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Mathematical modeling and optimal control of a deterministic SHATR model of HIV/AIDS with possibility of rehabilitation: a dynamic analysis

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Abstract. In the present work, we developed a deterministic SHATR (Susceptible - HIV infected -AIDS infected - Antiretroviral Treatment - Recovered) compartment model for HIV/AIDS. This model considers the disease outbreak due to a lack of awareness and treatment. The steady states of the proposed model system are obtained and analyzed by using the nonlinear stability theory of differential equations. The basic reproduction number is derived and explored to determine the stability and sensitivity index of some important relative parameters. Further, to know the global behavior of the model one parameter bifurcation study is discussed. Moreover, the optimal control theory has been applied to identify the optimal strategy by taking treatment and awareness for safe intercourse as control parameters. The control problem is solved analytically by using Pontryagin's maximum principle. Finally, the model is simulated to describe the optimality under various assumptions and the stability of equilibrium points.

Keywords. Antiretroviral therapy (ART), basic reproduction number, lyapunov, optimal control, Pontryagin's maximum principle

1 Introduction

Nowadays, infectious epidemic diseases are the leading cause of death in modern society and continue to spread worldwide despite the huge number of investments made in Fighting against them. AIDS (acquired immunodeficiency syndrome) is one of them caused by infection with HIV (Human Immunodeficiency Virus). The present spread of HIV infection influences increasing the occurrence of other diseases such as TB globally [1].
HIV is a virus that affects our body by weakening the immune system and leaving it vulnerable to other disease-causing organisms. HIV viral transmission may happen due to contaminated blood products, syringes, unsafe intercourse, and mother-to-child during birth or through breast-feeding [2]. The human immune system, preferably Cytotoxic T Lymphocytes (CTLs), has a vital role in defending against HIV infection by suppressing the viral replication process and increasing the CD4 cell count. Therefore, CTL cells play an important role in determining the viral load. Although modern therapies are more advanced, they have failed to eliminate the

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disease. Current Antiretroviral Therapy (ART) comprises two or more antiviral drugs chosen from two classes: Reverse Transcriptase Inhibitors (RTIs) and Protease Inhibitors (PIs). Reverse Transcriptase Inhibitors block the new infection while Protease Inhibitors block the production of new infectious viruses [3]. Hence, the immune response of an individual after viral infection is necessary to control disease transmission. It was estimated that 38 million people were living with HIV globally in 2019, but only 25.4 million people were accessing ART [4]. So, we need more efforts to control the epidemic disease. The reasons for fewer individuals undergoing ART can be due to their being unaware of their infection or due to fear of wastage of money because, even after investing a large amount in ART, the patient's immunity is temporary. Although there is a decrement in the incidence of HIV patients every year since the introduction of ARTs, it only helps to increase the life span of patients for some more years by suppressing the viral load and making them free from HIV symptoms.

Mathematical models have always been very useful in public health planning and policy-making as they can help in determining the outcome of an epidemic by estimating mortality, explaining the re-emergence of diseases, etc. Therefore, mathematical and computational modeling of HIV/AIDS plays a vital role in defining the disease dynamics and preventing it from spreading among people by reducing the risk factors. The controlling mechanisms of the disease can be investigated through the concept of optimal control theory. The theory has some valuable principles that justify, how the disease can be controlled using given biological controls.

In the last decade, various mathematical models have been developed in the field of epidemiology to understand the dynamics of HIV disease with control or without control. Such as Aldila et al. [5] proposed a model that includes the vertical transmission from infected parents to their newborn babies. They found that vertical transmission of HIV from infected parents is essential to control HIV. Dubey et al. [6] established a model for HIV/AIDS to study the role of immune response and ART. They observed that the combination of therapy reduces viral load and enhances the lifespan of HIV-infected patients. Some researchers, such as Kaymakamzade et al. [7], Kaur et al. [8], and Ghosh et al. [9], formulated the models by taking the effects of media awareness, psychological fear, etc. Their study suggested that awareness programs through media campaigns and the strength of psychological fear will surely decrease the epidemic potential in any society. Further, Yusuf et al. [10] introduced a strategy for finding the optimal combination of two control measures that will minimize the cost of the control efforts as well as the incidence of the disease. Rana, and Sharma [11] defined a simple compartmental SI model for HIV/AIDS, analyzed the stability, and concluded that giving early Anti-Retroviral Therapy to AIDS patients can prolong their lives by giving them a quality life. Similarly, Jana et al. [12] developed the SIR compartment model by taking the treatment function in saturated form and discussed the global dynamics, bifurcation, and optimal control of the system. They further stated that optimal control would be a good technique to minimize the infection and total treatment cost. Mastroberardino et al. [13] presented a mathematical model to study the HIV dynamics in Cuba and suggested that their national prevention program had an enormous impact on the exceptionally low prevalence rate with respect to other countries in the Caribbean. Similarly, Ayele et al. [1], did a case study of Ethiopia and showed that the combination of preventive and screening strategies are the best cost-effective strategies to reduce the disease burden. Many researchers did case studies of other countries too [14], [15]. Further, Ali et al. [16] developed a fractional order model for HIV/AIDS and obtained that the smaller values of fractional order have better performance than larger values.

As per the literature, until now no one proposed and analyzed the HIV/AIDS model with recovery and treatment compartments, assuming that even after ART treatment, patients can either transfer into the AIDS class or the HIV class. This model considers that the recovered compartment includes those susceptible individuals who modified their sexual habits by taking safety mea-

sures for intercourse throughout their entire life. Hence, they are gaining permanent immunity from HIV infection through sexual contact. The treatment compartment includes those infected individuals (HIV or AIDS), who are undergoing Antiretroviral therapy (ART). The model was solved and the stability of equilibrium points is discussed analytically. Furthermore, the control problem is formulated that minimizes the number of HIV/AIDS-infected individuals, the cost of treatment, and the cost of awareness about safe intercourse by implementing an optimal theory. The graphical results of the model have been presented to discuss the proposed strategies with control and without control. The numerical result suggested that more efforts should be given to make individuals aware of safe sexual intercourse.

2 Mathematical Model of HIV/AIDS Disease

Deterministic mathematical models for epidemics are fundamental to understanding the disease, which further helps to plan effective control strategies. We considered a region with a homogenously mixed population, which is split up into five distinct sub-classes or compartments; Susceptible compartment (S), HIV positive compartment (H), AIDS-infected compartment (A), ART treatment compartment (T), and Recovered compartment (contains individuals who took safety measures for safe intercourse for the rest of their lives) (R). So, they are unaffected of HIV infection by sexual contact. Thus, the total population at any time (T) is denoted by $N(t)$ and defined as $N(t) = S(t) + H(t) + A(t) + T(t) + R(t)$.

The population is recruited into susceptible class (involving birth and immigration) at λ_1 rate. The susceptible class contains healthy individuals that can come in close contact with HIV-positive individuals at β rate and become HIV infected. The model considers the standard incidence rate of infection that is mostly applicable to sexually transmitted diseases [17]. The shifting rate of individuals from HIV class to AIDS class is denoted by α. Similarly, the treatment rates of individuals in HIV and AIDS classes are a_1 and a_2 respectively. While b_1 and b_2 are the rate of treated individuals returning to $H(T)$ and $A(T)$ classes respectively. This represents that everyone is not completing the ART course, some are dropping out in the middle due to a financial crisis or some other issues. Further, d is an additional death rate induced by AIDS infected $A(T)$, and under-treatment individuals $T(t)$. The symbol μ_1 defines the proportion rate of susceptible that recovered from the illness due to changes in their sexual habits. The natural death rate is denoted by μ and assumed to be identical for all the compartments. The schematic flow diagram for the proposed mathematical model (2.1) is depicted in figure 1.

The model system is governed by the following differential equations

$$\begin{aligned}
\frac{dS}{dt} &= \lambda_1 - \beta\frac{SH}{N} - (\mu + \mu_1)S \\
\frac{dH}{dt} &= \beta\frac{SH}{N} - (a_1 + \mu + \alpha)H + b_1T \\
\frac{dA}{dt} &= \alpha H - (a_2 + \mu + d)A + b_2T \\
\frac{dT}{dt} &= a_1H + a_2A - (b_1 + b_2 + \mu + d)T \\
\frac{dR}{dt} &= \mu_1S - \mu R
\end{aligned} \tag{2.1}$$

with initial conditions $S_0 > 0$, $H_0 > 0$, $A_0 > 0$, $T_0 > 0$ and $R_0 > 0$.

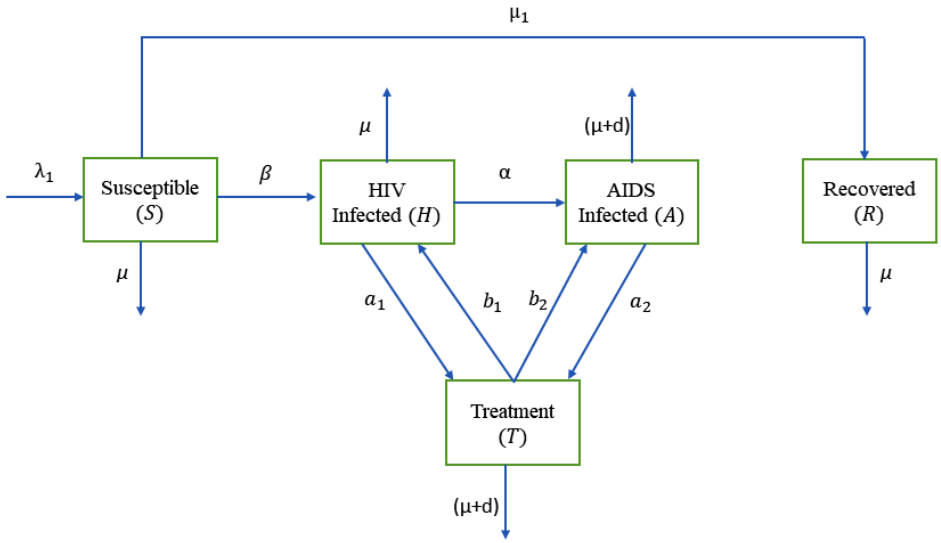


Figure 1: Transmission Flow Dynamics of a deterministic SHATR model for HIV/AIDS.

3 Positivity and Boundedness of Solutions

Lemma 3.1. *Let initially $S_0 \geq 0$, $H_0 \geq 0$, $A_0 \geq 0$, $T_0 \geq 0$, $R_0 \geq 0$ then the solutions of model system Eq. (2.1) are positive for all $t > 0$.*

Proof. Let $t_1 = sup\{t > 0 : t \in [\,0, t]$ *and* $S_0 \geq 0$, $H_0 \geq 0$, $A_0 \geq 0$, $T_0 \geq 0$, $R_0 \geq 0\,\}$.
Let $\lambda(t) = \beta \frac{H}{N}$, then now taking the first equation of system Eq. (2.1)

$$\begin{aligned} &\frac{dS}{dt} = \lambda_1 - \lambda(t)S - \mu S - \mu_1 S \\ \implies &\frac{dS}{dt} + \lambda(t)S + \mu S + \mu_1 S = \lambda_1 \\ &\frac{d}{dt}\,[S(t)\exp\{\,\textstyle\int_0^t \lambda(t)\,d\tau + (\mu+\mu_1)t\}] = \lambda_1 \exp\{\,\textstyle\int_0^t \lambda(t)\,d\tau + \mu t + \mu_1 t\} \end{aligned} \tag{3.1}$$

So, now solving this we have,

$$\begin{aligned} S(t_1)\,\exp\{\,\textstyle\int_0^{t_1} \lambda(t)\,d\tau + (\mu+\mu_1)t\} - S_0 &= \textstyle\int_0^{t_1}\, \lambda_1\, \exp\{\,\int_0^x \lambda(\nu)\,d\nu + (\mu+\mu_1)x\}\,dx \\ S(t_1) = S_0\,\exp\{-\textstyle\int_0^{t_1} \lambda(t)\,d\tau - (\mu+\mu_1)t\} + \exp\{-\textstyle\int_0^{t_1} \lambda(t)\,d\tau - (\mu+\mu_1)t\} \\ \times \textstyle\int_0^{t_1}\, \lambda_1\, \exp\{\,\int_0^x \lambda(\nu)\,d\nu + (\mu+\mu_1)x\}\,dx \end{aligned} \tag{3.2}$$

which implies $S(t_1) > 0$. Similarly, it can be shown that $H(t) \geq 0$, $A(t) \geq 0$, $T(t) \geq 0$, $R(t) \geq 0$ for all $t > 0$. Thus the solutions (S, H, A, T, R) of the system remain positive forever. This proves that the model variables are biologically meaningful. □

Lemma 3.2. *The system (2.1) is eventually bounded in the region R_+^5.*

Proof. Now using the non-negativity of state variables. The rate of total population can be obtained by adding all the equations of Eq. (2.1). Hence,

$$\begin{aligned} &\frac{dN}{dt} = \frac{dS}{dt} + \frac{dH}{dt} + \frac{dA}{dt} + \frac{dT}{dt} + \frac{dR}{dt} \\ \Longrightarrow\ &\frac{dN}{dt} = \lambda_1 - \mu N - (A+T)d \leq \lambda_1 - \mu N \\ \Longrightarrow\ &\frac{dN}{dt} \leq \lambda_1 - \mu N \end{aligned} \tag{3.3}$$

By comparison principle, we get that,

$$\lim_{t\to\infty} Sup(N(t)) \ \leq \frac{\lambda_1}{\mu} \tag{3.4}$$

Thus, every solution of system (2.1) is eventually bounded in R^5_+. □

4 Equilibrium and Stability Analysis

We studied the model in R^5_+ (described in Lemma 3.2), which is a positive and compact attracting set for our model system (2.1). Hence, it attracts all solutions initiated in it. We will discuss the qualitative behavior of the system through an equilibrium solution that does not change with time. Further, for the full characterization of a model, the stability of equilibrium points is discussed through Lyapunov and La Salle invariance principle [18]. The results on the stability of equilibrium points are stated in the following subsections. The model Eq. (2.1) has two equilibrium points namely disease-free equilibrium (DFE) and endemic equilibrium (EE). The DFE is obtained, when there is no disease i.e., $H = 0$, which gives the following point;

$$E^0 = (S_0, H_0, A_0, T_0, R_0) = \Big(\frac{\lambda_1}{(\mu+\mu_1)}, 0, 0, 0, \frac{\lambda_1\mu_1}{\mu(\mu+\mu_1)}\Big). \tag{4.1}$$

4.1 The Basic Reproduction Number

The Basic Reproduction Number is the threshold parameter that gives a borderline between disease persistence and eradication. To compute the basic reproduction number, the next generation matrix method is utilized. Let Eq.(2.1) can be written as $\dot{x} = F(x) - V(x)$, where $F(x)$ corresponds to new infection terms while $V(x)$ corresponds to the remaining transfer terms. Now writing the system in sequence $x = (H, A, T, S, R)^T$, we have

$$F(x) = \begin{bmatrix} \beta\frac{SH}{N} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \qquad V(x) = \begin{bmatrix} (a_1+\mu+\alpha)H - b_1T \\ (a_2+\mu+d)A - \alpha H - b_2T \\ (b_1+b_2+\mu+d)T - a_1H - a_2A \\ -\lambda_1 + \beta\frac{SH}{N} + \mu s \\ \mu R - \mu_1 S \end{bmatrix} \tag{4.2}$$

As the infected compartments are only H, A and T so, at DFE, $F_{3\times3}$ and $V_{3\times3}$ are as follows:

$$F(x) = \begin{bmatrix} \beta\frac{\mu}{(\mu+\mu_1)} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} and V(x) = \begin{bmatrix} (a_1+\mu+\alpha) & 0 & -b_1 \\ -\alpha & (a_2+\mu+d) & -b_2 \\ -a_1 & -a_2 & (b_1+b_2+\mu+d) \end{bmatrix} \tag{4.3}$$

At DFE point E^0 finding the eigenvalues of FV^{-1}, the basic reproduction number R_0 for the model can be given as;

$$\begin{aligned} R_0 &= \rho(FV^{-1}) \\ &= \frac{\beta\mu\{(a_2+\mu+d)(b_1+b_2+\mu+d)-a_2b_2\}}{(\mu+\mu_1)[(a_1+\mu+\alpha)\{(a_2+\mu+d)(b_1+b_2+\mu+d)-a_2b_2\}-b_1\{\alpha a_2+a_1(a_2+\mu+d)\}]} \end{aligned}$$

Now, simplifying the numerator term gives

$$\{(a_2+\mu+d)(b_1+b_2+\mu+d)-a_2b_2\} = \{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2)\} \tag{4.5}$$

$$\begin{aligned} R_0 &= \frac{\beta\mu\{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2)\}}{(\mu+\mu_1)[(a_1+\mu+\alpha)\{(a_2+\mu+d)(b_1+\mu+d)+(\mu+d)b_2\}-b_1\{\alpha a_2+a_1(a_2+\mu+d)\}]} \\ \implies R_0 &= \frac{\beta\mu}{(\mu+\mu_1)[(a_1+\mu+\alpha)-\frac{b_1\{\alpha a_2+a_1(a_2+\mu+d)\}}{\{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2)\}}]} \end{aligned} \tag{4.6}$$

4.2 Stability of Disease-Free Equilibrium Point

Theorem 4.1. *The disease-free equilibrium point is globally asymptotically stable whenever* $R_0 \leq 1$ *and unstable if* $R_0 > 1$.

Proof. Now to prove the global stability of DFE, we introduced a Lyapunov function V such that $V = H + mA + nT$. Taking the time derivative of V, $\dot{V} = \dot{H} + m\dot{A} + n\dot{T}$.
Now substituting the values of $\dot{H}$, $\dot{A}$, and $\dot{T}$ from our model system (2.1), in the above expression

$$\dot{V} = \beta\frac{SH}{N} - (a_1+\mu+\alpha)H + b_1T + m[\alpha H + b_2T - (a_2+\mu+d)A] + n[a_1H + a_2A - (b_1+b_2+\mu+d)T]. \tag{4.7}$$

At DFE point, from equation (4.1)

$$S^0 = \frac{\lambda_1}{(\mu+\mu_1)}, \quad R^0 = \frac{\lambda_1\mu_1}{\mu(\mu+\mu_1)} \tag{4.8}$$

$$\dot{V} \leq H[\frac{\beta\lambda_1}{N(\mu+\mu_1)} - (a_1+\mu+\alpha) + m\alpha + na_1] + A[-m(a_2+\mu+d) + na_2] + T[b_1 + mb_2 - n(b_1+b_2+\mu+d)]. \tag{4.9}$$

Choosing

$$m = \frac{a_2b_1}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2}, \quad n = \frac{b_1(a_2+\mu+d)}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2} \tag{4.10}$$

We get

$$\begin{aligned} \dot{V} &\leq H[\frac{\beta\mu}{(\mu+\mu_1)} - (a_1+\mu+\alpha) + \frac{b_1\{\alpha a_2+a_1(a_2+\mu+d)\}}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2}] \\ \implies \dot{V} &\leq H[\frac{\beta\mu}{(\mu+\mu_1)} - \{(a_1+\mu+\alpha) - \frac{b_1\{\alpha a_2+a_1(a_2+\mu+d)\}}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2}\}] \end{aligned} \tag{4.11}$$

from equation (4.6)

$$R_0 = \frac{\beta\mu}{(\mu+\mu_1)[(a_1+\mu+\alpha)-\frac{b_1\{\alpha a_2+a_1(a_2+\mu+d)\}}{\{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2)\}}]} \tag{4.12}$$

So, we have that

$$\dot{V} \leq \{(a_1+\mu+\alpha) - \frac{b_1\{\alpha a_2 + a_1(a_2+\mu+d)\}}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2}\} \times \{R_0 - 1\}H$$
$$\dot{V} \leq \frac{(a_1+\mu+\alpha)[(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2] - b_1\{\alpha a_2 + a_1(a_2+\mu+d)\}}{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2} \times \{R_0-1\}H \tag{4.13}$$

Implies $\dot{V} \leq 0$ whenever $R_0 \leq 1$ with $\dot{V} = 0$ only if $H = T = A = 0$ for $R_0 < 1$, while for $R_0 = 1$, $\dot{V} = 0$ if and only if $H = 0$ or $S = S^0, R = R^0$. Now substitute $H = T = A = 0$ in the model system (2.1), and we have $S \to \frac{\lambda_1}{\mu+\mu_1}$ and $R \to \frac{\lambda_1\mu_1}{\mu\{\mu+\mu_1\}}$ as $t \to \infty$. Hence, the largest compact invariant set in $\{(S,H,A,T,R) \in \Omega \colon \dot{V} = 0\}$ is single $\{E^0\}$. Therefore, applying LaSalle invariance principle [18], every solution of model system (2.1) approaches to E^0 as $t \to \infty$ when $R_0 \leq 1$. Hence disease-free equilibrium is GAS $R_0 \leq 1$ while unstable for $R_0 > 1$. □

4.3 Stability of Endemic Equilibrium Point

Now, the condition for the existence of endemic equilibrium point of the model is that the disease should be present in the population i.e $H^* \neq 0, A^* \neq 0$. Hence, the endemic equilibrium point $E^*(S^*, H^*, A^*, T^*, R^*)$ is obtained below as:

$$S^* = \frac{N}{\beta}\,[(a_1+\mu+\alpha) - b_1\frac{T^*}{H^*}], \quad H^* = \frac{(a_2+\mu+d)A^* - b_2T^*}{\alpha}$$
$$A^* = \frac{(\lambda_1 - \mu N)[\alpha(b_1+b_2+\mu+d)+a_1b_2]}{d[(a_2+\mu+d)a_1 + a_2\alpha + \alpha(b_1+b_2+\mu+d)+a_1b_2]} \tag{4.14}$$
$$T^* = \frac{(\lambda_1-\mu N)}{d} - A^*, \quad R^* = \frac{\mu_1}{\mu}S^*$$

Theorem 4.2. *The endemic equilibrium state is globally asymptotically stable in R^5_+ whenever $R_0 > 1$.*

Proof. To prove the global stability of the endemic point we considered only four equations of the system (2.1) because R doesn't appear in the first four equations. Let us consider the Lyapunov function V as

$$V = S - S^* \ln S + B(H - H^* \ln H) + C(A - A^* \ln A) + D(T - T^* \ln T) \tag{4.15}$$

Differentiating

$$\dot{V} = \dot{S}(1 - \frac{S^*}{S}) + B\dot{H}(1 - \frac{H^*}{H}) + C\dot{A}(1 - \frac{A^*}{A}) + D\dot{T}(1 - \frac{T^*}{T})$$
$$\implies \dot{V} = (1 - \frac{S^*}{S})(\lambda_1 - \beta\frac{SH}{N} - (\mu+\mu_1)S) + B(1 - \frac{H^*}{H})(\beta\frac{SH}{N} - (a_1+\mu+\alpha)H + b_1T)$$
$$+C(1 - \frac{A^*}{A})(\alpha H + b_2T - (a_2+\mu+d)A) + D(1 - \frac{T^*}{T})(a_1H + a_2A - (b_1+b_2+\mu+d)T) \tag{4.16}$$

Since, E^* satisfies the following equations

$$\lambda_1 - \beta\frac{S^*H^*}{N} - (\mu+\mu_1)S^* = 0, \qquad \beta\frac{S^*H^*}{N} - (a_1+\mu+\alpha)H^* + b_1T^* = 0$$
$$\alpha H^* + b_2T^* - (a_2+\mu+d)A^* = 0, \qquad a_1H^* + a_2A^* - (b_1+b_2+\mu+d)T^* = 0 \tag{4.17}$$

let's take, $\frac{S}{S^*} = x$, $\frac{H}{H^*} = y$, $\frac{A}{A^*} = z$, $\frac{T}{T^*} = w$, then

$$\begin{aligned}\dot{V} &= -\frac{(1-x)^2}{x}(\mu+\mu_1)S^* + \beta\frac{S^*H^*}{N}(1-xy-\frac{1}{x}+y) + B\beta\frac{S^*H^*}{N}(1+xy-x-y)\\ &+ Bb_1T^*(w-y-\frac{w}{y}+1) + C\alpha H^*(y-z-\frac{y}{z}+1) + Cb_2T^*(w-z-\frac{w}{z}+1)\\ &+ Da_1H^*(y-w-\frac{y}{w}+1) + Da_2A^*(z-w-\frac{z}{w}+1).\end{aligned} \tag{4.18}$$

Now, by equating the coefficients of xy, y, w and z to zero we have,

$$\begin{aligned} B-1=0, \qquad (1-B)\beta\frac{S^*H^*}{N} - Bb_1T^* + C\alpha H^* + Da_1H^* = 0,\\ Da_2A^* - C\alpha H^* - Cb_2T^* = 0, \qquad Bb_1T^* + Cb_2T^* - Da_1H^* - Da_2A^* = 0.\end{aligned} \tag{4.19}$$

Solving, these linear equations in B, C, and D, we obtained

$$B=1, \quad C = \frac{b_1a_2T^*A^*}{\alpha a_2H^*A^* + (\alpha H^* + b_2T^*)a_1H^*}, \quad D = \frac{(\alpha H^* + b_2T^*)b_1T^*}{\alpha a_2H^*A^* + (\alpha H^* + b_2T^*)a_1H^*} \tag{4.20}$$

Now substituting the values of B, C, and D, in Eq. (4.18)

$$\begin{aligned}\dot{V} &= -\frac{(1-x)^2}{x}(\mu+\mu_1)S^* + \beta\frac{S^*H^*}{N}(2-x-\frac{1}{x}) + C\alpha H^*(1-\frac{y}{z}) + Cb_2T^*(1-\frac{w}{z})\\ &+ Da_1H^*(1-\frac{y}{w}) + Da_2A^*(1-\frac{z}{w}) + b_1T^*(1-\frac{w}{y})\\ \implies \dot{V} &= -\frac{(1-x)^2}{x}(\mu+\mu_1)S^* + \beta\frac{S^*H^*}{N}(2-x-\frac{1}{x}) + \hat{f}(S,H,A,T,R)\\ \implies \dot{V} &= U + \hat{f}(S,H,A,T,R)\end{aligned} \tag{4.21}$$

Now, applying the property that the Algebraic mean is always greater and equal to the Geometric mean (A.M. $\geq$ G.M.), we have $2-x-\frac{1}{x} \leq 0$, implies $U \leq 0$. Now following the approach defined in [11, 23, 24], $\hat{f}(S,H,A,T,R)$ is non–positive for all $S,H,A,T,R \geq 0$. Hence, we found that $\dot{V} \leq 0$, and $\dot{V} = 0$, whenever $x = 1(S = S^*), H = H^*, A = A^*, T = T^*, R = R^*$. Thus, the EE point $\{E^*\}$ is the only singleton for which $\dot{V} = 0$. Applying the La Salle invariance principle, it can be verified that $\{E^*\}$ is globally asymptotically stable whenever $R_0 > 1$. □

5 Sensitivity Analysis

Sensitivity analysis of the model allows us to identify the behavior of a system variable relative to the most influential parameters. Following [19], the normalized forward sensitivity index of a variable that depends differentially on a parameter h is defined as $\gamma_h^{R_0} = \frac{h}{R_0} \times \frac{\partial R_0}{\partial h}$. Taking the parameter values from Table 2, the sensitivity indices of some important parameters are listed in Table 1, and portrayed in the Figure 2. It was detected that N is the least sensitive parameter, whereas β and λ_1 are equally the most sensitive parameters.

$$\begin{aligned}\gamma_{a_1}^{R_0} &= -\frac{a_1(\mu+d)(a_2+b_2+\mu+d)}{[(a_1+\mu+\alpha)\{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2\} - b_1\{\alpha a_2 + a_1(a_2+\mu+d)\}]},\\ \gamma_{\alpha}^{R_0} &= -\frac{\alpha(\mu+d)(a_2+b_1+b_2+\mu+d)}{[(a_1+\mu+\alpha)\{(b_1+\mu+d)(a_2+\mu+d)+(\mu+d)b_2\} - b_1\{\alpha a_2 + a_1(a_2+\mu+d)\}]},\\ \gamma_{\mu_1}^{R_0} &= -\frac{\mu_1}{(\mu+\mu_1)}\end{aligned} \tag{5.1}$$

Here, it was observed that β and λ_1 have the same sensitivity indices with a positive sign, which means 10% increment (or decrement) in β and λ_1 makes 10% increment (or decrement) in R_0. The sensitivity index of N is a negative sign, which implies 10% expansion (decrement) in N results in 10% decrement (or expansion) in R_0. Similarly, a 10% decrease (expansion) in α produces 2.8903% expansion (decrement) in R_0.

6 Change in Equilibrium Curve through One-parameter Bifurcation

From the sensitivity analysis of the model, the parameters β, λ_1 and a_1, and are identified as the three most sensitive parameters (see Table 1). For these parameters, the qualitative behavior for the range of parameters is investigated through one-parameter bifurcation diagrams in Figures 3, 4 and 5. The variations in the equilibrium curve for the range of parameters $a_1 \in [0, 1]$, $\beta \in [0, 5]$, and $\lambda_1 \in [0, 3.5]$ are clearly depicted in those Figures. The sharp decline in HIV-infected and AIDS-infected populations is evident with respect to parameter $a_1 \in [0, 1]$ whereas a sharp increase is evident with respect to parameter $\lambda_1 \in [0, 3.5]$. Consequently, the recovered populations increase with respect to parameters $a_1 \in [0, 1]$ but decreases with parameter $\beta \in [0, 5]$. All compartment populations H, A, T, and R increase with parameter $\lambda_1 \in [0, 3.5]$ as it is associated with the growth of the S compartment. The deviation in variables for a range of parameters is clearly depicted in Figures 3, 4 and 5.

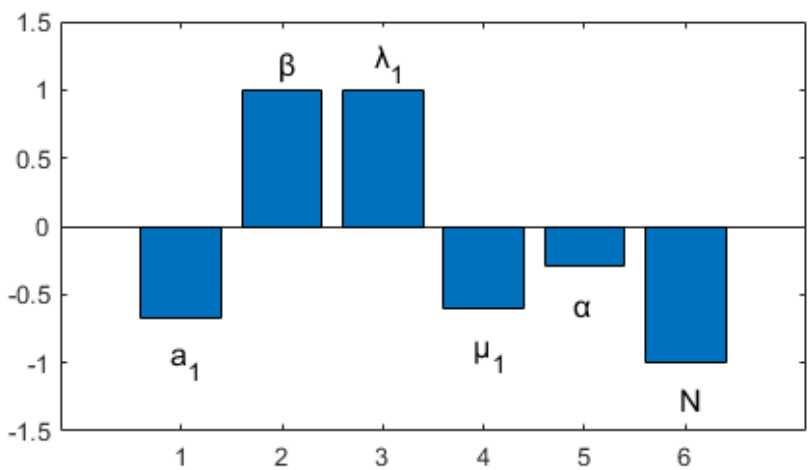


Figure 2: Diagram showing sensitivity of R_0.

7 Optimal Control Model

When the disease becomes out of control, we need to control the spread of the disease, then optimal control theory produces an effective way to procure the optimum strategy. It helps to identify the best intervention strategy to eradicate the disease in the specified time. Therefore,

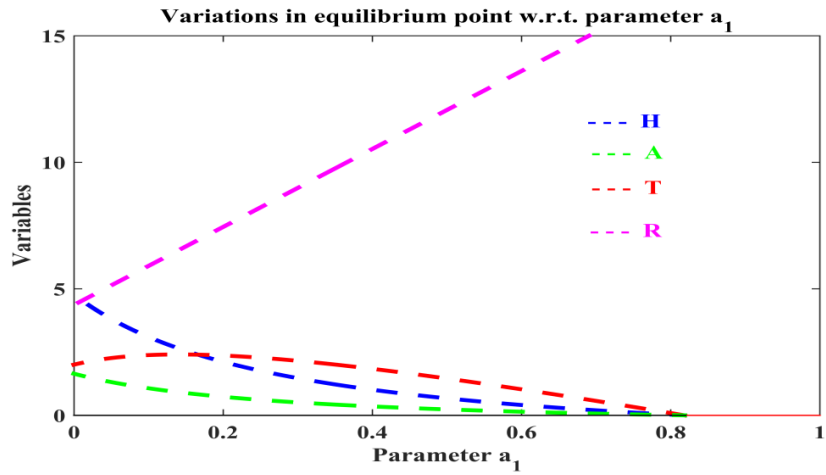


Figure 3: One-parameter bifurcation diagram with respect to parameter for the range $(0, 1)$.

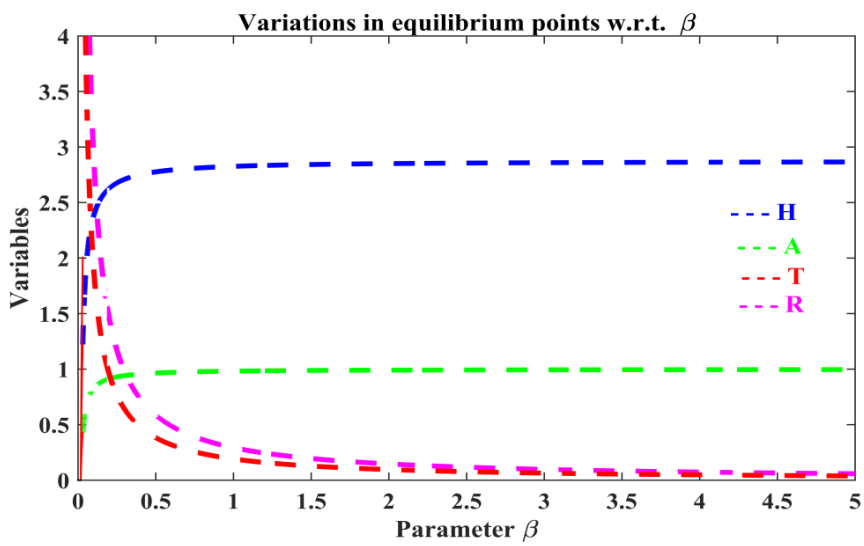


Figure 4: One-parameter bifurcation diagram with respect to parameter for the range $(0, 5)$.

Serial No	Parameter	Sensitivity Index
1	a_1	-0.67286
2	β	1
3	$\lambda 1$	1
4	μ_1	-0.60484
5	α	-0.28903
6	N	-1

Table 1: Sensitivity Indices of Parameters

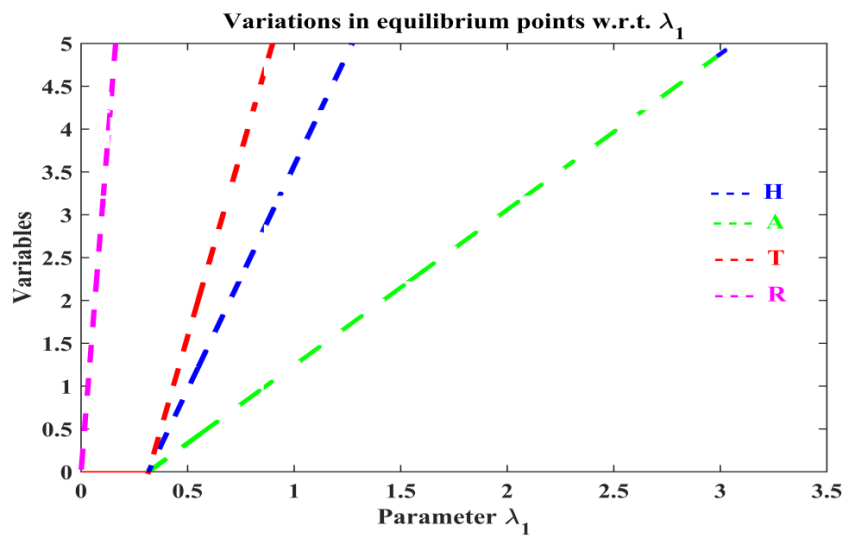


Figure 5: One-parameter bifurcation diagram with respect to parameter for the range $(0, 3.5)$.

we formulated a control problem and solved it to obtain the optimum strategy that reduces the number of infected individuals with the minimum cost.

7.1 Formulation of Optimum Control Problem:

Now, to find the optimum strategy, we incorporate two control parameters; treatment control and sexual habit awareness control. Following [20], we look forward to minimizing the following constructed objective function;

$$J(\mu_1, a_1, a_2) = \int_0^{t_1} (BH + \frac{1}{2}(B_1\mu_1^2 + B_2a_1^2 + B_3a_2^2)\, dt. \tag{7.1}$$

Where, B is the constant associated with HIV infection defined as per capita loss due to the presence of HIV-infected individuals while B_1, B_2 and B_3 are the weights for the control efforts

of μ_1, a_1 and a_2 respectively. The cost of giving awareness about safe sexual intercourse to susceptible is given by $\frac{1}{2}(B_1\mu_1^2)$. On the other hand, $\frac{1}{2}(B_2a_1^2)$ and $\frac{1}{2}(B_3a_2^2)$ are presented as the costs for the treatment of HIV-infected and AIDS-infected individuals respectively. All the controls are defined in the finite time horizon $[0, t_1]$. We aim to find an optimum control (μ_1^*, a_1^*, a_2^*) such that the total loss due to the occurrence of HIV infection and the total cost of the treatment and awareness of safe intercourse can be minimized.

$$J(\mu_1^*, a_1^*, a_2^*) = min_{(\mu_1,a_1,a_2)\in\theta} J(\mu_1, a_1, a_2), \tag{7.2}$$

where, $\theta = \{(\mu_1, a_1, a_2) : 0 \leq \mu_1(t), a_1(t), a_2(t) \leq 1, \text{ for } t \in [0, 1]\}$ is the control set for the problem. Here, the control parameters can attempt the highest value 1, when everyone getting treatment and awareness of safe sexual control while assuming the value 0 when no one is getting treatment and none are aware of sexual control too. Otherwise, we can take a value between 0 and 1.

Now, to solve the objective functional the Lagrangian can be given as

$$L(H, \mu_1, a_1, a_2) = BH + \frac{1}{2}(B_1\mu_1^2 + B_2a_1^2 + B_3a_2^2). \tag{7.3}$$

By using Pontryagin's maximum principle [21], The Hamiltonian H_1 for the problem is

$$\begin{aligned} H_1 &= BH + \frac{1}{2}(B_1\mu_1^2 + B_2a_1^2 + B_3a_2^2) + \lambda_1\frac{dS}{dt} + \lambda_2\frac{dH}{dt} + \lambda_3\frac{dT}{dt} + \lambda_4\frac{dA}{dt} + \lambda_5\frac{dR}{dt} \\ H_1 &= BH + \frac{1}{2}(B_1\mu_1^2 + B_2a_1^2 + B_3a_2^2) + \lambda_1\{\lambda - \beta\frac{SH}{N} - (\mu + \mu_1)S\} + \lambda_2\{\beta\frac{SH}{N} - (a_1 + \mu + \alpha)H \\ &+ b_1T\} + \lambda_3\{a_1H - (b_1 + b_2 + \mu + d)T + a_2A\} + \lambda_4\{\alpha H - (a_2 + \mu + d)A + b_2T\} + \lambda_5\{\mu_1S - \mu R\}. \end{aligned} \tag{7.4}$$

Where $\lambda_i^{'}s$ are the costate variables or adjoint variables corresponding to S, H, T, A, R determined by solving the following differential equations.

$$\begin{aligned} \dot{\lambda}_1(t) &= -\frac{\partial H_1}{\partial S} = \lambda_1\{\beta\frac{H}{N} + (\mu + \mu_1)\} - \lambda_2(\beta\frac{H}{N}) - \lambda_5(\mu_1) \\ \dot{\lambda}_2(t) &= -\frac{\partial H_1}{\partial H} = -B + \lambda_1\beta\frac{S}{N} - \lambda_2\{\beta\frac{S}{N} - (a_1 + \mu + \alpha)\} - \lambda_3a_1 - \lambda_4\alpha \\ \dot{\lambda}_3(t) &= -\frac{\partial H_1}{\partial T} = -\lambda_2b_1 + \lambda_3(b_1 + b_2 + \mu + d) - \lambda_4b_2 \\ \dot{\lambda}_4(t) &= -\frac{\partial H_1}{\partial A} = -\lambda_3a_2 + \lambda_4(a_2 + \mu + d) \\ \dot{\lambda}_5(t) &= -\frac{\partial H_1}{\partial R} = \lambda_5\mu \end{aligned} \tag{7.5}$$

Where the costate variables satisfy the transversality conditions at t_1 i.e. $\lambda_i(t_1) = 0$ for all $i = 1, 2, 3, 4, 5$.

Next, we will show the existence of optimum control. For which we used the following theorem that analyzes the sufficient condition for the existence of optimality.

Theorem 7.1. *There exists an optimum control (μ_1^*, a_1^*, a_2^*) that minimizes our objective functional $J(\mu_1, a_1, a_2)$ over control set θ.*

Proof. Proof of this theorem is based on conditions listed below given by Fleming and Rischel [22].
(1). The set of all solutions of system Eq. (2.1) with associated control functions in θ is non-empty.
(2). The right-hand side of system Eq. (2.1) is bounded by linear function in state and control.
(3). L is convex in and closed in θ , with respect to control $J(\mu_1, a_1, a_2)$, further there exist $L \geq C_1|(\mu_1, a_1, a_2)|^k - C_2$ such that $C_1, C_2 > 0$ and $k > 1$.
Using similar arguments as Ishaku et al. (2020) conditions (1) and (2) hold. Also, L is convex on θ, and $L \geq C_1\Big((|\mu_1|^2 + |a_1|^2 + |a_2|^2)^{k/2}\Big) - C_2$ means L is bounded below. Now using the Pontryagin's maximum principle we stated the following theorem. □

Theorem 7.2. *The optimum control (μ_1^*, a_1^*, a_2^*) that minimizes our objective functional J over θ is given by $\mu_1^* = max\{0, min(\overline{\mu}_1, 1)\}, a_1^* = max\ 0, min(\overline{a}_1, 1)\}$ and $a_2^* = max\{0, min(\overline{a}_2, 1)\}$ where $(\overline{\mu}_1)$ can be obtained by $\frac{\partial H_1}{\partial \mu_1} = 0$ and a_1, a_2 by $\frac{\partial H_1}{\partial a_1} = 0$ and $\frac{\partial H_1}{\partial a_2} = 0$ respectively.*

Proof. Now applying the optimality conditions, we have

$$\frac{\partial H_1}{\partial \mu_1} = B_1\overline{\mu}_1 - \lambda_1\overline{S} + \lambda_5\overline{S} = 0, \implies \overline{\mu}_1 = \frac{(\lambda_1 - \lambda_5)\overline{S}}{B_1}$$

$$Similarly \ \ \frac{\partial H_1}{\partial a_1} = B_2\overline{a}_1 - \lambda_2\overline{H} + \lambda_3\overline{H} = 0, \implies \overline{a}_1 = \frac{(\lambda_2 - \lambda_3)\overline{H}}{B_2} \text{ and}$$

$$\frac{\partial H_1}{\partial a_2} = B_3\overline{a}_2 - \lambda_4\overline{A} + \lambda_3\overline{A} = 0, \implies \overline{a}_2 = \frac{(\lambda_4 - \lambda_3)\overline{A}}{B_3}.$$

All these controls are bounded below by 0 and bounded above by 1. Hence, we get the optimum control as,

$$\mu_1^* = max\Big\{0, min\Big(\frac{(\lambda_1 - \lambda_5)\overline{S}}{B_1}, 1\Big)\Big\}$$

$$a_1^* = max\Big\{0, min\Big(\frac{(\lambda_2 - \lambda_3)\overline{H}}{B_2}, 1\Big)\Big\}$$

$$\mathrm{a}_2^* = max\Big\{0, min\Big(\frac{(\lambda_4 - \lambda_3)\overline{A}}{B_3}, 1\Big)\Big\}$$

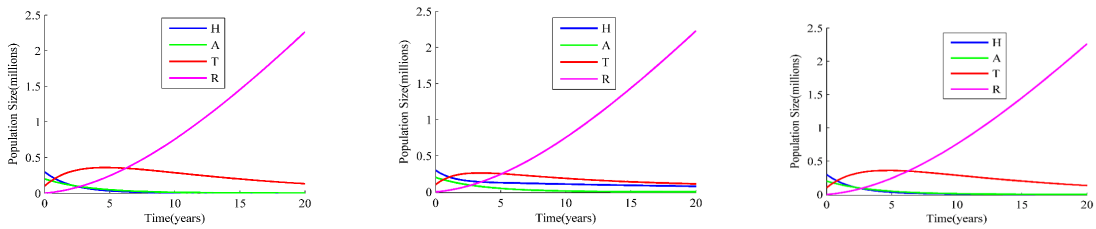
□

8 Numerical Illustrations for Stability

This section includes the validation of obtained analytical findings on the stability of equilibrium points through numerical simulation. Initial population strength in million has been taken as $S(0) = 0.5, H(0) = 0.3, A(0) = 0.2, T(0) = 0.1, R(0) = 0$. Now, choosing $b_1 = b_2 = 0.001$ and $N = 0.7$ then substituting all the values in the expression of R_0 , we obtained $R_0 = 0.9243 < 1$. Hence, the existence of disease-free equilibrium E^0 is confirmed. Now, in terms of stability, Figure 6(a) clearly shows that individuals suffering from only HIV and only AIDS will eventually decrease to zero. Hence, the disease-free equilibrium point is globally asymptotic stable for a given set of parameter values.

Parameter	Explanation	Estimated Value	Source
$\lambda 1$	Recruitment rate	0.55 pop/year	[9]
β	Transmission Coefficient	0.03/year	[3]
μ	Natural death rate	0.0196/year	[9]
μ_1	rate of Susceptible individual	0.03/year	[3]
α	Progression rate from H to A class	0.15/year	Estimated
d	AIDS-induced death rate	0.0667/year	[9]
a_1	Progression rate to T from H	0.35/year	Estimated
b_1	Proportion of Successful treatment	0.001/0.2	Assumed
a_2	Progression rate to T from A	0.35/year	Estimated
b_2	Proportion of treatment failure	0.001	Assumed
N	Population size	0.7/1	Assumed

Table 2: Description and data sources for the estimation of parameter values



(a) $R_0 < 1$ (b) $R_0 > 1$ (c) $R_0 = 1$

Figure 6: Showing the stability of equilibrium points

Now, choose $b_1 = 0.2$ and $b_2 = 0.001$ and $N = 1$, gives $R_0 = 1.746 > 1$. As a result, Figure 6(b) clearly shows that HIV and AIDS individuals initially decrease due to treatment therapy, but after a period of time, both remain constant, implying that the disease will persist in the population indefinitely. Therefore, we concluded that the endemic point is globally asymptotically stable in the population. Similarly, it can be seen from Figure 6c that the disease could be eradicated from the population in the near future.

9 Numerical illustrations for Optimal Control

We have discussed analytically, the optimal control to minimize the total cost. Here, we simulated the optimality system using MATLAB software by choosing the same parameter values from Table 2, and the Runge- Kutta fourth-order method to obtain the optimal control and treatment strategies. The initial population size in millions was taken as $S(0) = 0.5, H(0) = 0.3, A(0) = 0.2, T(0) = 0.1, R(0) = 0$. For this purpose, the treatment control and awareness of sexual habits are taken as control parameters and considered four different control strategies; (i) When both control strategies are active (a_1, a_2, and μ_1 are all non-zero), (ii) When neither control strategy is active (all a_1, a_2, and μ_1 are zero), (iii) When only the treatment control is used (a_1, a_2 are non zero whereas μ_1 is zero) (iv) When only safety control is used (a_1, a_2 are zero while μ_1 is

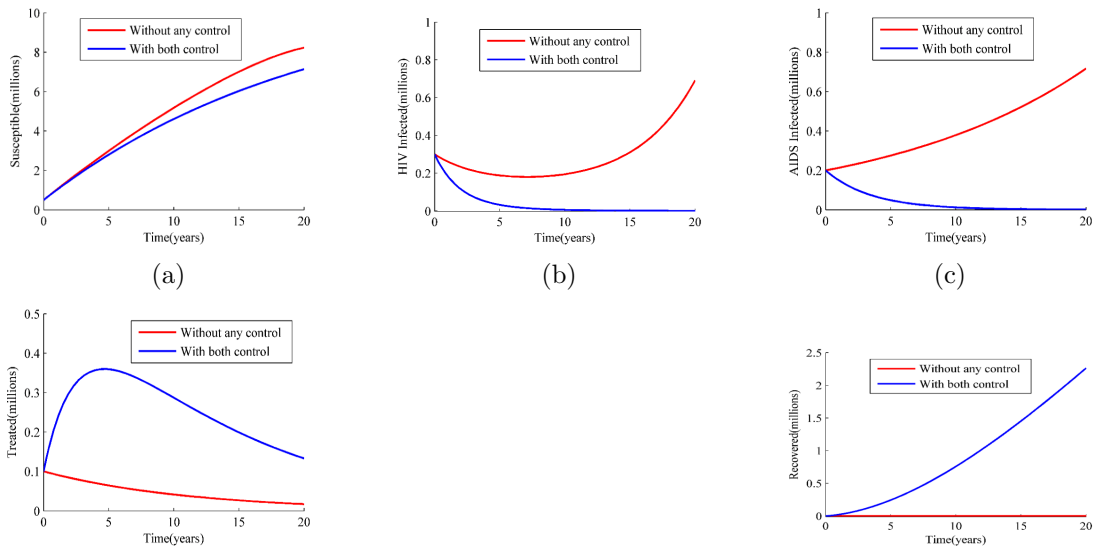


Figure 7: Simulations of optimal control with strategy (i) and strategy (ii) .

non zero). Figure 7a -7e depicts various class solutions using strategies (i) and (ii). Figure 7a depicts the behavior of susceptible in the presence of both controls and in the absence of control strategies. Similarly, Figure 7b and 7c show that when both control strategies are used optimally, the number of people infected with HIV and AIDS are significantly reduced. From, Figure 7d, we can see that the treated population is increasing when both the control strategies have been implemented. Furthermore, Figure 7e shows that the number of recovered individuals increases when both control strategies are implemented, whereas the number of recovered individuals is negligible when neither control strategy is implemented.

Similarly, Figures 8a - 8e show the same behavior of the compartments when at least one strategy is employed (either treatment or awareness of sexual control). Figure 8a clarifies that treatment control has more impact on susceptible individuals. Likewise, Figures 8b and 8c show that HIV and AIDS infections are increasing in the absence of treatment control. Furthermore, as shown in Figure 8d, when treatment control is used, the treated population grows. Figure 8e depicts that by taking awareness of sexual safety precautions more people can recover from HIV/AIDS.

10 Conclusion

In the present work, we developed an HIV/AIDS compartment model that includes important compartments such as HIV, AIDS, and Treatment. The analysis and complex behavior of the presented model have been studied and some suitable strategies for controlling HIV/AIDS are enumerated. The important properties of dynamical systems like positivity and boundedness of solution are henceforth substantiated. The threshold parameter (R_0) basic reproduction number for the model is derived using the next-generation matrix approach and it is evidenced that if $R_0 \leq 1$ then HIV disease can be abolished from the population, although for $R_0 > 1$ infection

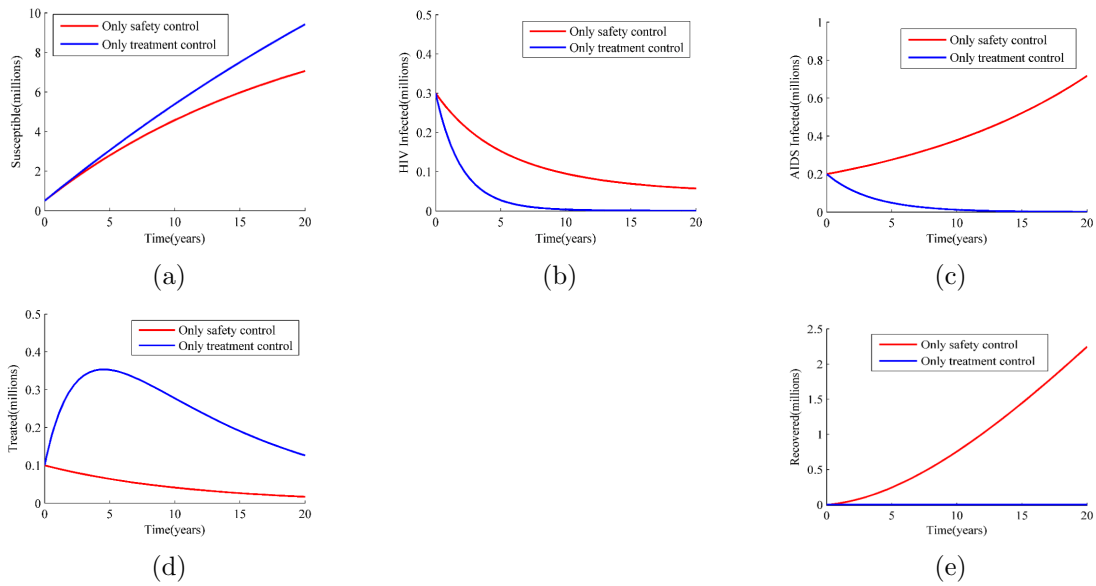


Figure 8: Simulations of optimal control with strategy (iii) and strategy (iv)

remains persistently in the population under certain conditions. Further, the normalized forward sensitivity index of the basic reproduction number (R_0) with respect to some important model parameters has been evaluated and concluded that N is the least sensitive parameter while β and λ_1 are equally the most sensitive parameters of the model. In addition to the above, an optimal control technique has been applied and the optimum objective function has been derived to minimize the HIV-infected individuals as well as the total cost associated with treatment and awareness of sexual activity. The simulation results support and enhance our analytical results for stability and optimal control. Moreover, our results specify that a combination of optimal control strategies helps to reduce the number of HIV and AIDS-infected individuals significantly. It is observed that a combination of treatment control and awareness of safe intercourse control can reduce the number of HIV/AIDS-infected patients more quickly. In fact, if an emergency occurs, then the government should majorly focus on making aware of people about safe sexual intercourse, rather than ART treatment.

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