MATHEMATICAL MODELING OF DUAL PROTECTION AND ART ADHERENCE FOR A HIGH RISK HIV POPULATION

BY

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Declaration

This thesis is my own work and has not been presented for a degree award in any other institution.

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This thesis has been submitted for examination with our approval as the university supervisors.

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Dedication

This thesis is dedicated to my mother Luciana Ayako Fanuel

Abstract

The spread of HIV/AIDS remains a major concern to public health enthusiasts world over. In spite of interventions such as medical male circumcision, condom use, treatment using Antiretroviral Therapy (ART), as well as use of Pre-Exposure Prophylaxis, the number of new HIV/AIDS infections in Sub-Sahara Africa remains high. This may be attributed to factors such as PrEP failure and inconsistency in condom use especially among the high risk group. The effectiveness of condoms depends on quality and proper use, while the success of ART largely depends on adherence. Mathematical models for these interventions exist in literature. However the challenges associated with the use of a single approach consequently necessitate the use of dual protection for better outcome against infection especially for the high risk population. In this study, a mathematical model for dual protection, incorporating PrEP and Condom use, and ART adherence is formulated, based on a system of ordinary differential equations and analyzed. The results obtained from stability analysis indicate that provided the basic reproductive number (R_0) is less than unity, the disease free equilibrium point is both locally and globally asymptotically stable, while provided that R_0 is greater than unity, the endemic equilibrium point is locally asymptotically stable. Sensitivity analysis showed that the most sensitive parameter is β_1, the mean contact rate with undiagnosed infectives. Numerical simulation results revealed that dual protection and ART adherence are key in the fight against the spread of HIV among the high risk population. These findings will help in reducing the number of new HIV infections as well as lower the infectivity of those who are already infected.

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Introduction

1.1 Background of the study

Numerous efforts have been made in an attempt to control the spread of HIV, with the aim of reducing its effects. According to the UNAIDS fact sheet 2019, at least 1.7 million new HIV infections were reported by the end of the year 2018 [18]. This in turn calls for the need to protect those at high risk from being infected by the virus. Scientific as well as public health interventions such as testing and counseling, circumcision, use of PrEP (Pre-Exposure Prophylaxis), PeP (Post-Exposure Prophylaxis), condom use, and antiretroviral therapy have been proposed and utilized in an attempt to achieve this objective. The choice of a given prevention measure depends on its proven level of success.

Traditional methods such as medical male circumcision, condom use, abstinence, as well as behaviorial and risk awareness programs remain the first line of defense among heterosexuals at high risk of contracting the HIV virus [11]. However, these methods may not be applicable to high

risk populations such as commercial sex workers, who often fall prey to their clients who use threats, or financial powers to influence their decision to use protection when engaging in sexual acts. In this case, circumcision, and or abstinence may not be adequately relied upon to prevent such a group from being infected. Consistent use of condoms can result to 80% reduction in HIV incidence among the heterosexual population [2], while the effectiveness of condom use for men who have sex with men is 70% [3]. Here, consistent use has been defined as use in every heterosexual act. In the event of serodiscordant couples, or when one is under substance abuse, or during oral sex, condom use may not be a viable alternative. Proper use (correctly and consistently) as well as quality concerns have been directly attributed to the success of this approach.

In 2012, the U.S Food and Drug Administration (FDA) approved the use of Truvada for PrEP as an oral pill taken once a day, which works by preventing the virus from making several more copies of itself in one's body [19]. Numerous efficacy trials(by iPrEX, Partners PrEP, TDF2, e.t.c) have since been conducted to ascertain the potential of PrEP to prevent HIV infection. The iPrEX trial demonstrated that PrEP has the potential of reducing the risk of HIV infection among transgender women, bisexual men, as well as men who have sex with men [12]. Two major studies; Partners PrEP, and TDF2 demonstrated the effectiveness of PrEP among heterosexual men and women whereas the Bangkok Tenofovir study focused on injecting drug users. Out of all these studies, none displayed a 100% effectiveness [16].

Adherence has been found to be directly correlated with the effectiveness of PrEP [16]. When taken daily for seven days, there is a reduction in

the risk of HIV infection of approximately 99%, when taken for four of the days in a week, the reduction in risk of infection is 96%, while when taken for just two of the seven days of a week, there is a 76% reduction in risk of being infected [13]. Moreover, it should be noted that before one is fully protected by PrEP, it takes about 7 days of consistent use, and while stopping, one should continue using it for at least four weeks after the last significant exposure [13]. This points to lack of full protection against HIV infection by PrEP users when starting, or just after stopping its use, which calls for the need for alternative means of protection.

In the absence of adherence, which guarantees efficacy, PrEP failures have been characterized by; system failures, people failures, Doctor failures, drug failures, as well as assay failures [13]. System failures entail the lack of or limited access to PrEP as a result of unavailability, cost, or lack of awareness by people at high risk of HIV infection. People failures happen when there is inconsistent use of PrEP. Doctor failures are caused by reluctance to rule out the availability of an infection before prescribing the use of PrEP whereas assay failures may be as a result of challenges in HIV diagnosis caused by the low sensitivity of the testing equipment. Drug failures on the other hand are accompanied by resistance of PrEP by some uninfected individuals, or low efficacy although this is less likely to happen [13]. These failures expose PrEP users to the risk of HIV infection hence the need for additional protection whenever PrEP use has been utilized.

The challanges experienced when various approaches are employed in an attempt to control the spread of HIV infection in a high risk population form the basis for the need to use combinations of preventon strategies in

order to achieve maximum protection. Whereas condom use emphasizes on consistency and correct use, that is use in every heterosexual act, it is often challenging to always achieve the desired levels of proper use.For instance, when one is a victim of substance abuse, or in the absence of the consent of the other partner, or when one is out to conceive for the case of serodiscordant couples. Only 16% of the men who have sex with men reported to have used condom protection during their sexual encounters with their partners despite not knowing their HIV status [3]. The nature of storage, and date of manufacture also determine their quality. Religious as well as socio-cultural beliefs may also to some extent limit the use of condoms.

PrEP on the other hand requires high adherence levels in order to attain the desired efficacy levels. 100% adherence is less likely to be achieved since one could forget to take the drug, or may not gain access to the drug due to unavailability or the cost. In the presence of PrEP, there is the temptation for the uninfected to engage in risky behavior, which increases the chances of an infection. Therefore, for people at high risk of HIV infection, PrEP can serve as the best complement to condom use. A combination prevention approach as proposed in [9], based on proven efficacy interventions, provides one with the best opportunity to curb the spread of HIV among the high risk population.

1.2 Basic Concepts

In this section, some of the theorems and definitions of terms used in the subsequent sections of this study are given as follows.

Definition 1.2.1 (Antiretroviral Therapy(ART))

Treatment of human immunodefficiency virus (HIV) is called antiretroviral therapy. It entails taking of anti HIV drugs by persons infected by the virus with the aim of suppressing its replication.

Definition 1.2.2 (Pre-Exposure Prophylaxis (PrEP))

Refers to medicine taken by people at high risk of HIV infection to prevent them from getting infected.

Definition 1.2.3 (High Risk vs Low risk)

High risk activities entail practicing irresponsible sexual behavior such as engaging in unprotected sex, and sharing of syringes while low risk activities involve practicing safe sexual behavior, and taking of medications to reduce the risk of infection. In this study, commercial sex workers, men who have sex with men (MSM), as well as serodiscordant couples are considered to be at high risk of infection.

Definition 1.2.4 (Equilibrium)

Consider a general autonomous vector field

$$\dot{x} = f(x), x \in \mathbb{R}^n. \tag{1.1}$$

An equilibrium solution of (1.1)*, also called fixed point, steady state, or critical point, is a point* $\bar{x} \in \mathbb{R}^n$ *such that* $f(\bar{x}) = o$*. For the case of a nonautonomous vector field* $\dot{x} = f(x,t)$*, it is given as* $f(\bar{x},t) = o$ *[21].*

Definition 1.2.5 (Asymptotic Stability)

Let $\bar{x}(t)$ *be any solution of* (1.1)*. Then,* $\bar{x}(t)$ *is said to be stable if solutions starting "close" to* $\bar{x}(t)$ *at a given time remain close to* $\bar{x}(t)$ *for all later times. It is* ***asymptotically stable*** *if nearby solutions not only stay close, but also converge to* $\bar{x}(t)$ *as* $t \to \infty$ *[21].*

Definition 1.2.6 (Descartes' Rule of Signs)

The rule is used to check the number of possible real roots in a polynomial. It states that the number of positive real roots in a polynomial say $p(\lambda)$ *is the same as or less than by an even number as he number of changes in the sign of the coefficients of its terms while the number of negative real roots of* $p(\lambda)$ *is equal to the number of changes in the sign of the coefficients of the terms of* $p(-\lambda)$ *or less than this by an even number [22]. Consider a polynomial with real coefficients of the form;*

$$p(\lambda) = a_0\lambda^n + a_1\lambda^{n-1} + ... + a_{n-1}\lambda + a_n, a_i \in \mathbb{R}, a_0 \neq 0. \tag{1.2}$$

Given that $a_n, a_{n-1}, ..., a_1, a_0$ *is the sequence of coefficients of* (1.2)*, if* K *is the total number of sign changes from one coefficient to the next in the sequence, then the number of positive real roots of the polynomial is either equal to* K *or* K *minus a positive even integer. For the case of* $K = 1$*, there exists exactly one positive real root.*

Definition 1.2.7 (Routh-Hurwitz Criterion)

It states that negative trace and a positive determinant guarantee that the eigenvalues of the jacobian matrix will have negative real parts [21].

1.3 Statement of the problem

The introduction of PrEP as a preventive measure against HIV infection has been hailed as a significant milestone against the infection. However, PrEP failure is a reality and challenge that threatens the success of this venture. The effectiveness of condom use on the other hand depends on

quality, consensus between the users, and proper use. The challenges with these two preventive measures consequently necessitate the use of dual protection, for better outcomes, against infection especially for the high risk population. Efficacy levels of these preventive measures is not 100%, and thus making it difficult to completely rule out chances of an infection when the two are used, thus prompting the need for adherence to ART in the event that an infection happens.

1.4 Objectives of the study

General objective

The main objective of this study was to formulate and analyze a mathematical model with dual protection against HIV infection and ART adherence for a high risk population.

Specific objectives

The specific objectives of this research were;

(i) To formulate a mathematical model based on a system of ordinary differential equations for HIV dynamics, incorporating the use of condoms, PrEP and ART adherence.

(ii) To analyze the dynamics of the model developed in (i) above.

(iii) To numerically simulate the effect of dual protection and ART adherence in preventing the spread of HIV/AIDS infection in a high risk population.

1.5 Significance of the study

This study explores the prospects of better outcomes in the fight against HIV infection by incorporating a combination of approaches as opposed to a single approach. This in turn will make it possible to compensate the failure of one approach by the other approach, thus providing a suitable alternative for use by those at high risk of contracting the virus. The findings of this study will help in preventing new HIV infections as well as lower the infectivity of those who are already infected.

Chapter 2

Literature Review

Mathematical models play an important role in aiding optimal planning with regard to strategies to be employed to control and prevent the spread of infectious diseases such as HIV. This is often achieved by studying the dynamics of the disease, particularly examining its infectiousness and making forward projections based on the results obtained. A vast literature exists on mathematical models of HIV infection.

A mathematical model analyzed by Malunguza *et, al* [15], and that of Smith *et al* [3] demonstrated the level of success achieved by the use of both male and female condoms in preventing HIV infection. Their ability to prevent both heterosexual and gay population from getting infected has also been highlighted. The impact of condom use in a heterosexual population in prevention of the spread of HIV was modelled by the authors in [15]. In their findings, they suggested that the use of both male and female condoms among heterosexuals had the potential of reducing the reproductive number significantly to levels below unity. However, to achieve this, it requires high levels of compliance by the user. The study further cites that such high levels of proper and consistent use of condoms

which may guarantee better protection were unattainable. Consequently, the study suggests the use of other preventive as well as therapeutic strategies in controlling the spread of HIV. On the other hand, the effectiveness of condom use in preventing HIV infection among men who have sex with men (Gay and Bisexual) in the United States has also been studied [3]. The study highlighted the correlation between consistency of use and effectiveness. The findings indicated a 70% effectiveness when consistently used during intercourse by men with their male partners, which is slightly lower than the 80% effectiveness when used during heterosexual intercourse. However, despite receiving behavior interventions, and HIV risk awareness, most of the men reported low rates of consistency of condoms use during any sexual activity with their partners. It also points out the potential of pre-sex infection as a limitation in estimating the actual effectiveness of condoms in preventing HIV infection, which motivates the need for multiple prevention as suggested in this study.

Since its introduction, PrEP use has been found to be an effective biomedical method of preventing the spread of HIV virus [19]. However, [8] cites its implication in terms of behavior change. The study showed that there had been a decline in the use of condoms especially for commercial sex workers, despite being part of the high risk population, upon the introduction of PrEP. The result of this was an increase in the risk of infections among female sex workers who had abandoned condom use while in pursuit for PrEP. Moreover, a study by Lewis and Camley found out that the average number of sex partners per year, and improper PrEP usage can potentially minimize its long term effectiveness [11]. Dual protection will be used in this study to make up for such behavior change among

high risk individuals which may lead to a rise in infections.

A mathematical model of HIV/AIDS population dynamics with ARV treatment and PrEP in South Africa was developed and analyzed in [14]. In this model, it was found out that early treatment of those found to be infected by the virus is necessary in averting HIV related mortality whereas PrEP has the potential to prevent new HIV infections from happening. The study highlighted that these control strategies ought to be channeled towards the high risk population in South Africa, who include truckers, commercial sex workers, discordant couples, and men who have sex with men. However, stigma, lack of proper support systems and sensitization campaigns remain the greatest barriers to the success of combining PrEP and ART in managing HIV infection. By incorporating adherence to ART in addition to dual protection, this study provides extended protection options to the high risk population.

Anti-Retroviral Treatment has also been found to play a significant role in combination HIV prevention techniques [9]. The study found out that antiretroviral drugs had the potential to prevent uninfected individuals from getting infected by way of PrEP and at the same time reduce subsequent transmission of the virus among infected individuals. However, they noted that the success of ARV's is dependent on their combination with other HIV prevention techniques due to the cost and availability concerns associated with PrEP. In their model, they demonstrated the potential of a combination of PrEP and early ART treatment in reducing incidence, prevalence as well as AIDS related mortality [9].

The impact of the use of ART by incorporating adherence was analyzed in

[6], pointing out the extent to which low levels of adherence has hampered the benefits of this approach. Their study emphasizes the need for ART adherence in achieving adequate viral load suppression. This makes the infected become less infectious. By focusing on the infected, the study fails to take into account methods of preventing the susceptible from being infected. In yet another study, Tireito *et al* performed a mathematical analysis of HIV/AIDS prophylaxis treatment [7]. They found out that PrEP use is an effective defense mechanism against HIV infection among the high risk population. However, their findings were pegged on the condition that the PrEP must be taken effectively to guarantee its efficacy. It is a reality that very high adherence to PrEP uptake cannot be achieved by all, as a result of other factors such as cost and availability to those using it, and therefore condom protection serves as a complement. This study therefore models dual protection as the first line of defense by the high risk population to make up for possible PrEP failure as a result of low adherence.

A sex structured population model of HIV in Kenya was developed [4]. The results from the study showed that HIV infection was more prevalent among the female population than in their male counterpart. Furthermore, the authors studied the dynamics of the disease when PrEP is incorporated as a preventive measure against HIV infection. The results showed that PrEP would effectively limit this spread of the disease. Sensitivity analysis of their mathematical model showed that reducing the effective contact between infectives and susceptible individuals would help reduce inter-gender infection. By assuming heterosexual intercourse as the main channel of transmission of the infection, the study fails to

account for men who have sex with men (MSM), yet they too fall in the category of people at high risk of HIV infection. This study proposes a mathematical model that will incorporate the MSM thus making it valid not only in Kenya but also in countries whose population may be largely homosexual.

In this study, a mathematical model of dual protection against HIV infection by the use of condoms and PrEP, and adherence to ART treatment is formulated, while focusing on the high risk population collectively. Earlier studies as highlighted above have either narrowed down to a particular category of persons at high risk of infection, or have used a combination of prevention techniques where one technique acts as a supplement to the other. Incorporating dual protection in this study aims at reducing the number of new HIV infections especially among the high risk group, while adherence to ART targets those who are already infected with the aim of making them less infectious.

Chapter 3

Model Formulation, Analysis and Discussion

3.1 Introduction

In this chapter, a mathematical model is formulated, based on a system of ordinary differential equations, incorporating the impact of dual protection and ART adherence in preventing HIV transmission among persons at high risk of infection. Positivity and boundedness of each solution is conducted to ascertain its biological feasibility. The Next Generation Matrix approach is used to calculate the basic reproductive number for the model as outlined in [20]. The local stability of the Disease Free Equilibrium point is analyzed using the Routh-Hurwitz criteria, while Castillo-Chavez's theorem is used to investigate its global stability [1]. Descartes' Rule of Signs [22] is applied to check the existence and stability of the Endemic Equilibrium point. Sensitivity analysis is done to establish how sensitive each of the model parameters is. Numerical simulations are performed using MATLAB to predict future dynamics of the

disease.

3.2 Model Description and Formulation

In this mathematical model, the human population under study is subdivided into the classes; Susceptible, Infected, and Aids individuals. The susceptible class has further been subdivided into two compartments on the basis of degree of risk of infection. These include susceptible individuals at high risk of infection, denoted by (S_H), and those at low risk, denoted by (S_L). The high risk population incorporates mainly commercial sex workers, men who have sex with men (MSM), and HIV-Discordant couples [12]. The infected class is subdivided into two compartments; those who are unaware of their HIV status (I), and those who have been diagnosed and consequently enrolled for antiretroviral treatment (T_D). The individuals who are unaware of their HIV status may progress to the T_D compartment after successful HIV awareness campaigns that will persuade them to get tested, or when they develop HIV symptoms and consequently enroll for ART treatment. If ART treatment fails, the individual progresses to the AIDS compartment. This happens when there is lack of adherence to ART, which allows the virus to multiply, thus increasing the plasma viral load. This results in weakening of the immune system and hence the AIDS symptoms begin to manifest. The AIDS compartment, denoted by A, comprises of those who posses full blown symptoms, and are sexually inactive, they thus do not significantly contribute to the spread of the disease. Exit from the AIDS class is through natural or disease induced death. Thus, considering a population of size

$N(t)$, at a time t,

$$N(t) = S_H(t) + S_L(t) + I(t) + T_D(t) + A(t). \tag{3.1}$$

3.2.1 Model Assumptions

(i) HIV transmission within the population from the infected individuals, to the susceptible population is mainly through sexual contact. This allows for incorporation of the key intervention strategy in the model which is dual protection by use of PrEP and condoms, which may not be relevant to other forms of transmission such as mother to child, or by sharing of syringes by injecting drug users, or through blood transfusion.

(ii) Infected individuals who have developed AIDS symptoms do not contribute to the transmission of the virus due to their chronic illness condition that makes them sexually inactive.

Movement of individuals from the susceptible to infected and then to the AIDS classes is illustrated by the compartmental model shown in Figure 3.1. The following interventions have been incorporated in the model;

(a) $0 \leq \phi_1 \leq 1$ - measures PrEP effectiveness, including its awareness and proper use as a means to prevent susceptible individuals from being infected. Thus, $(1 - \phi_1)$ measures PrEP failure.

(b) $0 \leq \phi_2 \leq 1$ - measures condom effectiveness as a result of proper use, following adequate awareness campaigns and availability. Thus, $(1 - \phi_2)$ measures condom failure.

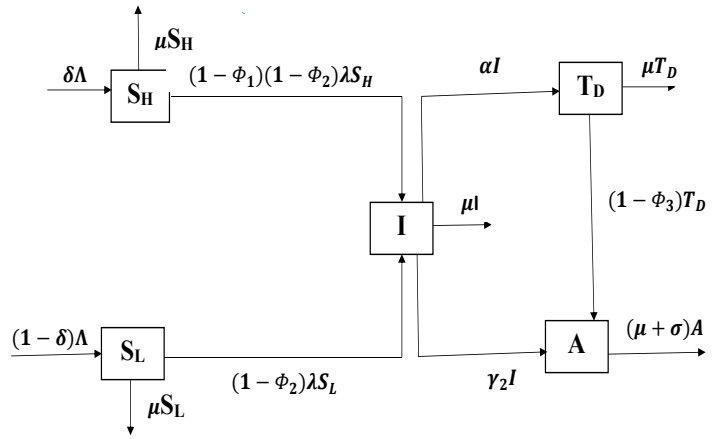

Figure 3.1: Compartmental Model.

(c) $0 \leq \phi_3 \leq 1$ - measures the efficacy of ART, including uptake with proper adherence, with the aim of reducing the plasma viral load and reconstructing the individual's immune system hence making them less infectious.

Table 3.1 presents a summary of the model variables and parameter description.

Symbol	Description
S_H	susceptible individuals at high risk of HIV infection.
S_L	susceptible individuals at low risk of HIV infection.
I	individuals who are unaware of their HIV status.
T_D	individuals who have been diagnosed and consequently enrolled for antiretrovira
A	individuals with AIDS symptoms.
Λ	constant rate of recruitment of susceptible upon becoming sexually active.
δ	proportion of susceptible individuals at high risk of infection.
$(1-\delta)$	proportion of susceptible population at low risk of HIV infection.
λ	rate of acquisition of an infection by susceptibles.It is given by; $\lambda = \left(\frac{\beta_1 I + \beta_2 T_D}{N}\right)$, where β_1, and β_2 are the mean contact rates for the susceptible individuals with I and T_D respectively.
μ	natural removal rate by death.
σ	aids induced mortality.
α	represents the proportion of infected individuals who upon being tested and found to be HIV positive,they enroll for ART treatment.
γ_2	represents the proportion of infected individuals who do not get tested hence remain undiagnosed until they begin to exhibit AIDS symptoms. Thus, γ

Table 3.1: Variables and Parameter Description

3.2.2 Model Equations

From the dynamics described above, the system (3.2) of ordinary differential equations is formulated as below

$$\begin{aligned}
\frac{dS_H}{dt} &= \delta\Lambda - (1-\phi_1)(1-\phi_2)\lambda S_H - \mu S_H \\
\frac{dS_L}{dt} &= (1-\delta)\Lambda - (1-\phi_2)\lambda S_L - \mu S_L \\
\frac{dI}{dt} &= (1-\phi_1)(1-\phi_2)\lambda S_H + (1-\phi_2)\lambda S_L - \alpha I - \gamma_2 I - \mu I \\
\frac{dT_D}{dt} &= \alpha I - (\gamma_3 + \mu) T_D \\
\frac{dA}{dt} &= \gamma_2 I + \gamma_3 T_D - (\mu + \sigma) A, \qquad (3.2)
\end{aligned}$$

where $\gamma_3 = 1 - \phi_3$.

3.3 Model Analysis

In order to give meaning to the model, and achieve the specific objectives of this study, the following approaches are utilized.

3.3.1 Well-Posedness of the Model

Analysis of the well posedness of the model is done to ensure it is both mathematically as well as biologically meaningful. This is achieved by checking for the positivity and boundedness of the solutions.

(a) Positivity of Solutions

Since the model monitors populations, the initial conditions of the system (3.2) are assumed to be non-negative such that;
$S_H(0) > 0$, $S_L(0) > 0$, $I(0) \geq 0$, $T_D(0) \geq 0$, and $A(0) \geq 0$, and the total population satisfies

$$\frac{dN}{dt} = \Lambda - \mu N - \sigma A. \tag{3.3}$$

.

Theorem 1

Let the initial conditions be $S_H(0) > 0$, $S_L(0) > 0$, $I(0) \geq 0$, $T_D(0) \geq 0$, *and* $A(0) \geq 0$. *Then the solution set* $\{S_H(t), S_L(t), I(t), T_D(t), A(t)\}$ *of the model system is positive for all* $t > 0$.

Proof. Assuming that

$$\tilde{t} = \sup\{t > 0 : S_H(0) > 0, S_L(0) > 0, I(0) > 0, T_D(0) > 0, A(0) > 0\} \in [0, t]. \tag{3.4}$$

From the first line of the system (3.2),

$$\frac{dS_H}{dt} = \delta\Lambda - (1-\phi_1)(1-\phi_2)\lambda S_H - \mu S_H = \delta\Lambda - (\lambda_* + \mu)S_H, \tag{3.5}$$

where $\lambda_* = (1-\phi_1)(1-\phi_2)\lambda$.
Thus

$$\frac{d}{dt}\left[S_H(t)\exp\left(\mu t + \int_0^t \lambda_*(u)du\right)\right] = \delta\Lambda\exp\left(\mu t + \int_0^t \lambda_*(u)du\right). \tag{3.6}$$

Hence

$$S_H(t)\exp\left(\mu t+\int_0^t\lambda_*(u)du\right)-S_H(0)=\int_0^t\delta\Lambda\exp\left(\mu t_1+\int_0^{t_1}\lambda_*(u)du\right)dt_1. \tag{3.7}$$

Therefore,

$$S_H(t)=\left[S_H(0)+\int_0^t\delta\Lambda\exp\left(\mu t_1+\int_0^{t_1}\lambda_*(u)du\right)dt_1\right]\exp\left(-\left(\mu t+\int_0^t\lambda_*(u)du\right)\right)>0. \tag{3.8}$$

Similarly, it can be shown that $S_L(t) > 0$, $I(t) \geq 0$, $T_D(t) \geq 0$, and $A(t) \geq 0$, for all $t > 0$. □

(b) Boundedness of Solutions

Theorem 2

The model solutions are bounded in the feasible region

$$\Gamma=\left\{(S_H(t),S_L(t),I(t),(T_D(t),A(t))\in\mathbb{R}_+^5:N(t)\leq\frac{\Lambda}{\mu}\right\}, \tag{3.9}$$

with the initial conditions given in Theorem (1).

Proof. From equation 3.1, $0 < S_H(t) \leq N(t), 0 < S_L(t) \leq N(t), 0 < I(t) \leq N(t), 0 < T_D(t) \leq N(t)$, and $0 < A(t) \leq N(t)$. Since the initial conditions for the system (3.2) are non-negative, then

$$\begin{aligned}\frac{dN(t)}{dt} &= \frac{dS_H(t)}{dt}+\frac{dS_L(t)}{dt}+\frac{dI(t)}{dt}+\frac{dT_D(t)}{dt}+\frac{dA(t)}{dt}\\ &= \Lambda-\mu N(t)-\sigma A.\end{aligned} \tag{3.10}$$

It then follows that,

$$\Lambda - (\mu + \sigma)N(t) \leq \frac{dN}{dt} < \Lambda - \mu N(t). \tag{3.11}$$

Thus,

$$\frac{\Lambda}{\mu + \sigma} \leq \liminf_{t\to\infty} N(t) \leq \limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}, \tag{3.12}$$

so that, $\limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}$.
Next, we show that Γ is indeed the feasible region for the model solutions. Now, from the model (3.2), it follows that $\frac{dN}{dt} \leq \Lambda - \mu N$.

$$\Rightarrow N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right). \tag{3.13}$$

In particular, $N(t) \leq \frac{\Lambda}{\mu}$ if $N(0) \leq \frac{\Lambda}{\mu}$. □
Since the solutions of the system (3.2) are non-negative for all time $t > 0$ and bounded in the region Γ, the model is mathematically well posed and biologically meaningful in the feasible region Γ. Therefore, it is sufficient to consider the dynamics of the system (3.2) in Γ.

3.3.2 Local Stability of the Disease Free Equilibrium

In this study, two types of equilibrium points are considered. They include; Disease Free Equilibrium (D.F.E), and Endemic Equilibrium (E.E). The disease free equilibrium point of the mathematical model represented by the system (3.2) is the steady state solution at which there is no HIV infection in the population under study. It symbolizes the absence of dis-

ease in the population. The Endemic equilibrium point is the steady state solution at which the disease is persistent in the population. An equilibrium point is studied in order to aid in predicting long term behavior of solutions of the model. Linearization of the system of ordinary differential equations (3.2) around the endemic equilibrium point is undertaken in order to aid in studying the behavior of solutions in passing time.

Theorem 3

The Disease Free Equilibrium of system (3.2) *is given by*

$$E_0 = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}, 0, 0, 0 \right). \tag{3.14}$$

PROOF. The D.F.E is denoted by $E_0 = (S_H^*, S_L^*, I^*, T_D^*, A^*)$ and the "disease" classes at D.F.E defined as $I^* = T_D^* = A^* = 0$.
At equilibrium, $\frac{dS_H}{dt} = \frac{dS_L}{dt} = \frac{dI}{dt} = \frac{dT_D}{dt} = \frac{dA}{dt} = 0$. From the first line of the system (3.2),

$$\delta\Lambda - \mu S_H^* = 0 \Rightarrow S_H^* = \frac{\delta\Lambda}{\mu}. \tag{3.15}$$

Also, from the second line of the system (3.2),

$$(1-\delta)\Lambda - \mu S_L^* = 0 \Rightarrow S_L^* = \frac{(1-\delta)\Lambda}{\mu}. \tag{3.16}$$

Thus $E_0 = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}, 0, 0, 0 \right)$ is the disease free equilibrium point of the model. The disease free equilibrium is indeed an equilibrium point of the mathematical model represented by the system (3.2) since by substituting $E_0 = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}, 0, 0, 0 \right)$ in the system, all derivatives equal to zero. □

The Basic Reproductive Number R_0 and Stability Analysis

The Basic Reproductive Number (R_0) refers to the mean number of secondary infections caused by a single infected agent during his/her entire infectious period, in a completely susceptible population [20]. In this study, the basic reproductive number of the model is defined as the average number of secondary HIV infections caused by a single HIV infected individual during his/her entire life as a HIV infective. It forms the threshold upon which the researcher is able to tell whether the disease will persist in the population or it will die out, thus making it possible to project future dynamics of the disease and plan appropriately. If R_0 is greater than unity, i.e $R_0 > 1$, this means that each infected individual will infect more than one susceptible individual and thus the disease will spread in the population. If R_0 is found to be less than unity, i.e $R_0 < 1$, this implies that each infected member of the population will infect less than one susceptible individual in their entire infectious period, causing the disease to die out. In this mathematical model, R_0 is derived using the next generation algorithm as proposed by Van den Driessche & Wotmough [20].

Let Z be the next generation matrix made up of two $m \times m$ matrices F and V such that $Z = FV^{-1}$ where F is the Jacobian of $\mathbf{f}$ evaluated at the disease free equilibrium state (E_0), and V is the Jacobian of $\mathbf{v}$ evaluated at E_0. $\mathbf{f} = \begin{pmatrix} f_I \\ f_{T_D} \end{pmatrix}$ represents the rate of appearance of new infections in the compartments I and T_D while $\mathbf{v} = \begin{pmatrix} v_I \\ v_{T_D} \end{pmatrix}$ represents the rate of transfer of individuals from compartments I and T_D by all other means.

$\mathbf{v} = \mathbf{v}^- - \mathbf{v}^+$, where $\mathbf{v}^-$ is the rate of transfer of individuals out of compartments I and T_D and $\mathbf{v}^+$ is the rate of transfer of individuals into compartments I and T_D by all other means. The spectral radius of matrix Z represents the basic reproduction number R_0.

Using the third and fourth lines of the system (3.2), which represent the diseased compartments,

$$\mathbf{f} = \begin{pmatrix} (1-\phi_1)(1-\phi_2)(\frac{\beta_1 I + \beta_2 T_D}{N})S_H + (1-\phi_2)(\frac{\beta_1 I + \beta_2 T_D}{N})S_L \\ 0 \end{pmatrix}$$

and

$$\mathbf{v} = \begin{pmatrix} (\alpha + \gamma_2 + \mu)I \\ -\alpha I + (\gamma_3 + \mu)T_D \end{pmatrix}.$$

The Jacobian matrix of $\mathbf{f}$ is given by

$$J_{\mathbf{f}} = \begin{pmatrix} (1-\phi_1)(1-\phi_2)\beta_1\frac{S_H^*}{N} + (1-\phi_2)\beta_1\frac{S_L^*}{N} & (1-\phi_1)(1-\phi_2)\beta_2\frac{S_H^*}{N} + (1-\phi_2)\beta_2\frac{S_L^*}{N} \\ 0 & 0 \end{pmatrix}.$$

The Jacobian of $\mathbf{f}$ evaluated at D.F.E yields F, given by

$$= \begin{pmatrix} (1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1 & (1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2 \\ 0 & 0 \end{pmatrix}$$

$$F = \begin{pmatrix} \beta_3 & \beta_4 \\ 0 & 0 \end{pmatrix},$$

where $\beta_3 = (1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1$, and

$\beta_4 = (1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2$.

The Jacobian matrix of $\mathbf{v}$ is given by

$$J_{\mathbf{v}} = \begin{pmatrix} \alpha + \gamma_2 + \mu & 0 \\ -\alpha & \gamma_3 + \mu \end{pmatrix}.$$

The Jacobian of $\mathbf{v}$ evaluated at D.F.E yields

$$\begin{aligned} V &= \begin{pmatrix} \alpha + \gamma 2 + \mu & 0 \\ -\alpha & \gamma_3 + \mu \end{pmatrix} \\ &= \begin{pmatrix} Q_1 & 0 \\ -\alpha & Q_2 \end{pmatrix}, \end{aligned}$$

where $Q_1 = \alpha + \gamma_2 + \mu$, $Q_2 = \gamma_3 + \mu$,$\gamma_2 = (1 - \alpha)$, and $\gamma_3 = (1 - \phi_3)$. Computing V^{-1} gives

$$V^{-1} = \begin{pmatrix} \frac{1}{Q_1} & 0 \\ \frac{\alpha}{Q_1 Q_2} & \frac{1}{Q_2} \end{pmatrix}.$$

The product of F and V^{-1} is therefore given by

$$FV^{-1} = \begin{pmatrix} \frac{\beta_3}{Q_1} + \frac{\alpha\beta_4}{Q_1 Q_2} & \frac{\beta_4}{Q_2} \\ 0 & 0 \end{pmatrix}. \tag{3.17}$$

The basic reproductive number R_0 is obtained by taking the dominant eigenvalue of the matrix in equation (3.17) [1], which is

$$R_0 = \frac{\beta_3}{Q_1} + \frac{\alpha\beta_4}{Q_1 Q_2}. \tag{3.18}$$

Substituting for $\beta_3 = (1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1$, and $\beta_4 = (1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2$ in equation (3.18) yields

$$\begin{aligned} R_0 &= \frac{(1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1}{\alpha+\gamma_2+\mu} \\ &\quad + \frac{\alpha\left[(1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2\right]}{(\alpha+\gamma_2+\mu)(\gamma_3+\mu)}. \end{aligned} \tag{3.19}$$

The basic reproductive number obtained above is the sum of reproduction numbers in the sub-populations I and T_D representing the contribution of individuals in these compartments in the transmission of the virus, that is, $R_{0I} = \frac{(1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1}{\alpha+\gamma_2+\mu}$ and $R_{0T_D} = \frac{\alpha\left[(1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2\right]}{(\alpha+\gamma_2+\mu)(\gamma_3+\mu)}$.

3.3.3 Local Stability of the Disease Free Equilibrium

Theorem 4

The Disease Free Equilibrium is locally asymptotically stable whenever $R_0 < 1$ and unstable whenever $R_0 > 1$.

Proof. The Jacobian matrix of system (3.2) evaluated at the disease free equilibrium i.e, J_{E_0} is given by

$$J_{E_0} = \begin{pmatrix} -\mu & 0 & -(1-\phi_1)(1-\phi_2)\delta\beta_1 & -(1-\phi_1)(1-\phi_2)\delta\beta_2 & 0 \\ 0 & -\mu & -(1-\phi_2)(1-\delta)\beta_1 & -(1-\phi_2)(1-\delta)\beta_2 & 0 \\ 0 & 0 & \beta_3 - Q_1 & \beta_4 & 0 \\ 0 & 0 & \alpha & -Q_2 & 0 \\ 0 & 0 & \gamma_2 & \gamma_3 & -Q_3 \end{pmatrix},$$

where $Q_3 = \mu + \sigma$. An equilibrium point is locally asymptomatically

stable if the Jacobian matrix of the system has eigenvalues with negative real part. The Jacobian matrix J_{E_0} above has three negative eigenvalues given by $-\mu$, $-\mu$, and $-Q_3$. The nature of the remaining eigenvalues is studied from the reduced matrix B given by

$$B = \begin{pmatrix} \beta_3 - Q_1 & \beta_4 \\ \alpha & -Q_2 \end{pmatrix}.$$

The Routh Hurwitz criterion which states that a negative trace and a positive determinant guarantees that the eigenvalues of the matrix will have negative real part is thus applied. The trace of matrix B, denoted as Tr_B is given by

$$Tr_B = \beta_3 - Q_1 - Q_2. \tag{3.20}$$

Making Q_1 the subject of equation (3.18) yields

$$Q_1 = \frac{\beta_3}{R_0} + \frac{\alpha\beta_4}{R_0 Q_2}. \tag{3.21}$$

Substituting (3.21) into (3.20) yields

$$\begin{aligned} Tr_B &= \beta_3 - \frac{\beta_3}{R_0} - \frac{\alpha\beta_4}{R_0 Q_2} - Q_2 \\ &= \beta_3 \left(1 - \frac{1}{R_0}\right) - \frac{\alpha\beta_4}{R_0 Q_2} - Q_2 < 0 \text{ iff } R_0 < 1. \end{aligned}$$

This implies that the trace of matrix B is negative whenever $R_0 < 1$.

The determinant of matrix B, denoted as det_B is given by;

$$\begin{aligned} det_B &= -Q_2(\beta_3 - Q_1) - \alpha\beta_4 \\ &= Q_1Q_2 - (\beta_3 Q_2 + \alpha\beta_4) \\ &= \left[1 - \left(\frac{\beta_3}{Q_1} + \frac{\alpha\beta_4}{Q_1Q_2}\right)\right] Q_1Q_2 \\ &= [1 - R_0]\, Q_1Q_2 > 0 \text{ iff } R_0 < 1. \end{aligned}$$

This implies that the determinant of matrix B is positive whenever $R_0 < 1$. Matrix B has a negative trace and a positive determinant provided $R_0 < 1$ and thus the Routh Hurwitz condition is satisfied. Therefore, the eigenvalues of matrix B will have a negative real part if $R_0 < 1$. Since all the eigenvalues of the Jacobian matrix of the system have negative real part, the desease free equilibrium is locally asymptotically stable whenever $R_0 < 1$. □

Mathematically, this implies that whenever there is a small perturbation on the system, the system returns to the disease free equilibrium. Epidemiologically, this implies that when a few HIV infectious individuals are introduced in a population that is fully susceptible to HIV infection, the disease dies out whenever $R_0 < 1$, otherwise, the disease will spread.

3.3.4 The Global Stability of Disease Free Equilibrium

Following [1], the system (3.2) can be written in the form

$$\frac{d\mathbf{X}}{dt} = F(\mathbf{X}, \mathbf{Z})$$
$$\frac{d\mathbf{Z}}{dt} = G(\mathbf{X}, \mathbf{Z}),$$

where $\mathbf{X} = (S_H, S_L), \mathbf{X} \in \mathbb{R}^2$ denotes (its components) the uninfected individuals while $\mathbf{Z} = (I, T_D, A), \mathbf{Z} \in \mathbb{R}^3$ denotes (its components) the infected individuals. The Disease Free Equilibrium E_0 is therefore given as $E_0 = (\mathbf{X}^*, \mathbf{Z}^*) = (\mathbf{X}^*, \mathbf{0}), \mathbf{X}^* = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}\right)$. The following two conditions H_1 and H_2 must be met to guarantee local asymptotic stability.
H_1: For $\frac{d\mathbf{X}}{dt} = F(\mathbf{X}, \mathbf{0})$, $\mathbf{X}^*$ is global asymptotically stable,
$H_2 : G(\mathbf{X}, \mathbf{Z}) = P\mathbf{Z} - \tilde{G}(\mathbf{X}, \mathbf{Z}), \tilde{G}(\mathbf{X}, \mathbf{Z}) \geq \mathbf{0}$ for $(\mathbf{X}, \mathbf{Z}) \in \Gamma$, where Γ is the region where the model represented by system (3.2) is biologically feasible, and $P = D_{\mathbf{Z}}G(\mathbf{P}, \mathbf{0})$; P is a Metzler matrix (i.e off diagonal entries are non-negative. The following theorem commonly known as Castillo Chavez's theorem [1] is used to investigate the global stability of the Disease Free Equilibrium of a model.

Theorem 5 ([1])

The Disease Free Equilibrium E_0 of a system is globally asymptotically stable provided that $R_0 < 1$ (local asymptotic stability) and that the assumptions H_1 and H_2 above are satisfied.

Thus, the following theorem can be proved,

Theorem 6

The Disease Free Equilibrium $E_0 = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}, 0, 0, 0\right)$ *of the system* (3.2) *is globally asymptotically stable whenever* $R_0 < 1$.

PROOF. Adopting the notation established above, $E_0 = (\mathbf{X}^*, \mathbf{0})$, $\mathbf{X} = (S_H, S_L), \mathbf{X}^* = \left(\frac{\delta\Lambda}{\mu}, \frac{(1-\delta)\Lambda}{\mu}\right)$ and $\mathbf{Z} = (I, T_D, A)$.

Now;

$$\frac{d\mathbf{X}}{dt} = F(\mathbf{X},\mathbf{0}) = \begin{pmatrix} \frac{dS_H}{dt} \\ \frac{dS_L}{dt} \end{pmatrix} = \begin{pmatrix} \delta\Lambda - \mu S_H \\ (1-\delta)\Lambda - \mu S_L \end{pmatrix}.$$

Solving for $S_H(t)$ and $S_L(t)$, we obtain

$$S_H(t) = \frac{\delta\Lambda}{\mu} + S_H(0)e^{-\mu t}$$

and

$$S_L(t) = \frac{(1-\delta)\Lambda}{\mu} + S_L(0)e^{-\mu t}.$$

Thus,

$$\lim_{t\to\infty} S_H(t) = \frac{\delta\Lambda}{\mu}$$

and

$$\lim_{t\to\infty} S_L(t) = \frac{(1-\delta)\Lambda}{\mu}.$$

Hence

$$\lim_{t\to\infty} \mathbf{X}(t) = \mathbf{X}^*(t),$$

implying that $\mathbf{X}^*(t)$ is globally asymptotically stable. Hence condition

H_1 is satisfied. For H_2:$G(\mathbf{X},\mathbf{Z}) = P\mathbf{Z} - \tilde{G}(\mathbf{X},\mathbf{Z})$, matrix P is given by

$$\begin{pmatrix} \frac{h_1\beta_1 S_H}{N} + \frac{(1-\phi_2)\beta_1 S_L}{N} - (\alpha+\gamma_2+\mu) & \frac{h_1\beta_2 S_H}{N} + \frac{(1-\phi_2)\beta_2 S_L}{N} & 0 \\ \alpha & -(\gamma_3+\mu) & 0 \\ \gamma_2 & \gamma_3 & -(\sigma+\mu) \end{pmatrix},$$

where $h_1 = (1-\phi_1)(1-\phi_2)$, and $P\mathbf{Z}$ is given by

$$\begin{pmatrix} \frac{h_1\beta_1 I S_H}{N} + \frac{(1-\phi_2)\beta_1 I S_L}{N} - (\alpha+\gamma_2+\mu) + \frac{h_1\beta_2 T_D S_H}{N} + \frac{(1-\phi_2)\beta_2 T_D S_L}{N} \\ \alpha I - (\gamma_3+\mu)T_D \\ \gamma_2 I + \gamma_3 T_D - (\sigma+\mu)A \end{pmatrix}.$$

Moreover, $G(\mathbf{X},\mathbf{Z})$ is given by

$$\begin{pmatrix} (1-\phi_1)(1-\phi_2)\left(\frac{\beta_1 I + \beta_2 T_D}{N}\right) S_H + (1-\phi_2)\left(\frac{\beta_1 I + \beta_2 T_D}{N}\right) S_L - (\alpha+\gamma_2+\mu)I \\ \alpha I - (\gamma_3+\mu)T_D \\ \gamma_2 I + \gamma_3 T_D - (\sigma+\mu)A \end{pmatrix},$$

and therefore $\tilde{G}(\mathbf{X},\mathbf{Z}) = P\mathbf{Z} - G(\mathbf{X},\mathbf{Z}) = \begin{pmatrix} \tilde{G}_1(\mathbf{X},\mathbf{Z}) \\ \tilde{G}_2(\mathbf{X},\mathbf{Z}) \\ \tilde{G}_3(\mathbf{X},\mathbf{Z}) \end{pmatrix} = \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}$. Hence condition H_2 is satisfied. Also from Theorem 4, E_0 is locally asymptotically stable whenever $R_0 < 1$. Therefore following Castillo Chavez's theorem (Theorem 5), E_0 is globally asymptotically stable whenever $R_0 < 1$, as desired. □

This implies that with a large perturbation of the disease free equilibrium, solutions of the model represented by the system (3.2) converge to D.F.E whenever $R_0 < 1$. Epidemiologically, this implies that if a sufficiently

large number of HIV infected individuals are introduced in a population that is fully susceptible to HIV infection, the disease will die out whenever $R_0 < 1$.

3.3.5 Existence of the Endemic Steady State

The mathematical model represented by the system (3.2) is reproduced here for ease of reference.

$$\begin{aligned}
\frac{dS_H}{dt} &= \delta\Lambda - (1-\phi_1)(1-\phi_2)\lambda S_H - \mu S_H \\
\frac{dS_L}{dt} &= (1-\delta)\Lambda - (1-\phi_2)\lambda S_L - \mu S_L \\
\frac{dI}{dt} &= (1-\phi_1)(1-\phi_2)\lambda S_H + (1-\phi_2)\lambda S_L - \alpha I - \gamma_2 I - \mu I \\
\frac{dT_D}{dt} &= \alpha I - (\gamma_3 + \mu) T_D \\
\frac{dA}{dt} &= \gamma_2 I + \gamma_3 T_D - (\mu + \sigma) A. \qquad (3.22)
\end{aligned}$$

Theorem 7

An endemic equilibrium point $E_1 = (S_H^{**}, S_L^{**}, I^{**}, T_D^{**}, A^{**})$, *of the system* (3.22) *exists whenever* $R_0 > 1$.

Proof. Equating the right hand side of each equation in the system

(3.22) to zero and simplifying yields;

$$\delta\Lambda - (1-\phi_1)(1-\phi_2)\left(\frac{\beta_1 I^{**} + \beta_2 T_D^{**}}{N}\right) S_H^{**} - \mu S_H^{**} = 0, \tag{3.23}$$

$$(1-\delta)\Lambda - (1-\phi_2)\left(\frac{\beta_1 I^{**} + \beta_2 T_D^{**}}{N}\right) S_L^{**} - \mu S_L^{**} = 0, \tag{3.24}$$

$$(1-\phi_1)(1-\phi_2)\left(\frac{\beta_1 I^{**} + \beta_2 T_D^{**}}{N}\right) S_H^{**} +$$

$$(1-\phi_2)\left(\frac{\beta_1 I^{**} + \beta_2 T_D^{**}}{N}\right) S_L^{**} - Q_1 I^{**} = 0, \tag{3.25}$$

$$\alpha I^{**} - Q_2 T_D^{**} = 0, \tag{3.26}$$

$$\gamma_2 I^{**} + \gamma_3 T_D^{**} - Q_3 A^{**} = 0, \tag{3.27}$$

where $Q_1 = \alpha + \gamma_2 + \mu$, $Q_2 = \gamma_3 + \mu$, and $Q_3 = \mu + \sigma$.

From equation (3.26), $T_D^{**} = \frac{\alpha}{Q_2} I^{**}$.

Substituting for T_D^{**} in equation (3.27) and simplifying gives

$A^{**} = \left(\frac{\gamma_2}{Q_3} + \frac{\alpha\gamma_3}{Q_2 Q_3}\right) I^{**}$.

Substituting T_D^{**} into equation (3.23) yields

$$\delta\Lambda N - (1-\phi_1)(1-\phi_2)\left(\beta_1 + \frac{\beta_2\alpha}{Q_2}\right) I^{**} S_H^{**} - \mu N S_H^{**} = 0,$$

$$\Rightarrow S_H^{**} = \frac{\delta\Lambda N}{a_1 I^{**} + \mu N},$$

where $a_1 = (1-\phi_1)(1-\phi_2)\left(\beta_1 + \frac{\beta_2\alpha}{Q_2}\right)$.

In a similar manner, S_L^{**} is expressed as

$S_L^{**} = \frac{(1-\delta)\Lambda N}{a_2 I^{**} + \mu N}$, where $a_2 = (1-\phi_2)\left(\beta_1 + \frac{\beta_2\alpha}{Q_2}\right)$.

Using equation (3.25) and substituting for S_H^{**} and S_L^{**},we obtain

$$\frac{a_1 I^{**}\delta\Lambda}{a_1 I^{**} + \mu N} + \frac{a_2 I^{**}(1-\delta)\Lambda}{a_2 I^{**} + \mu N} - Q_1 I^{**} = 0. \tag{3.28}$$

Thus from equation (3.28),

$$\left(\frac{a_1\delta\Lambda}{a_1I^{**}+\mu N}+\frac{a_2(1-\delta)\Lambda}{a_2I^{**}+\mu N}-Q_1\right)I^{**}=0. \tag{3.29}$$

From equation (3.29), $I^{**}=0$ corresponds to the disease free equilibrium point of the system (3.2), denoted by (E_0). The other solution of (3.29) when $I^{**}\neq 0$ corresponds to the endemic equilibrium point of the system such that,

$$\frac{a_1\delta\Lambda}{a_1I^{**}+\mu N}+\frac{a_2(1-\delta)\Lambda}{a_2I^{**}+\mu N}-Q_1=0. \tag{3.30}$$

Multiplying equation (3.30) through by $(a_1I^{**}+\mu N)(a_2I^{**}+\mu N)$, results in

$$CI^{**2}+DI^{**}+E=0. \tag{3.31}$$

where: $C=-Q_1a_1a_2$,

$D=(a_1a_2\delta\Lambda+a_1a_2(1-\delta)\Lambda)-(Q_1a_1\mu N+Q_1a_2\mu N)$,

$E=a_1\delta\Lambda\mu N+a_2(1-\delta)\Lambda\mu N-Q_1\mu N\mu N$.

The endemic equilibrium of the system exists if the roots of equation (3.31) are real and positive. Descarte's rule of signs is used to check the possible number of real roots of the polynomial. The number of positive real roots is equal to the number of sign changes in the coefficients of the terms of a polynomial [22].

Considering that all the parameters used are positive, the sign of C is negative. The sign of E is then checked as follows;

$E = a_1\delta\Lambda\mu N + a_2(1-\delta)\Lambda\mu N - Q_1\mu N\mu N$. Since $a_1 = (1-\phi_1)(1-\phi_2)\left(\beta_1 + \frac{\beta_2\alpha}{Q_2}\right)$, $a_2 = (1-\phi_2)\left(\beta_1 + \frac{\beta_2\alpha}{Q_2}\right)$, and the limiting value of $N = \frac{\Lambda}{\mu}$,

$$\begin{aligned} E &= \left[(1-\phi_1)(1-\phi_2)\delta\beta_1 + (1-\phi_2)(1-\delta)\beta_1\right]\Lambda^2 + \\ &\quad \left[(1-\phi_1)(1-\phi_2)\delta\beta_2 + (1-\phi_2)(1-\delta)\beta_2\right]\frac{\alpha\Lambda^2}{Q_2} - Q_1\Lambda^2 \\ &= \beta_3\Lambda^2 + \frac{\alpha\Lambda^2}{Q_2}\beta_4 - Q_1\Lambda^2 \\ &= \left[\frac{\beta_3}{Q_1} + \frac{\alpha\beta_4}{Q_1Q_2} - 1\right]Q_1\Lambda^2 \\ &= \left[R_0 - 1\right]Q_1\Lambda^2 \end{aligned}$$

Thus $E > 0$ iff $R_0 > 1$. Since C is negative, and E is positive, if $R_0 > 1$, there is at least one sign change regardless of the sign of D. This implies that equation (3.31) has at least one positive real root. Hence an endemic equilibrium point of the system (3.2) exists whenever $R_0 > 1$. □

3.3.6 Local Stability of the Endemic Equilibrium

At the endemic equilibrium, there is persistence of HIV infection in the population.

Theorem 8

The endemic equilibrium point $E_1 = (S_H^{**}, S_L^{**}, I^{**}, T_D^{**}, A^{**})$ *of system* (3.2) *is locally asymptotically stable if* $R_0 > 1$.

Proof. The Jacobian matrix of the system 3.2 evaluated at endemic

equilibrium is $J(E_1)=\begin{pmatrix} -b_1 & 0 & -b_2 & -b_3 & 0 \\ 0 & -b_4 & -b_5 & -b_6 & 0 \\ b_7 & b_8 & b_9-Q_1 & b_{10} & 0 \\ 0 & 0 & \alpha & -Q_2 & 0 \\ 0 & 0 & \gamma_2 & \gamma_3 & -Q_3 \end{pmatrix}$

where

$b_1 = \frac{(1-\phi_1)(1-\phi_2)(\beta_1 Q_2+\beta_2\alpha)\mu I^{**}+Q_2\mu\Lambda}{Q_2\Lambda}$,

$b_2 = \frac{(1-\phi_1)(1-\phi_2)\beta_1 a_1\delta\Lambda I^{**}}{a_1 I^{**}+\Lambda}$,

$b_3 = \frac{(1-\phi_1)(1-\phi_2)\beta_2 a_1\delta\Lambda I^{**}}{a_1 I^{**}+\Lambda}$,

$b_4 = \frac{(1-\phi_2)(\beta_1 Q_2+\beta_2\alpha)\mu I^{**}+Q_2\mu\Lambda}{Q_2\Lambda}$,

$b_5 = \frac{(1-\phi_2)(1-\delta)\Lambda\beta_1 a_2 I^{**}}{a_2 I^{**}+\Lambda}$,

$b_6 = \frac{(1-\phi_2)(1-\delta)\Lambda\beta_2 a_2 I^{**}}{a_2 I^{**}+\Lambda}$,

$b_7 = \frac{(1-\phi_1)(1-\phi_2)(\beta_1 Q_2+\beta_2\alpha)\mu I^{**}+Q_2\mu\Lambda}{Q_2\Lambda}$,

$b_8 = \frac{(1-\phi_2)(\beta_1 Q_2+\beta_2\alpha)\mu I^{**}+Q_2\mu\Lambda}{Q_2\Lambda}$,

$b_9 = \frac{(1-\phi_1)(1-\phi_2)\beta_1 a_1\delta\Lambda I^{**}}{a_1 I^{**}+\Lambda} + \frac{(1-\phi_2)(1-\delta)\Lambda\beta_1 a_2 I^{**}}{a_2 I^{**}+\Lambda}$,

$b_{10} = \frac{(1-\phi_1)(1-\phi_2)\beta_2 a_1\delta\Lambda I^{**}}{a_1 I^{**}+\Lambda} + \frac{(1-\phi_2)(1-\delta)\Lambda\beta_2 a_2 I^{**}}{a_2 I^{**}+\Lambda}$.

Clearly, $-Q_3$ is an eigenvalue of the Jacobian matrix $J(E_1)$. The other eigenvalues can be computed by finding the solution to the equation

$P(\lambda) = \begin{vmatrix} \lambda+b_1 & 0 & -b_2 & -b_3 \\ 0 & \lambda+b_4 & -b_5 & -b_6 \\ b_7 & b_8 & \lambda-(b_9-Q_1) & b_{10} \\ 0 & 0 & \alpha & \lambda+Q_2 \end{vmatrix}$=0, which is equivalent to

$$P(\lambda) = \lambda^4 + c_0\lambda^3 + c_1\lambda^2 + c_2\lambda + c_3 = 0, \tag{3.32}$$

where;

$c_0 = b_1 + b_4 - b_9 - Q_1 + Q_2$,

$c_1 = b_1b_4 + b_2b_7 + b_5b_8 - b_1b_9 - b_4b_9 - \alpha b_{10} - b_1Q_1 - b_4Q_1 + b_1Q_2 + b_4Q_2 -$

$b_9Q_2 - Q_1Q_2$,

$c_2 = -\alpha b_3b_7 + b_2b_4b_7 + b_1b_5b_8 - \alpha b_6b_8 - b_1b_4b_9 - \alpha b_1b_{10} - \alpha b_4b_{10} - b_1b_4Q_1 + b_1b_4Q_2 + b_2b_7Q_2 + b_5b_8Q_2 - b_1b_9Q_2 - b_4b_9Q_2 - b_1Q_1Q_2 - b_4Q_1Q_2$,

$c_3 = -\alpha b_3b_4b_7 - \alpha b_1b_6b_8 - \alpha b_1b_4b_{10} + b_2b_4b_7Q_2 + b_1b_5b_8Q_2 - b_1b_4b_9Q_2 - b_1b_4Q_1Q_2$.

The number of negative zeros of equation (3.32) depends on the signs of c_0, c_1, c_2 and c_3. Descarte's Rule of Signs is applied to study the number of negative real roots of the polynomial$P(\lambda_1)$ comprising of the coefficients c_0, c_1, c_2 and c_3 given by;

$$P(\lambda_1) = c_0\lambda^3 + c_1\lambda^2 + c_2\lambda + c_3 = 0. \tag{3.33}$$

Descarte's rule of signs states that the number of negative real zeros of $P(\lambda)$ is either equal to the variations in sign of $P(-\lambda)$ or less than this by an even number [22]. The possibilities of negative real zeros of $P(\lambda)$, is as summarized in Table 3.2. The maximum number of variations of signs in $P(-\lambda)$ is 3, hence the characteristic polynomial (3.33) has three negative roots. Thus $P(-\lambda) = \lambda^4 - c_0\lambda^3 + c_1\lambda^2 - c_2\lambda + c_3 = 0$ has negative roots. Therefore, given that cases 1-16 in Table 3.2 are satisfied, the endemic equilibrium point of the system (3.2) is locally asymptotically stable whenever $R_0 > 1$. □

This implies that for a small perturbation of the E_1, solutions of the mathematical model represented by the system (3.2) always converge to E_1, whenever $R_0 > 1$. Epidemiologically, it implies that if a few HIV infected individuals are introduced in a fully susceptible population, the disease will persist provided $R_0 > 1$.

Table 3.2: The Zeros of the characteristic equation (3.32) for $R_0 > 1$.

Cases	c_0	c_1	c_2	c_3	Sign Change	No. of $-ve$ Roots
1	+	−	−	+	2	2 or 0
2	+	−	+	+	2	2 or 0
3	−	−	+	−	2	2 or 0
4	+	+	−	−	1	0
5	−	−	+	+	1	0
6	+	+	+	−	1	0
7	−	+	−	+	3	3 or 1
8	−	−	−	−	0	0
9	−	−	−	+	1	0
10	−	+	−	−	2	2 or 0
11	−	+	+	−	2	2 or 0
12	−	+	+	+	1	0
13	+	+	+	+	0	0
14	+	+	−	+	2	2 or 0
15	+	−	+	−	3	3 or 1
16	+	−	−	−	1	0

3.4 Sensitivity Analysis

In mathematical modeling, Sensitivity refers to the degree to which a given input parameter in a mathematical model influences its output. Sensitive parameters are thus those that cause a significant impact on the disease transmission dynamics. Sensitivity analysis will aid in identifying the parameters which greatly impact on the value of the basic reproductive number R_0, and hence ought to be targeted when coming up with intervention strategies. The sensitivity of model parameters is calculated using the normalized forward sensitivity index. The normalized forward sensitivity index [10] of the basic reproductive number is given by $S_w^{R_0} = \frac{\partial R_0}{\partial w} \times \frac{w}{R_0}$, where w is the parameter whose sensitivity is to be determined.

R_0 is given by

$$\begin{aligned} R_0 &= \frac{(1-\phi_1)(1-\phi_2)\beta_1\delta + (1-\phi_2)(1-\delta)\beta_1}{\alpha+\gamma_2+\mu} \\ &\quad + \frac{\alpha\left[(1-\phi_1)(1-\phi_2)\beta_2\delta + (1-\phi_2)(1-\delta)\beta_2\right]}{(\alpha+\gamma_2+\mu)(\gamma_3+\mu)}. \end{aligned} \tag{3.34}$$

$$\text{For } \beta_1, S_{\beta_1}^{R_0} = \frac{\beta_1(\gamma_3+\mu)}{\beta_1(\gamma_3+\mu)+\alpha\beta_2}. \tag{3.35}$$

$$\text{For } \beta_2, S_{\beta_2}^{R_0} = \frac{\alpha\beta_2}{\beta_1(\gamma_3+\mu)+\alpha\beta_2}. \tag{3.36}$$

$$\text{For } \alpha, S_{\alpha}^{R_0} = \frac{[\beta_2(\alpha+\gamma_2+\mu)-(\beta_1(\gamma_3+\mu)+\alpha\beta_2)]\alpha}{(\alpha+\gamma_2+\mu)(\beta_1(\gamma_3+\mu)+\alpha\beta_2)}. \tag{3.37}$$

$$\text{For } \gamma_2, S_{\gamma_2}^{R_0} = (\alpha\gamma_2+\gamma_2^2+\mu\gamma_2)\ln|\alpha+\gamma_2+\mu|. \tag{3.38}$$

$$\text{For } \gamma_3, S_{\gamma_3}^{R_0} = \frac{-\alpha\beta_2\gamma_3}{(\beta_1(\gamma_3+\mu)^2+\alpha\beta_2(\gamma_3+\mu)}. \tag{3.39}$$

$$\text{For } \delta, S_{\delta}^{R_0} = \frac{-\phi_1\delta}{1-\delta\phi_1} \tag{3.40}$$

$$\text{For } \mu, S_{\mu}^{R_0} = \frac{[(\alpha+\gamma_2+\mu)(\gamma_3+\mu)\beta_1+((\gamma_3+\mu)\beta_1+\alpha\beta_2)(\alpha+\gamma_2+\gamma_3+2\mu)]\mu}{(\alpha+\gamma_2+\mu)(\gamma_3+\mu)(\beta_1(\gamma_3+\mu)+\alpha\beta_2)}. \tag{3.41}$$

Based on the sensitivity indices in Table 3.3, the drivers of infection are β_1 and β_2, whose sensitivity indices are 0.72345 and 0.27654 respectively. The most sensitive parameter to the value of R_0 is β_1, the mean contact rate with undiagnosed infectives. $S_{\beta_1}^{R_0} = 0.72345$ means that increasing (or decreasing) the value of β_1 by 10%, increases (or decreases) the value of R_0 by 7.2345. This implies that in order to control the spread of HIV in a high risk population, efforts should be geared towards reducing the number of those who are undiagnosed. This can be achieved via testing and enrolling them on ART. This in turn lowers their infectivity as well as chances of progressing to the AIDS class.

Table 3.3: Sensitivity Indices for the Model Parameters

Parameter	Description	Sensitivity Index
δ	Proportion of high risk sussceptibles	-0.36986
ϕ_1	PreP effectiveness	-0.041095
ϕ_2	Condom effectiveness	-0.11111
γ_3	ART Failure	-0.27182
β_1	Mean contact rate with I	0.72345
β_2	Mean contact rate with T_D	0.27654
α	Progression from I to T_D	-0.40225
γ_2	Progression from I to A	-0.05123
μ	Natural mortality rate	-0.02969

3.5 Numerical Simulation

Numerical simulation is carried out in order to predict future disease dynamics. Upon defining the initial conditions, the system (3.2) is coded and input in a mathematical software for simulation purposes. Parameters values obtained from secondary data are used to simulate the effect of dual protection and ART adherence. The parameter values given in Table 3.4 are used.

Table 3.4: Parameter Values for the Model

Parameter	Description	Value	Units	Source
Λ	Constant rate of recruitment.	0.55	*perday*	[17]
δ	Proportion of high risk sussceptibles	0.3		Assumed
ϕ_1	Prep effectiveness	$0.1 \leq \phi_1 \leq 0.9$		[5]
ϕ_2	Condom effectiveness	$0.1 \leq \phi_2 \leq 0.9$		[5]
ϕ_3	Efficacy of ART	$0.1 \leq \phi_3 \leq 0.9$		[5]
β_1	Mean contact rate with I	0.8	*perday*	[5]
β_2	Mean contact rate with T_D	0.8	*perday*	[5]
α	Progression from I to T_D	0.35	*perday*	[17]
γ_2	Progression from I to A	0.15	*perday*	[17]
σ	Aids induced mortality	0.0013	*perday*	[6]
μ	Natural mortality rate	0.01562	*perday*	[6]

3.5.1 Simulation Results for Dual Protection versus Single Method of protection

In this section, the impact of dual protection versus single prevention approach is investigated. The effect of low, moderate, and high levels of PrEP use and condom effectiveness is demonstrated by setting $\phi_1 = \phi_2 = 0.1$, $\phi_1 = \phi_2 = 0.85$, $\phi_1 = \phi_2 = 0.9$. It can be seen from Figure 3.2 that the higher the value of the ϕ's, the longer the time taken for the susceptible population to be infected. Thus high levels of PrEP uptake and condom use among the high risk population lowers their chances of getting infected.

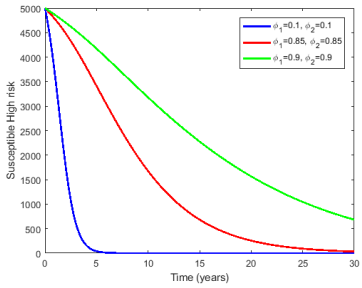

Figure 3.2: Varying the levels of Dual Protection (PrEP and Condom Use).

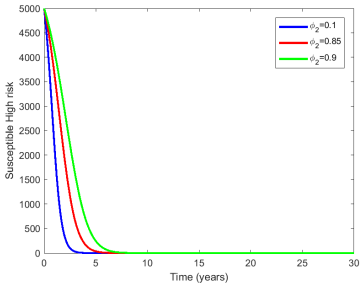

Figure 3.3: Use of a single Prevention approach(Condom Use)

The effect of low, moderate and high use of a single prevention approach (condom use) is demonstrated by setting $\phi_2 = 0.1, \phi_2 = 0.85$, and $\phi_2 = 0.9$. It can be seen from Figure 3.3 that when there is high condom effectiveness, i.e $\phi_2 = 0.9$, fewer susceptibles get infected as compared to when $\phi_2 = 0.1$. This implies that the success of condom use in preventing the high risk population from HIV infection depends on proper

use, which guarantees its effectiveness.

Comparing the effect of dual protection versus a single prevention approach, Figure 3.2 shows that with PrEP and Condom use, i.e $\phi_1 = \phi_2 = 0.85$, it takes more than 25 years for all the susceptible individuals to get infected whereas when only condom use is utilized, i.e $\phi_2 = 0.85$, it takes about five years for all susceptibles in the population to get infected as shown in Figure 3.3. This points to a lower infection rate when dual protection is used as compared to when a single prevention approach. Therefore, dual protection is an integral tool in protecting the high risk population from HIV infection. It slows down the disease transmission within a population, thus making it possible for other prevention ventures to come into play hence prevent further infectivity.

3.5.2 Simulating the Dynamics of HIV with ART Adherence

Here, ϕ_3 is varied and its effect on the number of people progressing to the AIDS class examined. Setting $\phi_3 = 0.1$, $\phi_3 = 0.7$, and $\phi_3 = 0.9$, it is observed in Figure 3.4 that when ϕ_3 is low, i.e "0.1", more people will move to the AIDS class while when ϕ_3 is high, i.e "0.9", few people tend to progress to the AIDS class. The higher the levels of ART adherence, the fewer the number of people who move to AIDS class. ART adherence is thus essential in controlling the spread of HIV among the high risk population.

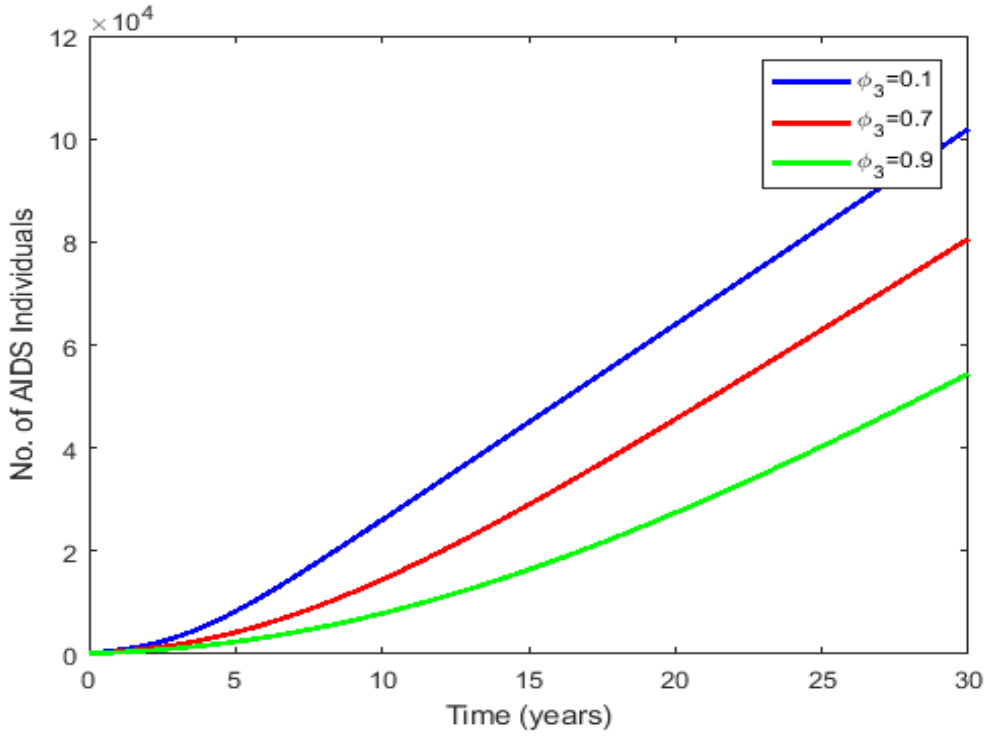

Figure 3.4: Effect of varying the levels of ART Adherence

Chapter 4

Conclusion and Recomendation

4.1 Conclusion

In this study, a mathematical model has been formulated based on a system of ordinary differential equations, incorporating the impact of dual protection and ART adherence in preventing the spread of HIV among persons at high risk of infection. Upon checking for positivity and boundedness of solutions the results indicate that there exists a region where the model is well posed both mathematically and epidemiologically. The basic reproduction number R_0 is computed using the Next Generation Matrix approach. It was shown that there is no HIV transmission within the population provided the basic reproductive number is below unity. Stability analysis of the model was done and depicted that when $R_0 < 1$, the disease free equilibrium is both locally and globally asymptotically stable. Existence of the endemic equilibrium was proved by applying Descarte's Rule of Signs. The Endemic Equilibrium point was shown to

be locally asymptotically stable whenever $R_0 > 1$, implying that there is persistence of HIV infection in the population provided that R_0 is greater than unity. Sensitivity analysis was conducted, depicting that the most sensitive parameter is β_1, the mean contact rate with the un-diagnosed infectives. Thus, in an attempt to control the spread of HIV among the high risk population, efforts ought to be geared towards reducing the number of those who are undiagnosed by frequently testing and enrolling them on ART treatment. Numerical simulation results point to the need for dual protection in preventing the high risk population. It slows down the rate of HIV transmission within the population. ART adherence guarantees low viral load within the infected individual, making them less infective. Thus, Dual protection and ART adherence are essential in the fight against the spread of HIV among the high risk population.

4.2 Recommendation

The findings of this study illustrate that control of the spread of HIV in a population can be achieved by targeting the high risk population. The optimality of the intervention strategies has not been studied. This can be considered as a future extension of the work. Furthermore, bifurcation analysis of this model is recommended.

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Appendix

```
[t,y]=ode45('functoriedo',[0,30],[5000 2000 1000 500 100]);
    [t2,y2]=ode45('functoriedo2',[0,30],[5000 2000 1000 500 100]);
    [t3,y3]=ode45('functoriedo3',[0,30],[5000 2000 1000 500 100]);
    plot(t,y(:,5),'b',t2,y2(:,5),'r',t3,y3(:,5),'g','linewidth', 2)
    hold on
    legend('$\phi_3 = 0.1$','$\phi_3 = 0.7$','$\phi_3 = 0.9$'); xlabel('Time (years)');
    ylabel('No. of AIDS Individuals');
    hold off
```