Modelling HIV/AIDS infection dynamics in the presence of interfered interventions

Hillary Kiprop Kosgei (hillary@aims.ac.za)
African Institute for Mathematical Sciences (AIMS)

Supervised by: Professor Farai Nyabadza
University of Johannesburg, South Africa

23 May 2019

Submitted in partial fulfillment of a structured masters degree at AIMS South Africa

Abstract

Mathematical models are invaluable tools in describing and understanding disease dynamics. In this study, we propose and analyse a model for HIV/AIDS to assess the impact of interventions on the disease dynamics in presence of interference. The model enables us to study the role of treatment in the presence interfered interventions, as a control strategy for reducing the HIV pandemic. We performed thorough qualitative analysis on the reproduction number of the model, $\mathcal{R}_0$. The global and local dynamics of the system are also considered, that is, we analyse the two equilibria states of the model: disease-free and a unique disease-persistent equilibria. We justified that the disease-free steady state is globally asymptotically stable whenever $\mathcal{R}_0 < 1$ and the endemic equilibrium is globally asymptotically stable whenever $\mathcal{R}_0 > 1$. We conducted numerical simulations to support the analytic results. The results of the model analysis indicated that interference have the effect of reducing the uptake of treatment and increasing the rates of drop-out. The results have implications in the designing of policies in countries with war, economic turmoil or any other form of disturbances.

Keywords: HIV/AIDS, Interference, Reproduction number, Treatment, Mathematical model.

Declaration

I, the undersigned, hereby declare that the work contained in this research project is my original work, and that any work done by others or by myself previously has been acknowledged and referenced accordingly.

Hillary Kiprop Kosgei, 23 May 2019

Contents

1. Introduction

HIV virus which causes AIDS still poses a serious public health threat in various parts of the globe especially in the Sub-Saharan Africa. According to WHO (2018), approximately 36.9 million individuals globally were living with the HIV virus in 2017, of whom about 21.7 million were on antiretroviral therapy (ART). In an attempt to combat the onward transmission of HIV pandemic, UNAIDS implemented prevention strategies in 2014 with an ambitious goal of reducing new infections to less than 500,000 by 2020 (UNAIDS , 2018). The control mechanisms proposed and implemented by World Health Organization (WHO) and UNAIDS include the use of female and male condoms, antiretroviral treatment to suppress the viral load in HIV patients, pre-exposure prophylaxis (PrEP) for those who are at risk of acquiring the infection, voluntary male circumcision, educational campaigns, provision of opiate therapy, use of clean syringes and needles among others.

However, according to WHO (2018), the new infections recorded in 2015 were about four-times the 2020 target despite the implementation of the WHO guidelines, indicating that more effort is still required in the war against the HIV epidemic. The high HIV incidences can be attributed to some situations that make the implementation of these HIV interventions difficult. For instance, conditions such as war and conflicts, political instability, poverty, migration and economic challenges limit the implementation of prevention mechanisms hence fuelling the transmission of the disease (WHO , 2018). Occurrence of disasters such as wars and conflicts subject people to harsh conditions which makes them vulnerable to human rights abuses such as rape and mass displacement. Furthermore, such calamities also interrupt the access of health care services making it difficult for HIV/AIDS victims and other patients to access treatment services (Januaris Saint Fores , 2018).

According to UNAIDS, there is no single control mechanism that has a powerful impact in lowering HIV prevalence and incidence levels, but a combination of several intervention strategies can significantly reduce new infections. However, failure to implement some of the proven HIV interventions systematically and consistently have slowed down the reduction in new HIV infections (UNAIDS , 2018). The cases of drop outs or failure to adhere to antiretroviral treatment enhances HIV transmission since it has been established that routine monitoring of the viral load is an effective HIV prevention tool (WHO , 2018). Adherence to antiretroviral drugs suppresses the viral load in HIV patients to undetectable levels and such patients cannot transmit the virus to others (UNAIDS , 2018). Therefore, poor adherence to antiretroviral therapy not only facilitate HIV transmission but also increases the mortality rates of the infected individuals.

1.1 Related literature

Mathematical models have played an important role in understanding and describing the epidemiological patterns for the proliferation and control of HIV pandemic and incorporation of HIV interventions in these model systems has attracted significant attention recently. A combination of early diagnosis followed by immediate treatment to suppress the viral load have been proposed as effective interventions in minimizing the HIV incidence in numerous models. In this section, we will review some mathematical models for HIV/AIDS with interventions.

Malunguza et al. (2010) presented a deterministic model for HIV/AIDS to investigate the impact of condom use alone in HIV prevention. They modelled the use of condoms for male only and the use of both female and male condoms simultaneously. Moreover, they extended their model to account for

the effects of ART treatment also as a single control mechanism for HIV. They realised that the use of condoms was effective in slowing HIV progression. However, their results also suggested that the use of treatment was not very effective since treated patients would indulge in risk sexual behaviours. Thus, they suggested that treatment should be followed by intense educational programmes to help in changing the attitude of HIV patients under treatment to practice safe sexual behaviours. They proposed effective medication and use of condoms as the two control measures that can assist to contain HIV/AIDS epidemic.

Nyabadza et al. (2011) formulated a deterministic model system of HIV that incorporated control strategies such as condom use, behaviour change, sexual partner acquisition as well as treatment. In their work, they concluded that behaviour change especially by those individuals who are sexually active is essential in reducing the HIV/AIDS pandemic. Furthermore, Safiel et al. (2012) proposed a compartmental model based on non linear equations to examine the impact of treatment and screening of individuals who are unaware of their HIV status on the spread of HIV/AIDS in a community. From their analysis, they noted that the screening and enrolling those who test HIV positive on treatment is beneficial in mitigating HIV/AIDS infection.

Okosun et al. (2013) presented a model based on ordinary differential equations to determine the effects of prevention intervention strategies on the spread of HIV. After rigorous analysis, they concluded that screening of unaware individuals was effective in curbing the endemicity of the infection since HIV awareness enable infectives to take necessary precautions not to transmit the virus. Therefore, control programs such as screening of HIV infections, treatment and effective use of condoms are vital in reducing the transmission. Similarly, in the study conducted by Thiébaut and May (2013) they also highlighted that the use ART, on HIV patients and PrEP, for uninfected individuals who are at risk, were effective according to the recent clinical trials.

Birger et al. (2013) proposed a mathematical model for HIV/AIDS pandemic to describe the dynamics of the disease in Newark, USA. Their key objective was to assess the effect of HIV interventions alongside continuum care in reducing the spread of HIV in Newark. They found that improving adherence to treatment as well as increasing HIV screening coverage and frequency was counter-productive in combating HIV pandemic. Therefore, their results reinforced the significance of continuum care in the fight against HIV/AIDS.

In their study, Kim et al. (2014) constructed an HIV infection model using the deterministic approach to assess the effectiveness of multiple HIV prevention measures in impacting local HIV spread in South Korea. The interventions studied included early diagnosis, early treatment (PrEP and ART) and the combination of these measures. The results of their model indicated that PrEP would be the most effective public health prevention measure. However, PrEP effectiveness would be decreased by increased engagement in unprotected sex behaviour. Early diagnosis also decreased HIV/AIDS incidence, but early ART on infected individuals failed to indicate considerable effectiveness. Therefore, in their model, they suggested the implementation of combined interventions (early diagnosis, PrEP and immediate treatment) as an effective measure to combat HIV/AIDS in South Korea.

Similarly, Huo and Chen (2015) in their work, revealed that early treatment of HIV was effective in the fight against HIV. In their study, Luo et al. (2015) modelled the effect of test-and-treat HIV prevention strategy among men having sex with other men (MSM) in China. They formulated a dynamic mathematical model to predict HIV incidence and prevalence among MSM in China over 10 years. They found that the implementation of test-and-treat would reduce new infections among MSM by 50.6 - 70.9%. Therefore, they recommended the scaling of HIV screening rate and treatment coverage among MSM in China since this strategy would significantly slow HIV progression much faster than any other

HIV control mechanism for MSM in China.

Su et al. (2016) also established a deterministic mathematical model to study the transmission dynamics of HIV. They calibrated their model using treatment and surveillance data from 2005-2008. After comparing the predicted value of the prevalence of HIV in 2010 to the predicted value of the prevalence data of HIV obtained in 2010, they established that the population-based control programs for the disease were effective in slowing down the HIV incidence. Hence, they recommended the scaling up of HIV testing as well as treatment.

Omondi et al. (2018a) developed a deterministic mathematical model based on non-linear differential equations to assess the effect of preventing, testing and treating HIV patients with ART. Sensitivity analysis results indicated that HIV proliferation was fuelled through contact rates and ART efficacy proved to be an effective public health intervention in reducing HIV incidence. Similarly, in their other work, Omondi et al. (2018b) used a model based on non-linear equations to investigate HIV dynamics in Kenya. They incorporated sexual orientation to understand the severity of HIV infection according to gender. Their findings indicated that the female population recorded higher infectivity compared to males. They further extended their model to incorporate the impact of PrEP as a control strategy against HIV/AIDS infection. Their results showed that the introduction of PrEP was effective in limiting HIV transmission across the gender divide.

1.2 Motivation

According to WHO (2018), emergency crises do not only subject affected individuals to the risk of acquiring HIV virus but also disrupt the existing HIV/AIDS programmes thus fuelling the transmission of the disease. Considering all the mathematical models mentioned above, none of them takes into account situations such as war, political instability, poverty, economic challenges, drought, nutritional challenges and other factors that impede HIV interventions. Therefore in this study, we propose a mathematical model for HIV epidemic that does not only incorporate HIV interventions but also focuses on the factors that can hinder smooth implementation of these prevention strategies aimed at stopping the HIV/AIDS transmission chain. Numerous qualitative studies have proposed HIV medication as an highly effective control mechanism since it does not only reduce HIV transmission but also keeps HIV patients healthy by reducing the viral load to undetectable amounts (UNAIDS , 2018). So, in this paper we will also assess the effect of treatment on the disease dynamics to ascertain their claims.

1.3 Aims of the study

The primary focus of this study is to model HIV/AIDS infection dynamics in presence of interfered interventions. The effect of factors that hamper HIV prevention strategies are considered in detail. In this project, the following specific objectives will be addressed through analytical techniques and numerical simulations of the model:

1. To model HIV/AIDS in the presence of interference in HIV transmission.
2. To assess the impact of treatment on the proliferation of HIV/AIDS in the presence of interference.
3. To establish the basic properties of the model and analyse the local and global dynamics of the system.

4. To determine the model's basic reproduction number using the next-generation matrix approach and investigate how model parameters impact this threshold value of the infection.
5. To numerically solve the model and investigate the impact of selected parameters.

2. Model Formulation and Analysis

2.1 System description

We formulate a new mathematical model based on a susceptible-infected (SI) deterministic model to understand and describe HIV transmission dynamics in presence of interference. We present a model that partitions the total human population $N(t)$ into four mutually-exclusive classes: $S(t), I(t), T(t)$ and $A(t)$. We assume that the total human population $N(t)$ at any given time t is denoted by Equation (2.1.1)

$$N(t) = S(t) + I(t) + T(t) + A(t). \tag{2.1.1}$$

The first class $S(t)$ represents the susceptible individuals, $I(t)$ consists of HIV-positive patients at asymptomatic stage of the infection, $T(t)$ comprises of HIV-positive individuals receiving ART treatment and lastly $A(t)$ represents patients at the symptomatic stage of HIV infection. We categorize the stages of HIV/AIDS infection into two, that is, infected people in the asymptomatic stage (I and T) of the infection and those in pre-AIDS stage or full-blown AIDS (A).

Interfered interventions have devastating impact on the spread of HIV/AIDS. In this study, we will utilize the standard incidence to model HIV/AIDS transmission dynamics. Therefore, the total number of new HIV infections triggered by infected individuals at the asymptomatic stage of HIV infection and HIV victims under treatment are obtained by using the force of infection λ, which can be modified as

$$\lambda = \begin{cases} (\beta_{max} + \varepsilon_1\omega)(I + \eta T), \\ \beta_{max} e^{-\varepsilon_2\omega}(I + \eta T), \\ \frac{\beta_{max}}{1+Ke^{-\varepsilon_3\omega}}(I + \eta T), \end{cases}$$

where β_{max} represents the effective transmission rate for the HIV virus, K represents the scale parameter, $\varepsilon_1, \varepsilon_2, \varepsilon_3$ represents the shape parameters that determines how fast the impacts of the disease can be felt, ω is the level of interference and η is the relative infectivity of T with respect to I, $\eta \in (0, 1)$. The forms of λ presented here, present the various possibilities or probable function that can used to measure the increased infection rate due to interference.

In this project, we propose a force of infection λ, that is dependent on the presence of interfered interventions given by,

$$\lambda = C(\omega)(I + \eta T),$$

where the function $C(w)$ describes the effective contact rate is given by

$$C(\omega) = \frac{\beta_{max}}{1 + Ke^{-\varepsilon\omega}}. \tag{2.1.2}$$

In the model, when $\omega = 0$ then there are no processes that can hamper HIV interventions and the disease spreads normally in the population at a rate β_{max}. However, maximum interference on HIV interventions is experienced when $\omega = 1$. We choose parameters K and ε carefully such that maximum HIV transmission rate, β_{max} occurs when $\omega = 1$. Therefore transmission dynamics of the disease depends on the value of ω as described in Figure 2.1.

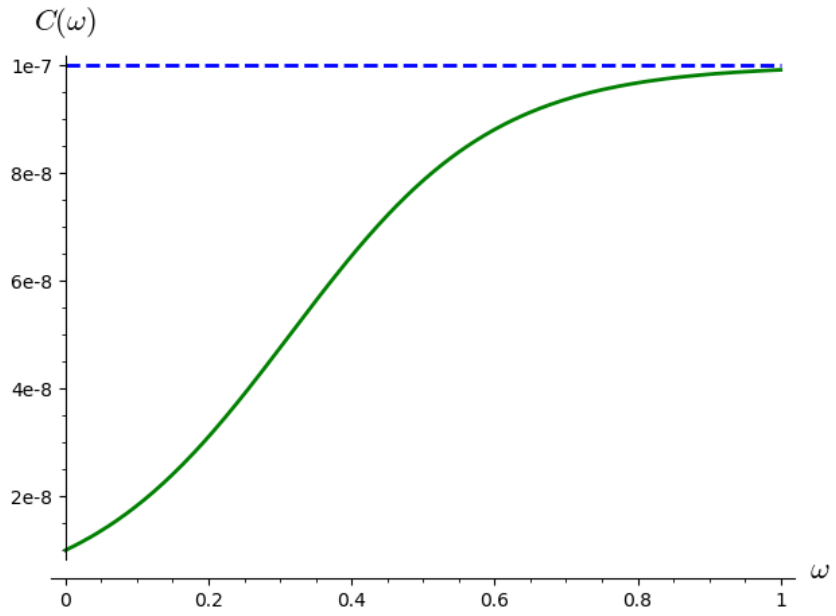

Figure 2.1: Graphical representation of HIV infection rate in presence of processes that limit interventions with $(\beta_{max} = 1 \times 10^{-7}, K = 9, \varepsilon = 7)$.

From Figure 2.1, it can be observed that there is a functional relationship between $C(\omega)$ and ω. Therefore, Equation (2.1.2) predicts that as the factors that hinder HIV interventions increases then the HIV infection rate in the population increase gradually initially, then rapidly, slows down again as ω approaches 1 and reaches its maximum value when $\omega = 1$.

A schematic representation of HIV/AIDS transmission dynamics in the presence of interfered interventions is shown in the Figure 2.2

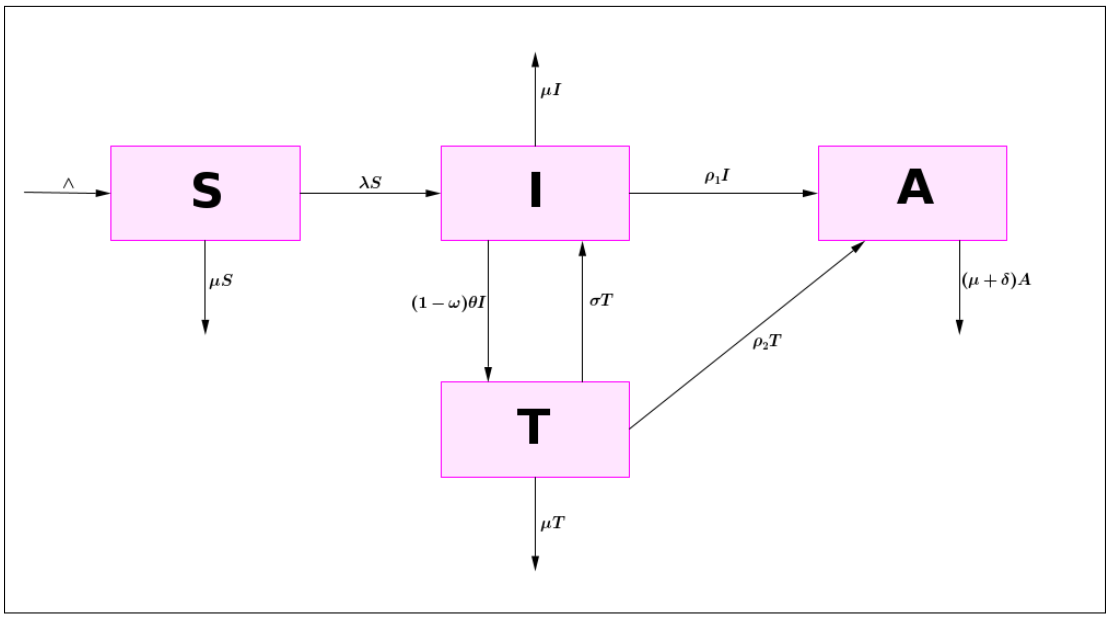

Figure 2.2: A model for HIV/AIDS infection dynamics in presence of processes that limit interventions.

2.1.1 Model assumptions. The key assumptions made in the model include:

1. There is homogeneous spatial distribution (mixing) of infected and HIV-negative individuals.
2. HIV virus is transmitted via heterosexual means.
3. HIV patients at the symptomatic stage of the HIV infection (class A) are at the terminal stage of the HIV infection and they do not contribute to the spread of the disease since they are unable to transmit the virus via sexual activity.

Now we consider the movement of populations between compartments in Figure 2.2 with time. Firstly, we assume that the population is recruited into susceptible class at a constant rate Λ and μ is the natural death rate for all compartments. Individuals in the susceptible class can acquire HIV virus with the force of infection λ. Each newly HIV infected individual in susceptible class (S) progresses to infected class (I) at a rate λ and those screened for the virus and put on ART treatment move to compartment (T) at a rate $(1-\omega)\theta$. Note here that as ω increases the rate of movement from compartment I to T slows down, that is, interference is assumed to slow uptake into treatment programs. So, we assume that interference increases the infection rate and reduces the uptake into a treatment program. The processes that impede HIV treatment have been incorporated in the model and $0 \leq \omega \leq 1$ measures the impact of any process that hinder HIV treatment. From the model, we can observe that as ω increases the rate of the infected people accessing medication decreases and no HIV patient can access treatment services when we have maximum interference, when $\omega = 1$. Persons who withdraw from ART therapy can either return to the infected class at a rate σ or move to full-blown AIDS stage (A) at a rate ρ_2. HIV patients in the infected class (I) can also move directly to the symptomatic stage of the HIV infection (A) at the rate ρ_1. In addition, we assume that the infected individuals in the symptomatic stage of HIV/AIDS infection (A) experience an additional mortality rate δ; due to AIDS unlike the other individuals in the other compartments.

2.1.2 Model Equations. The dynamics described in the Figure 2.2 is governed by the following non-linear system of differential equations

$$\left.\begin{aligned} \frac{dS}{dt} &= \Lambda - \mu S - \lambda S, \\ \frac{dI}{dt} &= \lambda S - \mu I - (1-\omega)\theta I - \rho_1 I + \sigma T, \\ \frac{dT}{dt} &= (1-\omega)\theta I - \mu T - \sigma T - \rho_2 T, \\ \frac{dA}{dt} &= \rho_1 I + \rho_2 T - (\mu + \delta) A, \end{aligned}\right\} \tag{2.1.3}$$

with the following initial conditions

$$S(0) \geq 0, I(0) \geq 0, T(0) \geq 0 \quad \text{and} \quad A(0) \geq 0.$$

NOTE: All parameters and state variables in model system (2.1.3) are strictly positive for all time $t \geq 0$ since it monitors the population of humans.

A summary of the model parameters are given in Table 2.1

Parameter	Description
β_{max}	Effective contact rate (Infection rate)
Λ	Recruitment rate
ω	Level of interference
θ	Rate of treatment
ρ_1, ρ_2	Progression rates to full-blown AIDS
σ	Drop out rate
μ	Natural death rate
δ	HIV/AIDS related death
η	Relative infectivity of I with respect to T
K	Scale parameter
ε	Shape parameter

Table 2.1: Description of parameters

2.2 Model properties

In this section, we focus on the basic properties of the system (2.1.3). We show that all the state variables of system (2.1.3) will remain non-negative and that all its solutions with positive initial conditions will remain non-negative for all $t > 0$.

2.2.1 Boundedness of model solutions.

2.2.2 Theorem. *The invariant region Ω for the given mathematical model defined by*

$$\Omega = \left\{ (S, I, T, A) \in \mathbb{R}^4_+ \quad \textit{such that} \quad 0 \leq N(t) \leq \frac{\Lambda}{\mu} \right\}, \tag{2.2.1}$$

with initial conditions $S(0) \geq 0, I(0) \geq 0, T(0) \geq 0, A(0) \geq 0$ is positively invariant for all $t \geq 0$.

Proof. The total human population is given by Equation (2.1.1) and at any given time, the rate change in the population is given by

$$\begin{aligned} \frac{dN}{dt} &= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dA}{dt}, \\ &= \Lambda - \mu N - \delta A. \end{aligned} \tag{2.2.2}$$

Assuming that mortality due to AIDS is zero, that is $\delta = 0$ in (2.2.2), then we have

$$\frac{dN}{dt} + \mu N \leq \Lambda. \tag{2.2.3}$$

Solving (2.2.3) using the integrating factor technique we get the solution $N(t)$ such that

$$N(t) = \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu} \right) e^{-\mu t}. \tag{2.2.4}$$

The solution has the property

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu} \right) e^{-\mu t},$$

where $N(0)$ represents initial human population. From Equation (2.2.4), we can note that $N \longrightarrow \frac{\Lambda}{\mu}$ as time, $t \longrightarrow \infty$. Therefore, $N(t)$ is bounded above by $\frac{\Lambda}{\mu}$. If $N(0) \leq \frac{\Lambda}{\mu}$, then we can infer that $N(t)$ tends to $\frac{\Lambda}{\mu}$ as time increases. Conversely, $N(t)$ will decrease to $\frac{\Lambda}{\mu}$ if $N(0) > \frac{\Lambda}{\mu}$. In other words, if $N(0) > \frac{\Lambda}{\mu}$ then the solutions $(S(t), I(t), T(t), A(t)$ approaches $\frac{\Lambda}{\mu}$ asymptotically. Therefore, the solutions of system (2.1.3) are bounded. □

2.2.3 Positivity of solutions.

2.2.4 Theorem. *Given that the initial conditions of the system* (2.1.3) *are* $S(0) \geq 0, I(0) \geq 0, T(0) \geq 0$ *and* $A \geq 0$ *then it follows that the resulting solutions* $S(t), I(t), T(t)$ *and* $A(t)$ *are all non-negative for all* $t > 0$.

Proof. To prove Theorem 2.2.4 we need to show that each of the trajectories of the model system (2.1.3) is positive for all $t > 0$. We let

$$\bar{t} = \sup\{t > 0 : S > 0, I > 0, T > 0, A > 0\} \in [0, t].$$

So $\bar{t} > 0$ and from the first equation of the system (2.1.3), it follows that

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - (\mu + \lambda)S \\ &\geq -(\mu + \lambda)S. \end{aligned} \tag{2.2.5}$$

When we separate variables in Equation (2.2.5) and integrate both sides with respect to t over the interval [0, t] we get:

$$S(t) \geq S(0)e^{-(\mu+\lambda)t} \geq 0.$$

Thus, when $t = 0, S(t)$ is never negative.

For the second equation in system (2.1.3), we have that

$$\frac{dI}{dt} \geq -(\mu + \rho_1 + (1 - \omega)\theta)I. \tag{2.2.6}$$

Separating variables in Equation (2.2.6) and integrating both sides with respect to t over the interval [0, t] we obtain

$$I(t) \geq I(0)e^{-(\mu+\rho_1+(1-\omega)\theta)t} \geq 0.$$

Thus, when $t = 0, I(t)$ is non negative.

Using the same technique we obtain the following solutions to the third and fourth equations in system (2.1.3)

$$\begin{aligned} T(t) &= T(0)e^{-(\sigma+\mu+\rho_2)t} \geq 0, \\ A(t) &= A(0)e^{-(\mu+\delta)t} \geq 0. \end{aligned}$$

We can note that when $t = 0$, $T(t)$ and $A(t)$ are positive. Therefore $S(t) \geq 0$, $I(t) \geq 0$, $T(t) \geq 0$ and $A(t) \geq 0$ for all $t \geq 0$. □

The model is well-posed epidemiologically and mathematically since all solutions of system (2.1.3) remain non-negative and bounded in the invariant set Ω. Therefore, it is sufficient to analyse the dynamics of the proposed model in Ω.

2.3 Disease-free equilibrium (DFE) and reproduction number ($\mathcal{R}_0$)

At DFE, we assume that the total population has not experienced HIV virus infection, the community remains free of the virus. Then it folows that the entire population becomes susceptible to the infection.Therefore, to obtain the DFE we let all the infected classes to be zero, that is $I = 0, T = 0$ and $A = 0$. We consider with the first equation in the model system (2.1.3) and equate it to zero, that is

$$\frac{dS}{dt} = \Lambda - (\mu + \lambda)S = 0.$$

We get

$$\Longrightarrow S = \frac{\Lambda}{(\mu + \lambda)},$$

Note that $\lambda = 0$ at DFE.

Hence in this model, the disease-free equilibrium is given by

$$E_0 = \left(S^0, I^0, T^0, A^0\right) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right).$$

In this model, we assume that the new HIV infections are generated by infected individuals in compartments I and T. Reproduction number $\mathcal{R}_0$ represents the average number of new infections generated by an infectious individual in the population of wholly susceptible individuals (Van den Driessche and Watmough, 2002). The next-generation matrix technique defined in Van den Driessche and Watmough (2002) is used to compute $\mathcal{R}_0$.

We consider the compartments that contribute to new HIV infections. We have that the matrix of new infections F and the matrix of transitions V are given by

$$F = \begin{pmatrix} \frac{C(\omega)\Lambda}{\mu} I + \frac{C(\omega)\Lambda\eta}{\mu} T \\ 0 \end{pmatrix},$$
$$V = \begin{pmatrix} (\mu + (1-\omega)\theta + \rho_1)I - \sigma T \\ -(1-\omega)\theta I + (\sigma + \mu + \rho_2)T \end{pmatrix}.$$

Now evaluating the matrices for the states F and V at the DFE yields

$$F = \begin{pmatrix} \frac{C(\omega)\Lambda}{\mu} & \frac{C(\omega)\Lambda\eta}{\mu} \\ 0 & 0 \end{pmatrix},$$
$$V = \begin{pmatrix} H_1 & -\sigma \\ -H_2 & H_3 \end{pmatrix}.$$

Here

$$H_1 = \mu + (1-\omega)\theta + \rho_1,$$
$$H_2 = (1-\omega)\theta,$$
$$H_3 = \mu + \sigma + \rho_2.$$

We have that

$$FV^{-1} = \begin{pmatrix} \frac{C(\omega)\Lambda}{\mu(H_1H_3-\sigma H_2)}(H_3+\eta H_2) & \frac{C(\omega)\Lambda}{\mu(H_1H_3-\sigma H_2)}(\sigma+\eta H_1) \\ 0 & 0 \end{pmatrix}.$$

The dominant eigenvalue of the matrix FV^{-1} gives the reproduction number $\mathcal{R}_0$ of system (2.1.3). Thus

$$\begin{aligned} \mathcal{R}_0 &= \varphi(FV^{-1}) \\ &= \frac{C(\omega)\Lambda}{\mu(H_1H_3-\sigma H_2)}\Big(H_3+\eta H_2\Big). \end{aligned} \tag{2.3.1}$$

We can note that

$$\begin{aligned} H_1H_3-\sigma H_2 &= H_1H_3\left(1-\frac{\sigma H_2}{H_1H_3}\right) \\ &= H_1H_3\left(1-\phi\right), \end{aligned}$$

where

$$\left(\frac{\sigma}{H_3}\right)\left(\frac{(1-\omega)\sigma}{H_1}\right) = \phi < 1.$$

Therefore, the reproduction number $\mathcal{R}_0$ becomes

$$\mathcal{R}_0 = \frac{C(\omega)\Lambda}{\mu H_1H_3\left(1-\phi\right)}\Big(H_3+\eta H_2\Big). \tag{2.3.2}$$

Substituting for the values of $C(\omega), H_1, H_2$ and H_3 in Equation (2.3.2) gives

$$\begin{aligned} \mathcal{R}_0 &= \frac{\beta_{max}\Lambda}{\mu(\mu+(1-\omega)\theta+\rho_1)(\mu+\sigma+\rho_2)(1+Ke^{-\epsilon\omega})\left(1-\phi\right)}((\mu+\sigma+\rho_2)+\eta((1-\omega)\theta)) \\ &= \frac{\beta_{max}\Lambda}{J}\Big[(\mu+\sigma+\rho_2)+\eta\theta(1-\omega)\Big], \end{aligned} \tag{2.3.3}$$

where $J = \mu\left[\mu+(1-\omega)\theta+\rho_1\right](\mu+\sigma+\rho_2)(1+Ke^{-\epsilon\omega})\left(1-\phi\right)$.

From Equation (2.3.3), we note that

$$\mathcal{R}_0 = \mathcal{R}_I + \mathcal{R}_T$$

where

$$\mathcal{R}_I = \frac{\beta_{max}\Lambda(\mu+\sigma+\rho_2)}{J}$$

and

$$\mathcal{R}_T = \frac{\eta\beta_{max}\Lambda(1-\omega)\theta}{J}.$$

Here we note that $\mathcal{R}_I$ is the contribution of individuals in compartment I to HIV/AIDS infections while $\mathcal{R}_T$ is contribution of infected individuals in compartment T.

2.3.1 Local stability of the DFE.

2.3.2 Theorem. *The DFE of the model system (2.1.3) is locally asymptotically stable when $\mathcal{R}_0 < 1$ and unstable otherwise.*

Proof. We employ the idea of stability matrix to prove Theorem 2.3.2 above. Thus the Jacobian matrix of system (2.1.3) is given as

$$J(S,I,T,A) = \begin{pmatrix} -(\mu + C(\omega)I + C(\omega)\eta T) & -C(\omega)S & -C(\omega)\eta S & 0 \\ C(\omega)I + C(\omega)\eta T & C(\omega)S - [(1-\omega)\theta + \mu + \rho_1] & C(\omega)\eta S + \sigma & 0 \\ 0 & (1-\omega)\theta & -(\sigma + \mu + \rho_2) & 0 \\ 0 & \rho_1 & \rho_2 & -(\mu + \delta) \end{pmatrix}.$$

Now evaluating the stability at the DFE, we obtain

$$J(\frac{\Lambda}{\mu},0,0,0) = \begin{pmatrix} -\mu & -C(\omega)\frac{\Lambda}{\mu} & -C(\omega)\eta\frac{\Lambda}{\mu} & 0 \\ 0 & C(\omega)\frac{\Lambda}{\mu} - [(1-\omega)\theta + \mu + \rho_1] & C(\omega)\eta\frac{\Lambda}{\mu} + \sigma & 0 \\ 0 & (1-\omega)\theta & -(\sigma + \mu + \rho_2) & 0 \\ 0 & \rho_1 & \rho_2 & -(\mu + \delta) \end{pmatrix}$$

$$= \begin{pmatrix} -\mu & -C(\omega)\frac{\Lambda}{\mu} & -C(\omega)\eta\frac{\Lambda}{\mu} & 0 \\ 0 & C(\omega)\frac{\Lambda}{\mu} - H_1 & C(\omega)\eta\frac{\Lambda}{\mu} + \sigma & 0 \\ 0 & H_2 & -H_3 & 0 \\ 0 & \rho_1 & \rho_2 & -(\mu + \delta) \end{pmatrix}.$$

We notice that by expanding the determinant of the characteristic equation $|J(E_0) - aI|$, we obtain two eigenvalues of the stability matrix $J(E_0)$, that is

$$\begin{aligned} a_1 &= -\mu, \qquad \text{(from the first column)}, \\ a_2 &= -(\mu + \delta), \qquad \text{(from the fourth column)}. \end{aligned}$$

The other two eigenvalues are obtained from the non-zero roots of 2×2 Jacobian matrix

$$J(E_0^\star) = \begin{pmatrix} C(\omega)\frac{\Lambda}{\mu} - H_1 & C(\omega)\eta\frac{\Lambda}{\mu} + \sigma \\ H_2 & -H_3 \end{pmatrix}$$

with the characteristic polynomial $P(a)$ given by

$$P(a) = a^2 + Xa + Y = 0, \tag{2.3.4}$$

where

$$X = C(\omega)\frac{\Lambda}{\mu} - (H_1 + H_3)$$

and

$$\begin{aligned}
Y &= -H_3\left(C(\omega)\frac{\Lambda}{\mu} - H_1\right) - H_2\left(C(\omega)\eta\frac{\Lambda}{\mu} + \sigma\right) \\
&= (H_1H_3 - \sigma H_2) - H_3C(\omega)\frac{\Lambda}{\mu} - H_2C(\omega)\eta\frac{\Lambda}{\mu} \\
&= \frac{\mu(H_1H_3 - \sigma H_2) - C(\omega)\Lambda(H_3 + \eta H_2)}{\mu} \\
&= (H_1H_3 - \sigma H_2)\left(\frac{\mu(H_1H_3 - \sigma H_2) - C(\omega)\Lambda(H_3 + \eta H_2)}{\mu(H_1H_3 - \sigma H_2)}\right) \\
&= (H_1H_3 - \sigma H_2)(1 - \mathcal{R}_0) \\
&= H_1H_3\left(1 - \frac{\sigma H_2}{H_1H_3}\right)(1 - \mathcal{R}_0) \\
&= H_1H_3(1 - \phi)(1 - \mathcal{R}_0).
\end{aligned}$$

It is evident that the eigenvalues a_1 and a_2 have negative real parts. Similarly, according to the Routh-Hurwitz criterion, the characteristic Equation (2.3.4) will have negative real eigenvalues if its coefficients are strictly positive, that is $X > 0$ and $Y > 0$ (DeJesus and Kaufman, 1987). We note that for $Y > 0$ then $\mathcal{R}_0 < 1$. Hence, the DFE is locally asymptotically stable if all the eigenvalues of the stability matrix at DFE have negative real parts. This implies that for our system, when $\mathcal{R}_0 < 1$ and $X > 0$ then the DFE is locally asymptotically stable and it is unstable otherwise. □

Theorem 2.3.2 tells us that the HIV infection can die out slowly and end up being eliminated from the community if $\mathcal{R}_0 < 1$.

2.3.3 Global stability of the DFE.

2.3.4 Theorem. *The DFE of the model system (2.1.3) is globally asymptotically stable whenever $\mathcal{R}_0 < 1$ and unstable otherwise. There is a unique equilibrium state when $\mathcal{R}_0 \leq 1$, the disease-free equilibrium, DFE in system (2.1.3).*

Proof. We let the Lyapunov candidate function for the global stability which involves compartments that contribute to the HIV infection in the population be

$$L = \psi_1 I + \psi_2 T$$

where the constants ψ_1 and ψ_2 are non-negative. To find these constants, we compute the time derivative of L, that is

$$\begin{aligned}
\frac{dL}{dt} &= \psi_1\frac{dI}{dt} + \psi_2\frac{dT}{dt} \\
&\leq \psi_1\left[\left(\frac{C(\omega)\Lambda}{\mu} - H_1\right)I + \left(\frac{C(\omega)\Lambda\eta}{\mu} + \sigma\right)T\right] + \psi_2\left[H_2I - H_3T\right] \\
&= \left[\psi_1\left(\frac{C(\omega)\Lambda}{\mu} - H_1\right) + \psi_2H_2\right]I + \left[\psi_1\left(\frac{C(\omega)\Lambda\eta}{\mu} + \sigma\right) - \psi_2H_3\right]T. \qquad (2.3.5)
\end{aligned}$$

Now equating the coefficient of the component T in (2.3.5) to zero, that is

$$\psi_1\left(\frac{C(\omega)\Lambda\eta}{\mu} + \sigma\right) - \psi_2H_3 = 0 \qquad (2.3.6)$$

and evaluating Equation (2.3.6) for the coefficients of the Lyapunov candidate function L we get

$$\begin{aligned}\psi_1 &= H_3,\\ \psi_2 &= \frac{C(\omega)\Lambda\eta}{\mu} + \sigma.\end{aligned}$$

Now substituting the constants ψ_1 and ψ_2 into Equation (2.3.5) gives

$$\begin{aligned}\frac{dL}{dt} &\leq \left[H_3\left(\frac{C(\omega)\Lambda}{\mu} - H_1\right) + \left(\frac{C(\omega)\Lambda\eta}{\mu} + \sigma\right)H_2\right] I\\ &= \left[\frac{C(\omega)\Lambda(H_3 + \eta H_2) - \mu(H_1H_3 - \sigma H_2)}{\mu(H_1H_3 - \sigma H_2)}\right](H_1H_3 - \sigma H_2)I\\ &= (\mathcal{R}_0 - 1)(H_1H_3 - \sigma H_2)I\\ &= H_1H_3(\mathcal{R}_0 - 1)(1-\phi)I.\end{aligned}$$

Therefore, it follows that $\frac{dL}{dt} < 0$ whenever $\mathcal{R}_0 < 1$ and $\frac{dL}{dt} = 0$ if and only if either $I = 0$ or $\mathcal{R}_0 = 1$. The largest non-negative compact invariant subset of the set

$$\left\{S(t), I(t), T(t), A(t) \in \Omega : \frac{dL}{dt} = 0\right\}$$

if $\mathcal{R}_0 \leq 1$ is E_0. Hence by the Lyapunov LaSalles's Invariance Principle defined in LaSalle (1976), the DFE is globally asymptotically stable in Ω if $\mathcal{R}_0 < 1$. □

2.4 Existence of the endemic equilibrium

2.4.1 Lemma. Whenever $\mathcal{R}_0 > 1$, then the proposed model system (2.1.3) has a unique endemic equilibrium given by

$$E_1 = (S^\star, I^\star, T^\star, A^\star)\,.$$

Proof. To obtain the disease-persistent steady state of the model (2.1.3) in terms force of the infection and the model parameters, we set the right-hand side of the model to zero, that is

$$\left.\begin{aligned}&\Lambda - (C(\omega)I^\star + C(\omega)\eta T^\star + \mu)S^\star = 0,\\ &(C(\omega)I^\star + C(\omega)\eta T^\star)S^\star - H_1I^\star + \sigma T^\star = 0,\\ &H_2I^\star - H_3T^\star = 0,\\ &\rho_1I^\star + \rho_2T^\star - H_4A^\star = 0,\end{aligned}\right\} \tag{2.4.1}$$

where

$$H_1 = \mu + (1-\omega)\theta + \rho_1, \quad H_2 = (1-\omega)\theta, \quad H_3 = \mu + \sigma + \rho_2 \quad \text{and} \quad H_4 = \mu + \delta.$$

We compute the endemic equilibrium by solving the simultaneous equations in system (2.4.1) for $S^\star, I^\star, T^\star$ and $A^\star$.

Now from the third equation in the system (2.4.1), we have

$$T^\star = \frac{H_2}{H_3} I^\star. \tag{2.4.2}$$

Then by substituting (2.4.2) into the fourth equation in system (2.4.1) gives

$$A^\star = \left(\frac{H_3\rho_1 + \rho_2 H_2}{H_4 H_3} \right) I^\star.$$

Similarly, substituting (2.4.2) into the second equation in system (2.4.1), we obtain

$$I^\star \left[\left(C(\omega) + \frac{C(\omega)\eta H_2}{H_3} \right) S^\star - H_1 + \frac{\sigma H_2}{H_3} \right] = 0. \tag{2.4.3}$$

Solving equation (2.4.3) for $I^\star$ and $S^\star$, we get

$$I^\star = 0 \quad \text{(corresponds to the disease-free equilibrium)}$$

and

$$\begin{aligned} S^\star &= \frac{H_1 H_3 - \sigma H_2}{C(\omega)H_3 + C(\omega)\eta H_2} \\ &= \frac{\Lambda}{\mu \mathcal{R}_0}. \end{aligned} \tag{2.4.4}$$

Now we substituting Equations (2.4.4) and (2.4.2) into the first equation in system (2.4.1) yields

$$\begin{aligned} \Lambda - \left(C(\omega) I^\star + \frac{C(\omega)\eta H_2}{H_3} I^\star + \mu \right) \left(\frac{H_1 H_3 - \sigma H_2}{C(\omega)H_3 + C(\omega)\eta H_2} \right) &= 0 \\ \Lambda - \left(C(\omega) I^\star + \frac{C(\omega)\eta H_2}{H_3} I^\star + \mu \right) \frac{\Lambda}{\mu \mathcal{R}_0} &= 0 \\ \mu \mathcal{R}_0 - \left(C(\omega) I^\star + \frac{C(\omega)\eta H_2}{H_3} I^\star + \mu \right) &= 0 \\ I^\star = \frac{\mu H_3 (\mathcal{R}_0 - 1)}{C(\omega)H_3 + C(\omega)\eta H_2}. \end{aligned} \tag{2.4.5}$$

Therefore using Equation (2.4.5), we have

$$T^\star = \frac{\mu H_2 H_3 (\mathcal{R}_0 - 1)}{C(\omega)H_3(H_3 + \eta H_2)} \quad \text{and} \quad A^\star = \left(\frac{(H_3\rho_1 + \rho_2 H_2)(\mu H_3(\mathcal{R}_0 - 1))}{C(\omega)H_3 H_4 (H_3 + \eta H_2)} \right).$$

It can be observed that whenever $\mathcal{R}_0 = 1$, then the disease-persistent equilibrium becomes the disease-free equilibrium. Similarly, the results indicate that the disease-persistent equilibrium is unique and exists only and only if $\mathcal{R}_0 > 1$. □

2.5 Global stability of endemic steady state

2.5.1 Theorem. *The disease-persistent equilibrium (E_1) of the model is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. As noted earlier, N approaches $\frac{\Lambda}{\mu}$ as t approaches ∞. So from Equation (2.1.1), we have the relation

$$S = \frac{\Lambda}{\mu} - I - T - A. \tag{2.5.1}$$

Substituting (2.5.1) in the equations that contribute to HIV infection in model (2.1.3) yields the limiting system

$$\left.\begin{aligned} \tfrac{dI}{dt} &= \lambda\left(\tfrac{\Lambda}{\mu} - I - T - A\right) - H_1 I - \sigma T, \\ \tfrac{dT}{dt} &= H_2 I - H_3 T. \end{aligned}\right\} \tag{2.5.2}$$

Expressing system (2.5.2) in terms of the force of infection, we get

$$\left.\begin{aligned} \tfrac{dI}{dt} &= (C(\omega)I + C(\omega)\eta T)\left(\tfrac{\Lambda}{\mu} - I - T - A\right) - H_1 I - \sigma T, \\ \tfrac{dT}{dt} &= H_2 I - H_3 T. \end{aligned}\right\} \tag{2.5.3}$$

Now applying the Dulac's multiplier $\pi_2(I,T) = \frac{1}{IT}$ as used in Mukandavire et al. (2009) and Omondi et al. (2018a), then we have

$$\begin{aligned} \partial\pi_2 &= \frac{\partial}{\partial I}\left[\frac{(C(\omega)I + C(\omega)\eta T)}{IT}\left(\frac{\Lambda}{\mu} - I - T - A\right) - \frac{H_1}{T} + \frac{\sigma}{I}\right] + \frac{\partial}{\partial T}\left[\frac{H_2}{T} - \frac{H_3}{I}\right] \\ &= \frac{\partial}{\partial I}\left[-\frac{C(\omega)}{T}I + \frac{C(\omega)\eta\Lambda}{I\mu} - \frac{C(\omega)\eta T}{I} - \frac{C(\omega)\eta A}{I} + \frac{\sigma}{I}\right] + \frac{\partial}{\partial T}\left[\frac{H_2}{T}\right] \\ &= -\frac{C(\omega)}{T} - \frac{C(\omega)\eta\Lambda}{\mu I^2} + \frac{C(\omega)\eta T}{I^2} + \frac{C(\omega)\eta A}{I^2} - \frac{\sigma}{I^2} - \frac{H_2}{T^2} \\ &= -\left[\frac{C(\omega)}{T} + \frac{C(\omega)\eta}{I^2}\left(\frac{\Lambda}{\mu} - (T+A)\right) + \frac{\sigma}{I^2} + \frac{H_2}{T^2}\right]. \end{aligned}$$

We note that $\partial\pi_2 < 0$ since $\frac{\Lambda}{\mu} \geq (T+A)$ in Ω. Therefore, by the Dulac's criterion, no closed or periodic orbits exist in Ω. Then according to the Poincare-Bendixon Theorem, all the solutions of system (2.5.3) starting in Ω remains in Ω for all time t, since the endemic steady state exists if $\mathcal{R}_0 > 1$ and Ω is positively invariant (Perko, 2013). Additionally, having no periodic orbits in Ω means that the unique disease-persistent steady state of model system (2.1.3) is globally asymptotically stable if $\mathcal{R}_0 > 1$.

□

3. Numerical Simulation Results and Discussion

In this section, we present results of the simulations for the model system (2.1.3). We will estimate parameter values and hypothetically choose the initial population values. We will carry out sensitivity analysis to identify model parameters that highly influences the reproduction number $\mathcal{R}_0$. We will also solve model system (2.1.3) for DFE and disease-persistent equilibrium to confirm if its results are consistent with the analytic results obtained in stability analysis in Sections 2.3 and 2.4. We will also look at how selected parameters in the model influences the reproduction number $\mathcal{R}_0$.

3.1 Estimation of parameter values

We need to determine the values of model parameters to carry out simulations and draw vital information and insights from the system. To begin with, we estimate the values of parameters basing on the existing literature which agrees with biological facts and experimental data.

We approximate the rate at which population is recruited into susceptible class to be $\Lambda = 0.02N$ and natural death rate to be $\mu = \frac{1}{63}$. The Table 3.1 below shows the estimated values for the other parameters of model system (2.1.3).

Parameter	**Estimate value/year**	Source
δ	0.09	Estimated
ω	$0 \leq \omega \leq 1$	Estimated
θ	$0 \leq \theta \leq 1$	Estimated
ρ_1	0.1	Estimated
ρ_2	0.05	Estimated
σ	$0 \leq \sigma \leq 1$	Estimated
η	$0 \leq \eta \leq 1$	Estimated
ε	7	Estimated
K	9	Estimated
β_{max}	$0.000000001 \leq \beta_{max} \leq 0.00000001$	Estimated

Table 3.1: Estimation of parameter values for system (2.1.3).

3.2 Sensitivity analysis

Sensitivity analysis is a technique that is used to determine how epidemiological quantities such as disease prevalence and reproduction number respond to variations in parameter values. For instance, through sensitivity analysis we can tell which parameters have high effect on reproduction number and target them to reduce HIV transmission. In this project, it is crucial to evaluate the robustness of the system predictions to the estimated parameter values through sensitivity analysis since the approximation of parameters were associated with uncertainties. The model parameters which are most sensitive to the reproduction number contributes largely to the spread of the disease. Therefore, carrying out sensitivity or uncertainty analysis can help in identifying the parameters to target in the intervention strategies since it provides information on the role played by different parameter values in the dynamics of HIV epidemic.

We employ the concept of elasticity (normalized sensitivity index) to examine the sensitivity of $\mathcal{R}_0$ with respect to changes in its parameters as described in Hamby (1994), Kalula (2011), Rodrigues et al. (2013), Omondi et al. (2018d) and Omondi et al. (2018a). It important to note that the higher the absolute values of the sensitivity index of $\mathcal{R}_0$ with respect to the parameter, the bigger the impact that the parameter has on $\mathcal{R}_0$.

3.2.1 Definition. If $\mathcal{R}_0$ is differentiable with respect to each of its parameters, then the expression for normalized sensitivity index $(S_\xi^{\mathcal{R}_0})$ of $\mathcal{R}_0$ to the parameter ξ, is given by

$$S_\xi^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \xi} \times \frac{\xi}{\mathcal{R}_0}. \tag{3.2.1}$$

Note that $\frac{\xi}{\mathcal{R}_0}$ is introduced to remove the effect of units in $S_\xi^{\mathcal{R}_0}$.

Additionally, in (3.2.1) we assume that the contribution of partial derivatives of higher order are negligible and no correlation exist between the parameters. Now applying the explicit sensitivity index formula provided in Equation (3.2.1) with model parameters values given in Table 3.1, we get sensitivity indices for each parameter in $\mathcal{R}_0$ which are shown in the Table 3.2.

Parameter	Sensitivity index
μ	-1.1385
ω	+1.1031
Λ	+1.0000
β_{max}	+1.0000
ε	+0.9651
K	-0.6894
θ	-0.5520
ρ_2	-0.3001
ρ_1	-0.2724
σ	+0.2631
η	+0.1324

Table 3.2: Sensitivity index of $\mathcal{R}_0$

The sensitivity indices in Table 3.2.1 are arranged according to their magnitude (absolute values) in a descending order. Similarly, it is important to note that increasing the model parameters with the positive and negative sensitivity indices increase and decrease reproduction number $\mathcal{R}_0$ respectively.

We can observe from Table 3.2.1 that the most sensitive parameters to $\mathcal{R}_0$ are level of interference ω, recruitment rate Λ and contact rate β_{max}. For $\omega = +1.1031$ implies that a 11.031% increase (decrease) in ω causes $\mathcal{R}_0$ to increase (decrease) by the same rate. Similarly, $\Lambda = +1.0000$ tells us that a 10% increase (decrease) in Λ makes $\mathcal{R}_0$ to increase (decrease) by 10%. The sensitivity analysis results indicate that $\mathcal{R}_0$ increases with increase in ω. We can also observe as we increase the rate of treatment θ, $\mathcal{R}_0$ also decreases. From the given model parameters, we focus on θ, σ and η and we can observe that the disease progression can be lowered by increasing the rate of treatment θ, reducing drop out rate σ and ensuring that treatment is very effective by lowering the value of η.

3.3 Simulations results

In this section, we use Matlab to solve Equations in the model system (2.1.3) and simulate the results to verify theoretical conclusions drawn in Sections 2.3 and 2.4 regarding stability analysis of the model. We also vary the parameters to understand the impact of treatment on HIV transmission dynamics in presence of interference. For illustrative purposes, we consider a hypothetical total population of 18200000 individuals, with the initial conditions $S(0) = 12000000, I(0) = 650000, T(0) = 5500000$ and $A(0) = 50000$.

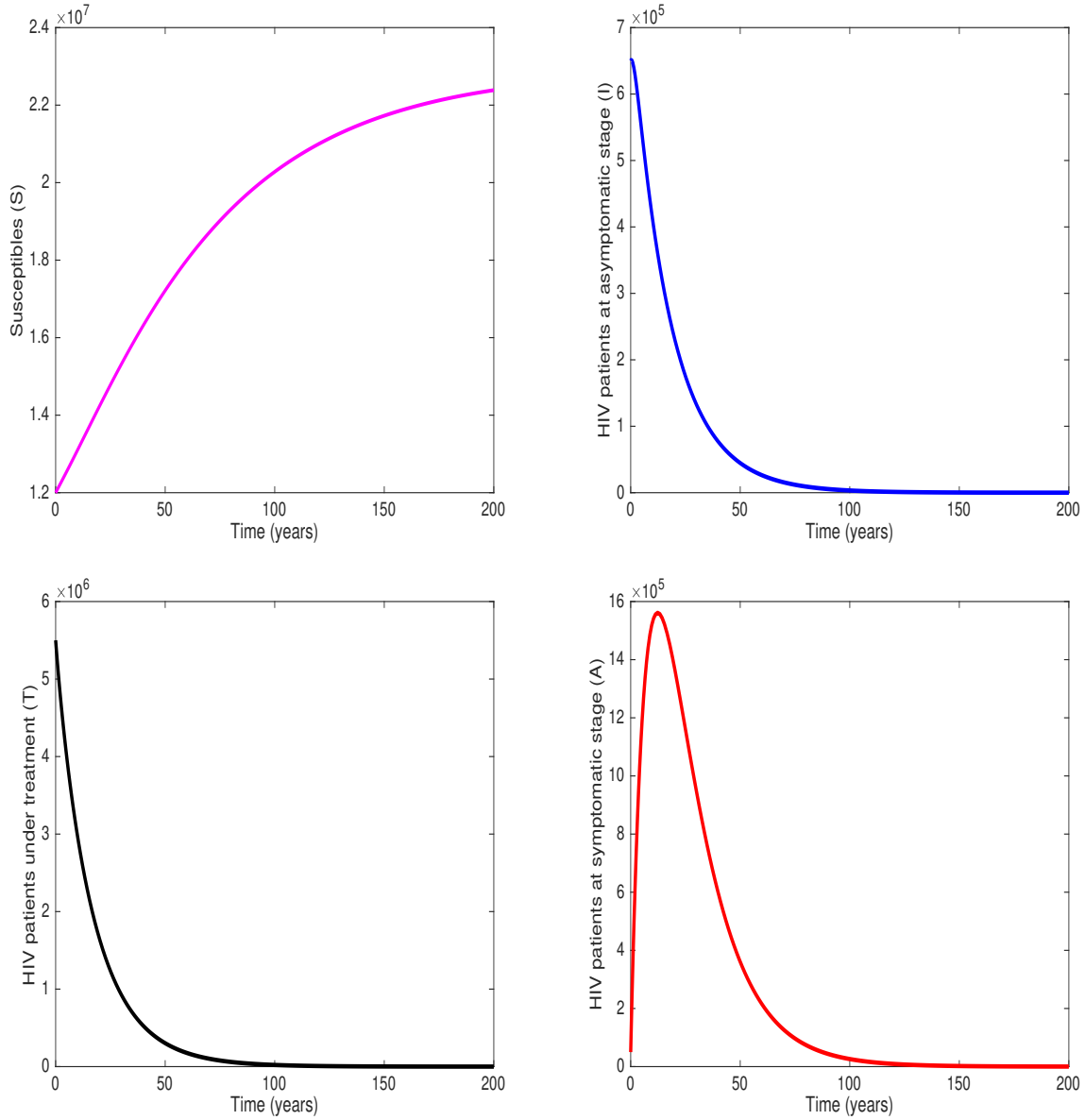

Figure 3.1: Indicates the results of simulations at DFE for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \theta = 0.6, \sigma = 0.06, \eta = 0.04, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \delta = 0.09$ and $\beta_{max} = 0.00000002$. Here the value of reproduction number is $\mathcal{R}_0 = 0.4473$.

Figure 3.1 presents very exciting results, we can observe that the disease can be eliminated from the entire population after sometime when $\mathcal{R}_0 < 1$. The populations of HIV-infected individuals (I), infected under treatment (T) and those in full-blown AIDS stage declines to zero with time. On contrary, we can observe that the susceptible population S keeps increasing with time until it approaches a constant value of $\frac{\Lambda}{\mu}$. This is consistent with the theoretical results that we obtained in stability analysis, it agrees with Theorem 2.3.2 in that the HIV infection may die out in approximately 100 years if appropriate control measures that ensures that the reproduction number $(\mathcal{R}_0)$ is kept below unity are undertaken.

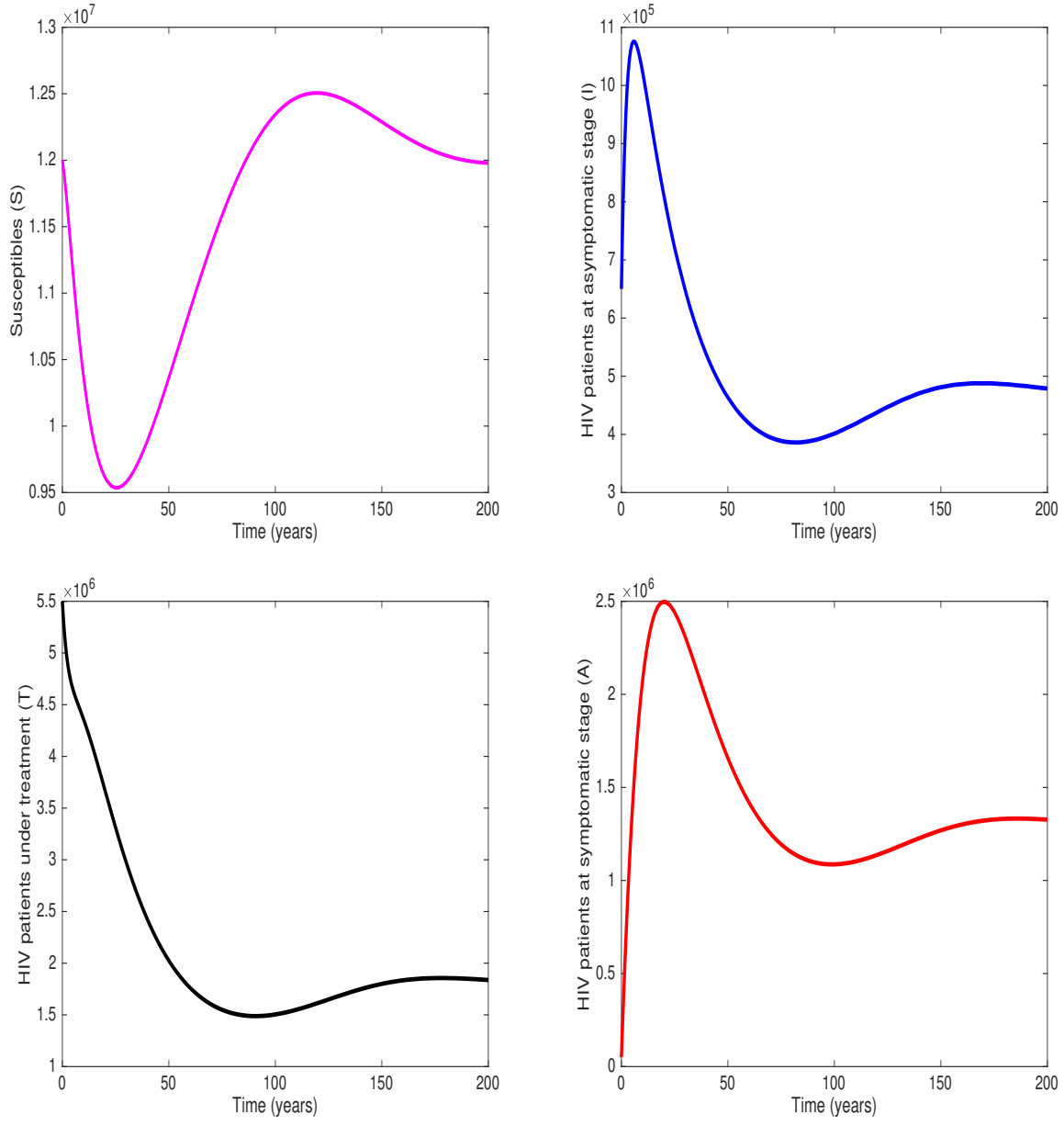

Figure 3.2: Shows the result of simulations for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \theta = 0.6, \sigma = 0.06, \eta = 0.04, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \delta = 0.09$ and $\beta_{max} = 0.000000085$. Here the value of reproduction number $\mathcal{R}_0 = 1.9010$.

The graphical representation in Figure 3.2 also concurs with our stability analysis results in Section 2.4. We observe that initially there is a short-term increase in the population of HIV patients at asymptomatic stage (I) and infected individuals at AIDS stage (A), but after sometime all compartments with the infections decline and stabilizes at different heights. This indicates that the model system (2.1.3) levels off at disease-persistent steady state as stipulated in Theorem 2.5.1. Therefore, that HIV epidemic persists in the community when $\mathcal{R}_0 > 1$ hence verifying the fact that the disease-persistent equilibrium is globally asymptotically stable $\mathcal{R}_0 > 1$.

3.4 Impact of model parameters on the reproduction number $\mathcal{R}_0$

It is important to investigate how reproduction number is influenced by some model parameters since it provides vital information regarding the spread of the infection. To start with, we fix all the other model parameter values and vary reproduction number $\mathcal{R}_0$ with the factors that hinder interventions for different values of the relative infectivity of T with respect to I as shown in Figure 3.3.

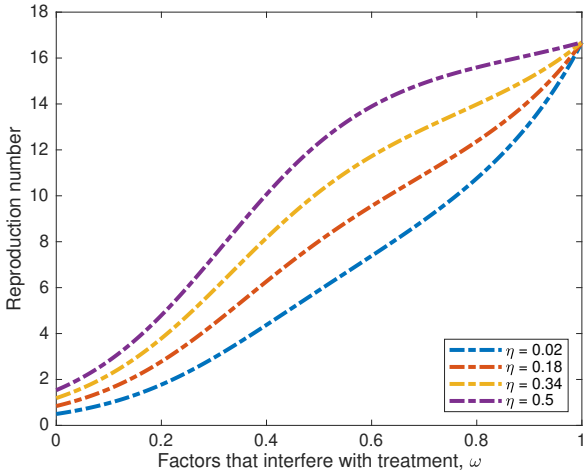

Figure 3.3: Shows how reproduction number $\mathcal{R}_0$ evolves with the level of interference ω for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \theta = 0.6, \sigma = 0.06, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \delta = 0.09, \beta_{max} = 0.000000085$ with four values of η, 0.02, 0.18, 0.34, and 0.5.

Figure 3.3 highlights some very interesting results on the relationship between the reproduction number $\mathcal{R}_0$ and the level of interference ω for different values of η. We can observe that if treatment is very effective in reducing the infection, that is for low values of η, then the rate at which $\mathcal{R}_0$ increases is lower compared to when η is high. Therefore, we can note that even with increased interference, as long as treatment is effective the disease progression is low. However, if treatment has a low impact to disease transmission then increased interference has increased propensity to raise the value of $\mathcal{R}_0$. So we need an effective treatment regime even if the inference is high.

Figure 3.4 provides crucial information about the impact of interference on disease progression for different values of drop out rate σ. If treatment is effective, we note that if drop out rate is increased, the reproduction number also increases. So, a reduction in the number of drop out cases is essential even in the presence of interference. On the contrary, if η is high indicating that the treatment is less effective then the changes in the rates of drop out does not significantly change the growth of $\mathcal{R}_0$ as

the factors that hinder interventions increase, in fact $\mathcal{R}_0$ increases significantly even with low drop out rates as shown in Figure 3.5. Therefore, effective treatment (low value of η) is essential in the presence interference.

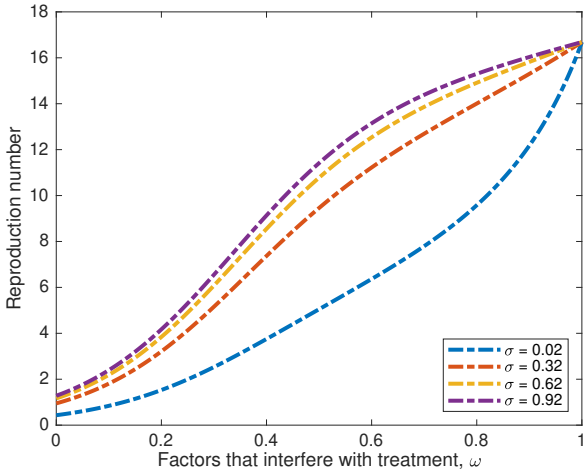

Figure 3.4: Shows how reproduction number $\mathcal{R}_0$ evolves with the level of interference ω for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \theta = 0.6, \sigma = 0.06, \eta = 0.04, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \delta = 0.09, \beta_{max} = 0.000000085$ with four values of σ, 0.02, 0.32, 0.62, and 0.92.

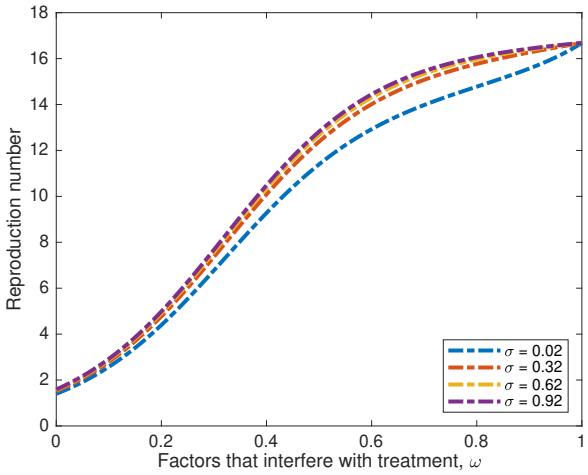

Figure 3.5: Shows how reproduction number $\mathcal{R}_0$ evolves with the level of interference ω for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \theta = 0.6, \sigma = 0.06, \eta = 0.45, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \delta = 0.09, \beta_{max} = 0.000000085$ with four values of σ, 0.02, 0.32, 0.62, and 0.92.

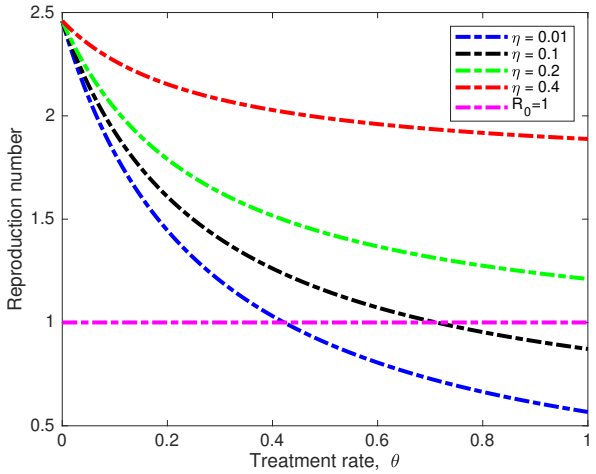

Figure 3.6: Shows how reproduction number $\mathcal{R}_0$ evolves with the treatment rate θ for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.2, \sigma = 0.06, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \beta_{max} = 0.00000004$ with four values of η, 0.01, 0.1, 0.2, and 0.4.

Figure 3.6 shows that when $\eta = 0.01$ and $\eta = 0.1$ then we need treatment rates to be above 0.45 and 0.75 respectively for its effect to be essential in reducing the spread of HIV virus. In addition, the graphical representation also illustrates that the disease progression decreases at a lower rate when η is high. Therefore, treatment is effective in controlling new HIV infections.

To get a better understanding on how rate of treatment, level of interference and drop out rates the impact reproduction number $\mathcal{R}_0$, we plot contours which shows how $\mathcal{R}_0$ changes with two parameters simultaneously.

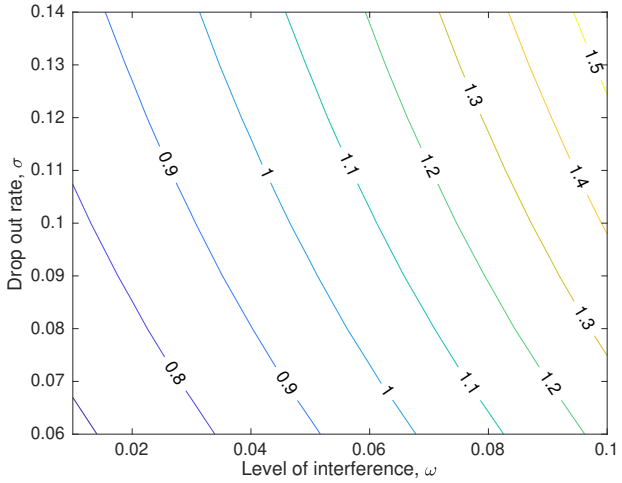

Figure 3.7: The diagram shows how drop out rate σ, and interference level ω, influences the reproduction number $\mathcal{R}_0$ for the following values of parameters: $\Lambda = 364000, \mu = \frac{1}{63}, \theta = 0.4, \eta = 0.04, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \beta_{max} = 0.00000008$.

Figure 3.7 illustrates the relationship between interference level and the drop out rates. We can note

from the graphical representation as the interference level and drop out rate increase then $\mathcal{R}_0$ also increases. The disease progresses much faster when both the level of interference and drop out rates are high. Therefore, if treatment is effective as indicated by the value of η then it is important to minimize the drop out cases as much as possible even in presence of interference.

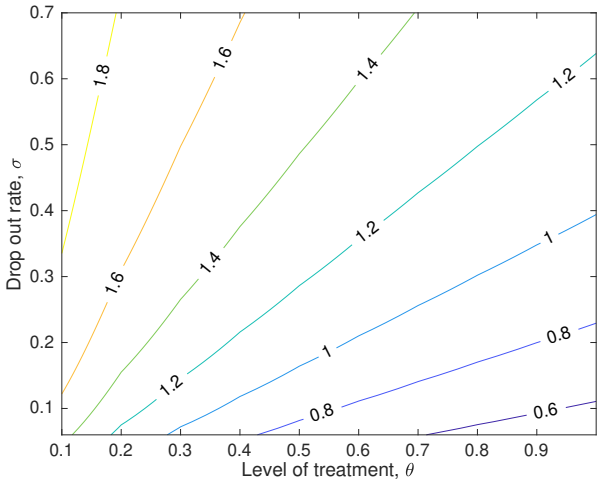

Figure 3.8: Shows contour plot shows how drop out rate σ, and treatment rate θ, influences the reproduction number $\mathcal{R}_0$, for the following parameter values: $\Lambda = 364000, \mu = \frac{1}{63}, \omega = 0.03, \eta = 0.04, \rho_1 = 0.1, \rho_2 = 0.05, K = 9, \varepsilon = 7, \beta_{max} = 0.000000085$.

Figure 3.8 tells us that increase in treatment rate has the greatest potential to lower disease progression since $\mathcal{R}_0$ values decrease much faster as the rate of treatment increases. The graphical description also indicates that reducing the drop out rate can only be effective in controlling HIV transmission. Therefore our graphical simulation results reiterate the significance of very effective treatment regime even in presence of interference to reduce the proliferation of HIV infection.

4. Conclusion

In this research project, we proposed and analysed a mathematical model for HIV to further understand the HIV infection dynamics. We discussed the mathematical features of the system which include: boundedness and positivity of solutions, threshold value of HIV epidemic and stability of the equilibria states. We determined the basic properties of the model and proved that all solutions of the system are non-negative and bounded. We also noted that the reproduction number of the model has two components, contribution of infected individuals not in treatment, $\mathcal{R}_I$ and that of those under medication, $\mathcal{R}_T$.

We used an appropriate Lyapunov candidate function and LaSalle invariance principle to establish the global stability of disease-free equilibrium. We found that when the threshold value of the epidemic is less that unity, that is $\mathcal{R}_0 < 1$, then the disease-free steady state of the system is locally and globally attractive. This implies that when $\mathcal{R}_0 < 1$, then the cases of new HIV infections generated is less than the number of infected individuals spreading the disease meaning that the epidemic can be eliminated from the community. Therefore, HIV/AIDS pandemic can be controlled effectively if intervention strategies are targeted towards minimizing the value of $\mathcal{R}_0$ to less than unity. However, whenever $\mathcal{R}_0 > 1$, the disease-free equilibrium becomes unstable. In addition, we showed that the system has a unique disease-persistent equilibrium which is globally asymptotically stable whenever $\mathcal{R}_0 > 1$.

Moreover, we observed that presence of interference fuels the spread of HIV/AIDS and a worst case scenario may be experienced when level interference is high and drop out from treatment is high. We investigated the effect of model parameters on $\mathcal{R}_0$ and found that interference have effect of reducing the uptake of treatment and increasing the rates of drop-out. Therefore, scaling-up of effective HIV treatment and lowering drop out rates even in presence of interference is crucial in reducing onward transmission of HIV/AIDS infections.

We acknowledge that the presented model may have some shortfalls. For instance, we considered treatment alone as a control mechanism for HIV infection. However, additional of more controls such as HIV screening as well as other educational programs will definately enhance the understanding of HIV/AIDS pandemic. Furthermore, taking into account other HIV transmission routes like mother-to-baby during birth or breastfeeding, infected blood transfusions, sharing piercing equipment with infected individuals will provide more information regarding the transmission of HIV. Nevertheless, the results obtained from the proposed model provides adequate insights to describe and understand the spread of HIV even in presence of interference.

Acknowledgements

Special thanks goes to the Almighty God for His guidance, protection and strength throughout the essay period. To my supervisor Professor Farai Nyabadza, I am extremely thankful for your support, guidance and the sacrifices that you made to make this project a success, your expertise was of great help. I would also like to express my sincere appreciation to AIMS administration for giving me an opportunity to pursue a Masters Degree. Not forgetting my essay tutor Dr. Kenneth Dadedzi, thanks so much for your support and wise counsel. My profound gratitude also goes to the entire AIMS fraternity: Lecturers, IT department, facilities management, tutors and my colleagues for their support in one way or another. Lastly, I would like to acknowledge my parents, siblings and friends for their prayers, unequivocal support and encouragements.

References

Birger, R. B., Hallett, T. B., Sinha, A., Grenfell, B. T., and Hodder, S. L. Modeling the impact of interventions along the HIV continuum of care in Newark, New Jersey. *Clinical Infectious Diseases*, 58(2):274–284, 2013.

DeJesus, E. X. and Kaufman, C. Routh-hurwitz criterion in the examination of eigenvalues of a system of nonlinear ordinary differential equations. *Physical Review A*, 35(12):5288, 1987.

Hamby, D. A review of techniques for parameter sensitivity analysis of environmental models. *Environmental Monitoring and Assessment*, 32(2):135–154, 1994.

Huo, H.-F. and Chen, R. Stability of an HIV/AIDS treatment model with different stages. *Discrete Dynamics in Nature and Society*, 2015.

Januaris Saint Fores (2018). 10 major factors that contribute to the spread of HIV/AIDS in the developing world. https://owlcation.com/stem/What-Factors-Contribute-to-the-Spread-of-HIVAIDS-in-Kenya, Accessed April 2019.

Kalula, A. S. *Modelling the dynamics of methamphetamine abuse in the Western Cape*. PhD thesis, Stellenbosch: University of Stellenbosch, 2011.

Kharsany, A. B. and Karim, Q. A. HIV infection and AIDS in sub-Saharan Africa: current status, challenges and opportunities. *The Open AIDS Journal*, 10:34, 2016.

Kim, S. B., Yoon, M., Ku, N. S., Kim, M. H., Song, J. E., Ahn, J. Y., Jeong, S. J., Kim, C., Kwon, H.-D., Lee, J., et al. Mathematical modeling of HIV prevention measures including pre-exposure prophylaxis on HIV incidence in South Korea. *Public Library of Science*, 9(3):e90080, 2014.

LaSalle, J. P. *The stability of dynamical systems*, volume 25. Siam, 1976.

Luo, S., Han, L., Lu, H., Dou, Z., Tao, Q., Khoshnood, K., Wu, Z., and Xu, J. Evaluating the impact of test-and-treat on the HIV epidemic among MSM in China using a mathematical model. *Public Library of Science*, 10(6):e0126893, 2015.

Malunguza, N., Mushayabasa, S., Chiyaka, C., and Mukandavire, Z. Modelling the effects of condom use and antiretroviral therapy in controlling HIV/AIDS among heterosexuals, homosexuals and bisexuals. *Computational and Mathematical Methods in Medicine*, 11(3):201–222, 2010.

Mukandavire, Z., Gumel, A. B., Garira, W., and Tchuenche, J. M. Mathematical analysis of a model for HIV-Malaria co-infection. 2009.

Nyabadza, F., Mukandavire, Z., and Hove-Musekwa, S. Modelling the HIV/AIDS epidemic trends in South Africa: Insights from a simple mathematical model. *Nonlinear Analysis: Real World Applications*, 12(4):2091–2104, 2011.

Okosun, K., Makinde, O., and Takaidza, I. Impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives. *Applied Mathematical Modelling*, 37(6):3802–3820, 2013.

Omondi, E., Mbogo, R., and Luboobi, L. Mathematical modelling of the impact of testing, treatment and control of HIV transmission in Kenya. *Cogent Mathematics & Statistics*, 5(1):1475590, 2018a.

Omondi, E., Mbogo, R., and Luboobi, L. Mathematical analysis of sex-structured population model of HIV infection in Kenya. *Letters in Biomathematics*, 5(1):174–194, 2018b.

Omondi, E., Mbogo, R., and Luboobi, L. Modelling the trend of HIV transmission and treatment in Kenya. *International Journal of Applied and Computational Mathematics*, 4(5):123, 2018c.

Omondi, E. O., Orwa, T. O., and Nyabadza, F. Application of optimal control to the Onchocerciasis transmission model with treatment. *Mathematical Biosciences*, 297:43–57, 2018d.

Perko, L. *Differential equations and dynamical systems*. Springer Science & Business Media, 2013.

Rodrigues, H. S., Monteiro, M. T. T., and Torres, D. F. Sensitivity analysis in a dengue epidemiological model. In *Conference Papers in Science*. Hindawi, 2013.

Safiel, R., Massawe, E. S., and Makinde, O. Modelling the effect screening and treatment on transmission of HIV/AIDS infection in a population. *American Journal of Mathematics and Statistics*, 2(4):75–88, 2012.

Su, Z., Dong, C., Li, P., Deng, H., Gong, Y., Zhong, S., Wu, M., Ruan, Y., Qin, G., Yang, W., et al. A mathematical modeling study of the HIV epidemics at two rural townships in the Liangshan Prefecture of the Sichuan Province of China. *Infectious Disease Modelling*, 1(1):3–10, 2016.

Thiébaut, R. and May, M. T. Mathematical modelling of HIV prevention intervention. *AIDS*, 27(3): 475–476, 2013.

UNAIDS (2018). UNAIDS DATA 2018. UNAIDS, https://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf., Accessed April 2019.

Van den Driessche, P. and Watmough, J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1-2):29–48, 2002.

WHO (2018). HIV/AIDS-Global Health Observatory (GHO) data. WHO, http://www.who.int/gho/hiv/en/., Accessed April 2019.