An optimal control intervention for the interrelated dynamics of TB transmission in humans and animals amidst seasonal flux.

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Abstract

Tuberculosis (TB) is a global health concern, affecting both humans and animals. This paper provides a dynamic model to analyze the complicated dynamics of tuberculosis transmission, taking into account human-animal interactions and a saturated incidence rate with seasonal changes. Furthermore, the model accounts for the efficiency of measures targeted at reducing the spread of tuberculosis (TB). This study intends to give insights into the intricate interplay between TB transmission patterns, seasonal changes, and the efficacy of control measures by combining epidemiological concepts with ecological dynamics. The study uses simulation and analysis to support targeted intervention techniques and policy decisions for reducing tuberculosis transmission in a shared human-animal habitat. When both control measures are taken, the alpha parameter, which represents awareness among the general public, increases, the K_{Ea} parameter, which represents efficacy of drugs, increases, and the beta and b parameters decrease, and the population of infectious individuals decreases $v_j = 0, R_0 = 2.269426314$, when $v_j = 0.5, b_a = 0.05$ and $\beta_h = 0.04, R_0 = 0.575348645$ and when $v_1 = 1.1, v_2 = 1.5, b_a = 0.05$ and $\beta_h = 0.001, R_0 = 0.001144038597$). It is seen that increased awareness among the general public and the efficacy of therapy will subsequently prevent cases of infection at the end of the control program. It is concluded that public awareness and the efficacy of therapy should be incorporated into the control program for an optimal control strategy for TB infection to be curtailed in the hosts.

Keywords: Seasonal variations, TB spread, diverse populations, interconnected dynamics, and combined control techniques.

Introduction I

Tuberculosis (TB) is shorten for tubercles bacillus an airborne disease caused by the rod-shaped bacteria pathogen Mycobacterium tuberculosis bacillus (MTB).
Tuberculosis (TB) is a chronic sickness that kills individuals. Controlling the illness is difficult due to its complicated epidemiology and lack of understanding.
TB progression in susceptible persons starts with MTBC infection [1].
The sickness may remain latent for some years before becoming active. TB can also be acquired by co-infection with other diseases [2].
The mathematical model is a useful tool for evaluating infectious disease control efforts [3]. Mathematical models have substantially improved our understanding of the difficulties of TB transmission.
During the latent period, the pathogen has little metabolic activity until it is revived by a weakened host. Each year, tuberculosis kills over a million people, and in 2019, it was the largest cause of mortality from a single infectious agent. Over the last three decades, there have been several global attempts to combat tuberculosis (TB). The WHO's End TB Strategy intends to accelerate progress by lowering tuberculosis incidence and fatalities by 90% and 95%, respectively, between 2015 and 2035. Blower et al. developed the fundamental mathematical equations for TB in 1995 [12].
Several computational theories for TB have been created over time due to its preventability and curability concepts [10-21].

Introduction II

Despite various studies have been conducted on dynamical TB models transmitted between human beings, there has been less study on models' optimal control on the spread between humans and animals. The objectives of the model are as follows:

(i) To examine human-animal TB model optimal control strategies

(ii) To incorporate timely public awareness and efficacy of treatment in the control strategies

Materials and Methods

To accomplish the purpose of this study, a compartmental deterministic model was established and examined with a system of ordinary differential equations. The model's fundamental reproduction number is computed. The stability of the model's equilibrium points was investigated using Jacobian matrix theory and Routh-Hurwitz's criterion.

Mathematical Conceptions and Analogies I

A deterministic compartmental model of TB is proposed. The population most vulnerable is determined by the rate of birth and immigration, and the total population at any one moment is written as N_h & N_a. The dynamics of the spread of tuberculosis in an endemic population with effective strategy control are investigated. Exogenous reinfection happens shortly after the initial infection. Infected individuals have a higher chance of progressing and becoming infectious. Individuals who are infected but do not become infectious quickly may nevertheless acquire active tuberculosis by exogenous or endogenous reinfection, or both. Equation (1) describes the model and shows how exogenous reinfection affects the dynamics of tuberculosis.

Mathematical Conceptions and Analogies II

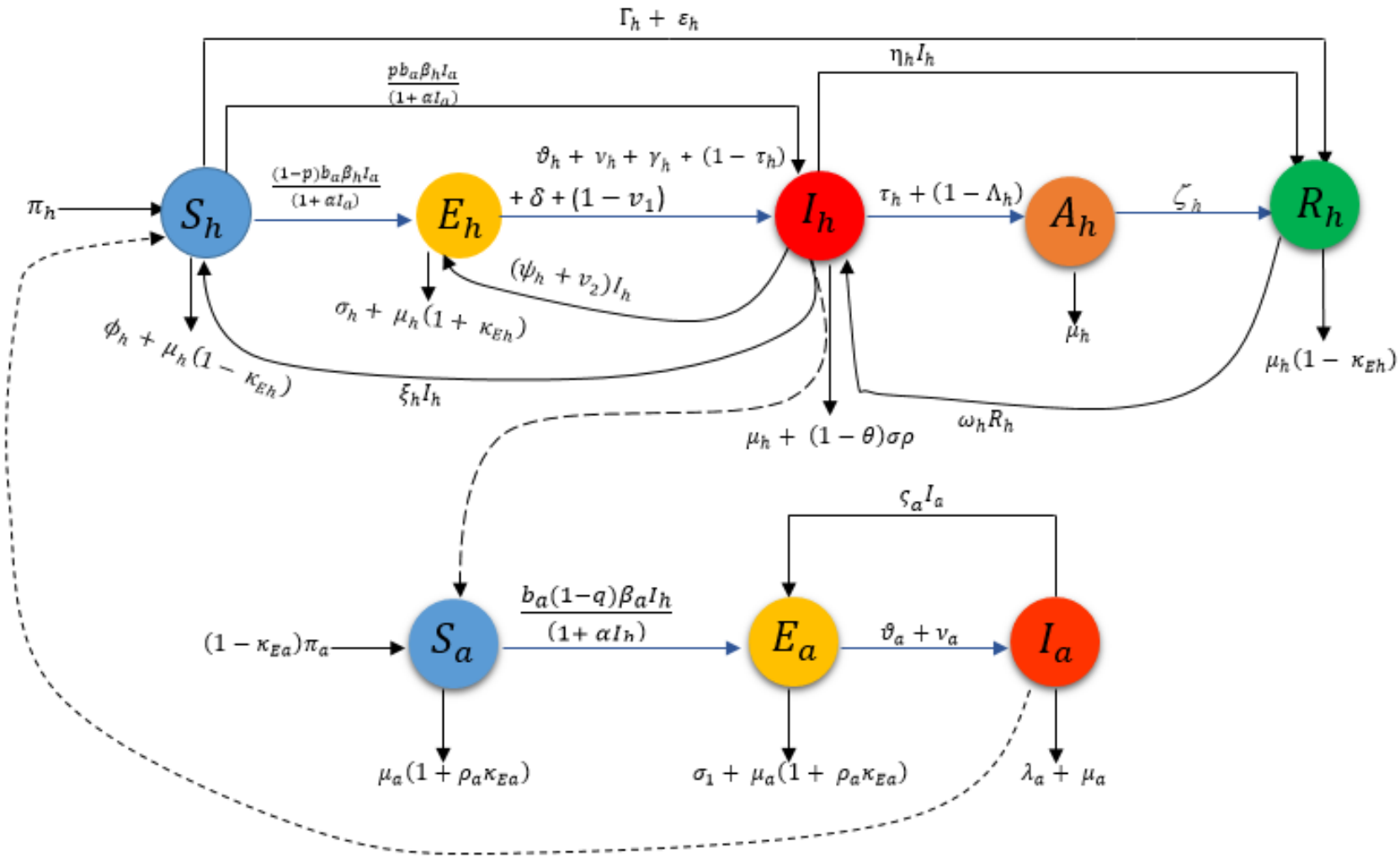

Figure:

Mathematical Conceptions and Analogies III

$$
\begin{aligned}
\frac{dS_h}{dt} &= \pi_h + (\Gamma_h + \varepsilon_h)R_h - \frac{b_a\beta_h I_a S_h}{(1+\alpha I_a)} - (\phi_h + \mu_h(1-k_{Eh}))S_h + \xi_h I_h \\
\frac{dE_h}{dt} &= \frac{b_a\beta_h(1-p)I_a S_h}{(1+\alpha I_a)} - (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1-\tau_h) + \mu_h(1+K_{Eh}))E_h - \delta E_h + v_2(t)I_h - (1-v_1(t))E_h, \\
\frac{dI_h}{dt} &= \frac{pb_a\beta_h I_a S_h}{(1+\alpha I_a)} + (\vartheta_h + \gamma_h + \nu_h + (1-\tau_h)\mu_h)E_h + \omega_h R_h - (\tau_h + \eta_h + \rho_h + (1-\wedge_h) + \xi_h + \mu_h + \psi_h)I_h + \\
&\delta E_h - (1-\theta)\sigma\rho I_h + (1-v_1(t))E_h - v_2(t)I_h \\
\frac{dA_h}{dt} &= (1-\wedge_h)I_h + (\tau_h + \rho_h)I_h - (\zeta_h + \mu_h)A_h, \\
\frac{dR_h}{dt} &= \zeta_h A - (\Gamma_h + \varepsilon_h + \mu_h)R_h - \omega_h R_h + \eta_h I_h, \\
\frac{dS_a}{dt} &= (1-K_{Ea})\pi_a - \frac{b_a\beta_a(1-q)I_h S_a}{(1+\alpha I_h)} - \mu_a(1+\rho_a K_{Ea})S_a. \\
\frac{dE_a}{dt} &= \frac{b_a\beta_a(1-q)I_h S_a}{(1+\alpha I_h)} - (\vartheta_a - \mu_a(1+\rho_a K_{Ea}))E_a + \zeta_a I_a. \\
\frac{dI_a}{dt} &= (\vartheta_a + \nu_a)E_a - (\zeta_a + \lambda_a + \mu_a)I_a.
\end{aligned}
\tag{1}
$$

Mathematical Conceptions and Analogies IV

Table: Variable and Parameter Descriptions

Variables	Descriptions
$S_h(t)$	The total population of vulnerable human's population
$E_h(t)$	The total population of unprotected human's population
$I_h(t)$	The total population of indicative or infected human's population
$A_h(t)$	Persons who are infectious but not infected, or the entire population of asymptomatic people
$R_h(t)$	The total population of recovered human's population
$S_a(t)$	The total population of exposed animals
$E_a(t)$	The total population of vulnerable animals
$I_a(t)$	The total population of vector-borne disease animals
$N_a(t)$	The total population of human
Parameter	
γ_h	Advancement from exposed
η_h	Cure rate
ω	Relapse to active TB
ζ_a	Quarantine rate of infected animal
q	Susceptible human who came in contact with infection animal
p	Susceptible animal who came in contact with infection human
K_{Ea}	Efficacy of treatment
$\delta(t)$	Seasonal variations
b_a	The average animal carrier rate
φ_h	The vulnerable protected
ρ	Vaccinated
β_h	Probability of infection of susceptible human population per animals
β_a	The probability of infection of susceptible vectors-borne per animals
π_h	The birth rate of human being
π_h	The birth rate of the animals

Mathematical Conceptions and Analogies V

Table: Variable and Parameter Descriptions

Parameters	Descriptions
ν_a	The per capital progression rate of exposed animals
μ_a	The natural death of animal
μ_h	The natural death of human's population
ξ_h	The reinfection rate of recovered human's population due to ineffective treatment
τ_h	Disease progression rate
$\wedge_a$	TB-induced death rate for infectious human's population
ϵ_h	The rate of recuperation (recovered) rate due to treatment
ν_h	Human's progression rate from exposed
Γ_h	Natural immunity gain in human population
$\frac{b_a\beta I}{1+\alpha I}$	Saturated incidence rate
	Individual moves back from to due to ineffective therapy
ψ_h	Public awareness of TB
α	Saturated incidence rate change into a symptomatic compartment
σ	Movement rate from treated
θ	Failure rate of treated human population
$\frac{b_a\beta_h(1-p)I_aS_h}{(1+\alpha I_a)}$	Exogenous reinfection
Control Parameter	
v_1	Immunization
v_2	Therapy

Population dynamics

The population of humans $N_h(t)$ h is expressed as follows:

$$N_h(t) = S_h + E_h + I_h + A_h + R_h, \tag{2}$$

Consequently, the overall number of animals $N_a(t)$ is being established as

$$N_b(t) = S_a + E_a + I_a, \tag{3}$$

The derivatives of equations (2) and (3) yield

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dE_h}{dt} + \frac{dI_h}{dt} + \frac{dA_h}{dt} + \frac{dR_h}{dt}, \tag{4}$$

and

$$\frac{dN_a}{dt} = \frac{dS_a}{dt} + \frac{dE_a}{dt} + \frac{dI_a}{dt}. \tag{5}$$

Combining equations (1), (4) and (5) together yield

$$\begin{aligned} \frac{dN_h}{dt} &= \pi_h - \mu_h N_h - (\phi_h + \mu_h k_{Eh})S_h - (\sigma_h + (1-\tau_h) + \tau_h\mu_h)E_h - \psi_h I_h + (1-\theta)\sigma\rho I_h, \\ \frac{dN_a}{dt} &= (1-K_{Ea})\pi_a - \mu_a N_a - \mu_a\rho_a K_{Ea} S_a + \mu_a(1+\rho_a K_{Ea}))E_a + \nu_a E_a - (\zeta_a + \lambda_a)I_a. \end{aligned} \tag{6}$$

Boundedness and Positivity of the Model's Solution I

The model system's fundamental features (1) are used to establish the criteria for solution positivity and system wellness. The feasibility of the model's solution (1) is evaluated based on its biological relevance in the researched location. The feasibility of the model which describes the region in which the solution of the model (1) is investigated because of its biological important.

Theorem

As t approaches ∞, the solution Ω of the model (1) with initial conditions in $\Re_+$ (set of vectors with eight non-negative components) approaches and remains in the solution's domain. Then, feasible The solution for the model is a positively invariant set provided by

$$\Omega = \Omega_h \times \Omega_v = \left\{(S_h + E_h + I_h + A_h + R + S_a + E_a + I_a) \in \Re_+^{\mathbf{8}} : N_h(t) \leq \frac{\pi}{\mu_h}, N_a(t) \leq \frac{(\mathbf{1}-K_{Ea})\pi_a}{\mu_a}\right\}. \quad (7)$$

From equation (6), In the absence of the disease

$$\frac{dN_h}{dt} = \pi_h - \mu_h N_h. \quad (8)$$

Following Birkhoff and Rota's (1989) equation yields

$$\frac{dN_h}{dt} \leq \pi_h - \mu_h N_h, \quad (9)$$

Boundedness and Positivity of the Model's Solution II

Integrating and assuming $0 \leq N_h \leq \frac{\pi_h}{\mu_h}$, the model Eq. (1) channels are confined. Therefore, the solution set for equation (7) is a compact forward persistent set for system equation (7).
When $N_h > \frac{\pi_h}{\mu_h}$ (exceeds $\frac{\pi_h}{\mu_h}$), $\frac{dN}{dt} < 0$. For $t > 0$, all solutions with a beginning condition in R_+^8 stay in the domain Ω_{ha}, a non-negatve invariant set under the model's flow (1). The system has epidemiological significance and is mathematically well-posed inside the domain Ω_{ha}.

Disease-free Stability of the System

To ensure that the population is free of bacteria, the diseased status will be set to zero. Equation (1) at DFE becomes

$$\begin{aligned}\mathbb{E}^0 &= (S_h^0, E_h^0, I_h^0, A_h^0, R_h^0, S_a^0, E_a^0, I_a^0) \\ &= \left(\frac{\pi_h}{(\phi_h + \mu_h(1-k_{Eh}))}, 0, 0, 0, 0, \frac{(1-K_{Ea})\pi_a}{\mu_a(1+\rho_a K_{Ea})}\right).\end{aligned} \tag{10}$$

The fundamental reproductive number of the mode l

To calculate the effective reproduction number R_0, the differential equations withing the compartments are employed to calculate the rate of fresh infection ($\mathcal{F}_i$), and transfer into and out of the infected and recovered compartments ($\mathcal{V}_i$) as shown in Figure **??**.

$$\mathcal{F}_i = \begin{pmatrix} \frac{b_a\beta_h(1-p)I_aS_h}{(1+\alpha I_a)} \\ \frac{pb_a\beta_hI_aS_h}{(1+\alpha I_a)} \\ 0 \\ \frac{b_a\beta_a(1-q)I_hS_a}{(1+\alpha I_h)} \\ 0 \end{pmatrix}, \tag{11}$$

At DFE, $I_h^0 = I_a^0 = 0$

$$\mathcal{F} = \begin{pmatrix} 0 & 0 & 0 & 0 & b_a\beta_h(1-p)S_h \\ 0 & 0 & 0 & 0 & pb_a\beta_hS_h \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & b_a\beta_a(1-q)S_a & 0 & 0 & 0 \end{pmatrix}. \tag{12}$$

$$\mathcal{V}_i = \begin{pmatrix} (\vartheta_h+\nu_h+\sigma_h+\gamma_h+(1-\tau_h)+\mu_h(1+K_{Eh}))E_h+\delta E_h - v_2(t)I_h+(1-v_1(t))E_h \\ -(\vartheta_h+\gamma_h+\nu_h+(1-\tau_h)\mu_h)E_h-\omega_hR_h+(\tau_h+\eta_h+\rho_h+(1-\wedge_h)+\xi_h+\mu_h+\psi_h)I_h-\delta E_h+ \\ (1-\theta)\sigma\rho I_h\ldots-(1-v_1(t))E_h+v_2(t)I_h \\ -(1-\wedge_h)I_h-(\tau_h+\rho_h)I_h+(\zeta_h+\mu_h)A_h \\ (\vartheta_a-\mu_a(1+\rho_aK_{Ea}))E_a-\zeta_aI_a \\ -(\vartheta_a+\nu_a)E_a+(\zeta_a+\lambda_a+\mu_a)I_a \end{pmatrix}, \tag{13}$$

The fundamental reproductive number of the mode II

Obtaining the partial derivatives of (13) with respect to E_h, I_h, A_h, E_a and I_a respectively yield

$$\mathcal{V} = \begin{bmatrix} X_1 & -v_2 & 0 & 0 & 0 \\ -X_6 & X_2 & 0 & 0 & 0 \\ 0 & X_7 & X_3 & 0 & 0 \\ 0 & 0 & 0 & X_4 & -\zeta_a \\ 0 & 0 & 0 & -X_8 & X_5 \end{bmatrix} \tag{14}$$

$X_1 = (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1-\tau_h) + \mu_h(1+K_{Eh}) + \delta + (1-v_1)), X_2 = (\tau_h + \eta_h + \rho_h + (1-\wedge_h) + \xi_h + \mu_h + \psi_h + v_2) + (1-\theta)\sigma\rho, X_3 = (\zeta_h + \mu_h), X_4 = (\vartheta_a - \mu_a(1+\rho_a K_{Ea})), X_5 = (\zeta_a + \lambda_a + \mu_a), X_6 = (\vartheta_h + \gamma_h + \nu_h + (1-\tau_h)\mu_h + \delta), X_7 = -(1 - \wedge_h + \tau_h + \rho_h), X_8 = (\vartheta_a + \nu_a)$

$$\mathcal{F}\mathcal{V}^{-1} = \begin{bmatrix} 0 & 0 & 0 & \frac{b_a\beta_h(1-p)S_hX_8}{X_5X_4 - X_8\zeta_a} & \frac{b_a\beta_h(1-p)S_hX_4}{X_5X_4 - X_8\zeta_a} \\ 0 & 0 & 0 & \frac{pb_a\beta_hS_hX_8}{X_5X_4 - X_8\zeta_a} & \frac{pb_a\beta_hS_hX_4}{X_5X_4 - X_8\zeta_a} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \frac{b_a\beta_a(1-q)S_aX_6}{X_2X_1 - X_6v_2} & \frac{b_a\beta_a(1-q)S_aX_1}{X_2X_1 - X_6v_2} & 0 & 0 & 0 \end{bmatrix} \tag{15}$$

The fundamental reproductive number of the mode III

Then the eigenvalues of the matrix (15) are computed with

$$\left.\begin{aligned}
\lambda_1 &= 0\\
\lambda_2 &= 0\\
\lambda_3 &= 0\\
\lambda_4 &= \frac{\sqrt{M\beta_a S_a S_h X_4\left(X_6\beta_h(1-p)+X_1 p\beta_h - qX_6\beta_h(1-p)-qX_1 p\beta_h\right)}b_a}{X_2X_1X_5X_4 - X_2X_1X_8\zeta_a - X_6v_2X_5X_4 + X_6v_2X_8\zeta_a}\\
\lambda_5 &= -\frac{\sqrt{M\beta_a S_a S_h X_4\left(X_6\beta_h(1-p)+X_1 p\beta_h - qX_6\beta_h(1-p)-qX_1 p\beta_h\right)}b_a}{X_2X_1X_5X_4 - X_2X_1X_8\zeta_a - X_6v_2X_5X_4 + X_6v_2X_8\zeta_a}.
\end{aligned}\right\}$$

Therefore, the basic reproduction number which is given by the largest eigenvalue for the model of TB denoted by R_0 is given by

$$R_0 = \rho(\mathcal{F}\mathcal{V}^{-1}) = max\left\{\lambda_4, \lambda_5\right\}. \tag{16}$$

$$\therefore \quad R_0 = \frac{\sqrt{M\beta_a S_a S_h X_4\left(X_6\beta_h(1-p)+X_1 p\beta_h - qX_6\beta_h(1-p)-qX_1 p\beta_h\right)}b_a}{X_2X_1X_5X_4 - X_2X_1X_8\zeta_a - X_6v_2X_5X_4 + X_6v_2X_8\zeta_a} \tag{17}$$

$M = (X_2X_1X_5X_4 - X_2X_1X_8\zeta_a - X_6v_2X_5X_4 + X_6v_2X_8\zeta_a)$

Remark

i. *If $R_0 \geq 1$ then the disease infectious I_h exists*

ii. *If $R_0 < 1$ then disease eradicated in the population i.e $I_h = 0$*

The model's ecological equilibrium I

Solving system of equation (1) simultaneously in terms of R_0 to obtain endemic equilibrium state yield the following

$$\mathbb{E}^* = \begin{cases} S_h^* = \dfrac{\pi_h}{(\phi_h + \mu_h(1-k_{Eh}))R_0} \\ E_h^* = \dfrac{[P_1 + P_2](R_0 - 1)}{R_0\left[R_0[(\vartheta_a - A_6)A_8 + A_9\zeta_a] + \alpha(1-K_{Ea})\pi_a(R_0-1)\right]A_7 B_1 G_1} \\ I_h^* = \dfrac{A_6(R_0-1)}{A_5 - \alpha A_6(R_0-1)} \\ A_h^* = \dfrac{A_2 A_6(R_0-1)}{A_3[A_5 - \alpha A_6(R_0-1)]} \\ R_h^* = \dfrac{[\zeta_h A_2 + \eta_h A_3]A_6(R_0-1)}{A_3 A_4[A_5 - \alpha A_6(R_0-1)]} \\ S_a^* = \dfrac{(1-K_{Ea})\pi_a}{\mu_a(1+\rho_a K_{Ea})R_0} \\ E_a^* = \dfrac{A_8(1-K_{Ea})\pi_a(R_0-1)}{[(\vartheta_a - A_6)A_8 + A_9\zeta_a]A_9 R_0} \\ I_a^* = \dfrac{(1-K_{Ea})\pi_a(R_0-1)}{R_0[(\vartheta_a - A_6)A_8 + A_9\zeta_a]} \end{cases} \tag{18}$$

Where,
$A_1 = (\Gamma_h + \varepsilon_h)$, $A_2 = (1 - \wedge_h + \tau_h + \rho_h)$, $A_3 = (\zeta_h + \mu_h)$, $A_4 = (\Gamma_h + \varepsilon_h + \mu_h + \omega_h)$, $A_5 = b_a\beta_a(1-q)$, $A_6 = \mu_a(1+\rho_a K_{Ea})$, $A_7 = (\phi_h + \mu_h(1-k_{Eh}))$, $A_8 = (\zeta_a + \lambda_a + \mu_a)$, $A_9 = (\vartheta_a + \nu_a)$, $B_1 = A_5 - \alpha A_6(R_0 - 1)$, $G_1 = (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1-\tau_h) + \mu_h(1+K_{Eh}) + \delta + (1 - v_1(t)))$, $P_1 = b_a\beta_h\pi_h\pi_a(1-p)(1-K_{Ea})B_1$, $P_2 = R_0\left(R_0((\vartheta_a - A_6)A_8 + A_9\zeta_a) + \alpha(1-K_{Ea})\pi_a(R_0-1)\right)A_7 v_2(t)A_6$

The model's ecological equilibrium II

Thus, if $R_0 > 1$, then $I_h^* > 0$ and $I_a^* > 0$ then model equation in Eq. (1) has a unique endemic equilibrium given by $\mathbb{E}^* = (S_h^*, E_h^*, I_h^*, A_h^*, R_h^*, S_a^*, E_a^*, I_a^*)$ which in the presence of infection (I$\neq$ 0) is defined.
Therefore, to ensure the existence of a positive endemic-equilibrium, it is required that $R_0 > 1$.
Since $(S_h^*, E_h^*, I_h^*, A_h^*, R_h^*, S_a^*, E_a^*, I_a^*) > 0$ (when $R_0 > 1$), the endemic-equilibrium $\mathbb{E}^*$ is positive and $I_{h,a}^* > 0$. This is the condition for the existence and uniqueness of the endemic-equilibrium state for the model (1).

Local stability analysis of the disease-free equilibrium state I

To determine the stability or otherwise of the disease - free equilibrium point $\mathbb{E}^0$, we examine the behaviour of the model population near the equilibrium solution. Here, we compute the Jacobian matrix J of model Eq. (1)
The method of trace and determinant was used to evaluate system of equations (1) without explicitly calculating eigenvalues.

Theorem

: The disease-free equilibrium state $\mathbb{E}^0$ is locally asymptotically stable if $R_0 < 1$ for $tr(J_{\mathbb{E}^0}) < 0$ and $det(J_{\mathbb{E}^0}) > 0$, and unstable if $R_0 > 1$ for $tr(J_{\mathbb{E}^0}) > 0$ and $det(J_{\mathbb{E}^0}) < 0$.

Proof. The Jacobian matrix evaluated at the DFE ($\mathbb{E}^0$) was constructed and obtained as:

$$J_{\mathbb{E}^0} = \begin{pmatrix} -W_1 & 0 & \xi_h & 0 & W_2 & 0 & 0 & -W_{13} \\ 0 & -W_3 & v_2 & 0 & 0 & 0 & 0 & W_{14} \\ 0 & W_4 & -W_5 & 0 & \omega_h & 0 & 0 & W_{15} \\ 0 & 0 & W_6 & -W_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & \eta_h & \zeta_h & -W_8 & 0 & 0 & 0 \\ 0 & 0 & W_{16} & 0 & 0 & -W_9 & 0 & 0 \\ 0 & 0 & W_{17} & 0 & 0 & 0 & -W_{10} & \zeta_a \\ 0 & 0 & 0 & 0 & 0 & 0 & W_{11} & -W_{12} \end{pmatrix} \tag{19}$$

The matrix $J^0(\mathbb{E}^0)$ in eqn. (19) of dimension (8) is stable if its trace is negative i.e $tr(J^0\mathbb{E}^0) < 0$ and its determinant is positive i.e $det(J^0\mathbb{E}^0)) \geq 0$.

Local stability analysis of the disease-free equilibrium state II

The trace of matrix $J^{0}(\mathbb{E}^{0})$ is obtained as:

$$\begin{aligned} tr(J^{+}) &= -W_1 - W_3 - W_5 - W_7 - W_8 - W_9 - W_{10} - W_{12} \\ &= -(W_1 + W_3 + W_5 + W_7 + W_8 + W_9 + W_{10} + W_{12}) \\ \therefore \quad & tr(\mathbb{E}^{0}) < 0 \end{aligned} \tag{20}$$

Also, the determinant of matrix $J^{0}(\mathbb{E}^{0})$ is generated as

$$detJ^{0}(\mathbb{E}^{0}) = [W_{10}W_{12}\left[W_8W_7W_3W_5 - \left(W_4W_8W_7\nu_2 + W_6\omega_hW_3\zeta_h + \omega_hW_3W_7\eta_h\right)\right] + W_4W_{11}W_8W_7\left(\zeta_a\nu_2 - W_{17}W_{14}\right)$$
$$W_3W_{11}\zeta_a\left(\omega_hW_6\zeta_h - W_8W_7W_5\right) + W_{11}W_3W_7\left(\zeta_a\omega_h\eta_h - W_8W_{17}W_{15}\right)]W_1W_9$$

Hence,

$$det(J^{+}) \geq 0$$

if and only if

$$W_8W_7W_3W_5 \geq \left(W_4W_8W_7\nu_2 + W_6\omega_hW_3\zeta_h + \omega_hW_3W_7\eta_h\right),$$
$$\zeta_a\nu_2 \geq W_{17}W_{14}, \omega_hW_6\zeta_h \geq W_8W_7W_5, \quad \text{and} \quad \zeta_a\omega_h\eta_h \geq W_8W_{17}W_{15}$$

Where,
$W_1 = (\phi_h + \mu_h(1 - k_{Eh}))$, $W_2 = (\Gamma_h + \varepsilon_h)$, $W_3 = (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1 - \tau_h) + \mu_h(1 + K_{Eh}) + \delta + (1 - \nu_1))$, $W_4 = (\vartheta_h + \gamma_h + \nu_h + (1 - \tau_h)\mu_h + \delta + (1 - \nu_1))$, $W_5 = (\tau_h + \eta_h + \rho_h + (1 - \wedge_h) + \xi_h + \mu_h + \psi_h + (1 - \theta)\sigma\rho + \nu_2)$, $W_6 = (1 - \wedge_h + \tau_h + \rho_h)$, $W_7 = (\zeta_h + \mu_h)$, $W_8 = (\Gamma_h + \varepsilon_h + \mu_h + \omega_h)$, $W_9 = \mu_a(1 + \rho_aK_{Ea})$, $W_{10} = (\vartheta_a - \mu_a(1 + \rho_aK_{Ea}))$, $W_{11} = (\vartheta_a + \nu_a)$, $W_{12} = (\zeta_a + \lambda_a + \mu_a)$, $W_{13} = \dfrac{-b_a\beta_h\pi_h}{(\phi_h + \mu_h(1 - k_{Eh}))}$, $W_{14} = \dfrac{b_a\beta_h(1 - p)\pi_h}{(\phi_h + \mu_h(1 - k_{Eh}))}$, $W_{15} =$

Local stability analysis of the disease-free equilibrium state III

$\frac{pb_a\beta_h\pi_h}{(\phi_h+\mu_h(1-k_{Eh}))}$, $W_{16} = \frac{-b_a\beta_a(1-q)(1-K_{Ea})\pi_a}{\mu_a(1+\rho_a K_{Ea})}$, $W_{17} = \frac{b_a\beta_a(1-q)(1-K_{Ea})\pi_a}{\mu_a(1+\rho_a K_{Ea})}$ From above result for the trace and determinant of the matrix which shows that $tr(J^0) < 0$ and $det(J^0) > 0$.
This proves that the disease-free equilibrium point is locally asymptotically stable. Biologically, this means that the disease dies out.

Conversely if $R_0 > 1$ then $tr(J^0) > 0$. This would cause the determinant to be negative (i.e $det(J^0) < 0$) and making the disease free-equilibrium point unstable. Biologically, this means that the disease persists.

Optimal Control Solution of the Model I

One of the early reasons for studying TB infection is to improve the control variables and finally to put down the infection of the population.
Optimal control theory is a useful mathematical analysis tool that can be used to make the best decisions in controlling a given problem at the minimum cost.
The optimal control theory, which was developed by Pontryagin and his co-workers in the late 1950s, has been applied to many areas including economics, management, engineering, biology, physiology, and medicine.
To describe the mathematical model presented in (1), the below objective functional (21) was employed.Our aim, objectives and goals here is to seek an optimal control strategy to put down TB infection from population by reducing the exposed $E_h(t)$ and infected $I_h(t)$ individuals and also increasing the recovered individuals $R_h(t)$ in a population and to minimizing the costs required to control the TB infection by using Immunization and therapy as the control variables $v_1(t)$ and $v_(t)$ respectively.
Given the objective functional subject to equation. (1) :

$$J(v_1, v_2) = \min_{v_1, v_2} \int_0^T \left[A_1 E_h(t) + A_2 I_h(t) + \frac{1}{2}\left(B_1 v_1^2 + B_2 v_2^2 \right) \right] dt \tag{21}$$

A_1 & A_2 are positive constants that are represented to keep a balance weight constants or balance factors in the size of $E_h(t)$ & $I_h(t)$ group respectively; B_1 and B_2 are constants relatively cost weights corresponding to the controls v_1 and v_2. For the control problem we assume that the initial time is zero,$t_0 = 0$, the final time $t_1 = T$.
Thus, the terms $B_1 v_1^2$ and $B_2 v_2^2$ represents the costs associated with immunization and therapy, respectively. The square of the control variables is taken here to remove the severity of the controls. The form is quadratic because we assume that costs are non-linear in its nature.

Optimal Control Solution of the Model II

Here is the Hamiltonian for the optimal control problem in Eqs. (1) and (21).

$$
\begin{aligned}
&H(S_h, V_h, E_h, I_h, Q, T, R, S_b, V_b, E_b, I_b, u_1, u_2, u_3; t) = A_1 E_h(t) + A_2 I_h(t) + \frac{B_1}{2} v_1^2 + \frac{B_2}{2} v_2^2 + \\
&\lambda_1(t)\left(\pi_h + (\Gamma_h + \varepsilon_h)R_h - \frac{b_a \beta_h I_a S_h}{(1+\alpha I_a)} - (\phi_h + \mu_h(1-k_{Eh}))S_h + \xi_h I_h\right) \\
&+ \lambda_2(t)\left(\frac{b_a \beta_h (1-p) I_a S_h}{(1+\alpha I_a)} - (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1-\tau_h) + \mu_h(1+K_{Eh}))E_h - \delta E_h + v_2(t) I_h - (1-v_1(t))E_h\right) + \\
&\lambda_3(t)\left(\frac{p b_a \beta_h I_a S_h}{(1+\alpha I_a)} + (\vartheta_h + \gamma_h + \nu_h + (1-\tau_h)\mu_h)E_h + \omega_h R_h - (\tau_h + \eta_h + \rho_h + (1-\wedge_h) + \xi_h + \mu_h + \psi_h)I_h + \right. \\
&\left. \delta E_h - (1-\theta)\sigma\rho I_h + (1-v_1(t))E_h - v_2(t) I_h\right) + \lambda_4(t)\left((1-\wedge_h)I_h + (\tau_h + \rho_h)I_h - (\zeta_h + \mu_h)A_h\right) + \\
&\lambda_5(t)\left(\zeta_h A - (\Gamma_h + \varepsilon_h + \mu_h)R_h - \omega_h R_h + \eta_h I_h\right) + \lambda_6(t)\left((1-K_{Ea})\pi_a - \frac{b_a \beta_a (1-q) I_h S_a}{(1+\alpha I_h)} - \mu_a(1+\rho_a K_{Ea})S_a\right) + \\
&\lambda_7(t)\left(\frac{b_a \beta_a (1-q) I_h S_a}{(1+\alpha I_h)} - (\vartheta_a - \mu_a(1+\rho_a K_{Ea}))E_a + \zeta_a I_a\right) + \lambda_8(t)\left((\vartheta_a + \nu_a)E_a - (\zeta_a + \lambda_a + \mu_a)I_a\right)
\end{aligned}
\tag{22}
$$

The following theorem holds.

Optimal Control Solution of the Model III

Theorem

(Necessary Conditions)
Given that $(S_h^*, E_h^*, I_h^*, T^*, R^*, S_a^*, E_a^*, I_a^*)$ *are optimal state solutions and* (v_1, v_2) *are associated optimal control variables for the optimal control problem* (1)*, then there exist eleven (11) adjoint variables* λ_i *for i=1,2,3,4,5,6,7,8 which satisfying*

$$\lambda_1' = \frac{-\partial H}{\partial S_h}, \lambda_2' = \frac{-\partial H}{\partial E_h}, \lambda_3' = \frac{-\partial H}{\partial I_h}, \lambda_4' = \frac{-\partial H}{\partial A_h}, \lambda_5' = \frac{-\partial H}{\partial R}, \lambda_6' = \frac{-\partial H}{\partial S_a}, \lambda_7' = \frac{-\partial H}{\partial E_a}, \lambda_8' = \frac{-\partial H}{\partial I_a} \tag{23}$$

with the transversality conditions (boundary conditions) or (final time conditions) $\lambda_i(T) = 0$*, (i=1,2,3....8). with the optimal control pair given by*

$$\left.\begin{aligned} v_1^*(t) &= min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2^*)E_h^*}{B_1}\right), 1\right\} \\ v_2^*(t) &= min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2)I_h^*}{B_2}\right), 1\right\}. \end{aligned}\right\} \tag{24}$$

Optimal Control Solution of the Model IV

Proof.

$$\frac{d\lambda_1}{dt} = [\lambda_1(t) - \lambda_2(t)]\frac{b_a\beta_h I_a}{(1+\alpha I_a)^2} + \lambda_1(t)(\phi_h + \mu_h(1-k_{Eh})) + [\lambda_2(t) - \lambda_3(t)]\frac{pb_a\beta_h I_a}{(1+\alpha I_a)^2}$$

$$\frac{d\lambda_2}{dt} = -A_1 + [\lambda_2(t) - \lambda_3(t)](\vartheta_h + \nu_h + \gamma_h + \delta + (1-\mu_h)(1-\tau_h) + (1-v_1(t))) + \lambda_2(t)\sigma_h + \lambda_2(t)(\mu_h(1+K_{Eh}))$$

$$\frac{d\lambda_3}{dt} = -A_2 + [\lambda_3(t) - \lambda_1(t)]\xi_h + [\lambda_3(t) - \lambda_2(t)]v_2(t) + \lambda_3(t)(\mu_h + \psi_h) - \lambda_3(t)(1-\theta)\sigma\rho + [\lambda_3(t) - \lambda_4(t)](1-\wedge_h)$$

$$+ [\lambda_3(t) - \lambda_4(t)]\tau_h + [\lambda_3(t) - \lambda_4(t)]\rho_h + [\lambda_3(t) - \lambda_5(t)]\eta_h + [\lambda_6(t) - \lambda_7(t)]\frac{b_a\beta_a(1-q)S_a}{(1+\alpha I_h)^2}$$

$$\frac{d\lambda_4}{dt} = [\lambda_4(t) - \lambda_5(t)]\zeta_h + \lambda_4(t)\mu_h$$

$$\frac{d\lambda_5}{dt} = -\lambda_1(t)\pi_h + [\lambda_5(t) - \lambda_1(t)](\Gamma_h + \varepsilon_h) + [\lambda_5(t) - \lambda_3(t)]\omega_h + \lambda_5(t)\mu_h$$

$$\frac{d\lambda_6}{dt} = [\lambda_6(t) - \lambda_7(t)]\frac{b_a\beta_a(1-q)I_h}{(1+\alpha I_h)^2} + \lambda_6(t)\mu_a(1+\rho_a K_{Ea})$$

$$\frac{d\lambda_7}{dt} = [\lambda_7(t) - \lambda_8(t)]\vartheta_a + \lambda_7(t)\mu_a(1+\rho_a K_{Ea}) - \lambda_8(t)\nu_a$$

$$\frac{d\lambda_8}{dt} = [\lambda_1(t) - \lambda_2(t)]\frac{b_a\beta_h S_h}{(1+\alpha I_a)^2} + [\lambda_2(t) - \lambda_3(t)]\frac{pb_a\beta_h S_h}{(1+\alpha I_a)^2} + [\lambda_8(t) - \lambda_7(t)]\zeta_a + \lambda_8(t)\lambda_a + \lambda_8(t)\mu_a \tag{25}$$

Optimal Control Solution of the Model V

Optimal controls obtained after differentiating H w.r.t. v_1 and v_2

$$\left.\begin{aligned} v_1^*(t) &= \frac{\left[\lambda_3^*(t) - \lambda_2^*(t)\right] E_h^*(t)}{B_1} \\ v_2^*(t) &= \frac{\left[\lambda_3^*(t) - \lambda_2^*(t)\right] I_h^*(t)}{B_2} \end{aligned}\right\} \tag{26}$$

$$\left.\begin{aligned}
\dot{S}_h^* &= \pi_h + (\Gamma_h + \varepsilon_h)R_h - \frac{b_a\beta_h I_a S_h}{(1+\alpha I_a)} - (\phi_h + \mu_h(1-k_{Eh}))S_h + \xi_h I_h \\
\dot{E}_h^* &= \frac{b_a\beta_h(1-p)I_a S_h}{(1+\alpha I_a)} - (\vartheta_h + \nu_h + \sigma_h + \gamma_h + (1-\tau_h) + \mu_h(1+K_{Eh}))E_h - \delta E_h + \\
&\left(min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2^*)I_h^*}{B_1}\right), 1\right\}\right)I_h - \left(1 - \left(min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2^*)E_h^*}{B_1}\right), 1\right\}\right)\right)E_h, \\
\dot{I}_h^* &== \frac{pb_a\beta_h I_a S_h}{(1+\alpha I_a)} + (\vartheta_h + \gamma_h + \nu_h + (1-\tau_h)\mu_h)E_h + \omega_h R_h - (\tau_h + \eta_h + \rho_h + (1-\wedge_h) + \xi_h + \mu_h + \psi_h)I_h + \\
&\delta E_h - (1-\theta)\sigma\rho I_h + \left(1 - \left(min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2^*)_h^*}{B_1}\right), 1\right\}\right)\right)E_h - \left(min\left\{max\left(0, \frac{(\lambda_3^* - \lambda_2^*)I_h^*}{B_1}\right), 1\right\}\right)I_h \\
\dot{A}_h^* &= (1-\wedge_h)I_h + (\tau_h + \rho_h)I_h - (\zeta_h + \mu_h)A_h, \\
\dot{R}_h^* &= \zeta_h A - (\Gamma_h + \varepsilon_h + \mu_h)R_h - \omega_h R_h + \eta_h I_h, \\
\dot{S}_a^* &= (1-K_{Ea})\pi_a - \frac{b_a\beta_a(1-q)I_h S_a}{(1+\alpha I_h)} - \mu_a(1+\rho_a K_{Ea})S_a. \\
\dot{E}_a^* &= \frac{b_a\beta_a(1-q)I_h S_a}{(1+\alpha I_h)} - (\vartheta_a - \mu_a(1+\rho_a K_{Ea}))E_a + \zeta_a I_a. \\
\dot{I}_a^* &= (\vartheta_a + \nu_a)E_a - (\zeta_a + \lambda_a + \mu_a)I_a.
\end{aligned}\right\} \tag{27}$$

Numerical Simulation I

Table: Parameter values of TB model

Symbol	Description	Symbol	Description
ϑ_h	0.05	b_a	0.05
ν_h	0.02	p	0.35
σ_h	0.01	ζ_a	0.02
γ_h	0.01	β_h	0.04
μ_h	0.05	ρ_h	0.04
K_{Eh}	0.001	q	0.09
K_{Ea}	0.9	ρ	0.01
δ	0.6	ϕ_h	0.6
η_h	0.06	π_h	1000
$\wedge_h$	0.0002	π_a	100
ξ_h	0.3	v_1	[0-1]
ψ_h	0.8	v_1	[0-1]
θ	0.26	α	[0.02 - 1.0]
σ	0.5	ν_h	0.0016
ζ_h	0.04	τ_h	0.05
μ_a	0.027	ϑ_a	0.07
ρ_a	0.73	ν_a	0.01
λ_a	0.05		

$$R_0 = \frac{\sqrt{M\beta_a S_a S_h X_4 \left(X_6\beta_h(1-p) + X_1 p\beta_h - qX_6\beta_h(1-p) - qX_1 p\beta_h\right)b_a}}{X_2X_1X_5X_4 - X_2X_1X_8\zeta_a - X_6v_2X_5X_4 + X_6v_2X_8\zeta_a} \tag{28}$$

Using the above parameters we will obtained the following
When,
$v_1 = 0.0, v_2 = 0.0, R_0 = 2.269426314,$
$v_1 = 0.5, v_2 = 0.5, R_0 = 0.5753486745$

Numerical Simulation II

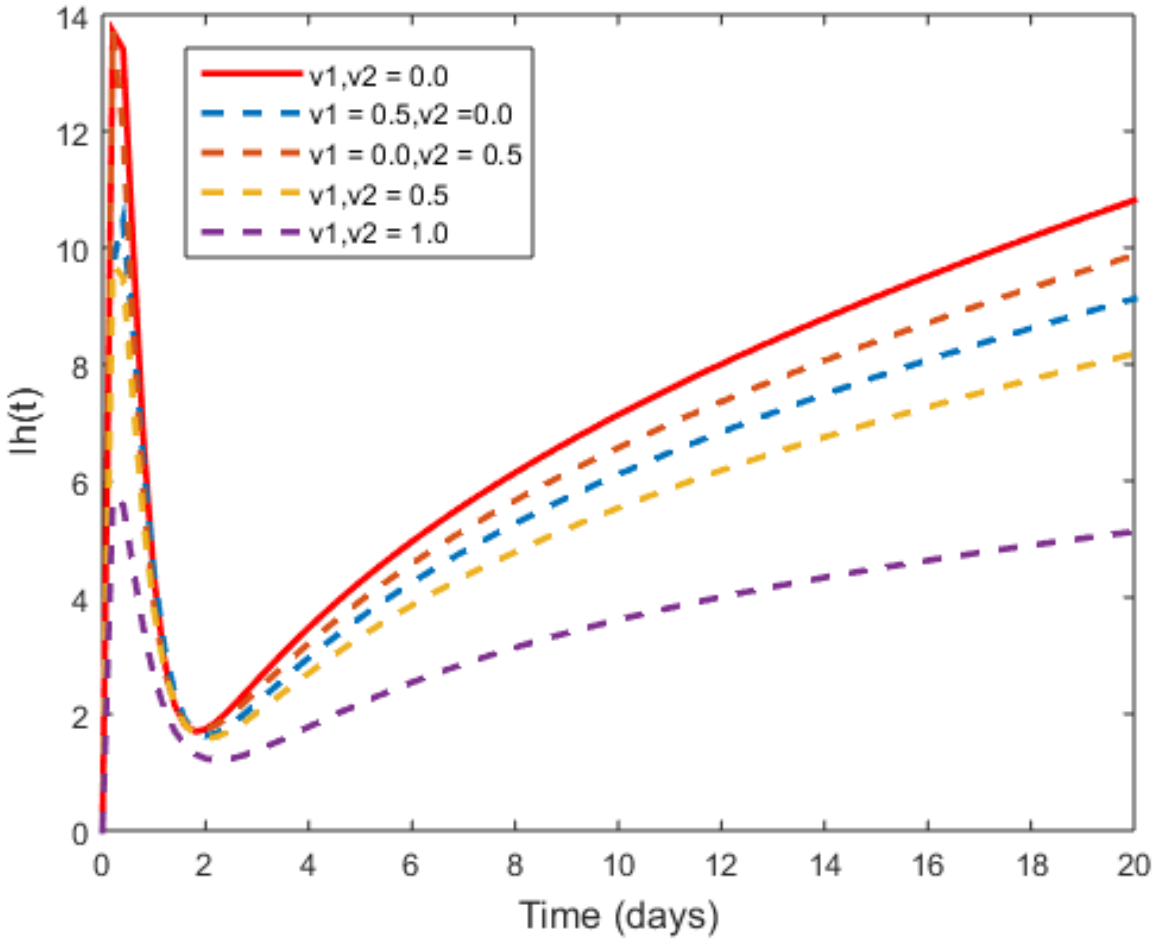

Figure: Infected Compartment against time using Control strategy

Numerical Simulation III

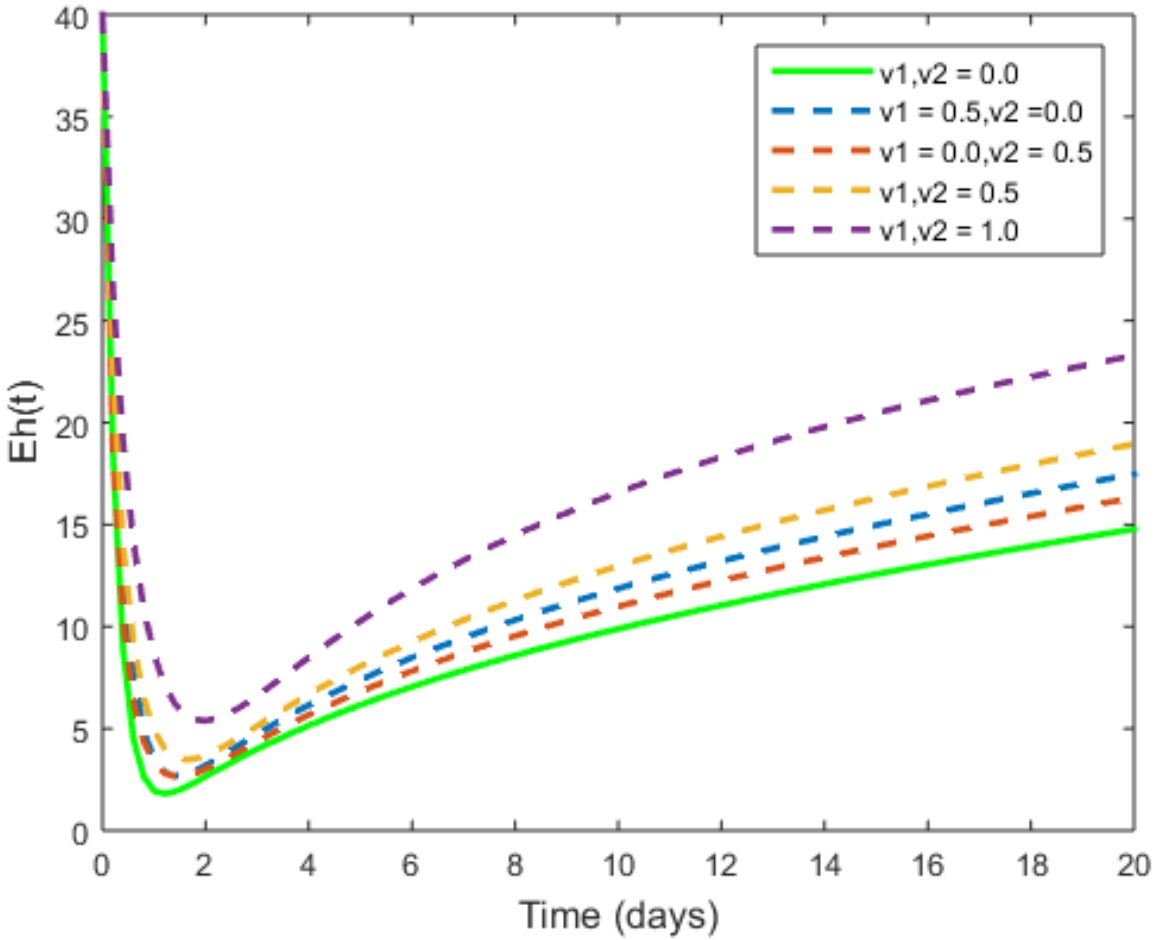

Figure: Exposed Compartment against time using Control strategy

Discussion I

The mathematical model used in the study to investigate the dynamics of TB transmission in both human and animal populations reveals a complex interplay of factors influencing disease propagation. Seasonal changes, saturation incidence rates, and therapeutic efficacy all contribute to a more thorough knowledge of how tuberculosis survives and evolves within communities. The model sheds light on an intriguing element of tuberculosis transmission: the seasonal flux. Seasonal fluctuations in temperature and environmental variables can have a considerable influence on disease dynamics, affecting both individual vulnerability and mycobacterium survival in the environment. Furthermore, the model emphasizes the idea of saturation incidence rates, in which the pool of susceptible people is depleted over time as a result of previous infections or therapies. As the frequency of TB in the community falls, so does the rate of new infections, eventually reaching saturation and making future reductions more difficult. This saturation effect emphasizes the significance of early and vigorous intervention methods to prevent the disease from becoming endemic. Furthermore, the success of treatments, such as vaccination campaigns, treatment programs, and public health initiatives, is critical in limiting TB transmission. The model enables researchers to investigate the possible effects of various intervention options and assess their efficacy in lowering disease burden. By optimizing resource allocation and adapting interventions to specific demographic features, TB control efforts will become more effective globally.

Conclusion I

Under certain conditions, the unique endemic equilibrium becomes globally asymptotically stable. Optimal control measures for tuberculosis bacteria include preventive and control education, prompt treatment, and enhanced efficacy. This control is situated between $0 \leq v_j \leq 1$, where $j = 1, 2$ and v_1, v_2 are immunization and therapy, respectively. If $v_1 = 0$ the use of personal protective measures such as drinking warm water, wearing facial masks, wearing a nasal guard, and avoiding dusty regions is ineffectual, then when v_j is greater than zero, such precautions are completely effective. More focused and effective ways for fighting this chronic global health issue are created as the comprehension of TB dynamics improves via mathematical modelling and empirical investigations.

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Thank You