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Analysis and Cost-Effecteveness of Hepatities B Virus (HBV) Model

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Abstract. This paper presents a mathematical model for Hepatitis B virus (HBV) dynamics. The model is analyzed to establish the existence, positivity, and uniqueness of its solutions, the derivation of the basic reproductive number (R_0), stability analysis of the disease-free equilibrium (DFE), sensitivity analysis is conducted to determine the impact of the parameters on $\mathcal{R}_0$. The model is extended to include optimal control variables that represent interventions aimed at reducing HBV transmission and minimizing associated costs. Several control strategies are presented supported by numerical simulations and graphical results.

1. Introduction

Hebatities B Virus (HBV) is the one of the most dangerous viruses that affect human health, causing serious disease, such as cirrhosis and liver cancer which affect the quality of the human life, making it a major challenge to compact. HBV is transmitted through contact with infected blood and body fluids. Effective interventions to reduce transmission such as, include raising awareness about the disease, ensuring the careful management of blood and blood products play a big rule in reducing the spread of the disease, also promoting vaccination, and providing treatment to infected individuals are essential to limit the spread and reducing its serious health consequences. Mathematical models are used to understand the dynamic of HBV transmission and guide control strategies. Khan [2] presents a mathematical models to describe the transmission dynamic of HBV in China, the models describes the interactions between different stages of the populations, providing insights into the spread of HBV within population. Kamyad [3] investigates the impact

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of vaccination and treatment on the transmission dynamic of HBV. Khatun [14] discuss the virus dynamics and provide understanding of the transmission including immune system. Elkhadir [4] extend SEIR model by incorporating immunized class and determine the impact of vaccination and treatment. M. Belay [7] presents a mathematical models incorporating a two dose vaccine series, providing insights into optimal vaccine. Yousuf [15] presents a mathematical model and provide control strategies to reduce the spreading of disease. In this study, we analyze the HBV model and find the basic reproductive number $R0$, then we extend the model to optimal control interventions including (transmission reduction, vaccination, treatment), and we use Pontagin Maximum Principle (PMP). We balance the costs of the burden disease against the costs of interventions, to identify the most effective intervention in reducing the spread of the disease and the total cost. We evaluated some interventions strategies: Implementing each intervention (at high or low levels), combining two interventions while excluding the third, applying all interventions (at high or low levels). We evaluated the effectiveness of these strategies by comparing the basic reproduction number R_0 and the total cost, with a discussion on which strategy is optimal.

2. Mathematical Formulation

We assume the total population $N(t)$ is divided into seven compartments: Susceptible $S(t)$, Exposed $E(t)$, Acute $A(t)$, Chronic $C(t)$, Treated $T(t)$, Vaccinated $V(t)$, and Recovered $R(t)$.

Susceptible $S(t)$**:** Increases through the birth of unvaccinated newborns at rate $\alpha N_0(1-\beta)$ and vaccinated individuals for whom the vaccination failed at rate ϵV. It decreases as individuals become infected through contact with Acute or Chronic cases at rate $\frac{\sigma}{N}(A+C)S$, transition to the vaccinated compartment at rate γS, or die from natural causes at rate μS.

Exposed $E(t)$**:** Increases as susceptible individuals become infected through contact with Acute or Chronic cases at rate $\frac{\sigma}{N}(A+C)S$. It decreases as exposed individuals move to the Acute compartment at rate λE or die from natural causes at rate μE

Acute $A(t)$**:** Increases as exposed individuals who develop severe symptoms move to the Acute compartment at rate λE, and decreases as Acute individuals move to the Chronic compartment at rate $\delta_1 A$, recover at rate $\delta_2 A$, or die from natural causes at rate μA.

Chronic $C(t)$**:** Increases as infected individuals transition from the Acute compartment at rate $\delta_1 A$, and decreases as Chronic individuals receive treatment and move to the Treated compartment at rate ηC, die due to disease at rate dC, or die from natural causes at rate μC.

Treated $T(t)$**:** Increases as Chronic individuals receive treatment and move to the Treated compartment at rate ηC, and decreases as Treated individuals recover and transition to the Recovered compartment at rate ψT or die from natural causes at rate μT.

Vaccinated $V(t)$**:** Increases as susceptible individuals receive the vaccine at rate γS, and decreases as vaccinated individuals move to the Recovered compartment at rate ϵV or die from natural causes at rate μV.

Recovered $R(t)$**:** Increases as Acute individuals recover at rate $\delta_2 A$ and treated individuals recover

at rate ψT. It decreases as recovered individuals die from natural causes at rate μR.
Figure 1 shows the flows of the population through the seven compartments. The following ODEs system represents the flows of the population through the seven compartments.

$$\begin{aligned}
\frac{dS}{dt} &= \alpha N_0(1-\beta) - \frac{\sigma}{N}(A(t)+C(t))S(t) - \gamma S(t) + \epsilon V(t) - \mu S(t),\\
\frac{dE}{dt} &= \frac{\sigma}{N}(A(t)+C(t))S(t) - \lambda E(t) - \mu E(t),\\
\frac{dA}{dt} &= \lambda E(t) - \delta_1 A(t) - \delta_2 A(t) - \mu A(t),\\
\frac{dC}{dt} &= \delta_1 A(t) - \eta C(t) - dC(t) - \mu C(t),\\
\frac{dT}{dt} &= \eta C(t) - \psi T(t) - \mu T(t),\\
\frac{dV}{dt} &= \alpha N_0 \beta + \gamma S(t) - \epsilon V(t) - \mu V(t),\\
\frac{dR}{dt} &= \delta_2 A(t) + \psi T(t) - \mu R(t),\\
N(t) &= S(t) + E(t) + A(t) + C(t) + T(t) + V(t) + R(t).
\end{aligned} \tag{2.1}$$

with initial conditions:

$$\{S(0), E(0), A(0), C(0), T(0), V(0), R(0)\} = \{S_0, E_0, A_0, C_0, T_0, V_0, R_0\} \tag{2.2}$$

$S_0, E_0, A_0, C_0, T_0, V_0, R_0$ all are positive. The description of the parameters is given in Table 1.

Parameter	Description
α	Birth rate
β	Vaccination coverage at birth
ϵ	Failure probability of vaccination
γ	Vaccination rate
μ	Natural death rate
σ	Transmission rate from Susceptible to Exposed
λ	Progression rate from Exposed to Acute
δ_1	Progression rate from Acute to Chronic
δ_2	Recovery rate from Acute infection
d	HBV induced death rate
η	Treatment rate for Chronic individuals
ψ	Recovery rate for Treated individuals

TABLE 1. The Description of the parameters

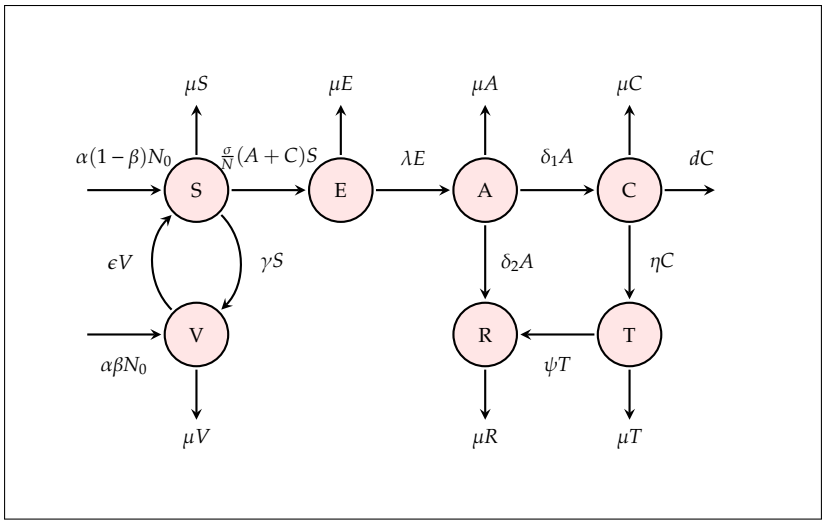

FIGURE 1. HBV model Compartments

3. Analysis of the Model

3.1. **Existence and Uniqueness of the Solutions.**

Definition 3.1 (Lipschitz continuity)**.** *A function $F : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n$ is said to be **Lipschitz continuous in** x if there exists a constant $L > 0$ such that for all x, y,*

$$\|F(x,t) - F(y,t)\| \leq L\|x - y\|$$

Theorem 3.1 (Picard–Lindelöf Theorem)**.** *Let $D \subseteq \mathbb{R}^n \times \mathbb{R}$ be an open set, and let $F : D \to \mathbb{R}^n$ satisfy the following conditions:*

*(1) $F(x,t)$ is **continuous** in t on D.*
*(2) $F(x,t)$ is **Lipschitz continuous** in x.*

Then, for any initial condition $x_i(t_0) = x_{i0}$ where $(x_{i0}, t_0) \in D$, there exists a unique solution $x_i(t)$ for the system

$$\frac{dx_i}{dt} = F_i(x_i, t), \quad i = 1, \ldots, n,$$

in a neighborhood of t_0.

From the theorem (3.1), the system (2.1) has a unique solution since its right-hand sides consist of linear and quadratic terms, which are continuous in t and Lipschitz continuous in $x = \{S, E, A, C, T, V, R\}$.

3.2. **Positivity of the Solutions.**

Theorem 3.2. *Let the initial conditions $\{S(0), E(0), A(0), C(0), T(0), V(0), R(0)\} = \{S_0, E_0, A_0, C_0, T_0, V_0, R_0\}$ are positive, then $S(t), E(t), A(t), C(t), T(t), V(t)$, and $R(t)$ remain positive for all $t > 0$.*

Proof. To prove the positivity of $S(t)$, we define

$$T = \sup\{t > 0 : S(\tau) > 0 \ \forall \tau \in [0, t]\}. \tag{3.1}$$

This means that since $S(0)$ is positive, $S(t)$ remains positive for all $t \in [0, T]$. In other words, T is the maximum time up to which $S(t)$ stays positive.
We can write the first equation in the system 2.1

$$\frac{dS}{dt} + P(t)S = Q(t)$$

where, $P(t) = \frac{\sigma}{N}(A(t) + C(t)) + \gamma + \mu$ and $Q(t) = \alpha N_0(1-\beta) + \epsilon V(t)$.
Let $\zeta(t) = \exp\left(\int P(t)dt\right)$, then equation (**??**) can be written as

$$\frac{d}{dt}(\zeta(t)S(t)) = \zeta(t)Q(t)$$

Integrating both sides from 0 to T gives

$$S(T)\zeta(T) - S(0)\zeta(0) = \int_0^T \zeta(\tau)Q(\tau)d\tau$$

$$S(T) = \frac{1}{\zeta(T)}\left(S(0)\zeta(0) + \int_0^T \zeta(\tau)Q(\tau)d\tau\right)$$

Since all the parameters $\alpha, \beta, \epsilon, \gamma, \mu$, and σ are positive, $0 < \beta < 1$, and $S(0), \zeta(0) > 0$, with $\zeta(\tau)$ and $Q(\tau)$ being positive $\forall \tau \in [0, T]$, we have $S(T) > 0$ and $S(T) \neq 0$. Therefore, from the continuity of $S(t)$, there exists $h > 0$ such that $S(T + h) > 0$, which contradicts the assumption that T is a supremum. Thus, $S(t)$ is positive $\forall t > 0$. We can prove by the same method the positivity of the remaining variables E, A, C, T, V, and R, which completes the proof. □

3.3. **Boundedness of the Solutions.** To prove the boundedness of the solutions $S(t), E(t), A(t), C(t), V(t), T(t), R(t)$, we consider the total population at any time t given by

$$N(t) = S(t) + E(t) + A(t) + C(t) + V(t) + T(t) + R(t).$$

Differentiating both sides, the rate of change of the total population $N(t)$ is given by

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dA}{dt} + \frac{dC}{dt} + \frac{dV}{dt} + \frac{dT}{dt} + \frac{dR}{dt}.$$

By substituting the rates of change of each compartment and simplifying, we obtain

$$\frac{dN}{dt} = \alpha N_0 - \mu N - dC.$$

since $C(t) \leq N(t)$ for all t, we can write

$$\frac{dN}{dt} \leq \alpha N_0 - (\mu + d)N.$$

By integrating both sides and using the initial condition $N(0) = N_0$, we get

$$N(t) \leq \frac{\alpha N_0}{\mu + d} + \left(N_0 - \frac{\alpha N_0}{\mu - d}\right)e^{-(\mu+d)t},$$

as $t \to \infty, N(t) \to N_\infty$, where

$$N_\infty = \frac{\alpha N_0}{\mu + d}$$

Thus, $N(t)$ is bounded above by N_∞. Since each compartment $S(t), E(t), A(t), C(t), T(t), V(t), R(t)$ is a subset of $N(t)$, they are also bounded. Hence, all compartments remain bounded for all $t \geq 0$. This establishes the feasible region:

$$\Omega = \{(S, E, A, C, V, T, R) \in \mathbb{R}^7_+ \mid 0 < S + E + A + C + V + T + R \leq N_\infty\}.$$

This means that once the system enters Ω, it will never leave it, ensuring that the system is biologically and mathematically realistic.

3.4. **Disease Free Equilibrium (DFE).** Disease Free Equilibrium (DFE) is the state where there are no infected individuals in the population, can be found by setting the infected compartments E, A, C, and T to zero in the system 2.1, and solving for the remaining compartments S, V, and R. we get:

$$P^0 = (S^0, E^0, A^0, C^0, T^0, V^0, R^0)$$

$$P^0 = \left(\frac{\alpha N_0(\epsilon + (1-\beta)\mu)}{\mu(\gamma + \epsilon + \mu)}, 0, 0, 0, 0, \frac{\alpha N_0 \beta + \gamma S^0}{\epsilon + \mu}, 0\right) \tag{3.2}$$

3.5. **The basic Reproduction Number $\mathcal{R}_0$.** : To analyze the stability of the model, we first derive the expression for the basic reproduction number. We use the next-generation method [5]. We define $\mathcal{F}$ (New infection rates) and $\mathcal{V}$ (Transition rates) for the infected compartments E, A, C, T as

$$\mathcal{F} = \begin{bmatrix} \frac{\sigma}{N}(A + C)S \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} (\lambda + \mu)E \\ -\lambda E + (\delta_1 + \delta_2 + \mu)A \\ -\delta_1 A + (\eta + d + \mu)C \\ -\eta C + (\psi + \mu)T \end{bmatrix}$$

The Jacobian matrix of $\mathcal{F}$ with respect to (E, A, C, T), at the disease-free equilibrium P_0 is

$$F = J(\mathcal{F})\Big|_{P_0} = \begin{bmatrix} 0 & \frac{\sigma S^0}{N} & \frac{\sigma S^0}{N} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & a_1 & a_2 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Similarly, the Jacobian matrix of $\mathcal{V}$ with respect to (E, A, C, T), at the disease-free equilibrium P_0 is

$$V = J(\mathcal{V})\Big|_{P_0} = \begin{bmatrix} \lambda + \mu & 0 & 0 & 0 \\ -\lambda & \delta_1 + \delta_2 + \mu & 0 & 0 \\ 0 & -\delta_1 & \eta + d + \mu & 0 \\ 0 & 0 & -\eta & \psi + \mu \end{bmatrix} = \begin{bmatrix} b_1 & 0 & 0 & 0 \\ b_2 & b_3 & 0 & 0 \\ 0 & b_4 & b_5 & 0 \\ 0 & 0 & b_6 & b_7 \end{bmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{-a_1b_2}{b_1b_3} + \frac{a_2b_2b_4}{b_1b_3b_5} & \frac{a_1}{b_3} - \frac{a_2b_4}{b_3b_5} & \frac{a_2}{b_5} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

The basic reproductive number $\mathcal{R}_0$ is the maximum eigenvalue of the matrix FV^{-1}, which gives

$$\mathcal{R}_0 = \frac{-a_1b_2}{b_1b_3} + \frac{a_2b_2b_4}{b_1b_3b_5}$$

substitute $a_1, a_2, b_1, b_2, b_3, b_4, b_5, b_6$ and S^0, we obtain

$$\mathcal{R}_0 = \frac{\alpha\lambda\sigma(\epsilon + \mu(1-\beta))(d + \delta_1 + \eta + \mu)}{(\lambda + \mu)((\mu + \epsilon + \gamma)\mu)(d + \eta + \mu)(\delta_1 + \delta_2 + \mu)} \tag{3.3}$$

Theorem 3.3 (Local Stability of the Disease-Free Equilibrium)**.** *The local asymptotic stability of the DFE is determined by the value of R_0:*

(1) If $R_0 < 1$, the Disease-Free Equilibrium (P^0) is locally asymptotically stable. This implies that if the system starts close enough to the DFE, it will return to the DFE over time, meaning the disease will die out.

(2) If $R_0 > 1$, the Disease-Free Equilibrium (P^0) is unstable. This implies that if a small number of infectious individuals are introduced into the population, the disease will initially grow and spread, moving the system away from the DFE.

4. Sensitivity Analysis of $\mathcal{R}_0$

We studied the sensitivity analysis, to show which parameters have the significant impact (positive or negative) on the reproduction number $\mathcal{R}_0$.

The sensitivity index of $\mathcal{R}_0$ to a given parameter P, is given by the following relation:

$$S_P^{\mathcal{R}_0} = \left(\frac{\partial \mathcal{R}_0}{\partial P}\right)\left(\frac{P}{R_0}\right),$$

or in other form,

$$S_P^{\mathcal{R}_0} = P\left(\frac{\partial}{\partial P}\left(\ln \mathcal{R}_0\right)\right),$$

Thus, we can evaluate the sensitivity index of $\mathcal{R}_0$ to each parameter as follows:

$$S_\alpha^{\mathcal{R}_0} = 1,$$

$$S_\lambda^{\mathcal{R}_0} = \lambda\left(\tfrac{1}{\lambda} - \tfrac{1}{\lambda+\mu}\right) = 1 - \tfrac{\lambda}{\lambda+\mu},$$

$$S_\sigma^{\mathcal{R}_0} = 1,$$

$$S_\epsilon^{\mathcal{R}_0} = \epsilon\left(\tfrac{1}{\epsilon+\mu(1-\beta)} - \tfrac{1}{\mu+\epsilon+\gamma}\right),$$

$$S_{\mu}^{\mathcal{R}_0} = \mu\left[\frac{1-\beta}{\epsilon+\mu(1-\beta)} + \frac{1}{d+\delta_1+\eta+\mu} - \frac{1}{\lambda+\mu} - \frac{1}{\mu} - \frac{1}{\mu+\epsilon+\gamma} - \frac{1}{d+\eta+\mu} - \frac{1}{\delta_1+\delta_2+\mu}\right],$$

$$S_{\beta}^{\mathcal{R}_0} = \beta\left(\frac{-\mu}{\epsilon+\mu(1-\beta)}\right),$$

$$S_{d}^{\mathcal{R}_0} = \left(\frac{1}{d+\delta_1+\eta+\mu} - \frac{1}{d+\eta+\mu}\right),$$

$$S_{\delta_1}^{\mathcal{R}_0} = \delta_1\left(\frac{1}{d+\delta_1+\eta+\mu} - \frac{1}{\delta_1+\delta_2+\mu}\right),$$

$$S_{\delta_2}^{\mathcal{R}_0} = \delta_2\left(-\frac{1}{\delta_1+\delta_2+\mu}\right),$$

$$S_{\eta}^{\mathcal{R}_0} = \eta\left(\frac{1}{d+\delta_1+\eta+\mu} - \frac{1}{d+\eta+\mu}\right),$$

$$S_{\gamma}^{\mathcal{R}_0} = \gamma\left(-\frac{1}{\mu+\epsilon+\gamma}\right)$$

The parameter values given in Table 2 and the calculated sensitivity indices are shown in Table 3 and Figure 2.

Parameter	**Meaning**	**Value**	**Source**
α	Birth rate	0.0096	[6]
β	Vaccination coverage at birth	0.85	[1]
σ	Transmission rate from Susceptible to Exposed	0.04	[1]
γ	Vaccination rate	0.045	[1]
ϵ	Failure probability of vaccination	0.02	[6]
μ	Natural death rate	0.0096	[6]
λ	Progression rate from Exposed to Acute	0.036	[1]
δ_1	Progression rate from Acute to Chronic	0.2028	[1]
δ_2	Recovery rate from Acute infection	3.8528	[1]
η	Treatment rate for Chronic individuals	0.0936	[1]
d	HBV induced death rate	0.0936	[4]
ψ	Recovery rate for Treated individuals	0.05	[1]

TABLE 2. Estimated values of the model parameters

Parameter	Value	Sensitivity Index $\left(S_P^{\mathcal{R}_0}\right)$
α	0.0096	+1.0000
β	0.85	-0.3806
σ	0.04	+1.0000
γ	0.045	-0.6032
ϵ	0.02	+0.6647
μ	0.0096	-1.4386
λ	0.036	+0.2105
δ_1	0.025	-0.3067
δ_2	0.025	-0.4195
η	0.0936	-0.0536
d	0.0936	-0.0536

TABLE 3. Sensitivity Indices for the parameters

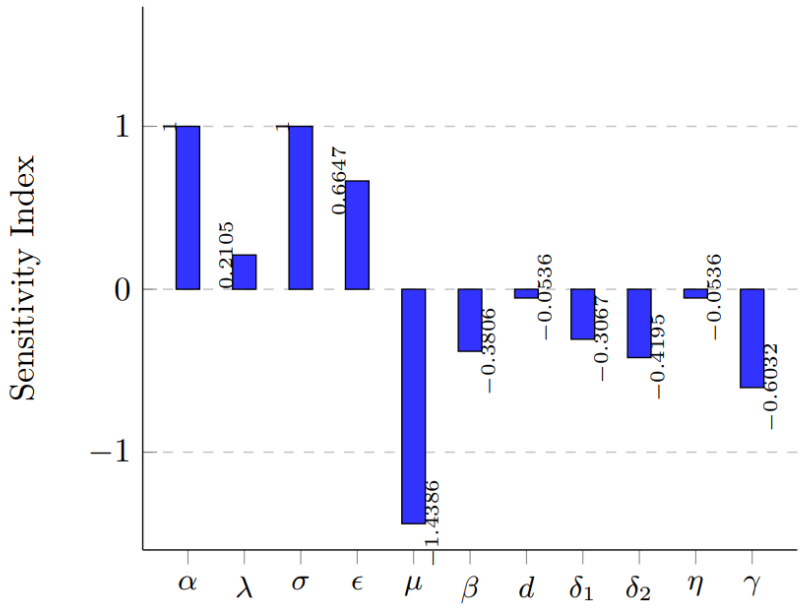

FIGURE 2. Sensitivity Indices for the Parameters

5. Optimal Control Model

Sensitivity analysis give us insight into which parameters have the most significant impact on the basic reproduction number $\mathcal{R}_0$, which represents as a measure of spreading the disease. from this analysis we find:

- The parameter σ showed high sensitivity index (+1), this means reducing transmision rate σ contributes to reduce $\mathcal{R}_0$. We introduce a control variable $u_1(t)$, where $0 \leq u_1(t) \leq u_1^{max} < 1$,

represents a combination of interventions to reduce transmission, such as (behavioral education and awareness, blood screening and safety, safe injection practices, avoiding the sharing of personal items with infected individuals), u_1^{max} is the maximum feasible interventions. With this control the transmission rate becomes $\sigma(1-u_1(t))$.

- The parameter γ showed sensitivity index (-0.6032). This means increasing vaccination rate reduces R_0. Define a control variable $u_2(t)$ where $0 \leq u_2(t) \leq u_2^{max} < 1$, represents the vaccination rate applied to susceptible at time t, u_2^{max} is the maximum feasible vaccination. With this, the vaccination rate becomes $(\gamma + u_2(t))$.
- The parameter δ_2 showed sensitivity index (-0.4195). Which means increasing δ_2 leads to decreasing $\mathcal{R}_0$. Define a control variable $u_3(t)$, where $0 \leq u_3(t) \leq u_3^{max} < 1$ represents the treatment rate applied to acute at time t, u_3^{max} is the maximum feasible treatment. With this the treatment rate becomes $\delta_2 + u_3(t)$.
- The parameters such as α, ϵ and μ showed high sensitivity index but they are non controllable demographic and biological parameters.
- The parameters β, δ_1, d and η, have low sensitivity index, we exclude them in optimal control.

We aim to minimize the total cost associated with infected individuals (exposed, acute or chronic) together with the cost of interventions u_1, u_2 and u_3 over the time interval $[0, T]$. Thus, the objective is to minimize the function:

$$\begin{aligned} J(u_1, u_2, u_3) = \int_0^T & [w_2 A(t) + w_3 C(t) + w_1 E(t) \\ & + \frac{B_1}{2} u_1(t)^2 + \frac{B_2}{2} u_2(t)^2 + \frac{B_3}{2} u_3(t)^2 \Big] dt \end{aligned} \tag{5.1}$$

Where, w_1, w_2 and w_3 represent the weights of the cost per infected individual in year in Exposed, Acute, and Chronic stages respectively. B_1, B_2, and B_3 represent the weights of the costs of the interventions (transmission reduction effort costs, treatment cost, vaccination costs respectively).

Minimize the function 5.1 subject to the population dynamics given by the system 2.1 with consider of inserting optimal control variables,

$$\begin{aligned} \frac{dS}{dt} &= \alpha N_0(1-\beta) - \Lambda(t)S(t) - (\gamma + u_2(t))S(t) + \epsilon V(t) - \mu S(t) \\ \frac{dE}{dt} &= \Lambda(t)S(t) - \lambda E(t) - \mu E(t) \\ \frac{dA}{dt} &= \lambda E(t) - \delta_1 A(t) - (\delta_2 + u_3(t))A(t) - \mu A(t) \\ \frac{dC}{dt} &= \delta_1 A(t) - \eta C(t) - dC(t) - \mu C(t) \\ \frac{dT}{dt} &= \eta C(t) - \psi T(t) - \mu T(t) \\ \frac{dV}{dt} &= \alpha N_0 \beta + (\gamma + u_2(t))S(t) - \epsilon V(t) - \mu V(t) \end{aligned} \tag{5.2}$$

$$\begin{aligned}\frac{dR}{dt} &= (\delta_2 + u_3(t))A(t) + \psi T(t) - \mu R(t)\\ N(t) &= S(t) + E(t) + A(t) + C(t) + T(t) + V(t) + R(t)\end{aligned}$$

where,

$$\Lambda(t) = \frac{\sigma(1-u_1(t))}{N(t)}(A(t) + C(t)) \tag{5.3}$$

6. Solution of the Optimal Control Problem

To find the optimal control $u_1^*(t), u_2^*(t), u_3^*(t)$, associated with the optimal solution $S^*(t), E^*(t), A^*, C^*, T^*, V^*, R^*$ we apply the Pontryagin Maximum Principle (PMP) [], to derive the necessary conditions of optimality.

Pontryagin Maximum Principle (PMP):

The Pontryagin Maximum Principle (PMP) provides necessary conditions for optimality in control problems. Consider a control system described by

$$\frac{dx_i}{dt} = f_i(t, x_i, u_j), \quad x_i(0) = x_{i0},,$$

where, $x_i(t), i = \{1, ..., n\}$ are the state vectors, and $u_j(t), j = \{1, ..., m\}$ are the control variables in a bounded and closed intervals U, then to find the optimal control $u_j^*(t)$ associated with the state vectors $x_i^*(t)$, that minimize the objective function

$$J(u_j) = \int_0^T L(t, x_i, u_j)dt$$

there exist a continuous costate vectors $\lambda_i(t)$ such that the following conditions are satisfied:

(1) The state variables $x_i^*(t)$ and the costate variables $\lambda_i(t)$ must satisfies the system:

$$\frac{dx_i^*}{dt} = \frac{\partial \mathbf{H}}{\partial \lambda_i} \qquad and \qquad \frac{d\lambda_i}{dt} = -\frac{\partial \mathbf{H}}{\partial x_i} \tag{6.1}$$

(2) The control $u_j^*(t)$ minimizes the Hamiltonian $\mathbf{H}$ almost everywhere, so

$$\left.\frac{\partial \mathbf{H}}{\partial u_j}\right|_{u_j = u_j^*} = 0 \tag{6.2}$$

(3) A transversality conditions

$$\lambda_i(T) = 0, \tag{6.3}$$

where $\mathbf{H}$ is the Hamiltonian function defined as

$$\mathbf{H}(t, x_i, u_j, \lambda_i) = L(t, x_i, u_j) + \lambda_i f_i(t, x_i, u_j)$$

Applying PMP in our model, the objective is to minimize the cost function 5.1, subject to the system 5.2. we can write the Hamiltonian function as:

$$\begin{aligned}\mathbf{H} = w_2 A + w_3 C + w_1 E + \frac{B_1}{2}u_1^2 + \frac{B_2}{2}u_2^2 + \frac{B_3}{2}u_3^2\\ + \lambda_1\left(\alpha N_0(1-\beta) - \Lambda S - u_2 S + \epsilon V - \mu S\right)\end{aligned}$$

$$
\begin{aligned}
&+ \lambda_2 (\Lambda S - \lambda E - \mu E) \\
&+ \lambda_3 (\lambda E - \delta_1 A - (\delta_2 + u_3) A - \mu A) \\
&+ \lambda_4 (\delta_1 A - \eta C - dC - \mu C) \\
&+ \lambda_5 (\eta C - \psi T - \mu T) \\
&+ \lambda_6 (\alpha N_0 \beta + (\gamma + u_2) S - \epsilon V - \mu V) \\
&+ \lambda_7 ((\delta_2 + u_3) A + \psi T - \mu R)
\end{aligned} \tag{6.4}
$$

(1) The The costate variables λ_i system is given by:

$$
\begin{aligned}
&\frac{d\lambda_1}{dt} = -\frac{\partial \mathbf{H}}{\partial S}, \qquad \frac{d\lambda_2}{dt} = -\frac{\partial \mathbf{H}}{\partial E}, \qquad \frac{d\lambda_3}{dt} = -\frac{\partial \mathbf{H}}{\partial A}, \qquad \frac{d\lambda_4}{dt} = -\frac{\partial \mathbf{H}}{\partial C}, \\
&\frac{d\lambda_5}{dt} = -\frac{\partial \mathbf{H}}{\partial T}, \qquad \frac{d\lambda_6}{dt} = -\frac{\partial \mathbf{H}}{\partial V}, \qquad \frac{d\lambda_7}{dt} = -\frac{\partial \mathbf{H}}{\partial R}
\end{aligned}
$$

which gives:

$$
\begin{aligned}
\frac{d\lambda_1}{dt} &= \left(\Lambda - \frac{\Lambda S}{N}\right)(\lambda_1 - \lambda_2) + (\gamma + u_2 + \mu)\lambda_1 - (\gamma + u_2)\lambda_6, \\
\frac{d\lambda_2}{dt} &= -w_1 + (\lambda + \mu)\lambda_2 - \lambda\lambda_3 + \frac{\Lambda S}{N}(\lambda_2 - \lambda_1), \\
\frac{d\lambda_3}{dt} &= -w_2 - \left(\frac{\sigma(1-u_1)}{N} - \frac{\Lambda}{N}\right) S(\lambda_2 - \lambda_1) \\
&\quad + (\delta_1 + \delta_2 + u_3 + \mu)\lambda_3 - \delta_1\lambda_4 - (\delta_2 + u_3)\lambda_7, \\
\frac{d\lambda_4}{dt} &= -w_3 - \left(\frac{\sigma(1-u_1)}{N} - \frac{\Lambda}{N}\right) S(\lambda_2 - \lambda_1) \\
&\quad + (\eta + d + \mu)\lambda_4 - \eta\lambda_5, \\
\frac{d\lambda_5}{dt} &= (\psi + \mu)\lambda_5 - \psi\lambda_7 + \frac{\Lambda S}{N}(\lambda_2 - \lambda_1), \\
\frac{d\lambda_6}{dt} &= -\epsilon\lambda_1 + (\epsilon + \mu)\lambda_6 + \frac{\Lambda S}{N}(\lambda_2 - \lambda_1), \\
\frac{d\lambda_7}{dt} &= \mu\lambda_7 + \frac{\Lambda S}{N}(\lambda_2 - \lambda_1),
\end{aligned} \tag{6.5}
$$

Here, we compute the partial derivative of Λ with respect to each variable S, E, A, C, T, V and R as follows:

$$
\begin{aligned}
&\frac{\partial \Lambda}{\partial S} = \frac{\partial}{\partial S}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = -\frac{\sigma(1-u_1)(A+C)}{N^2} = -\frac{\Lambda}{N}, \\
&\frac{\partial \Lambda}{\partial E} = \frac{\partial}{\partial E}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = -\frac{\Lambda}{N}, \\
&\frac{\partial \Lambda}{\partial A} = \frac{\partial}{\partial A}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = \frac{N\sigma(1-u_1) - \sigma(1-u_1)(A+C)}{N^2} = \frac{\sigma(1-u_1)}{N} - \frac{\Lambda}{N}, \\
&\frac{\partial \Lambda}{\partial C} = \frac{\partial}{\partial C}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = \frac{N\sigma(1-u_1) - \sigma(1-u_1)(A+C)}{N^2} = \frac{\sigma(1-u_1)}{N} - \frac{\Lambda}{N}, \\
&\frac{\partial \Lambda}{\partial T} = \frac{\partial}{\partial T}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = -\frac{\sigma(1-u_1)(A+C)}{N^2} = -\frac{\Lambda}{N}, \\
&\frac{\partial \Lambda}{\partial V} = \frac{\partial}{\partial V}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = -\frac{\sigma(1-u_1)(A+C)}{N^2} = -\frac{\Lambda}{N},
\end{aligned}
$$

$\frac{\partial \Lambda}{\partial R} = \frac{\partial}{\partial R}\left[\frac{\sigma(1-u_1)(A+C)}{N}\right] = -\frac{\sigma(1-u_1)(A+C)}{N^2} = -\frac{\Lambda}{N}$.

(2) The optimal control $u_j^*(t)$ must minimize the Hamiltonian $\mathbf{H}$ at each time t. This conditions is given by $\frac{\partial \mathbf{H}}{\partial u_j} = 0$.

$$\frac{\partial H}{\partial u_1} = B_1 u_1 + (\lambda_1 - \lambda_2)\left(\frac{\sigma}{N}(A+C)S\right) = 0 \implies u_1^* = \frac{1}{B_1}(\lambda_1 - \lambda_2)\frac{\sigma S(A+C)}{N} \tag{6.6}$$

$$\frac{\partial H}{\partial u_2} = B_2 u_2 + \lambda_1(-S) + \lambda_6 S = 0 \implies u_2^* = \frac{S}{B_2}(\lambda_1 - \lambda_6) \tag{6.7}$$

$$\frac{\partial H}{\partial u_3} = B_3 u_3 + \lambda_3(-A) + \lambda_7 A = 0 \implies u_3^* = \frac{A}{B_3}(\lambda_3 - \lambda_7) \tag{6.8}$$

Since the controls are bounded, $u_j \in [0, u_j^{max}]$, the optimal controls are given by:

$$u_1^*(t) = \max\left(0, \min\left(u_1^{max}, \frac{1}{B_1}(\lambda_1(t) - \lambda_2(t))\frac{\sigma S(t)(A(t)+C(t))}{N(t)}\right)\right) \tag{6.9}$$

$$u_2^*(t) = \max\left(0, \min\left(u_2^{max}, \frac{S(t)}{B_2}(\lambda_1(t) - \lambda_6(t))\right)\right) \tag{6.10}$$

$$u_3^*(t) = \max\left(0, \min\left(u_3^{max}, \frac{A(t)}{B_3}(\lambda_3(t) - \lambda_7(t))\right)\right) \tag{6.11}$$

(3) The transversality conditions are:

$$\lambda_i(T) = 0, \quad i \in \{1,2,3,4,5,6,7\} \tag{6.12}$$

7. Numerical Solution

Solving the system 5.2 of state equations forward in time from 0 to T with initial conditions 2.2, coupled with the system 6.5 of costate equations backward in time from T to 0 with boundary conditions 6.12, this coupled problem is solved numerically by Forward-Backward Sweep Method (FBSM), to find the optimal controls $u_j, \quad j = \{1,2,3\}$, with the corresponding state variables $S(t), E(t), A(t), C(t), T(t), V(t)$ and $R(t)$.

Steps of the Forward Backward Sweep Method (FBSM).

Step 1: Initialization:

- Choose an initial guess for the controls $u_j^{(0)}(t) = 0, \quad j = \{1,2,3\}$

- State the maximum iterations (Max), set the iteration index $k = 0$ and the convergence tolerance Tol.

Step 2: Forward Sweep:

Using the current controls solve the sate equation forward in time from $t = 0$ to $t = T$ using Runge Kutta method (RK4).

Step 3: Backward Sweep:

Solve the costate equation with the computed state variables and the current controls backward in time from $t = T$ tp $t = 0$ using Runge Kutta method (RK4).

Step 4: Update Control:

Update the control using the optimality condition:

$$u_j^{(k+1)}(t) = u_j^*, \text{where} \left(\frac{\partial \mathbf{H}}{\partial u_j} = 0 \right).$$

Step 5: Check the Convergence: If

$$\|u^{(k+1)} - u^{(k)}\| < Tol,$$

then stop, otherwise, increase k and repeat from Step 2.

	Description	**Target group**	**Weighted Cost**
w_1	Basic tests, Monitoring without symptoms.	Exposed	0.1
w_2	Medical visits, Initial diagnosis	Acute	0.5
w_3	Regular laboratory monitoring	Chronic	1
B_1	Awareness campaigns, blood screening, and preventive procedures	Susceptible	0.5
B_2	Enhancing Vaccination coverage	Susceptible	0.5
B_3	Short term treatment, Long term treatment	Acute and Chronic	1

TABLE 4. Disease costs and interventions costs

8. Results and Discussion

In this section, we present the numerical results based on the following:

(1) The initial total population $N_0 = 10^6$.
(2) The initial values:
$\{E_0, A_0, C_0, T_0, V_0, R_0\} = \{1000, 500, 100, 100, 0, \beta N_0\}$,
$S_0 = N_0 - E_0 - A_0 - C_0 - T_0 - V_0 - R_0$.
(3) Parameter values are given in Table 2.
(4) The maximum allowable values for the control interventions are:

$$u_1^{\max} = 0.7, \quad u_2^{\max} = 0.4, \quad u_3^{\max} = 0.5.$$

(5) The weighted costs w_1, w_2, w_3 and B_1, B_2, B_3 are provided in Table 4.

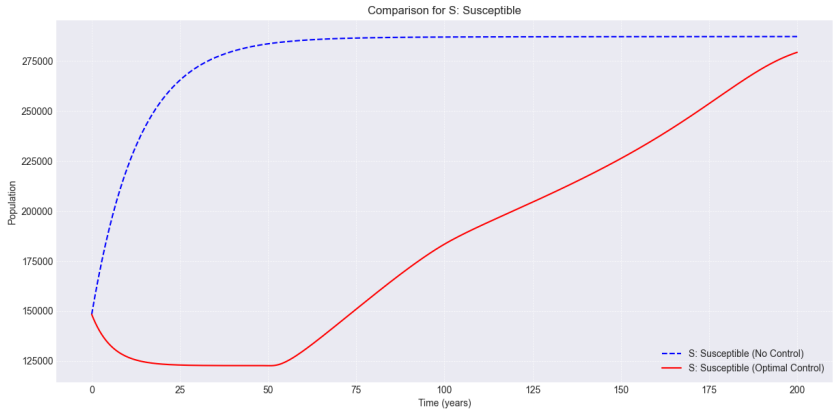

FIGURE 3. Dynamics of Susceptible with and without control

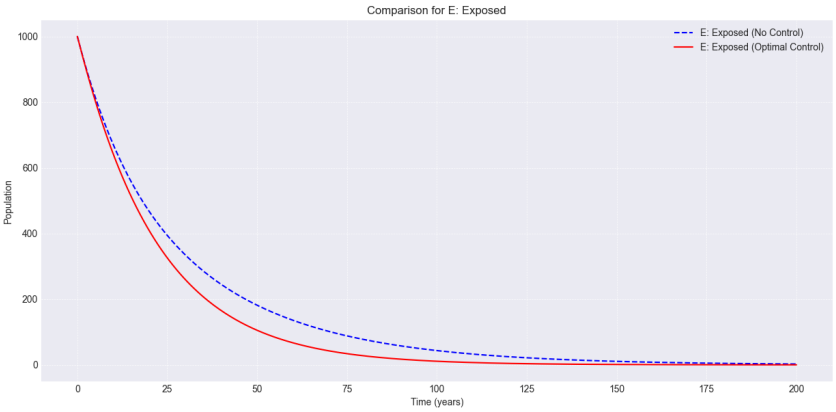

FIGURE 4. Dynamics of Exposed with and without control

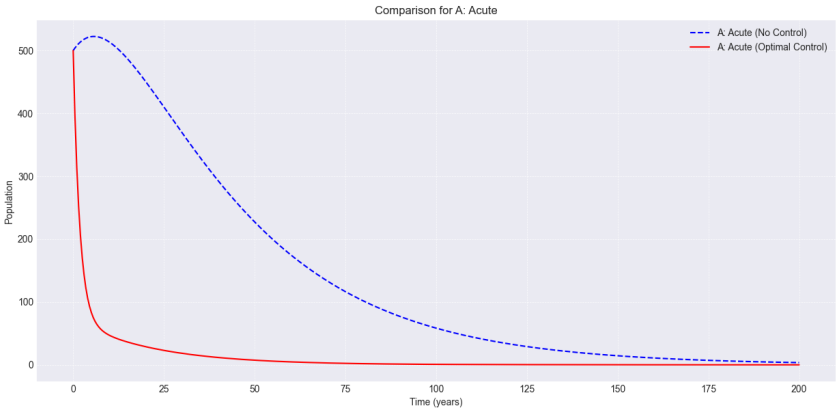

FIGURE 5. Dynamics of Acute with and without control

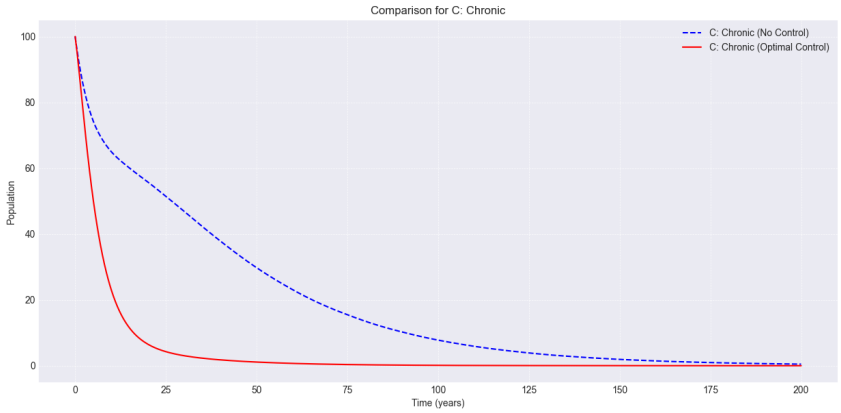

FIGURE 6. Dynamics of Chronic with and without control

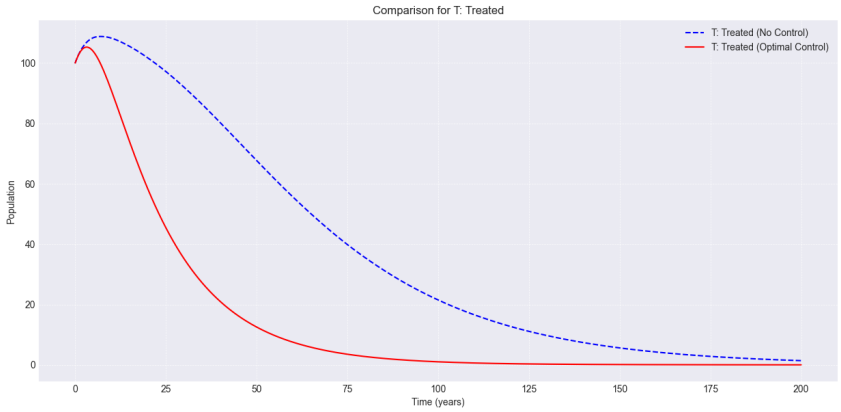

FIGURE 7. Dynamics of Treated with and without control

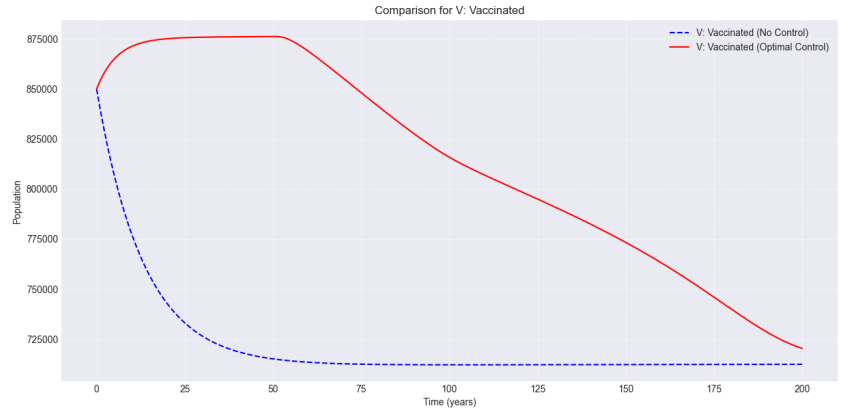

FIGURE 8. Dynamics of Vaccinated with and without control

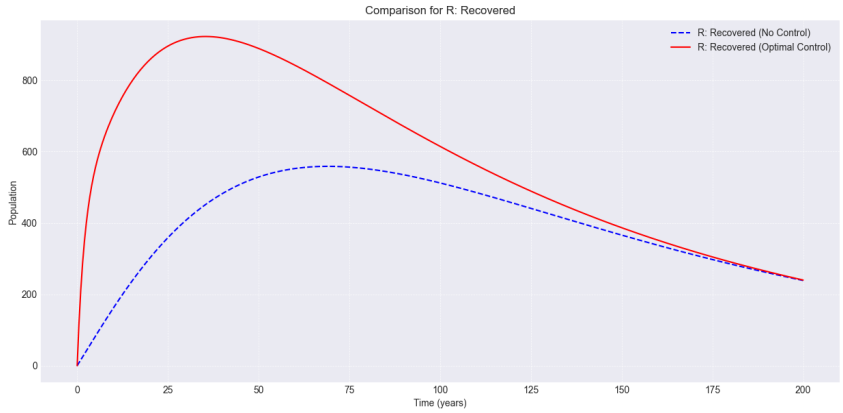

FIGURE 9. Dynamics of Recovered with and without control

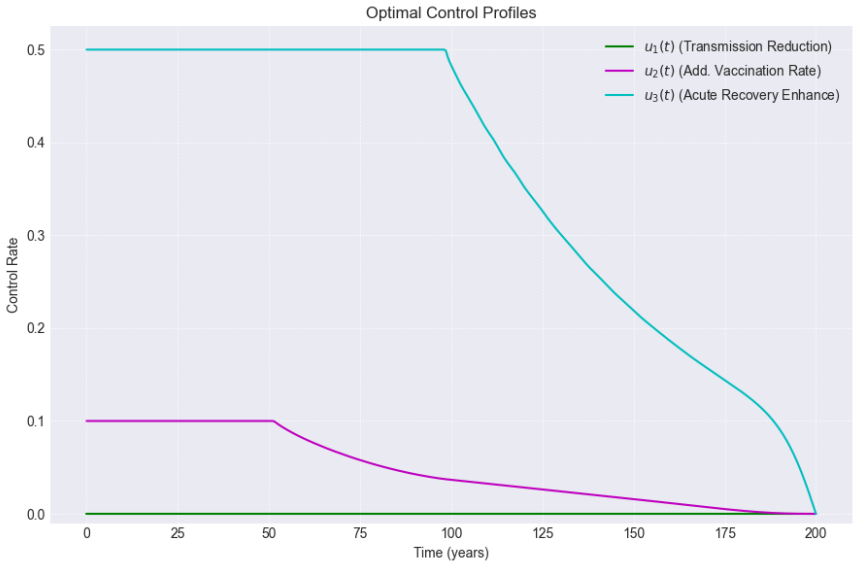

FIGURE 10. Optimal variables $u_1(t)$, $u_2(t)$, and $u_3(t)$

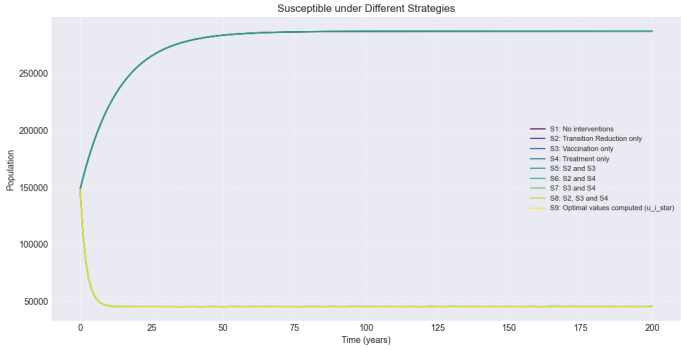

FIGURE 11. Dynamic of Susceptible under Different Strategies

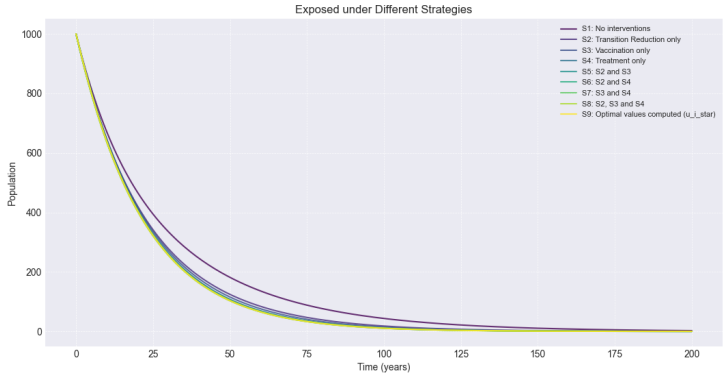

FIGURE 12. Dynamics of Exposed under Different Strategies

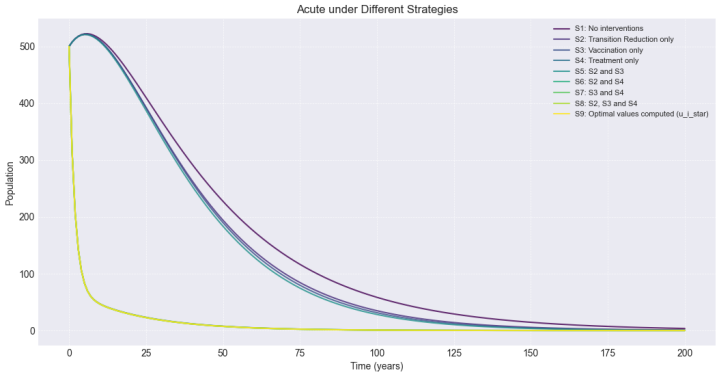

FIGURE 13. Dynamics of Acute under Different Strategies

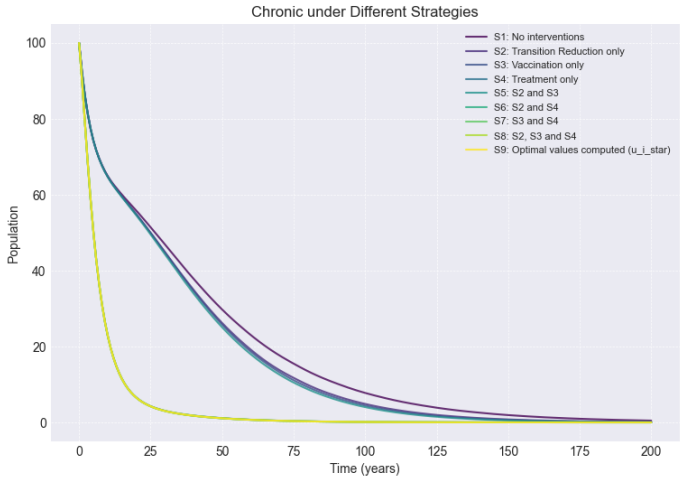

FIGURE 14. Dynamics of Chronic under Different Strategies

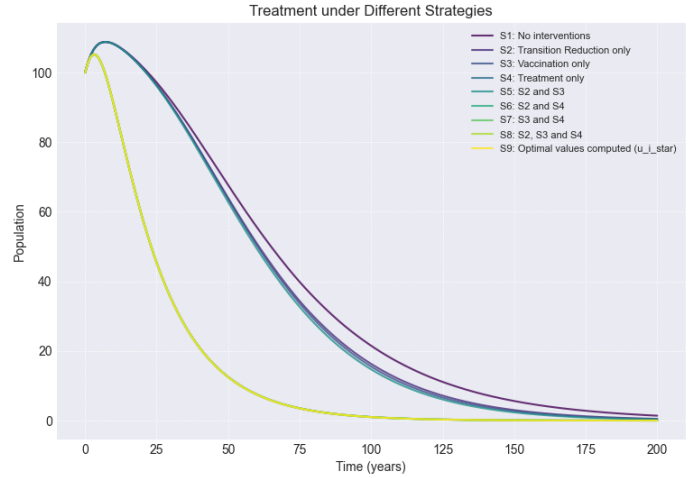

FIGURE 15. Dynamics of Treated under Different Strategies

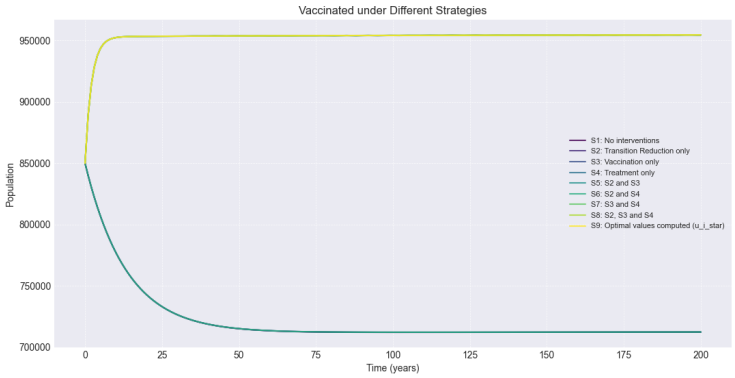

FIGURE 16. Dynamics of Vaccinated under Different Strategies

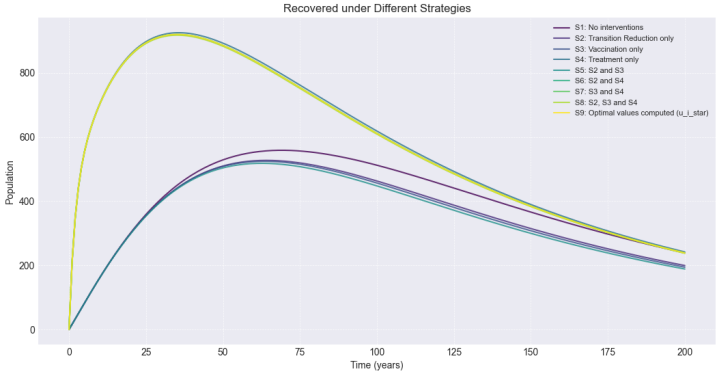

FIGURE 17. Dynamics of Recovered under Different Strategies

The table below summarizes the different intervention strategies, associated with the basic reproduction number $\mathcal{R}_0$, the burden costs, and the control costs in different values of the control variables.

Strategy	**Description and Control Values** (u_1, u_2, u_3)	$\mathcal{R}_0$
S1	No Interventions $(0,0,0)$	0.171622329
S2	Transmission Reduction Only $(u_1^{max}, 0, 0)$	0.051486699
S3	Vaccination Only $(0, u_2^{max}, 0)$	0.026976455
S4	Treatment Only $(0, 0, u_3^{max})$	0.018278575
S5	S2 and S3 $(u_1^{max}, u_2^{max}, 0)$	0.008092937
S6	S2 and S4 $(u_1^{max}, 0, u_2^{max})$	0.005483573
S7	S3 and S4 $(0, u_2^{max}, u_3^{max})$	0.002873118
S8	S2, S3 and S4 (all maximum) $(u_1^{max}, u_2^{max}, u_3^{max})$	0.000861935
S9	Optimal controls computed by (PMP) (u_1^*, u_2^*, u_3^*)	0.002873118

TABLE 5. Effects of different intervention strategies on the basic reproductive number R_0.

Strategy	**Burden Cost**	**Control Cost**	**Total Cost**
S1: No interventions	20760	0	20760
S2: Transition Reduction only	18138	24	18163
S3: Vaccination only	17811	8	17819
S4: Treatment only	4210	25	4235
S5: S2 and S3	17382	32	17415
S6: S2 and S4	4153	50	4203
S7: S3 and S4	4156	33	4189
S8: S2, S3 and S4	4137	57	4195
S9: Optimal values computed (u_i^*)	4156	33	4189

TABLE 6. Comparison of intervention strategies with associated costs.

9. CONCLUSION

This study presents a mathematical model for analyzing the transmission dynamics of the Hepatitis B Virus (HBV) and evaluating the effectiveness of three intervention strategies: transmission reduction, vaccination, and treatment. Mathematical analysis establish the existence and uniqueness of the solutions, derived the basic reproduction number $\mathcal{R}_0$, and analyzed the stability of the disease-free equilibrium.

Numerical simulations were conducted to assess the impact of various intervention strategies,

including individual interventions, pairwise combinations, and a combination of all three interventions. Table 5 summarizes the results of each strategy on the basic reproductive number $\mathcal{R}_0$. The results show the combination of all the three interventions at maximum value of the control variables give the minimum value of $\mathcal{R}_0$ (Strategy S8), followed by the optimal control strategy (S9), which yields the same $\mathcal{R}_0$ as the combined vaccination and treatment strategy (S7). Table 6 shows the results of the weighted disease burden costs and intervention costs. Strategy (S1), which represents no interventions gives the highest total cost. Strategy (S7) which represents treatment and vaccination at maximum value of controls, also strategy (S9) which represents the optimal values of the controls which computed by PMP, give the same lowest total cost.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

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