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Analyzing Stability and Bifurcation in an HIV Model with Treatment Interventions

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Abstract

This study presents a comprehensive mathematical model for HIV infection dynamics in the presence of treatment, focusing on stability analyses. The model incorporates treatment interventions and

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explores their impact on disease progression, viral load dynamics, and population-level outcomes. A stability analysis was conducted to investigate the existence and properties of equilibrium points, including disease-free and endemic equilibria. Analysis shows that there is existence of disease-free whenever the threshold quantity R_0 *is less than unity i.e.* $R_0 < 1$*, and otherwise epidemic when* $R_0 > 1$*. Utilizing mathematical techniques and computational simulations, we explore the stability of these equilibrium points under varying conditions and treatment scenarios. Our findings elucidate the critical role of treatment in mitigating HIV transmission, reducing viral replication, and preserving immune function. This research contributes valuable insights into the dynamics of HIV infection and the efficacy of treatment interventions in controlling the spread of the virus.*

Keywords: Diphtheria, Disease-Free, Reproduction number, Sensitivity, Simulation

INTRODUCTION

The Human Immunodeficiency Virus (HIV) is not merely a medical condition but a multifaceted challenge that impacts both individuals and societies on various levels. Its pervasive effects extend beyond the realm of healthcare, often resulting in profound economic and social consequences if not effectively managed (Adewale *et al.,* 2016a; Lu *et al.,* 2018; Akudibillah *et al.,* 2019; Saldaña *et al.,* 2019; Widyaningsih *et al.,* 2019; Ayele *et al.,* 2021; Omame *et al.,* 2021; Akinwumi *et al.,* 2021; Marsudi *et al.,* 2021; Ajao *et al.,* 2023). This virus, which causes HIV infection, not only threatens individual health but also poses significant challenges to public health systems worldwide (Grigorieva *et al.,* 2020; Cheneke *et al.,* 2021a). Developing a definitive cure for HIV has proven to be a significant challenge despite extensive research efforts. However, advancements in medical science have led to the development of Antiretroviral Therapy (ART) and combination therapies, which have revolutionized the management of HIV infection (Ilahi and Nurhalimah, 2019; Mayanja *et al.,* 2020; Cheneke *et al.,* 2021a; Seidu *et al.,* 2021). These treatments function by inhibiting the replication of the virus in the bloodstream, thereby preventing its progression to the more severe stage known as Acquired Immunodeficiency Syndrome (AIDS). By effectively controlling viral load and bolstering the immune system, ART has transformed HIV from a once-debilitating disease to a chronic yet manageable condition (Nkamba *et al.,* 2019; Rana & Sharma, 2020).

Understanding the progression of HIV infection is crucial for effective intervention and treatment. The disease unfolds in distinct stages, each characterized by specific clinical manifestations and implications for patient management (Saha *et al.,* 2019; Saha & Samanta, 2019). The primary stage, often asymptomatic, marks the initial presence of the virus in the bloodstream, posing challenges for early detection. As the infection progresses, individuals may enter the asymptomatic stage, where the virus remains dormant but detectable through medical testing. Subsequently, symptoms may manifest in the symptomatic stage, ranging from fatigue and weight loss to more severe complications. Without timely intervention, HIV can advance to the AIDS stage, where immune function is severely compromised, and susceptibility to opportunistic infections increases exponentially.

HIV transmission occurs through various routes, including unsafe sexual practices, exposure to infected blood, vertical transmission from mother to child during childbirth or breastfeeding, and contact with bodily fluids containing the virus. Addressing these modes of transmission requires comprehensive prevention strategies tailored to the needs of diverse populations and settings. By implementing evidence-based interventions and promoting safer behaviors, towards reducing the burden of HIV/AIDS and achieving epidemic control (Olopade *et al.,* 2016; Marsudi *et al.,* 2021). In contrast, adherence to safe

practices, such as the ABC principle (Abstinence, Be faithful, Use Condoms), serves as a cornerstone for preventing new infections and reducing transmission rates.

Effective control of the HIV epidemic requires a comprehensive approach that integrates medical, social, and behavioral interventions. Public health education, promotion of condom use, and access to timely treatment are critical components of this strategy (Widyaningsih *et al.,* 2019; Omame *et al.,* 2021; Marsudi *et al.,* 2021). By raising awareness, reducing stigma, and providing essential services, communities possess the capacity to empower individuals, enabling them to make informed decisions concerning their health and overall well-being.
A mathematical model is essential for representing biological and physical phenomena through equations, aiding HIV/AIDS policymakers. It helps compare interventions, generalize trial results, identify challenges, monitor program impact, and assess treatment strategies. These models bridge theory and practice, providing insights crucial for evidence-based decision-making in combating the epidemic. (Adewale *et al.,* 2015a, 2015b; Adesanya *et al.,* 2016a, 2016b; Cheneke *et al.,* 2021b, 2022c; Olopade *et al.,* 2024a, 2024b, 2024c). In the context of HIV, various mathematical models have been devised to elucidate the intricate dynamics of the virus. These models encompass a range of complexities and factors, aiming to capture the nuances of HIV transmission, progression, and intervention strategies.

Li & Xiao (2018) studied the immune response to HIV, focusing on viral load and treatment strategies. They analyzed the model's dynamics, influenced by HIV disposal and infected cell growth rates. Their research provides insights into HIV infection mechanisms and optimizing treatment regimens. Maimuna & Aldila (2018) studied the impact of ART on HIV spread using a mathematical model. They found that increasing the number of infected individuals in ART programs significantly reduced the basic reproductive number of HIV. This highlights that expanding ART treatment is crucial in curbing HIV transmission, underscoring the importance of proactive strategies in managing infectious diseases.

Naik *et al.,* (2020) introduced a nonlinear fractional order model to study HIV transmission and optimize control strategies. Their findings advocate for a dual approach to reduce HIV spread: promoting individual preventive measures like safe sex and barrier methods, and ensuring continuous monitoring and intervention by healthcare professionals to manage and contain the virus effectively. Tigabu *et al.,* (2021) conducted an HIV/AIDS model addressing undiagnosed infections, analyzing its equilibrium and stability with an emphasis on the reproductive number (Ro). They introduced an optimal control problem using prevention and screening. Their numerical results indicated that combining these strategies effectively lowered HIV/AIDS prevalence and costs.

This study delves into the intricate dynamics of an HIV model, exploring the intricate relationship between bifurcations and stability, particularly in the context of early treatment interventions for infected individuals and the parameters that fuel the rapid progression of HIV. HIV, a virus notorious for its ability to rapidly mutate and evade the immune system, presents a formidable challenge to public health efforts worldwide. By integrating the early treatment paradigm into the model framework, this research seeks to deepen our understanding of how timely interventions can influence the trajectory of the epidemic.

MATERIAL AND METHODS

Formulation of the Model

At a given time t, the total sexually active population can be represented by a subdivision into five mutually exclusive compartments: the susceptible class $S(t)$, latently infected individuals L_H, infected undetected individuals H_U, infected detected individuals H_D, and treated individuals H_T. Hence, the total population is $S(t)+L_H(t)+H_U(t)+H_D(t)+H_T(t)$. Individuals are presumed to enter the susceptible class at a consistent rate π. Susceptible individuals have the potential to become infected with HIV upon contact with infected individuals at a rate λ, where $\lambda=(L_H+\eta_U H_U+\eta_{dH}H_U+\eta_W H_T)$ and β_H is the transmission rates for HIV. The individuals in class H_D exhibit a higher level of infectiousness compared to those in class H_U. Therefore we have slow progressor ε_1 that moves from latently infected individuals to infected undetected class. Further information regarding additional parameters can be found in Table 1. The dynamics of the variables are described by

$$\left.\begin{aligned}
\frac{dS}{dt}&=\pi-\beta_H(L_H+\eta_U H_U+\eta_{dH}H_D+\eta_W H_T)S-\mu S\\
\frac{dL_H}{dt}&=(1-\varepsilon_1)\beta_H(L_H+\eta_U H_U+\eta_{dH}H_D+\eta_W H_T)S-(\kappa_H+\mu)L_H\\
\frac{dH_U}{dt}&=\varepsilon_1\beta_H(L_H+\eta_U H_U+\eta_{dH}H_D+\eta_W H_T)S+(1-\omega_1)\kappa_H L_H-(\gamma_{UH}+\mu+\delta_{UH})H_U\\
\frac{dH_D}{dt}&=\omega_1\kappa_H L_H+\gamma_{UH}H_U-(\tau_1+\mu+\delta_{dH})H_D\\
\frac{dH_T}{dt}&=\tau_1 H_D-\mu H_T
\end{aligned}\right\} \quad (1)$$

For better analysis, we have the below model;

$$\left.\begin{aligned}
\frac{dS}{dt}&=\pi-\beta_H\lambda S-\mu S\\
\frac{dL_H}{dt}&=(1-\varepsilon_1)\beta_H\lambda S-K_1L_H\\
\frac{dH_U}{dt}&=\varepsilon_1\beta_H\lambda S+(1-\omega_1)\kappa_H L_H-K_2H_U\\
\frac{dH_D}{dt}&=\omega_1\kappa_H L_H+\gamma_{UH}H_U-K_3H_D\\
\frac{dH_T}{dt}&=\tau_1 H_D-\mu H_T
\end{aligned}\right\} \quad (2)$$

Where

$$K_1=(\kappa_H+\mu),\ K_2=(\gamma_{UH}+\mu+\delta_{UH}),\ K_3=(\tau_1+\mu+\delta_{dH}),\ \lambda=(L_H+\eta_U H_U+\eta_{dH}H_D+\eta_W H_T)$$

Table 1. Description of Variables

Variables	Description
S	Susceptible
L_H	Latent HIV
H_D	Detected HIV
H_U	Undetected HIV
H_T	Treated HIV

Table 2. Description of Parameters

Parameters	Description			
π	Recruitment rate	2000	Assumed	
μ	Natural death rate		0.019	Ibrahim *et al.*, (2021)
τ_1	Treatment rate		0.1	Ibrahim *et al.*, (2021)
ε_1	Slow progressor	0.125	Assumed	
κ_H	Progression rate	0.068	Assumed	
ω_1	Progression rate	0.054	Assumed	
γ_{UH}	Detection rate		0.7	Assumed
β_H	Contact rate		0.2	Akinwumi *et al.*, (2021)
δ_{UH}, δ_{dH}	HIV-induced mortality rate		0.01	Akinwumi et al., (2021)
$\eta_U, \eta_{dH}, \eta_W$	HIV Modification parameters		0.001	Assumed

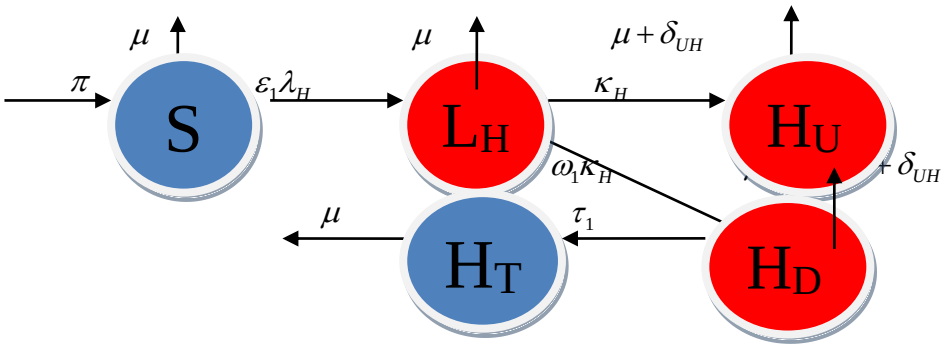

Figure 1. Diagram illustrating the HIV model.

Positivity of Solutions

To establish the epidemiological and mathematical validity of the Human Immunodeficiency Virus model, it is imperative to demonstrate that all state variables remain non-negative throughout time $(t > 0)$.

Theorem 1.

Let:

$$\{S(0) \geq 0,\ L_H(0) \geq 0,\ H_U(0) \geq 0,\ H_D(0) \geq 0,\ H_T(0) \geq 0\} \in \Gamma$$

Then, the solution $\{S(t), L_H(t), H_U(t), H_D(t), H_T(t)\}$ of the model system equation (1) are positive $\forall t \geq 0$.

Proof:

To establish theorem (1), we utilized the equations from system (1). Considering the first equation of the model (1):

$$\frac{dS}{dt} = \pi - \beta_H (L_H + \eta_U H_U + \eta_{dH} H_D + \eta_W H_T) S - \mu S$$

From which it follows that:

$$\frac{dS}{dt} =\geq -\mu S \tag{3}$$

Consequently:

$\frac{dS}{dt} + \mu S \geq 0$ is the first order homogeneous differential equation.

$$\text{I.F.} = \quad \ell^{\int \mu dt} = \ell^{\mu t} \tag{4}$$

Multiplying both sides by the integrating factor yields:

$$\ell^{\mu t} \frac{dS}{dt} + \mu S \ell^{\mu t} \geq 0 \tag{5}$$

It then follows that, $d(S\ell^{\mu t}) \geq 0 dt$

Integrating on both sides gives:

$S\ell^{\mu t} \geq C$,

$S(t) \geq C\ell^{-\mu t}$

Utilizing the initial condition that, when $t = 0$, $S(t) = S(0)$, we have:

$$S(0) \geq C \tag{6}$$

$$\text{Hence } S(t) \geq S(0)\ell^{-\mu t} \tag{7}$$

Since $\mu > 0 \, and \, S(0) \geq 0$, then:

$S(t) \geq 0$, if $t = 0 \, and \, t \to \infty$

Therefore: $S(t) \geq 0 \;\; \forall t \geq 0.$

Following the same procedure for the remaining variables L_H, H_U, H_D, H_T, therefore, The HIV model formulated is well posed both mathematically and epidemiologically.

Existence of Disease- free and Endemic Equilibrium

To determine critical points, we set:

$$\frac{dS}{dt} = \frac{dL_H}{dt} = \frac{dH_U}{dt} = \frac{dH_D}{dt} = \frac{dH_T}{dt} = 0 \tag{8}$$

At this free equilibrium, it is assumed that there is no infection, then $L_H = H_U = H_D = H_T = 0$

The disease-free equilibrium is:

$$\varepsilon_0 = \left\{ \frac{\pi}{\mu}, 0, 0, 0, 0 \right\} \tag{9}$$

Existence of Endemic Equilibrium (EE)

The endemic equilibrium points are $\varepsilon_0^* = (S^*, L_H^*, H_U^*, H_D^*, H_T^*)$

$$S^* = \frac{\pi}{\lambda\beta + \mu},$$

$$L_H^* = -\frac{\pi\lambda\beta(\varepsilon_1 - 1)}{K_1(\lambda\beta + \mu)},$$

$$H_U^* = \frac{\pi\lambda\beta(\kappa_H\varepsilon_1\omega_1 - \kappa_H\varepsilon_1 - \kappa_H\omega_1 + \varepsilon_1K_1 + \kappa_H)}{K_2K_1(\lambda\beta + \mu)}$$

$$H_D^* = \frac{\pi\lambda\beta(\gamma_{UH}\kappa_H\varepsilon_1\omega_1 - \kappa_H\varepsilon_1K_2\omega_1 - \gamma_{UH}\kappa_H\varepsilon_1 - \gamma_{UH}\kappa_H\omega_1 + \gamma_{UH}\varepsilon_1\omega_1K_1 + \kappa_HK_2\omega_1 + \gamma_{UH}\kappa_H)}{K_3K_2K_1(\lambda\beta + \mu)}$$

$$H_T^* = \frac{\pi\lambda\beta\tau_1(\gamma_{UH}\kappa_H\varepsilon_1\omega_1 - \kappa_H\varepsilon_1K_2\omega_1 - \gamma_{UH}\kappa_H\varepsilon_1 - \gamma_{UH}\kappa_H\omega_1 + \gamma_{UH}\varepsilon_1\omega_1K_1 + \kappa_HK_2\omega_1 + \gamma_{UH}\kappa_H)}{\mu K_3K_2K_1(\lambda\beta + \mu)}$$

$$\lambda = (L_H + \eta_U H_U + \eta_{dH} H_D + \eta_W H_T)$$

Stability of the HIV model

The basic reproduction number of the model (2) is determined through the utilization of the next generation matrix. (Akinola *et al.,* 2021; Olopade *et al.,* 2021a, 2021b). Using this approach, we have:

$$F = \begin{pmatrix} (1-\varepsilon_1)\beta_H & (1-\varepsilon_1)\beta_H\eta_U & (1-\varepsilon_1)\beta_H\eta_{dH} & (1-\varepsilon_1)\beta_H\eta_W \\ \varepsilon_1\beta_H & \varepsilon_1\beta_H\eta_U & \varepsilon_1\beta_H\eta_{dH} & \varepsilon_1\beta_H\eta_W \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{10}$$

$$V = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ -(1-\omega_1)\kappa_H & K_2 & 0 & 0 \\ -\omega_1K_H & -\gamma_{UH} & K_3 & 0 \\ 0 & 0 & -\tau_1 & \mu \end{pmatrix} \tag{11}$$

The reproduction number is the principal eigenvalue of the matrix $F \times V^{-1}$. Thus,

$$R_H = \frac{\left(\beta_H\left(\begin{pmatrix}((\eta_{dH}(\omega_1-1)\gamma_{UH} + (\eta_UK_3 - K_2\eta_{dH})\omega_1 - \eta_UK_3)\mu + \eta_T((\omega_1-1)\gamma_{UH} - \omega_1K_2)\tau_1) \\ (\varepsilon_1-1)\kappa_H + ((\eta_{dH}\gamma_{UH}K_1 + K_3(\eta_UK_1 - K_2))\varepsilon_1 + K_2K_3)\mu + \varepsilon_1\eta_T\gamma_{UH}K_1\tau_1\end{pmatrix}\right)\right)}{\mu K_1K_2K_3} \tag{12}$$

The threshold quantity R_H is the basic reproduction number of the normalized model system (2) for HIV infection in a population. It measures the average number of new secondary infections generated by a single infected individual in his or her infectious period in a susceptible population (Adewale *et al.,* 2015c, 2016b; Olopade *et al.,* 2017, 2022).

Local Stability of the Disease-Free Equilibrium

Theorem 2: The disease-free equilibrium of the system (2) demonstrates local asymptotic stability (LAS) if $R_H < 1$, and instability if $R_H > 1$.

Proof: To ascertain the local stability of the equilibrium point E_0, we compute the Jacobian matrix corresponding to it. Examining the stability of the disease-free equilibrium at the critical point ($\frac{\pi}{\mu}$, 0, 0, 0, 0), based on equation (2), yields:

$$J_H = \begin{pmatrix} -\mu & 0 & 0 & 0 & 0 \\ 0 & -K_1 & 0 & 0 & 0 \\ 0 & (1-\omega_1)\kappa_H & -K_2 & 0 & 0 \\ 0 & \omega_1\kappa_H & \gamma_{UH} & -K_3 & 0 \\ 0 & 0 & 0 & \tau_1 & -\mu \end{pmatrix} \tag{13}$$

Then the characteristic equations are obtained as, $|J_H - \lambda I| = 0$ (where I is a 5*5 identity matrix)

Hence, $|J_H - \lambda I| = 0$ implies that:

$$\begin{pmatrix} -\mu-\lambda_1 & 0 & 0 & 0 & 0 \\ 0 & -K_1-\lambda_2 & 0 & 0 & 0 \\ 0 & (1-\omega_1)\kappa_H & -K_2-\lambda_3 & 0 & 0 \\ 0 & \omega_1\kappa_H & \gamma_{UH} & -K_3-\lambda_4 & 0 \\ 0 & 0 & 0 & \tau_1 & -\mu-\lambda_5 \end{pmatrix} = 0 \tag{14}$$

From equation (14), clearly $\lambda_2 = -K_1,\ \lambda_3 = -K_2,\ \lambda_4 = -K_3$ and $\lambda_1, \lambda_5 = -\mu$ twice

Given that all real roots are negative, real, and distinct, it suggests that the disease-free equilibrium of HIV is locally asymptotically stable, which means the disease can be controlled without leading to full blown AIDS.

Global Stability of Disease-Free Equilibrium (HIV)

We study the global stability of equilibrium without disease and we implement the approach of (Phelimon *et al.,* 2023; Adesola *et al.,* 2024a, 2024b), then the equations of the model may be rewritten in the form;

$$\frac{dM}{dt} = F(M, I)$$
$$\frac{dI}{dt} = G(M, I) \tag{15}$$

With $G(P,0) = 0$, where $P \in R^1$ represents the uninfected classes (S) and $I \in R^4$ represents the infected classes $(L_H,\ I_U, I_D, H_T)$. Also, $E_o = (M^*, 0)$ denotes the disease-free equilibrium of the model.

The two conditions $(H1)$ and $(H2)$ stated below must be satisfied for the model to be globally stable.

$(H1)$: For $\frac{dM}{dt} = F(M,0)$, M^* is globally asymptotically stable

$(H2)$: $G(M,I) = AI - \hat{G}(M,I), \quad \hat{G}(M,I) \geq 0$ for $(M,I) \in D$

Where $A = D_I G(M^*, 0)$ is an M-matrix (the off-diagonal elements of A are non-negative) and D represents the feasible region where the model holds biological significance. If conditions $(H1)$ and $(H2)$ are met, then the following theorem applies.

Theorem 3: The disease-free equilibrium $E_o = (M^*, 0)$ is a globally asymptotically stable equilibrium of the model if $R_0 < 1$ and that the conditions $(H1)$ and $(H2)$ are satisfied

Proof:

Now $M = (S)$ and $I = (L_H,\ H_U, H_D,\ H_T)$

$$F(M,0)=(\pi-\mu S) \tag{16}$$

$$A=\begin{pmatrix}(1-\varepsilon_1)\beta_H-K_1 & (1-\varepsilon_1)\beta_H\eta_U & (1-\varepsilon_1)\beta_H\eta_{dH} & (1-\varepsilon_1)\beta_H\eta_W\\ \varepsilon_1\beta_H-(1-\omega_1)\kappa_H & \varepsilon_1\beta_H\eta_U-K_2 & \varepsilon_1\beta_H\eta_{dH} & \varepsilon_1\beta_H\eta_W\\ \omega_1\kappa_H & \gamma_{UH} & -K_3 & 0\\ 0 & 0 & \tau_1 & -\mu\end{pmatrix} \tag{17}$$

Then

$$\hat{G}(M,I)=\begin{pmatrix}(1-\varepsilon_1)\beta_H\left(1-\dfrac{S}{N}\right)\\ \varepsilon_1\beta_H\left(1-\dfrac{S}{N}\right)\\ 0\\ 0\end{pmatrix} \tag{18}$$

Since $0\le\varepsilon\le 1$, clearly $\hat{G}(M,I)\ge 0$, $E_o=\left(\dfrac{\pi}{\mu}\right)$ is a globally asymptotic stable equilibrium of the model equations. Hence, the two conditions above are satisfied. Therefore, the disease-free equilibrium is globally asymptotically stable. This implies biologically that the prevention of HIV leads to AIDS is independent of the initial sizes of the sub-populations whenever the basic production number is less than one.

Local Stability of Endemic Equilibrium

Bifurcation Analysis

Here, we delve into the potential for both backward and forward bifurcation, employing the center manifold theory. Initially, from equation (1), we undertake simplifications and a change of variables as follows. Let;

$$S=x_1, L_H=x_2, H_U=x_3, H_D=x_4, H_T=x_5 \tag{19}$$

$$N=x_1+x_2+x_3+x_4+x_5 \tag{20}$$

Further, utilizing vector notation $X=(x_1+x_2+x_3+x_4+x_5)^T$,

The HIV model in the form $\dfrac{dX}{dt}=(f_1,f_2,f_3,f_4,f_5)^T$, can be expressed as follows:

$$\left.\begin{aligned}
\frac{dx_1}{dt}&=f_1=\pi-\frac{\beta_H(x_1+\eta_U x_3+\eta_{dH}x_4+\eta_W x_5)}{(x_1+x_2+x_3+x_4+x_5)}x_1-\mu x_1\\
\frac{dx_2}{dt}&=f_2=\frac{(1-\varepsilon_1)\beta_H(x_1+\eta_U x_3+\eta_{dH}x_4+\eta_W x_5)}{(x_1+x_2+x_3+x_4+x_5)}x_1-K_1x_2\\
\frac{dx_3}{dt}&=f_3=\frac{\varepsilon_1\beta_H(x_1+\eta_U x_3+\eta_{dH}x_4+\eta_W x_5)}{(x_1+x_2+x_3+x_4+x_5)}x_1-K_2K_Hx_2+K_3x_3\\
\frac{dx_4}{dt}&=f_4=\omega_1K_Hx_2+\gamma_{UH}x_3-K_4x_4\\
\frac{dx_5}{dt}&=f_5=\tau_1x_4-\mu x_5
\end{aligned}\right\} \tag{21}$$

The Jacobian of the system (2) at the DFE is provided as

follows: $J(\varepsilon_0)=\begin{pmatrix} -\mu & -\beta_H & -\beta_H\eta_U & -\beta_H\eta_{dH} & -\beta_H\eta_W \\ 0 & (1-\varepsilon_1)\beta_H-K_1 & (1-\varepsilon_1)\beta_H\eta_U & (1-\varepsilon_1)\beta_H\eta_{dH} & (1-\varepsilon_1)\beta_H\eta_W \\ 0 & \varepsilon_1\beta_H+K_2\kappa_H & \varepsilon_1\beta_H\eta_U-K_3 & \varepsilon_1\beta_H\eta_{dH} & \varepsilon_1\beta_H\eta_W \\ 0 & \omega_1 K_H & \gamma_{UH} & -K_4 & 0 \\ 0 & 0 & 0 & \tau_1 & -\mu \end{pmatrix}$ (22)

In our analysis, we select $\beta_H=\beta^*$ as our bifurcation parameter, specifically when we examine the case of $R_H=1$ and determine β_H from:

$$R_H=\frac{\left(\beta_H\begin{pmatrix}((\eta_{dH}(\omega_1-1)\gamma_{UH}+(\eta_U K_3-K_2\eta_{dH})\omega_1-\eta_U K_3)\mu+\eta_T((\omega_1-1)\gamma_{UH}-\omega_1K_2)\tau_1)\\ (\varepsilon_1-1)\kappa_H+((\eta_{dH}\gamma_{UH}K_1+K_3(\eta_U K_1-K_2))\varepsilon_1+K_2K_3)\mu+\varepsilon_1\eta_T\gamma_{UH}K_1\tau_1\end{pmatrix}\right)}{\mu K_1K_2K_3}$$ (23)

Then, we have:

$$\beta_H=\beta^*\frac{\mu K_1K_2K_3}{\begin{pmatrix}((\eta_{dH}(\omega_1-1)\gamma_{UH}+(\eta_U K_3-K_2\eta_{dH})\omega_1-\eta_U K_3)\mu+\eta_T((\omega_1-1)\gamma_{UH}-\omega_1K_2)\tau_1)\\ (\varepsilon_1-1)\kappa_H+((\eta_{dH}\gamma_{UH}K_1+K_3(\eta_U K_1-K_2))\varepsilon_1+K_2K_3)\mu+\varepsilon_1\eta_T\gamma_{UH}K_1\tau_1\end{pmatrix}}$$ (24)

Thus, the center manifold theory provides a framework for analyzing the dynamics of equation (21) with $\beta_H=\beta^*$. It can be demonstrated that the Jacobian matrix of equation (24) at $\beta_H=\beta^*$ possesses a right eigenvector corresponding to the zero eigenvalues, denoted by $(\omega_1,\omega_2,\omega_3,\omega_4,\omega_5)^T$, with the associated right eigen-values.

$$\omega_1=-\frac{(\beta_H\omega_2+\beta_H\eta_H\omega_3+\beta_H\eta_{dH}\omega_4+\beta_H\eta_H\omega_5)}{\mu}$$

$$\omega_3=\frac{K_4\mu\omega_5-\tau(\omega_1\kappa_H)\omega_2}{\gamma_{UH}\tau_1}$$

$$\omega_4=\frac{\mu\omega_5}{\tau_1}$$

$\omega_2>0$ and $\omega_5>0$ are free right eigenvector.

The Jacobian matrix ε_0 possesses left eigenvectors (related to the zero eigenvalue), which are represented by $v=(v_1,v_2,v_3,v_4,v_5)$

This gives:

$v_1=0$

$$v_2=-\frac{[(\varepsilon_1\beta_H\eta_U-K_3)v_3+\gamma_{UH}v_4]}{(1-\varepsilon_1)\beta_H\eta_U}$$

$$v_3=\frac{-[\varepsilon_1\beta_H\eta_U v_2+\gamma_{UH}v_4]}{(1-\varepsilon_1)\beta_H\eta_U-K_3}$$

$$v_4=\frac{(1-\varepsilon_1)\beta_H\eta_{dH}v_2+\varepsilon_1\beta_H\eta_{dH}v_3+\tau_1v_5}{K_4}$$

$$v_5=\frac{((1-\varepsilon_1)\beta_H\eta_W)v_2+\varepsilon_1\beta_H\eta_W v_3}{\mu}$$

Next is the computation bifurcation coefficients of a and b

$$a = \sum_{k,i,j=1}^{s} v_k \omega_i \omega_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}$$

We start from v_2 since $v_1 = 0$

$$\frac{v_2\omega_2^2\partial^2 f_2}{\partial x_2^2} = -\frac{2\beta^*\mu\varepsilon_1}{\pi}, \quad \frac{v_2\omega_2\omega_3\partial^2 f_2}{\partial x_2\partial x_3} = -\frac{\eta_U\beta^*\mu\varepsilon_1}{\pi}, \frac{v_2\omega_2\omega_4\partial^2 f_2}{\partial x_2\partial x_4} = -\frac{\eta_{dH}\beta^*\mu\varepsilon_1}{\pi}$$

$$\frac{v_2\omega_2\omega_5\partial^2 f_2}{\partial x_2\partial x_4} = -\frac{\eta_W\beta^*\mu\varepsilon_1}{\pi}, \frac{v_2\omega_3^2\partial^2 f_2}{\partial x_3^2} = -\frac{2\beta^*\eta_U\mu\varepsilon_1}{\pi}, \frac{v_2\omega_3\omega_4\partial^2 f_2}{\partial x_2\partial x_4} = -\frac{\eta_{dH}\beta^*\mu\varepsilon_1}{\pi}$$

$$\frac{v_2\omega_3\omega_5\partial^2 f_2}{\partial x_3\partial x_5} = -\frac{\eta_W\beta^*\mu\varepsilon_1}{\pi}, \frac{v_2\omega_4^2\partial^2 f_2}{\partial x_4^2} = \frac{-2\eta_{dH}\beta^*\mu\varepsilon_1}{\pi}, \frac{v_2\omega_4\omega_5\partial^2 f_2}{\partial x_4\partial x_5} = -\frac{\varepsilon_1\beta^*\eta_W\mu}{\pi}$$

$$\frac{v_2\omega_5^2\partial^2 f_2}{\partial x_5^2} = -\frac{2\varepsilon_1\beta^*\eta_W\mu}{\pi}, \frac{v_3\omega_2^2\partial^2 f_3}{\partial x_3^2} = -\frac{2\beta^*\mu(1-\varepsilon_1)}{\pi}, \frac{v_3\omega_2\omega_3\partial^2 f_3}{\partial x_2\partial x_3} = -\frac{\eta_U\beta^*\mu(1-\varepsilon_1)}{\pi}$$

$$\frac{v_3\omega_2\omega_4\partial^2 f_3}{\partial x_2\partial x_4} = -\frac{\eta_{dH}\beta^*\mu(1-\varepsilon_1)}{\pi}, \frac{v_3\omega_2\omega_5\partial^2 f_3}{\partial x_2\partial x_4} = -\frac{\eta_W\beta^*\mu(1-\varepsilon_1)}{\pi}, \frac{v_3\omega_3^2\partial^2 f_3}{\partial x_3^2} = -\frac{2\beta^*\eta\mu(1-\varepsilon_1)}{\pi}$$

$$\frac{v_3\omega_3\omega_4\partial^2 f_3}{\partial x_2\partial x_4} = -\frac{\eta_{dH}\beta^*\mu(1-\varepsilon_1)}{\pi}, \frac{v_3\omega_3\omega_5\partial^2 f_3}{\partial x_3\partial x_5} = -\frac{\eta_w\beta^*\mu(1-\varepsilon_1)}{\pi}, \frac{v_3\omega_4^2\partial^2 f_3}{\partial x_4^2} = -2\eta_{dH}\beta^*\mu(1-\varepsilon_1),$$

$$\frac{v_3\omega_4\omega_5\partial^2 f_3}{\partial x_4\partial x_5} = -\frac{(1-\varepsilon_1)\beta^*\eta_W\mu}{\pi}, \frac{v_3\omega_5^2\partial^2 f_3}{\partial x_5^2} = -\frac{2\beta^*\eta_W\mu}{\pi}$$

From the expression above

$$a = \sum_{k,i,j=1}^{s} v_k \omega_i \omega_j \frac{\partial^2 f_k}{\partial x_i \partial x_j} =$$

$$-\frac{2\beta^*\mu}{\pi}\left[\begin{matrix}(\varepsilon_1 v_2(\omega_2+\omega_3+\omega_4+\omega_5)+(\varepsilon_1 v_3+v_3)(\omega_2+\omega_3+\omega_4+\omega_5)\\(\omega_2+\eta_U\omega_3+\eta_{dH}\omega_4+\eta_W\omega_5)\end{matrix}\right] \tag{25}$$

Equation (25) shows that $a < 0$

$$b = \sum_{i=j=1}^{s} v_k \omega_i \frac{\partial^2 f_k}{\partial x_i \partial \beta^*}$$

$$\frac{v_2\omega_2^2\partial^2 f_2}{\partial x_2\partial\beta_H} = \varepsilon_1, \frac{v_2\omega_3\partial^2 f_2}{\partial x_3\partial\beta_H} = \varepsilon_1\eta_U, \frac{v_2\omega_4\partial^2 f_2}{\partial x_4\partial\beta_H} = \varepsilon_1\eta_{dH}$$

$$\frac{v_2\omega_5\partial^2 f_2}{\partial x_5\partial\beta_H} = \varepsilon_1\eta_W, \frac{v_3\omega_2\partial^2 f_3}{\partial x_2\partial\beta_H} = (1-\varepsilon_1), \frac{v_3\omega_3\partial^2 f_2}{\partial x_3\partial\beta_H} = (1-\varepsilon_1)\eta_U$$

$$\frac{v_3\omega_4\partial^2 f_3}{\partial x_4\partial\beta_H} = (1-\varepsilon_1)\eta_{dH}, \frac{v_3\omega_5\partial^2 f_3}{\partial x_5\partial\beta_H} = (1-\varepsilon_1)\eta_W$$

$$b = \sum_{i=j=1}^{s} v_k \omega_i \frac{\partial^2 f_k}{\partial x_i \partial \beta^*} = \tag{26}$$

$$\left[(\varepsilon_1(v_3+v_3)+v_3)(\omega_2+\omega_3+\omega_4+\omega_5)(\omega_2+\eta_U\omega_3+\eta_{dH}\omega_4+\eta_W\omega_5)\right]$$

Equation (26) shows that $b > 0$

In the HIV model, a forward bifurcation occurs at $R_H = 1$, as evidenced by the non-negative parameters within model (1), leading us to infer that $a < 0$ and $b > 0$. From the analysis above, model (1) demonstrates a supercritical (forward) bifurcation when R_H surpasses the

threshold $R_H = 1$. This implies the existence of a locally asymptotically stable endemic equilibrium point, denoted as $\varepsilon_0^* = (S^*, L_H^*, H_U^*, H_D^*, H_T^*)$ for $R_H > 1$.

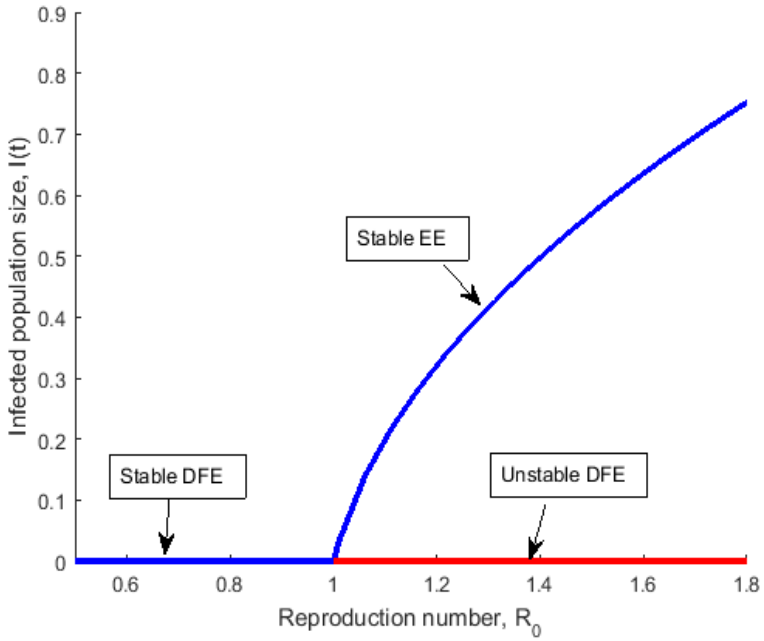

Figure 2; Forward bifurcation graph

Sensitivity analysis

This analysis helps determine how sensitive a variable is to the parameters affecting it. The normalized forward sensitivity index of a particular variable (denoted as R_0) with respect to a parameter (labeled as P) is formally defined as:

$$X_P^{R_0} = \frac{d\omega}{dP} \times \frac{P}{R_0} \tag{27}$$

Table 3.2 Numerical Sensitivity Index for HIV

Parameter	Sensitivity Value	Sensitivity Sign
β_H	1.00000	+
κ_H	0.62227	+
ω_1	0.50027	+
η_{dH}	0.20122	+
η_U	0.30142	+
η_W	0.20002	+
ε_1	0.45999	+
τ_1	-0.20755	-
γ_{UH}	-0.55371	-
μ	-0.21223	-
δ_{UH}	-0.10235	-
δ_{dH}	-0.12010	-

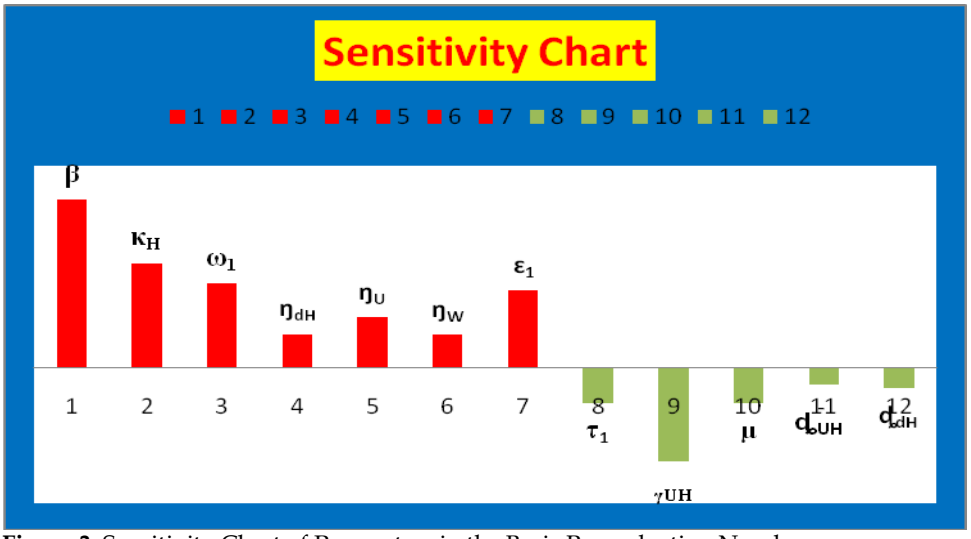

Figure 3: Sensitivity Chart of Parameters in the Basic Reproduction Number

Numerical Analysis

In this section, numerical simulations are utilized to visually demonstrate the analytical findings derived in the above analyses. To solve the system of equations (1), we utilize a fourth-order Runge-Kutta iterative scheme. The initial values for the variables of model (1) are as follows: $(S(0) = 2000, L_H(0) = 1000,\ H_U(0) = (500), H_D(0) = 700,\ H_T(0) = 300)$. Additionally, Table 2 provides both the values and the sources of the parameters utilized in the simulations.

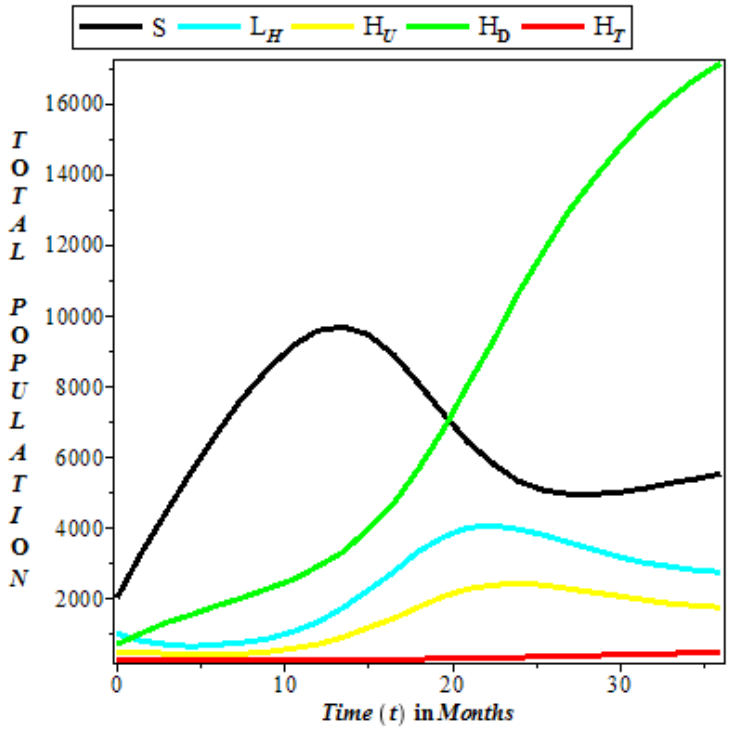

Figure 4 The total population of S_h, L_H, H_U, H_D & H_T when $\tau_1 = 0.0$

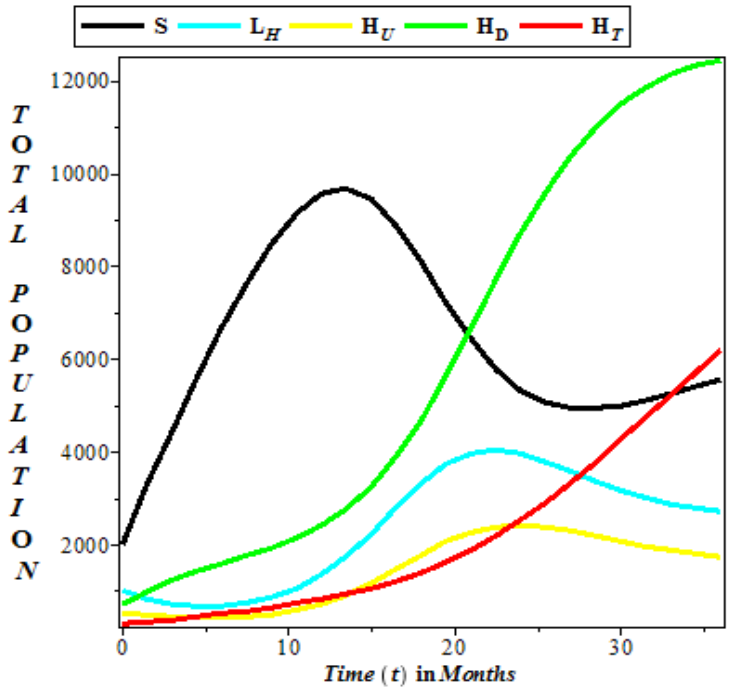

Figure 5 The total population of S_h, L_H, H_U, H_D & H_T when $\tau_1 = 0.25$

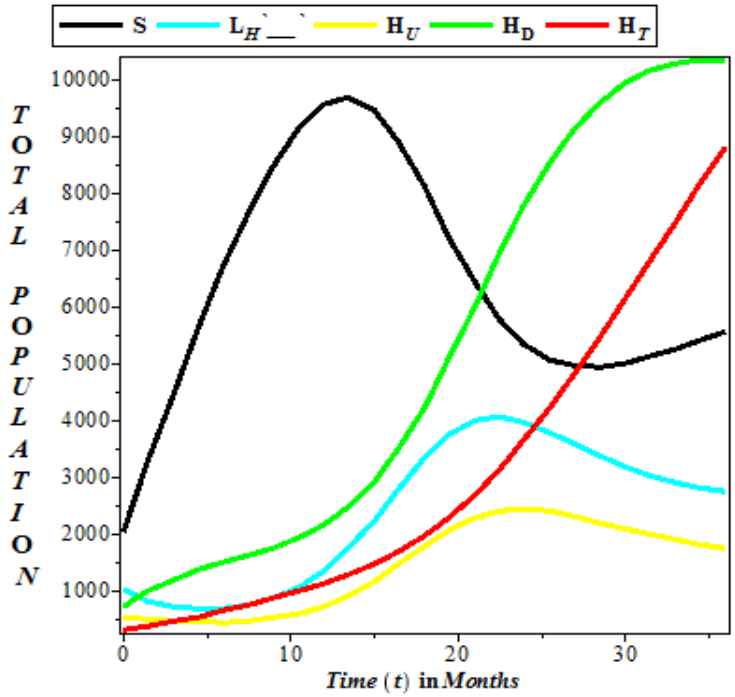

Figure 6 The total population of S_h, L_H, H_U, H_D & H_T when $\tau_1 = 0.5$

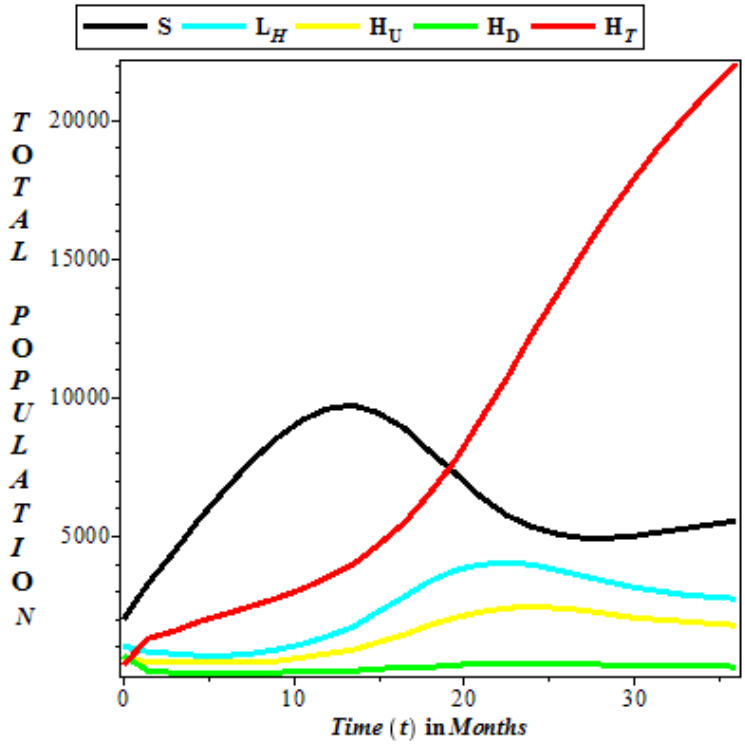

Figure 7 The total population of S_h, L_H, H_U, H_D & H_T when $\tau_1 = 1.0$

DISCUSSION

This study presents a comprehensive analysis of a non-linear deterministic model for HIV, with a focus on parameter sensitivity and stability considerations. By thoroughly examining the mathematical and epidemiological aspects of the model, our aim is to elucidate the significance of each parameter in determining the basic reproduction number. The mathematical and epidemiological viability of the model is rigorously assessed, with particular attention paid to the positivity of its solutions. This ensures that the model is well-posed both mathematically and epidemiologically. Upon analysis of the model, it becomes evident that the existence of disease-free and endemic equilibrium points is contingent upon the basic reproduction number, which plays a critical role in disease dynamics. Specifically, the disease is projected to either die out $(R_H < 1)$ or spread (when it exceeds one), based on the value of the R_H.

Furthermore, analyses of the disease equilibrium, both locally and globally, are performed to ascertain its stability under varying conditions. Bifurcation analysis was investigated on HIV, the analysis reveal that $R_H < 1$is a sufficient condition to control HIV progression to full blown AIDS. This provides valuable insights into the long-term behavior of the disease within the population. Furthermore, numerical simulations and sensitivity analyses are conducted using MAPLE 18 software to pinpoint parameters that play a substantial role in influencing the spread of HIV. The results of these simulations highlight parameters with negative indices, which mitigate disease spread, and those with positive indices, which amplify the basic reproduction number, thereby intensifying disease transmission.

From **figure 2**, it becomes evident that parameters associated with positive index values significantly influence the basic reproduction number. When this number surpasses unity, it signifies a potential escalation towards a more endemic scenario, potentially culminating in the development of full-blown AIDS. Notably, four parameters emerge as particularly

influential in determining the basic reproduction number: the infective contact rate, the two progression rates, and the rate of progression from slow progressors to HIV undetected individuals. Expanding on this observation, the infective contact rate represents a pivotal factor in the transmission dynamics of HIV, as it governs the likelihood of transmission from infected to susceptible individuals. Similarly, the two progression rates dictate the pace at which individuals' transition through different stages of HIV infection, influencing the overall disease progression within the population. Moreover, the rate of progression from slow progressors to HIV undetected individuals underscores the significance of early detection and intervention in mitigating the spread of the virus. By comprehensively analyzing the sensitivity of these parameters, we gain valuable insights into the mechanisms driving the dynamics of HIV transmission and progression. This understanding is essential for informing targeted intervention strategies aimed at curbing the epidemic and improving public health outcomes.

The importance of treatment in managing HIV cannot be overstated, particularly in preventing its progression to full-blown AIDS. Antiretroviral therapy (ART) stands as a cornerstone in the battle against HIV/AIDS, playing a pivotal role in managing the disease and improving the quality of life for those infected. By utilizing a combination of medications, ART effectively targets different stages of the virus's life cycle, preventing its replication and reducing its presence in the bloodstream. This reduction in viral load not only helps to preserve immune function but also diminishes the risk of progressing to AIDS. The graphical representation depicted in **Figure 4** vividly illustrates the progressive nature of HIV infection over time. The upward trajectory of viral load and the downward trend in CD4 cell count signify the unchecked replication of the virus and the consequential deterioration of the immune system. This visual depiction mirrors the natural course of HIV infection, where the virus proliferates within the body, causing gradual damage to immune cells and resulting in the advancement of the disease. **Figure 5** illustrates how initiating treatment at an early stage of infection leads to a rapid decline in viral load and preservation of CD4 cell count, compared to delayed treatment initiation. This highlights the pivotal role of early treatment in suppressing viral replication and preserving immune function, ultimately delaying disease progression and reducing the risk of developing AIDS-related complications. **Figure 6** delves deeper into the impact of comprehensive treatment on HIV outcomes. The graph demonstrates the significant benefits of comprehensive treatment in achieving viral suppression and immune reconstitution. It shows Individuals receiving treatment exhibit lower viral loads, higher CD4 cell counts, when treatment rate is 0.5, and improved clinical outcomes compared to those receiving partial or no treatment. This underscores the importance of adherence to treatment protocols and ensuring access to comprehensive care for all individuals living with HIV. Furthermore, **Figure 7** provides insights into the long-term effects of early and comprehensive treatment on HIV transmission dynamics within the population. By modeling the impact of treatment on viral load and transmission rates, the graph highlights the potential of early and comprehensive treatment to reduce HIV transmission and curb the spread of the virus. This underscores the dual benefits of treatment in improving individual health outcomes while also contributing to broader public health efforts to control the HIV epidemic.

CONCLUSION

Conclusively, while this research highlights the crucial significance of early and comprehensive treatment in HIV infection management, it is crucial to recognize certain limitations when discussing treatment-antiretroviral therapy (ART) and its role in HIV management. Firstly, the study may not fully capture the diverse socioeconomic and cultural factors that influence treatment accessibility and adherence, particularly in

marginalized communities. Additionally, the findings may be constrained by the study's scope and methodology, which may not encompass all variables relevant to treatment outcomes. Furthermore, the generalizability of the results may be limited by factors such as sample size and selection bias. Despite these limitations, the research underscores the essential role of timely intervention and treatment adherence in mitigating the impact of HIV infection on both individual health outcomes and population-level transmission dynamics.

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