Determining an Optimal Stage for Initiating ARV Treatment for HIV/AIDS Patients

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Abstract

There has been a lot of controversy on the most appropriate HIV infection stage to start ARV treatment in order to reduce the incidence to the barest minimal level. Various agencies have issued different guideline on when to initiate ARV treatment and this could bring confusion for clinicians, the infected individuals and policy makers when determining the optimal stage to initiate treatment. Optimizing the initiation of ARV treatment is clearly complex and must therefore be balanced for effective control in the morbidity and mortality of the disease. Our aim is to determine the optimal stage to initiate ARV treatment in order to reduce the incidence (new cases of the infection) to the barest minimal level. In order to achieve this, we developed an SI model with four disease stages, and incorporated control (prevention) measure and treatment parameters. The control is aimed at reducing the susceptibility since prevention is the only solution to an incurable disease, while the treatment will help to reduce the level of infectiousness of the infected individuals, improve their health and reduce mortality.

In this project, we have developed a model for the horizontal transmission of HIV infection. Simulation of our model has identified an optimal stage for initiating ARV treatment. It is optimal in the sense that starting the treatment at that stage reduces the incidence rate faster than at any other stage. We note that the key to controlling an infectious disease which has no cure, lies in a rapid reduction of the incidence rate.

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.

Simbiat Agnes Adefisan, 22 May 2014

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1. Introduction

HIV is an acronym which stands for Human Immunodeficiency Virus. It is responsible for causing AIDS (acquired immunodeficiency syndrome). This virus damages the immune system by attacking the $CD4^+$ T cells. These cells are responsible for fighting against infection in the body system. The strength of the immune system is directly proportional to the population and how active these cells are. Infected cells end up producing thousands of copies of viruses. This implies that the reduction in the $CD4^+$ T cells count in the body leads to dramatic increase in the virus population. It takes an average of $10 - 15$ for an infected individual to develop AIDS. Investigations revealed that the virus originated from Africa. Hunters contracted this virus from chimpanzee during hunting. The chimpanzee virus is known as Simian Immunodeficiency Virus (SIVcpz). Technological advancement brought about the wide spread of the infection world wide.

The virus resides in the body fluids and can be transmitted in a very large proportion from semen, pre-seminal fluid, vaginal secretion, blood and breast milk. Research have shown that they are also present in small quantity in saliva and tears. They can be contracted by sharing sharp objects such as: needles, razor blades, knives, clippers and scissors. WCAIDS.

HIV transmission modes are categorised into two namely: The vertical transmission and the horizontal transmission. Vertical transmission is also known as mother to child transmission (MTCT). This could happen during pregnancy, delivery, or breast feeding, while the horizontal transmission has to do with all other modes of transmission such as: sexual contact, transfusion of infected blood and the use of infected needle.

1.1 Motivation

The highest mode of transmission of HIV is through sexual intercourse/contact. Its greatest impact is found in Sub-Saharan Africa. In 2012, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organisation (WHO) estimated that 35.3 million of people were living with HIV infection, 2.3 millions are newly infected and 1.6 million AIDS death occurred world wide. Of these estimates, 25 million live in Sub-Saharan Africa, of which 1.6 million were newly infected and 1.2 million AIDS deaths occurred whereas as at 2010, 34.5 million were living with HIV, 2.5 million are newly infected and 1.9 million AIDS deaths HIVE. These estimates revealed that the prevalence of the infection has increased greatly compared to the incidence. This is as a result of the effort that has been put in place to control the morbidity and the mortality rates of the infection. More effort still have to be put in place in order to continue to ensure that both the incidence and the prevalence of the infection keep decreasing throughout the whole world and most especially in Sub-Saharan region of Africa where highest number of infection is being recorded on yearly basis.

1.2 Objectives

HIV infection is mostly spread through sexual contact. The category of people who are sexually active are those people within the age bracket of $15 - 49$ years, they are known as the *the risk group*. This group can be further categorised into two subgroup namely: *high risk group* and *low risk group*. The high risk group are those who engaged in unprotected sex with multiple sexual partners while the low

risk group also engaged in unprotected sex but with fewer partners. Millions of lives are lost as a result of the infection. In this essay, our aim is to develop a mathematical model, analyse it and propose the optimal stage to initiate ARV treatment for the infected patients which will yield the optimal result in reducing the incidences (new cases) and the mortality of the infection.

1.3 Methodology

In this project, we shall be solving system of first order differential equation. We shall be determining the equilibrium points, the basic reproduction number R_0 by evaluating the next generation matrix, and the condition for stability of the equilibrium points.

Determination of the equilibrium points also known as the steady state: The steady state is the state where the function does not change with time. The steady state of the system of the differential equation can be evaluated by equating the right hand side of each of the derivatives to zero. And then obtain values for each of the variables present in the equation in terms of the parameters.

Mainly, there are two steady states which are usually sort after in any epidemiological model namely, the Disease free equilibrium (DFE) and the Endemic Equilibrium (EE). The disease free equilibrium (DFE) is the situation whereby the population is completely free from the infection after certain number of years. Whereas, the endemic equilibrium (EE) is the state whereby the population is not free from the infection, but the infection stabilized to a certain level in the population after certain number of years.

The basic reproduction number R_0 can be define as the expected number of new infection/ secondary infection caused by introducing an infectious individual into a totally susceptible population. This number form the basis of any epidemiological model because it helps to predict the future occurrence of any infection under consideration and the type of intervention measure that has to be applied.

Stability analysis of steady states (equilibrium points) of the model shall be carried out through the application of the next-generation matrix in order to determine the R_0. In determining R_0, there must be distinction between new infections and all other changes in the population. Let $\mathcal{F}_i(x)$, $\mathcal{V}^+_{i(x)}$ and $\mathcal{V}^-_i(x)$ be continuously differentiable functions with $\mathcal{F}_i(x)$ being the appearance rate of new infection in compartment i, $\mathcal{V}^+_i(x)$ being the transfer rate of individuals into compartment i by all other means while $\mathcal{V}^-_i(x)$ represents the transfer rate of individual out of compartment i. Each of these functions is assumed to be differentiable atleast twice in each variable. The disease transmission is made up of non-negative initial conditions.

$$\dot{x} = \mathrm{f}_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x), \mathrm{i} = 1, ..., n,$$

where $\mathcal{V}_i = \mathcal{V}^-_i(x) - \mathcal{V}^+_i(x)$ where $\mathcal{F}_i(x) \geq 0$, $\mathcal{V}^-_i(x) \geq 0$, and $\mathcal{V}^+_i(x) \geq 0$ for all $\mathrm{i} = 1, ..., n$.

The Jacobian matrix of $\mathcal{F}_i(x)$ and $\mathcal{V}_i(x)$ is evaluated about the disease free equilibrium point.

$\mathrm{F} = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right]$ and $\mathrm{V} = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0)\right]$ with $1 \leq i, j \leq m$ where F and V are $m \times m$ matrix. Where, F is a non-negative and V is a non singular matrix. The basic reproduction number R_0 is evaluated as:

$$R_0 = \rho(\mathrm{FV}^{-1})$$

where ρ denotes the spatial radius of the matrix den Driessche and Watmough (2002).

Effective Reproduction number: In the basic model, the basic reproduction number is computed to determine how the infection spreads if an infective is introduced into a totally susceptible population. However, when control strategies are already in place or are possible, we are more interested in the effective reproduction number. This number is defined as the average number of secondary infection that arises as a result of one primary infection in the population that has the infection. It reflects the impact brought about by any control or prevention measure in place. Although they are not the same, the computation of the effective reproduction number is the same as that of the basic reproduction number R_0

1.4 Outline

Having highlighted the motivation and the general objective of this work, the rest of this essay is structured as follows:

In chapter 2, a simple basic SI (Susceptible-Infectious) model will be developed using ordinary differential equation to study the dynamics of the contagious and incurable disease in any given community. This will be followed by an SI model with vital dynamics such as: birth rate, natural death rate, migration and disease induced death to indicate the dynamics of the infection in the community since it usually persist in the community. In chapter 3, A within host dynamics of the HIV infection will be analysed in this chapter, an SI model with various infection stages as revealed by the within host model shall be analysed. Prevention measure will be incorporated into the model which help to reduce the level of susceptibility and treatment parameters will also be incorporated at various disease stages in order to determine the optimal stage to initialize treatment.The treatment is aimed at reducing the HIV-associated morbidity and mortality and also to help to reduce the risk of HIV transmission.

We shall do numerical simulation in chapter 4 using South African HIV/AIDS data from World bank, Statistical Release of South African and UNAIDS. Conclusion and recommendation will e discussed in chapter 5

2. Basic Model Analysis

In this chapter, we shall be describing the basic SI (Susceptible-Infectious) model. First, we start with the simplest form of any epidemiological model and then progress by including vital dynamics in terms of recruitment (birth and migration) rate, natural death and disease induced death.

2.1 A Basic SI (Susceptible - Infectious) Model

An SI model is used to describe the dynamics of a contagious and *incurable* disease in a population. Examples of such diseases include: those caused by the Ebola virus and HIV which causes AIDS (Acquired immunodeficiency syndrome). The model divides the population into two compartments namely: the susceptible and the infectious. The susceptible compartment is made up of individuals who have no immunity against the infection and can therefore become infected as a result of their interaction with infected individuals. The infected and the infectious are individuals that are presently infected and can transmit the disease to the susceptible. We will assume that the disease occurs on a time-scale much faster than other population processes (births and deaths) and there is no disease induced death, so the population remains constant over time.

Let $S(t)$, be the number of individuals who are susceptible to the disease and $I(t)$, the number of individuals that are infected and are infectious.

The dynamics of a basic SI model using *standard* incidence is given by:

$$\dot{S} = -\frac{\beta SI}{N} \tag{2.1.1}$$

$$\dot{I} = \frac{\beta SI}{N}. \tag{2.1.2}$$

We observed that $\dot{S} + \dot{I} = \frac{d}{dt}\{S + I\} = \frac{dN}{dt} = 0$, and so the total population N remains constant over time. Substituting $S(t) = N - I(t)$ into (2.1.2) gives the *logistic equation*

$$\dot{I} = \beta I \left(1 - \frac{I}{N}\right), \tag{2.1.3}$$

with two equilibrium solutions namely, $I_0 = 0$, which is unstable and $I_1 = N$, which is stable.

Solving equation (2.1.3), with initial condition $I(0) = I_0$, gives

$$I(t) = \frac{NI_0}{I_0 + (N - I_0)e^{-\beta t}} \tag{2.1.4}$$

It can be shown that $\lim_{t\to\infty} I(t) = N$, that is, the disease eventually spreads throughout the community. see figure (2.1).

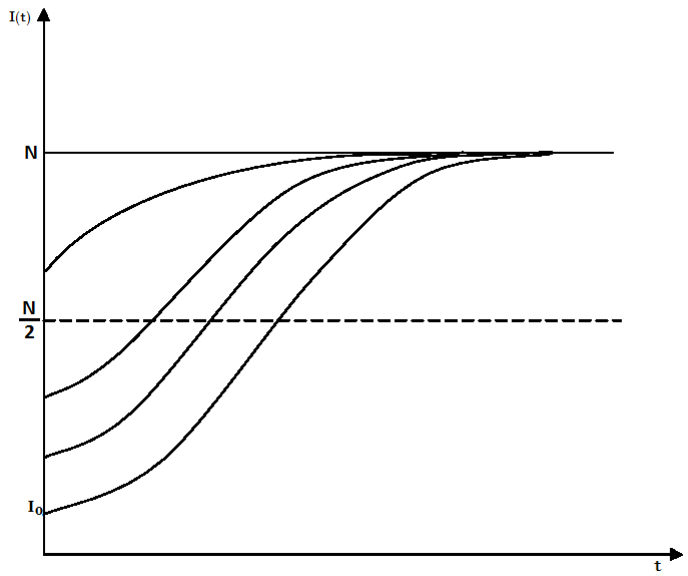

Figure 2.1: A plot of the solution in (2.1.4)

2.1.1 Basic SI model with disease induced death. When the disease is fatal. The basic model then take the form

$$\dot{S} = -\frac{\beta SI}{N} \tag{2.1.5}$$

$$\dot{I} = \frac{\beta SI}{N} - \delta I \tag{2.1.6}$$

where δ is the disease induced death rate. In this case, $\dot{S} + \dot{I} = \dot{N} = -\delta I$, indicating that the population decreases over time. Once again, substituting $S(t) = N - I(t)$, into (2.1.6) results in the *logistic equation*

$$\dot{I} = \beta I\left(1 - \frac{I}{N}\right) - \delta I \tag{2.1.7}$$

$$\dot{I} = (\beta - \delta)I\left(1 - \frac{\beta}{(\beta - \delta)}\frac{I}{N}\right) \tag{2.1.8}$$

with two equilibrium solutions namely, $I_0 = 0$, which is unstable and $I_1 = \left(1 - \frac{\delta}{\beta}\right)N$ which is stable.

Solving equation (2.1.8), with initial condition $I(0) = I_0$, gives

$$I(t) = \frac{(\beta - \delta)NI_0}{\beta I_0 + ((\beta - \delta)N - \beta I_0)e^{-(\beta-\delta)t}} \tag{2.1.9}$$

It follows that $\lim_{t\to\infty} I(t) = \frac{(\beta - \delta)}{\beta} N < N$, that is, the disease reduces the population.

2.2 SI model with vital dynamics

An infectious disease usually stay long in a community,in such situation, we have to incorporate vital dynamics (birth, death and migration) as well as disease induced death into the model. Since there is no cure for the disease, it is necessary to introduce some prevention measures in order to control the disease. A schematic diagram and the resulting dynamics are given below:

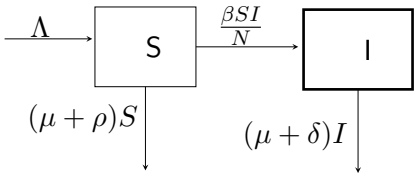

Figure 2.2: A schematic diagram for SI model with vital dynamics

The model below incorporates vital dynamics, disease induced death rate and prevention measures.

$$\dot{S} = \Lambda - \frac{\beta SI}{N} - (\mu + \rho)S \tag{2.2.1}$$

$$\dot{I} = \frac{\beta SI}{N} - \mu I - \delta I \tag{2.2.2}$$

where μ is natural death rate, β is the transmission rate, δ is the disease induce death rate, ρ is the prevention measure, Λ is the recruitment rate, and $N(t) = S(t) + I(t)$ is the total population which satisfies $\dot{N} = \dot{S} + \dot{I} = \Lambda - \mu N - \rho S - \delta I$

Parameter	Description
Λ	Recruitment rate
μ	Natural death rate
ρ	prevention rate
δ	Diseased induced death
β	Transmission rate

Table 2.1: Table showing the parameters of the SI model with vital dynamics

The region Ω described under the dynamics of equation (2.2.2) is defined by $\Omega = \left\{(S,\, I) \in \mathbb{R}^2_+ \,|\, S + I \leq \frac{\Lambda}{\mu}\right\}$ is positive everywhere where the limiting capacity of the population is given as $\lim_{t\to\infty} N(t) = \frac{\Lambda}{\mu}$ in the absence of disease induced death and prevention.

2.2.1 Lemma. *Ω is a compact attracting set (i.e. the Ω limit set of any region starting in $\mathbb{R}^2_+$ lies in Ω).*

Proof. Using the non-negativity of the model state variables and

$$\dot{N} = \Lambda - \mu N - \rho S - \delta I$$

for initial conditions $S(0)$, $I(0) \in \mathbb{R}^2_+$ and $t \geq 0$, we have $\dot{N} \leq \Lambda - \mu N$. This implies that

$$\frac{d}{dt}(N\mathrm{e}^{\mu t}) \leq \Lambda \mathrm{e}^{\mu t} \Longrightarrow N(t)\mathrm{e}^{\mu t} - N(0) \leq \frac{\Lambda}{\mu}(\mathrm{e}^{\mu t} - 1) \leq \frac{\Lambda}{\mu}\mathrm{e}^{\mu t}.$$

So, for all $t \geq 0$,

$$N(t) \leq N(0)\mathrm{e}^{-\mu t} + \frac{\Lambda}{\mu}. \tag{2.2.3}$$

If (S^*, I^*) is an Ω limit point of a region in $\mathbb{R}^2_+$, then there is a subsequence $t_i \to \infty$ such that

$$\lim_{t\to\infty}(S(t_i), I(t_i)) = (S^*, I^*).$$

Hence,

$$\lim_{t\to\infty} N(t_i) = N^* = S^* + I^*.$$

From equation (2.2.3) (by evaluating $t = t_i$ and passing to the limit $i \to \infty$), it follows that $N^* \leq \frac{\Lambda}{\mu}$ and hence, this shows that $(S^*, I^*) \in \Omega$.

Thus, for any initial starting point $(S_0, I_0) \in \mathbb{R}^2_+$, the trajectory lies within Ω. Therefore, the system is both mathematically and epidemiologically well posed. □

2.2.2 Lemma. *The region $\mathbb{R}^2_+$ is positive everywhere for the model described in (2.2.2)*

Proof. Let $t_1 = sup\{t > 0 \,|\, S \geq 0, I \geq 0 \in [0, t]\}$. From equation(2.2.2), we have

$$\dot{S} = \Lambda - (\lambda(t) + \mu + \rho)S, \text{ where } \qquad \lambda(t) = \frac{\beta I}{N}.$$

This is the same as

$$\dot{S} + (\lambda(t) + \mu + \rho)S = \Lambda,$$

and this implies that

$$\frac{d}{dt}\left(S(t)\, exp\left\{(\mu+\rho)t + \int_0^t \lambda(\tau)d\tau\right\}\right) = \Lambda\, exp\left\{(\mu+\rho)t + \int_0^t (\lambda(\tau))d\tau\right\}.$$

Thus,

$$S(t_1)\, exp\left\{(\mu+\rho)t_1 + \int_0^{t_1} \lambda(\tau)d\tau\right\} - S(0) = \int_0^{t_1} \Lambda\, exp\left\{(\mu+\rho)\phi + \int_0^{\phi} \lambda(\epsilon)d\epsilon\right\} d\phi.$$

Hence,

$$\begin{aligned} S(t_1) &= S(0)\, exp\left\{-\left((\mu+\rho)t_1 + \int_0^{t_1} \lambda(\tau)d\tau\right)\right\} \\ &+ exp\left\{-\left((\mu+\rho)t_1 + \int_0^{t_1} \lambda(\tau)d\tau\right)\right\} \\ &\times \int_0^{t_1} \Lambda\, exp\left\{(\mu+\rho)\phi + \int_0^{\phi} \lambda(\epsilon)d\epsilon\right\} d\phi \\ &\geq 0. \end{aligned}$$

Similarly, we can show that $I(t) \geq 0$. This completes the proof. □

The above lemma is important because it guarantees that the model variables are continuously biologically meaningful, since population size cannot be negative.

The steady state analysis of the model described in equation (2.2.1 and 2.2.2) reveals that the model has two equilibrium points. The disease free equilibrium DFE point gives $(S_0, I_0) = \left(\frac{\Lambda}{\mu+\rho}, 0\right)$ and the endemic equilibrium EE point gives $(S_E, I_E) = \left(\frac{\Lambda(\mu+\delta)}{\beta\mu}, \frac{\Lambda(\beta\mu-(\mu+\rho)(\mu+\delta))}{\beta\mu(\mu+\delta)}\right)$

2.3 The Stability analysis of the equilibrium points.

Determination of the condition for stability of disease free equilibrium point. The DFE is locally asymptotically stable if $\frac{\beta\mu}{(\mu+\delta)(\mu+\rho)} \leq 1$.

The Jacobian matrix of the system is

$$J(S,I) = \begin{pmatrix} -\frac{\beta\mu I}{\Lambda} - (\mu+\rho) & -\frac{\beta\mu S}{\Lambda} \\ \frac{\beta\mu I}{\Lambda} & \frac{\beta\mu S}{\Lambda} - (\mu+\delta) \end{pmatrix} \tag{2.3.1}$$

Evaluating Jacobian matrix at the disease free equilibrium point gives

$$J(S_0,\, I_0) = \begin{pmatrix} -(\mu+\rho) & -\frac{\beta\mu}{(\mu+\rho)} \\ 0 & \frac{\beta\mu}{(\mu+\rho)} - (\mu+\delta) \end{pmatrix} \tag{2.3.2}$$

The eigenvalues of the Jacobian matrix are $\lambda_1 = -(\mu+\rho)$ and $\lambda_2 = \frac{\beta\mu}{(\mu+\rho)} - (\mu+\delta)$.

Routh-Hurwitz stability criterion stated that a 2×2 matrix will have negative roots provided the tr < 0 and the det > 0, where tr and det represent the trace and the determinant of the matrix respectively.

Hence, the disease free equilibrium point will be locally asymptotically stable if $\frac{\beta\mu}{(\mu+\rho)} < \mu+\delta$, that is, $\frac{\beta\mu}{(\mu+\delta)(\mu+\rho)} \leq 1$. In that case, it is obvious that $J(S_0, I_0)$ will be unstable if $\frac{\beta\mu}{(\mu+\rho)} > \mu+\delta$, $\frac{\beta\mu}{(\mu+\delta)(\mu+\rho)} > 1$. Hence the effective reproduction number

$$\mathrm{R}_0(\rho) = \frac{\beta\mu}{(\mu+\delta)(\mu+\rho)}. \tag{2.3.3}$$

2.3.1 Remark. From equation (2.3.3), we see that if $\rho = 0$ (no prevention measures)

$$R_0(0) = \frac{\beta}{(\mu+\delta)} > \frac{\beta\mu}{(\mu+\delta)(\mu+\rho)} = \mathrm{R}_0(\rho).$$

The inequality implies that it will be easier to control the disease when prevention measures are in place.

The endemic equilibrium point can be written in term of $R_0(\rho)$ as:

$$(S_E, I_E) = \left(\frac{\Lambda}{\mathrm{R}_0(\rho)(\mu+\rho)}, \frac{\Lambda(\mu+\rho)}{\beta\mu}(\mathrm{R}_0(\rho)-1)\right). \tag{2.3.4}$$

2.3.2 Theorem. *The endemic equilibrium EE point is locally asymptotically stable if* $\mathrm{R}_0(\rho) > 1$.

Proof. Evaluating the Jacobian matrix at the endemic equilibrium point gives:

$$J_2 = J(S_E, I_E) = \begin{pmatrix} \frac{-\beta\mu I_E}{\Lambda} - (\mu+\rho) & \frac{-\beta\mu S_E}{\Lambda} \\ \frac{-\beta\mu I_E}{\Lambda} & \frac{\beta\mu S_E}{\Lambda} - (\mu+\delta) \end{pmatrix} \tag{2.3.5}$$

$$= \begin{pmatrix} -(\mu+\rho)R_0(\rho) & \frac{-\beta\mu}{(\mu+\rho)R_0(\rho)} \\ (\mu+\rho)(R_0(\rho)-1) & 0 \end{pmatrix} \tag{2.3.6}$$

By applying Routh-Hurwitz stability condition, trace$(J_2) < 0$ and det $(J_2) > 0$. Since all the parameters are non-negative, clearly, trace$(J_2) = -(\mu+\rho)R_0(\rho) < 0$ and Det$(J_2) = \frac{\beta\mu}{R_0(\rho)}(R_0(\rho)-1) > 0$ provided $R_0(\rho) > 1$. Hence, the endemic equilibrium point is locally asymptotically stable if $R_0(\rho) > 1$. This ends the proof □

3. SI model of HIV/AIDS

3.1 Within Host Model of the HIV/AIDS

Several models have been formulated to describe the dynamics of the HIV/AIDS pandemic within the host system. We studied a system of ordinary differential equation illustrating the changes that happened in the immune system as a result of the virus. This helps to test the responsiveness of the immune system to treatment. The virus attack certain white blood cells important to the functionality of the immune system. These cells are known as *helper T* cells (specifically, $CD4^+$ T cells). The $CD4^+$ T cells are white blood cells that help to organise the immune system which helps to fight against infection in the body. They are usually produced in the bone marrow. The $CD4^+$ T cells of an healthy individual is usually between 1000 and 1200 cells/mm^3, whereas as soon as an individual is infected with HIV, the number of the cells begin to drop Nowak and Bangham (1996).

Infection with this virus is characterized by a long asymptomatic period that lasts for several year. During this time, the viral load (the level of the virus in an individual) remains relatively stable, and the infection seems to be "latent". The first effective antiretroviral drugs (introduced around 1995) has revealed a highly dynamics picture of this "latency". As soon as the treatment commences, the viral load begins to fall typically several orders of magnitude within $1-2$ weeks. The drug blocks the infection of new cells, but does not affect the death of already infected cells nor have any role in the breakdown of the virus particles. Therefore, the rapid decline that was observed reflects the normal decay of infected cells and virus, which is, in the absence of treatment, balanced by equally fast production Muller (Accessed 2014).

The model below will be expatiating how the $CD4^+$ T cells population and the viral load changes within the host system. When an individual is infected with HIV, an immune response to the virus occurs and antibodies against the virus can be detected in the blood. At the end of the asymptomatic stage, the viral load increases and the immune system collapses. The infection results in a decrease in the number of $CD4^+$ T cells as the disease progresses Philips (1996).

The basic model for $CD4^+$ T cells and the virus dynamics is a system of three ordinary differential equations representing the number of uninfected $CD4^+$ T cells, infected $CD4^+$ T cells and the free virus which are represented as T, I and V respectively. In this model, the uninfected cell are assumed to be produced at the constant rate Λ, die at the rate μ_T per cell, and to be infected by the free virus, according to a simple mass action infection term βTV. This generates productively infected cells, I, which are lost at the rate μ_I, larger than μ_T, which is meant to reflect viral effects in shortening lifespan of the infected cell. Finally, free virus are produced by infected cells at constant $n\mu_I$ per cell, and are cleared from circulation at the rate c per virus Ribeiro and Pereson (2004).

The schematic diagram for the model is shown in figure (3.1) and the differential equations describing the model are:

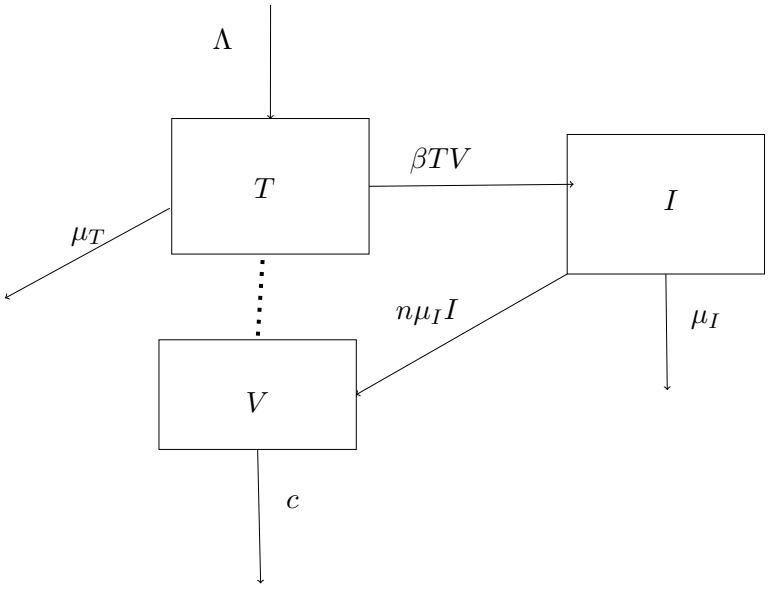

Figure 3.1: A schematic diagram for the within host model

$$\begin{aligned} \dot{T} &= \Lambda - \beta TV - \mu_T T \\ \dot{I} &= \beta TV - \mu_I T \\ \dot{V} &= n\mu_I - cV. \end{aligned} \tag{3.1.1}$$

Steady state analysis was carried out on equation (3.1.1), and the disease free equilibrium DFE point was obtained as

$$(T_0,\, I_0,\, V_0) = \left(\frac{\Lambda}{\mu_T},\, 0,\, 0\right).$$

and the endemic equilibrium EE point was obtained as

$$(T_E,\, I_E,\, V_E) = \left(\frac{c}{\beta n},\, \frac{n\beta\Lambda - c\mu_T}{n\beta\mu_I},\, \frac{n\beta\Lambda - c\mu_T}{c\beta}\right).$$

From the next generation matrix, the basic reproduction number is given as

$$R_0 = \frac{n\beta\Lambda}{c\mu_T}.$$

Hence, the endemic equilibrium points can be written in terms of R_0 as

$$(T_E,\, I_E,\, V_E) = \left(\frac{\Lambda}{R_0\mu_T},\, (R_0-1)\frac{c\mu_T}{n\mu_I\beta},\, (R_0-1)\frac{\mu_T}{\beta}\right).$$

The Jacobian matrix of the system is given as

$$J(T,I,V) = \begin{pmatrix} -\beta V - \mu_T & 0 & -\beta T \\ \beta V & -\mu_I & \beta T \\ 0 & n\mu_I & -c \end{pmatrix} \tag{3.1.2}$$

3.1.1 Theorem. *The disease free equilibrium point is locally asymptotically stable if* $R_0 < 1$.

Proof. The Jacobian matrix evaluated at disease free DFE equilibrium point is given as

$$J_0 = J(T_0, I_0, V_0) = \begin{pmatrix} -\mu_T & 0 & -\dfrac{\beta\Lambda}{\mu_T} \\ 0 & -\mu_I & \dfrac{\beta\Lambda}{\mu_T} \\ 0 & n\mu_I & -c \end{pmatrix} \tag{3.1.3}$$

One of the eigenvalues of J_0 is $\lambda_1 = -\mu$ and the other two eigenvalues can be obtained from the sub-matrix

$$J_0^s = \begin{pmatrix} -\mu_I & \dfrac{\beta\Lambda}{\mu_T} \\ n\mu_I & -c \end{pmatrix} \tag{3.1.4}$$

by applying Routh-Hurwitz stability criterion, $tr(J_0^s) = -(\mu_I + c) < 0$ and the $det(J_0^s) = c\mu_I - \dfrac{n\beta\mu_I\Lambda}{\mu_T} > 0$ implies that $c\mu_I > \dfrac{n\beta\mu_I\Lambda}{\mu_T}$ which result to $1 > \dfrac{n\beta\Lambda}{c\mu_T} = R_0$. Hence the disease free equilibrium DFE point is locally asymptotically stable provided that $R_0 < 1$ and unstable if otherwise. This ends the proof. □

3.1.2 Theorem. *The endemic equilibrium EE point is locally asymptotically stable if* $R_0 > 1$.

Proof. The Jacobian matrix evaluated at the endemic equilibrium point is given as

$$J_2 = J(T_E, I_E, V_E) = \begin{pmatrix} -\beta V_E - \mu_T & 0 & -\beta T_E \\ \beta V_E & -\mu_I & \beta T_E \\ 0 & n\mu_I & -c \end{pmatrix} \tag{3.1.5}$$

$$= \begin{pmatrix} -R_0\mu_T - \lambda & 0 & -\frac{\beta\Lambda}{R_0\mu_T} \\ (R_0 - 1)\mu_T & -\mu_I - \lambda & \frac{\beta\Lambda}{R_0\mu_T} \\ 0 & n\mu_I & -c - \lambda \end{pmatrix} \tag{3.1.6}$$

The characteristic polynomial resulting from this matrix is given as

$$P(\lambda_{1,2,3}) = \lambda^3 + (\mu_I + c + \mu_T R_0)\lambda^2 + (c + \mu_I)\mu_T R_0 + c\mu_I\mu_T(R_0 - 1) = 0.$$

By applying Routh- Hurwitz stability criterion, a polynomial of degree three, will have all its roots negative provided each of the coefficient is non-negative. For instance, $a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0$.

The polynomial has negative roots provided that $a_3 > 0$, $a_2 > 0$, $a_1 > 0$ $a_0 > 0$ and $a_2 a_1 > a_3 a_0$ since each of the parameters is non-negative,

$$\begin{aligned} a_3 &= 1 > 0 \\ a_2 &= \mu_T R_0 + \mu_I + c > 0 \\ a_1 &= (c + \mu_I)\mu_T R_0 > 0 \\ a_0 &= c\mu_T \mu_I (R_0 - 1) > 0 \implies R_0 > 1 \\ a_2 a_1 &= (\mu_T R_0 + \mu_I + c)(c\mu_T R_0 + \mu_I \mu_T R_0) \\ a_3 a_0 &= (c + \mu_I)\mu_T R_0 \\ (\mu_T R_0 + \mu_I + c)(c\mu_T R_0 + \mu_I \mu_T R_0) &> (c + \mu_I)\mu_T R_0 \end{aligned}$$

Clearly, $a_2 a_1 > a_3 a_0$ which implies that the polynomial has all its roots negative. Hence, the endemic equilibrium point is locally asymptotically stable provided that $R_0 > 1$. □

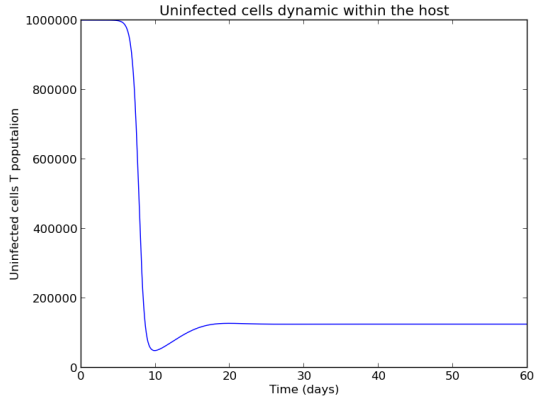

Figure 3.2: A plot of the Uninfected cells

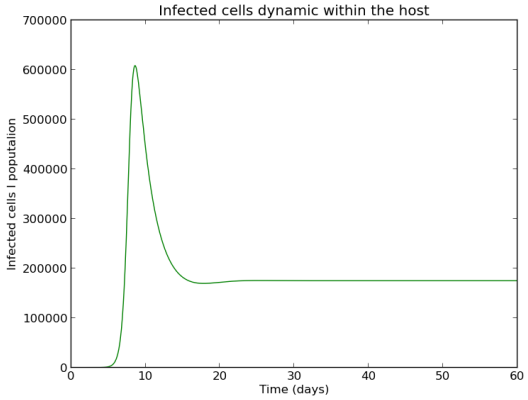

Figure 3.3: A plot of the infected cells

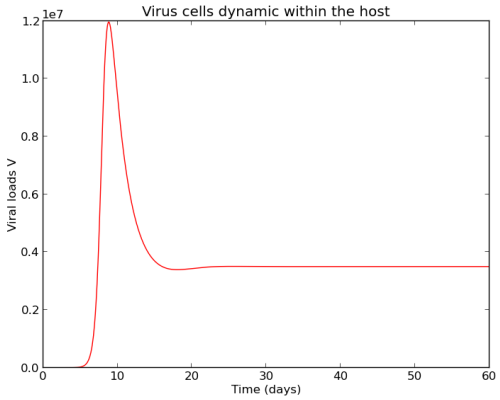

Figure 3.4: A plot of the virus

Figure (3.2), (3.3) and (3.4) show the dynamics of the uninfected cells, the infected cell and the virus respectively within the host body in the first 8^{th} weeks of the infection. These plots were produced using the following parameters: $\Lambda = 10^5$ cells day^{-1}, $\beta = 2 \times 10^{-7}$ cells^{-1} ml^{-1} day^{-1}, $n = 200$, $\mu_T = 0.1\, day^{-1}$, $\mu_I = 0.5\, day^{-1}$ and $c = 5\, day^{-1}$ (Allen, 2007)

3.2 Various stages of HIV infection

It is a known fact, that there are about $3 - 4$ stages of HIV infection. It has also been established that its transmission rate is not uniform. It differs from one stage of infection to another. Hence, epidemiological model must incorporate the stages of infection progression in order to capture the dynamics of the infection in the population. As an infected individual progresses from one infection stage to another, their level of infectiousness changes. Therefore, the transmission dynamics of the viruses can be categorised based on the infection stage progression of an infected individual C. et al. (2000). These stages are categorised into four and are explained below:

3.2.1 Stages of HIV infection. The HIV infection passes through a series of stages before it turns into AIDS. The immune system is progressively destroyed by the virus. This destruction can be observed in the number of $CD4^+T$ cells present in the blood. There is decrease in the immunity of the body system and this gives room for opportunistic infection to overwhelm the body. Opportunistic infections are caused by organisms that do not cause infections in healthy individuals.

The stages of the infection are outlined below:

- Primary stage: This stage occurs after acquiring the infection, it usually last for a very short period of about $2-6$ weeks. At this stage, the virus level is very high and as a result, the infected individual show certain symptoms of infections (flu like symptoms).
- Asymptomatic stage: This stage is free from major symptoms, the viral load present in the blood become very low. Although, the virus is not dominant at this stage, but they are very active and the infected individual remain infectious. The stage usually last for about $8 - 10$ years.
- Symptomatic stage: At this stage, the virus become more pathogenic (more stronger and varies) due to their year of activities and this leads to the destruction of the $CD4^+$ T cells. The body fails to keep replacing the $CD4^+$ T cells that are lost. Hence, the individual begins to show symptoms of the infection. This stage is also known as the pre AIDS stage. It usually last for about $2 - 3$ years. At this stage the number of the $CD4^+$ T cells < 350 cells/mm^3 in the blood plasma.
- Advance AIDS stage: This stage is characterized by severe immunodeficiency. There are signs of life-threatening infections and unusual tumours. These infections are as a result of the immune system inability to fight infections. The $CD4^+$ T cells of the individuals at this stage is < 200 cells/mm^3 AIDSP.

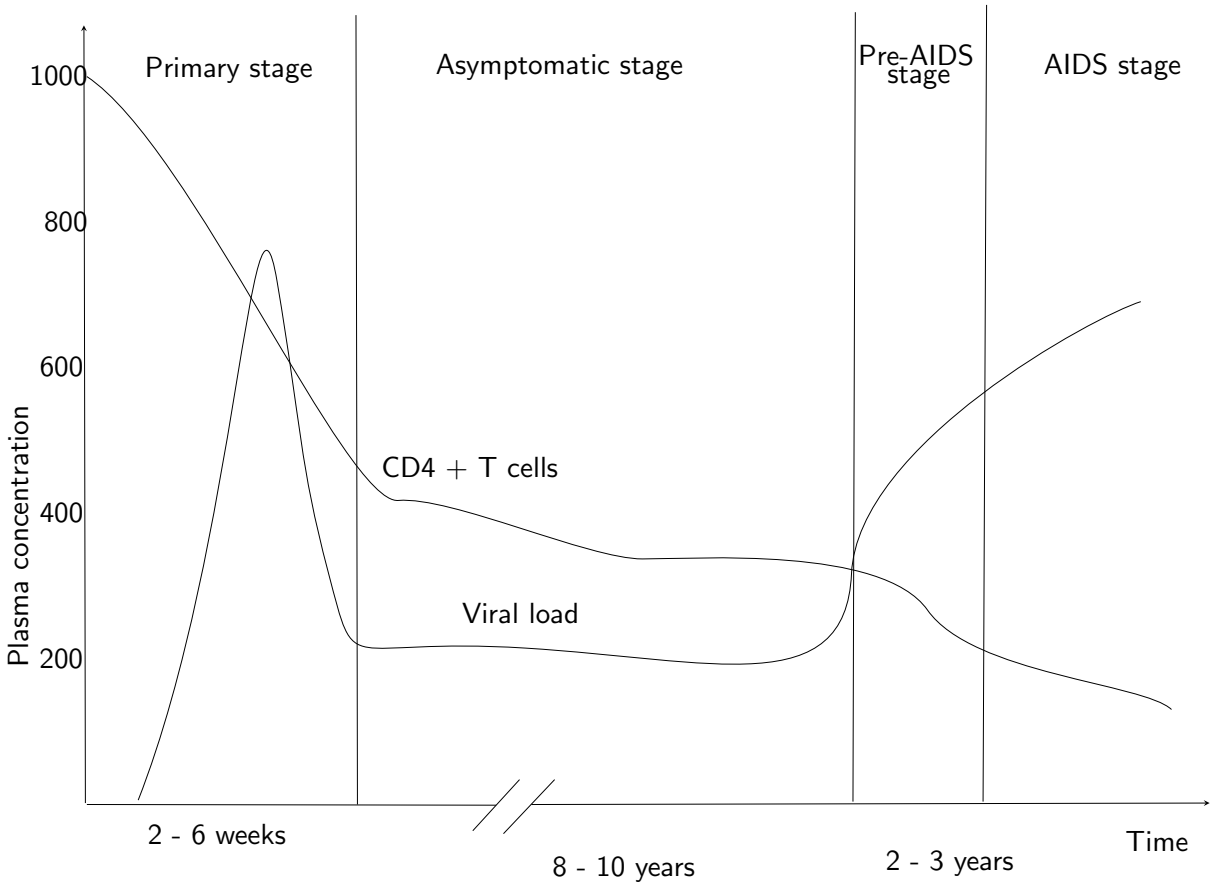

Figure 3.5: Figure showing the dynamics of HIV within the host system

3.3 Between Host model

We shall be analysing an SI model with four infection stages. A system of six ordinary differential equations shall be used for the model analysis. Incorporated into the model are the recruitment rate (birth rate and migration rate), natural death rate, disease induced death, prevention and treatment parameters.

We considered a sexually active population $N(t)$, divided into six compartments: $S(t)$, $I_1(t)$, $I_2(t)$, $I_3(t)$, $A(t)$ and $T(t)$. $S(t)$ represents the numbers of susceptible individuals, $I_1(t)$ represents the number of HIV positive individuals in the primary stage, $I_2(t)$ represents the numbers of HIV positive individuals in the asymptomatic stage, $I_3(t)$ represents the numbers of HIV positive individuals in the symptomatic or (Pre AIDS) stage, $A(t)$ represents the numbers of HIV positive individuals with advance (full blown) AIDS stage and $T(t)$ represent the numbers of HIV positive individuals receiving ARV treatment. Certain proportion of the susceptible population are removed. These are the people who have modified their sexual contact. They take up safe sexual habits and maintain the habits for the rest of their lives. The significance of this is that it emphasizes the importance of prevention as the control of the disease, since the infection is *incurable*. Increasing the number of these sets of individuals is a vital key in controlling the incidence of the disease.This model is somewhat similar to the model described in a paper presented by Yussuf and Benyah (2011) except for the fact that the primary stage

was considered as a compartment independent of the other compartments and the removed class was left out because they do not partake in the transmission of the infection.

3.3.1 Assumption about the model..

- The susceptible population $S(t)$ is homogeneous.
- Mechanism of infection is not assumed in the model, that is it could be homosexual or heterosexual.
- Certain proportion of the susceptible population are removed. They are considered to have modified their sexual behaviour, so we regard them as having literally immunity against the infection.
- Each compartment has different transmission rate with the primary stage having the highest transmission rate while the asymptomatic stage has the least transmission rate.
- The advanced AIDS patients are assumed not to transmit the infection because they are very weak, so they could not engage in any sexual activity.
- Treatment is administered to one group at a time. The primary group were never considered for treatment because they are not aware of their status.
- The treated group are assumed not to contribute to the transmission of the infection as a result of the constant counselling section they undergo.
- There is no disease induced death apart from those in the advanced AIDS stage.

The schematic diagram and the equations representing the dynamics of the infection are given in figure (3.6) and equation (3.3.1) respectively

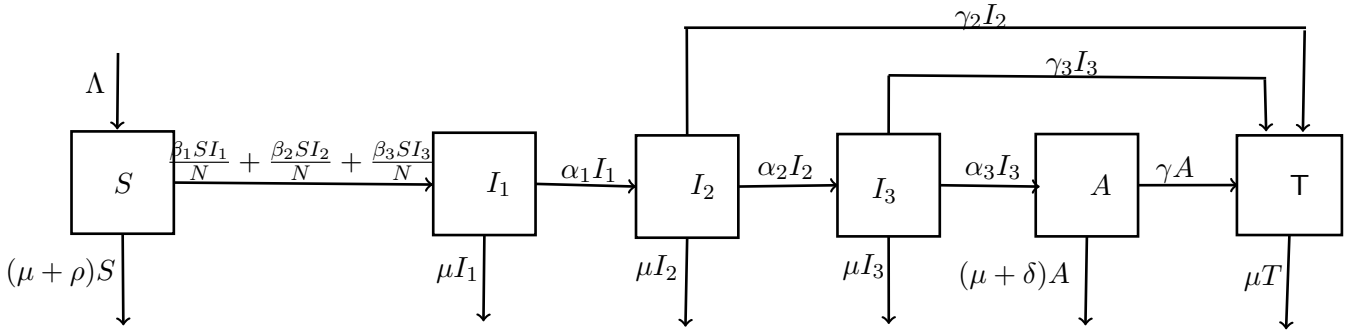

Figure 3.6: A schematic diagram for the spread of HIV infection

3.3.2 The model dynamics.

$$
\begin{aligned}
\dot{S} &= \Lambda - \left(\frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N}\right) S - (\mu+\rho)S \\
\dot{I}_1 &= \left(\frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N}\right) S - (\mu+\alpha_1)I_1 \\
\dot{I}_2 &= \alpha_1 I_1 - (\mu+\alpha_2+\gamma_2)I_2 \\
\dot{I}_3 &= \alpha_2 I_2 - (\mu+\alpha_3+\gamma_3)I_3 \\
\dot{A} &= \alpha_3 I_3 - (\mu+\delta_1+\gamma_A)A \\
\dot{T} &= \gamma_2 I_2 + \gamma_3 I_3 + \gamma_A A - \mu T
\end{aligned}
\tag{3.3.1}
$$

where $\beta_i = cp_i$, $i = 1, 2, 3$ is the product of the average number of sexual partners(c) and the probability (p_i) of the infection per partner with an infected individual in I_1, I_2, and I_3 respectively. The total population, $N(t)$ is given by

$$N = S(t) + I_1(t) + I_2(t) + I_3(t) + A(t) + T(t) \tag{3.3.2}$$

and it satisfies

$$\dot{N} = \Lambda - \mu N - \rho S - \delta A \tag{3.3.3}$$

where Λ is the recruitment rate, β_i, $i = 1, 2, 3$ is the transmission rate, μ is the natural death rate, α_i, $i = 1, 2, 3$ is the progression rate from one infection stage to another, ρ is the prevention measure, γ_i, $i = 2, 3, A$ is the treatment parameter and δ is the disease induced death rate. The table (3.1) presents the details of the parameters definitions

$Parameter$	The equations then becomes Description
β_1	Transmission rate of primary infectious individual
β_2	Transmission rate of asymptomatic infectious individual
β_3	Transmission rate of symptomatic infectious individual
Λ	Recruitment rate
μ	Natural death rate
α_1	Progression rate from the I_1 to I_2
α_2	Progression rate from the I_2 to I_3
α_3	Progression rate from the I_3 to A
δ	Diseased induced death
ρ	Rate of removal of susceptible
γ_2	Treatment rate for asymptomatic infectious individual
γ_3	Treatment rate for symptomatic infectious individual
γ_A	Treatment rate for advanced AIDS individual

Table 3.1: Parameters definition for the model

The system dynamics described in (3.3.1) will be studied in the region Ω, defined by

$$\Omega = \left\{ (S,\, I_1,\, I_2,\, I_3,\, A,\, T) \in \mathrm{R}^6_+ \,|\, S + I_1 + I_2 + I_3 + A + T \leq \frac{\Lambda}{\mu} \right\}$$

which is positively invariant.

3.3.3 Lemma. *The region $\mathbb{R}^6_+$ is positively everywhere for the model (3.3.1) (i.e the model does not predict negative values for the state variables at any future time).*

Proof. Let $t_1 = sup\{t > 0 \,|\, S \geq 0,\, I_1 \geq 0,\, I_2 \geq 0,\, I_3 \geq 0,\, A \geq 0,\, T \geq 0 \in [0, t]\}$. From equation(1), we have

$$\dot{S} = \Lambda - (\lambda(t) + \mu + \rho)S, \qquad \text{where} \qquad \lambda(t) = \frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N}.$$

This is the same as

$$\dot{S} + (\lambda(t) + \mu + \rho)S = \Lambda,$$

and this implies that

$$\frac{d}{dt}\left(S(t)\,exp\left\{(\mu+\rho)t+\int_0^t\lambda(\tau)d\tau\right\}\right)=\Lambda\,exp\left\{(\mu+\rho)t+\int_0^t\lambda(\tau)d\tau\right\}.$$

Thus,

$$S(t_1)\,exp\left\{(\mu+\rho)t_1+\int_0^{t_1}(\lambda(\tau)d\tau\right\}-S(0)=\int_0^{t_1}\Lambda\,exp\left\{(\mu+\rho)\phi+\int_0^{\phi}\lambda(\epsilon)d\epsilon\right\}d\phi.$$

Hence,

$$\begin{aligned}S(t_1)=S(0)\,exp&\left\{-\left((\mu+\rho)t_1+\int_0^{t_1}\lambda(\tau)d\tau\right)\right\}\\&+exp\left\{-\left((\mu+\rho)t_1+\int_0^{t_1}\lambda(\tau)d\tau\right)\right\}\\&\times\int_0^{t_1}\Lambda\,exp\left\{(\mu+\rho)\phi+\int_0^{\phi}\lambda(\epsilon)d\epsilon\right\}d\phi\\&\geq 0.\end{aligned}$$

Similarly, we can show that $I_1(t)\geq 0, I_2(t)\geq 0, I_3(t)\geq 0$, $A(t)\geq 0$ and $T(t)\geq 0$. This completes the proof. □

The above lemma is important because it guarantees that the model variables are continuously biologically meaningful, since population size cannot be negative.

3.3.4 Lemma. *Ω is a compact attracting set (i.e. the Ω limit set of any arbitrary starting in $\mathbb{R}^6_+$ lies in Ω).*

Proof. Using the non-negativity of the model state variables as established in the preceding lemma and

$$\dot{N}=\Lambda-\mu N-\rho S-\delta A$$

for initial conditions in $\mathbb{R}^6_+$ and $t\geq 0$, we have $\dot{N}\leq\Lambda-\mu N$. This implies that

$$\frac{d}{dt}(N\mathrm{e}^{\mu t})\leq\Lambda\mathrm{e}^{\mu t}\Longrightarrow N(t)\mathrm{e}^{\mu t}-N(0)\leq\frac{\Lambda}{\mu}(\mathrm{e}^{\mu t}-1)\leq\frac{\Lambda}{\mu}\mathrm{e}^{\mu t}.$$

So, for all $t\geq 0$,

$$N(t)\leq N(0)\mathrm{e}^{-\mu t}+\frac{\Lambda}{\mu}. \tag{3.3.4}$$

If $(S^*, I_1^*, I_2^*, I_3^*, A^*, T^*)$ is an Ω limit point of a region in $\mathbb{R}^6_+$, then there is a subsequence $t_i\to\infty$ such that

$$\lim_{t\to\infty}(S(t_i), I_1(t_i), I_2(t_i), I_3(t_i), A(t_i), T(t_i))=(S^*, I_1^*, I_2^*, I_3^*, A^*, T^*).$$

Hence,

$$\lim_{t\to\infty}N(t_i)=N^*=S^*+I_1^*+I_2^*+I_3^*+A^*+T^*.$$

From Equation (3.3.4) (by evaluating $t=t_i$ and passing to the limit $i\to\infty$) , it follows that $N^*\leq\frac{\Lambda}{\mu}$ and hence that $(S^*, I_1^*, I_2^*, I_3^*, A^*\,T^*)\in\Omega$.

Thus, for any initial starting point $(S(0), I_1(0), I_2(0), I_3(0), A(0), T(0))\in\mathbb{R}^6_+$, the trajectory lies within Ω. Therefore, the system is both mathematically and epidemiologically well posed. □

3.3.5 Analysis of the model. The stability analysis of the model revealed that the model is made up of two equilibrium points. The disease free equilibrium DFE point is given as:

$$(S,\, I_1,\, I_2,\, I_3,\, A,\, T) = \left(\frac{\Lambda}{\mu+\rho},\, 0,\, 0,\, 0,\, 0,\, 0\right)$$

while the endemic equilibrium point is given as:

$$S^* = \frac{\Lambda}{\lambda+\mu+\rho} \tag{3.3.5}$$

$$I_1{}^* = \frac{\lambda}{(\mu+\alpha_1)} S^* \tag{3.3.6}$$

$$I_2{}^* = \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} I_1{}^* \tag{3.3.7}$$

$$I_3{}^* = \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} \frac{\alpha_2}{(\mu+\alpha_3+\gamma_3)} I_1{}^* \tag{3.3.8}$$

$$A^* = \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} \frac{\alpha_2}{(\mu+\alpha_3+\gamma_3)} \frac{\alpha_3}{(\mu+\delta+\gamma_A)} I_1{}^* \tag{3.3.9}$$

$$T^* = \left[\frac{\gamma_2}{\mu} \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} + \frac{\gamma_3}{\mu} \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} \frac{\alpha_2}{(\mu+\alpha_3+\gamma_3)} + \frac{\gamma_A}{\mu} \frac{\alpha_1}{(\mu+\alpha_2+\gamma_2)} \frac{\alpha_2}{(\mu+\alpha_3+\gamma_3)} \frac{\alpha_3}{(\mu+\delta+\gamma_A)}\right] I_1{}^* \tag{3.3.10}$$

where $\lambda = \frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N}$.

3.4 Effective reproduction number analysis

This model is made up of five infectious compartments namely: the primary compartment I_1, the asymptomatic compartment I_2, the symptomatic compartment I_3, the advance AIDS compartment A and the treated compartment T. Compartments A and T are assumed not to contribute to the infection transmission because the individuals in compartment A are considered to be generally very weak and hence, could not partake in any sexual act, while those in compartment T are assumed to adhere to the counselling instructions that are provided to them . Although, we don't expect total compliance for abstinence. We assume that the transmission rate of those individuals that fail to comply are negligible.

The threshold quantity $R_0(\rho)$ for this model was evaluated using next generation matrix technique for compartmental models presented by den Driessche and Watmough (2002).

$$\mathcal{F} = \begin{pmatrix} \left(\frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N}\right) S \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{3.4.1}$$

$$\mathcal{V} = \begin{pmatrix} (\mu+\alpha_1)I_1 \\ -\alpha_1 I_1 + (\mu+\alpha_2+\gamma_2)I_2 \\ -\alpha_2 I_2 + (\mu+\alpha_3+\gamma_3)I_3 \\ -\alpha_3 I_3 + (\mu+\delta+\gamma_A)A \\ -\gamma_2 I_2 - \gamma_3 I_3 - \gamma_A A + \mu T \end{pmatrix} \tag{3.4.2}$$

By evaluating the Jacobian matrix at the disease free equilibrium of $\mathcal{F}$ and $\mathcal{V}$.
we obtain,

$$\mathrm{F} = \begin{pmatrix} \frac{\beta_1\mu}{\mu+\rho} & \frac{\beta_2\mu}{\mu+\rho} & \frac{\beta_3\mu}{\mu+\rho} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.4.3}$$

$$\mathrm{V} = \begin{pmatrix} (\mu+\alpha_1) & 0 & 0 & 0 & 0 \\ -\alpha_1 & (\mu+\alpha_2) & 0 & 0 & 0 \\ 0 & -\alpha_2 & (\mu+\alpha_3+\epsilon_1) & 0 & 0 \\ 0 & 0 & -\alpha_3 & (\mu+\delta+\gamma_2) & 0 \\ 0 & 0 & -\epsilon_1 & -\gamma_2 & \mu \end{pmatrix} \tag{3.4.4}$$

$$\mathrm{FV}^{-1} = \begin{pmatrix} M_{11} & M_{12} & M_{13} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.4.5}$$

$$M_{11} = \frac{\beta_1\mu}{(\mu+\rho)(\mu+\alpha_1)} + \frac{\alpha_1\beta_2\mu}{(\mu+\rho)(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1,\alpha_2\beta_3\mu}{(\mu+\rho)(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)} \tag{3.4.6}$$

$$M_{12} = \frac{\beta_3\mu}{(\mu+\rho)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_2\beta_2\mu}{(\mu+\rho)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)} \tag{3.4.7}$$

$$M_{13} = \frac{\beta_3\mu}{(\mu+\rho)(\mu+\alpha_3++\gamma_3)} \tag{3.4.8}$$

$R_0(\rho)$ is given as

$$R_0(\rho) = M_{11} = \frac{\beta_1\mu}{(\mu+\rho)(\mu+\alpha_1)} + \frac{\alpha_1\beta_2\mu}{(\mu+\rho)(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1,\alpha_2\beta_3\mu}{(\mu+\rho)(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)}$$

The basic reproduction number for the model is given as

$$R_0 = \frac{\beta_1}{(\mu+\alpha_1)} + \frac{\alpha_1\beta_2}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1\alpha_2\beta_3}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)}$$

$$R_0(\rho) = \frac{\mu}{(\mu+\rho)}R_0$$

where

1. $\frac{\alpha_1}{\mu+\alpha_1}$ is the probability that an infective progresses from I_1 to I_2.
2. $\frac{\alpha_2}{\mu+\alpha_2+\gamma_2}$ is the probability that an infective progresses from I_2 to I_3.
3. $\frac{\alpha_3}{\mu+\alpha_3+\gamma_3}$ is the probability that an infective progresses from I_3 to A.
4. $\frac{\mu}{\mu+\rho}$ is the proportion of the susceptible individual that died due to natural death.

from equation (3.3.6) we have

$$\begin{aligned}
\frac{{I_1}^*}{S^*} &= \frac{\lambda}{(\mu+\alpha_1)} \\
\frac{{I_1}^*}{S^*} &= \frac{1}{(\mu+\alpha_1)}\left(\frac{\beta_1 I_1 + \beta_2 I_2 + \beta_3 I_3}{N}\right) \\
\frac{N^*}{S^*} &= \frac{1}{(\mu+\alpha_1)}\left[\beta_1 + \frac{\beta_2 {I_2}^*}{{I_1}^*} + \frac{\beta_3 {I_3}^*}{{I_1}^*}\right] \\
\frac{N^*}{S^*} &= \frac{1}{(\mu+\alpha_1)}\left[\beta_1 + \frac{\alpha_1\beta_2}{(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1\alpha_2\beta_3}{(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)}\right] \\
\frac{N^*}{S^*} &= R_0
\end{aligned}$$

$$\begin{aligned}
R_0 &= \frac{N^*}{S^*} \\
&= \frac{S^* + {I_1}^* + {I_2}^* + {I_3}^* + A^* + T^*}{S^*} \\
&= 1 + \lambda\frac{1}{(\mu+\alpha_1)} + \lambda\frac{\alpha_1}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)} + \lambda\frac{\alpha_1\alpha_2}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)} \\
&+ \lambda\frac{\alpha_1\alpha_2\alpha_3}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)} \\
&+ \lambda\frac{\alpha_1}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)}\left[\frac{\gamma_2}{\mu} + \frac{\alpha_2\gamma_3}{\mu(\mu+\alpha_3+\gamma_3)} + \frac{\alpha_2\alpha_3\gamma_A}{\mu(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)}\right] \\
R_0 - 1 &= \lambda\pi \\
\lambda &= \frac{(R_0-1)}{\pi}
\end{aligned}$$

where π is the mean infective period given by

$$\pi = \frac{1}{(\mu+\alpha_1)} + \frac{\alpha_1}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1\alpha_2}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)} + \lambda\frac{\alpha_1\alpha_2\alpha_3}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)} + \frac{\alpha_1}{(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)}\left[\frac{\gamma_2}{\mu} + \frac{\alpha_2\gamma_3}{\mu(\mu+\alpha_3+\gamma_3)} + \frac{\alpha_2\alpha_3\gamma_A}{\mu(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)}\right]$$

by substituting λ into the endemic equilibrium (EE) points expressed in equation (3.3.5) – equation (3.3.9), we will obtain the endemic equilibrium points in term of R_0 to be

$$S^* = \left[\frac{\Lambda\pi}{(R_0-1)+\mu+\rho}\right] \tag{3.4.9}$$

$${I_1}^* = \left[\frac{(R_0-1)}{\pi(\mu+\alpha_1)}\right] S^* \tag{3.4.10}$$

$${I_2}^* = \left[\frac{\alpha_1}{\pi(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)}\right](R_0-1)S^* \tag{3.4.11}$$

$${I_3}^* = \left[\frac{\alpha_1\alpha_2}{\pi(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)}\right](R_0-1)S^* \tag{3.4.12}$$

$$A^* = \left[\frac{\alpha_1\alpha_2\alpha_3}{\pi(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)}\right](R_0-1)S^* \tag{3.4.13}$$

$$T^* = \frac{\alpha_1}{\pi(\mu+\alpha_1)(\mu+\alpha_2+\gamma_2)}\left[\frac{\gamma_2}{\mu} + \frac{\alpha_2\gamma_3}{\mu(\mu+\alpha_3+\gamma_3)} + \frac{\alpha_2\alpha_3\gamma_A}{\mu(\mu+\alpha_3+\gamma_3)(\mu+\delta+\gamma_A)}\right](R_0-1)S^* \tag{3.4.14}$$

Jacobian matrix of the system presented in (3.3.1) is given as

$$\mathbf{J} = \begin{pmatrix} -\frac{\beta_1 I_1}{N} - \frac{\beta_2 I_2}{N} - \frac{\beta_3 I_3}{N} - (\mu+\rho) & -\frac{\beta_1 S}{N} & -\frac{\beta_2 S}{N} & -\frac{\beta_3 S}{N} & 0 & 0 \\ \frac{\beta_1 I_1}{N} + \frac{\beta_2 I_2}{N} + \frac{\beta_3 I_3}{N} & \frac{\beta_1 S}{N} - (\alpha_1+\mu) & \frac{\beta_2 S}{N} & \frac{\beta_3 S}{N} & 0 & 0 \\ 0 & \alpha_1 & -(\alpha_2+\gamma_2+\mu) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & -(\alpha_3+\gamma_3+\mu) & 0 & 0 \\ 0 & 0 & 0 & \alpha_3 & -(\delta+\gamma_A+\mu) & 0 \\ 0 & 0 & \gamma_2 & \gamma_3 & \gamma_A & -\mu \end{pmatrix}$$

3.4.1 Theorem. *The disease free equilibrium DFE point is locally asymptotically stable if* $R_0(\rho) < 1$.

Proof. The Jacobian matrix $\mathbf{J}$ evaluated at disease free equilibrium (DFE) point is given as

$$\mathbf{J_0} = \begin{pmatrix} -(\mu+\rho) & -\frac{\beta_1\mu}{(\mu+\rho)} & -\frac{\beta_2\mu}{(\mu+\rho)} & -\frac{\beta_3\mu}{(\mu+\rho)} & 0 & 0 \\ 0 & \frac{\beta_1\mu}{(\mu+\rho)} - (\alpha_1+\mu) & \frac{\beta_2\mu}{(\mu+\rho)} & \frac{\beta_3\mu}{(\mu+\rho)} & 0 & 0 \\ 0 & \alpha_1 & -(\alpha_2+\gamma_2+\mu) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & -(\alpha_3+\gamma_3+\mu) & 0 & 0 \\ 0 & 0 & 0 & \alpha_3 & -(\delta+\gamma_A+\mu) & 0 \\ 0 & 0 & \gamma_2 & \gamma_3 & \gamma_A & -\mu \end{pmatrix}$$

Three of the eigenvalues of $\mathbf{J_0}$ are

$$\lambda_1 = -\mu, \qquad \lambda_2 = -(\mu+\rho), \qquad \lambda_3 = -(\delta+\gamma_A+\mu).$$

We now determine the eigenvalues of the sub-matrix J_0^s by applying the corollary of Greshgorin's circle theorem.

3.4.2 Corollary. (Corollary to Greshgorin's circle theorem) Let M be an $n \times n$ matrix with real entries m_{ij}, if the diagonal elements of M satisfy

$$\mathrm{m}_{ii} < -r_i \qquad \text{where } r_i = \sum_{j=1, j\neq i} |\mathrm{m}_{ij}| \qquad i,j = 1...n$$

then the eigenvalues of M are negative or have negative real parts Allen (2007)

$$J_0^s = \begin{pmatrix} \frac{\beta_1\mu}{(\mu+\rho)} - (\alpha_1+\mu) & \frac{\beta_2\mu}{(\mu+\rho)} & \frac{\beta_3\mu}{(\mu+\rho)} \\ \alpha_1 & -(\alpha_2+\gamma_2+\mu) & 0 \\ 0 & \alpha_2 & -(\alpha_3+\gamma_3+\mu) \end{pmatrix} \tag{3.4.15}$$

$$r_1: \qquad 1 > \frac{\beta_1\mu}{(\mu+\rho)(\alpha_1+\mu)} + \frac{\beta_2\mu}{(\mu+\rho)(\alpha_1+\mu)} + \frac{\beta_3\mu}{(\mu+\rho)(\alpha_1+\mu)} \tag{3.4.16}$$

$$r_2: \qquad 1 > \frac{\alpha_1}{(\alpha_2+\gamma_2+\mu)} \tag{3.4.17}$$

$$r_3: \qquad 1 > \frac{\alpha_2}{(\alpha_3+\gamma_3+\mu)} \tag{3.4.18}$$

(3.4.19)

where r_i, $i = 1,2,3$ stands for the rows in the matrix. By multiplying, second term of right hand side (rhs) of 3.4.16 by the term obtained in rhs of (3.4.17) and also by multiplying the third term of rhs of (3.4.16) by the terms obtain in rhs of (3.4.17) and (3.4.18). Hence we obtain

$$1 > \frac{\beta_1\mu}{(\mu+\alpha_1)(\mu+\rho)} + \frac{\alpha_1\beta_2\mu}{(\mu+\alpha_1)(\mu+\rho)(\mu+\alpha_2+\gamma_2)} + \frac{\alpha_1\alpha_2\beta_3\mu}{(\mu+\alpha_1(\mu+\rho))(\mu+\alpha_2+\gamma_2)(\mu+\alpha_3+\gamma_3)} = R_0(\rho)$$

which implies $R_0(\rho) < 1$, hence the disease free equilibrium point is locally asymptotically stable. □

3.4.3 Theorem. *The endemic equilibrium EE point is locally asymptotically stable if* $R_0(\rho) > 1$.

Proof. The Jacobian matrix evaluated at endemic equilibrium point gives

$$\mathbf{J_E} = \begin{pmatrix} -\lambda^* - (\mu+\rho) & -\frac{\beta_1}{R_0} & -\frac{\beta_2}{R_0} & -\frac{\beta_3}{R_0} & 0 & 0 \\ \lambda^* & \frac{\beta_1}{R_0} - (\alpha_1+\mu) & \frac{\beta_2}{R_0} & \frac{\beta_3}{R_0} & 0 & 0 \\ 0 & \alpha_1 & -(\alpha_2+\gamma_2+\mu) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & -(\alpha_3+\gamma_3+\mu) & 0 & 0 \\ 0 & 0 & 0 & \alpha_3 & -(\delta+\gamma_A+\mu) & 0 \\ 0 & 0 & \gamma_2 & \gamma_3 & \gamma_A & -\mu \end{pmatrix}$$

where $\lambda^* = \frac{\beta_1 I_1^*}{N^*} + \frac{\beta_2 I_3^*}{N^*} + \frac{\beta_3 I_3^*}{N^*}$ and $R_0 = \frac{N^*}{S^*}$.

Two of the eigenvalues of $\mathbf{J_E}$ are $\lambda_1 = -\mu$ and $\lambda_2 = -(\delta + \gamma_A + \mu)$

By applying the corollary of Greshgorin's circle theorem for the sub-matrix $\mathbf{J_E^s}$ given by

$$\mathbf{J_E^s} = \begin{pmatrix} -\lambda^* - (\mu+\rho) & -\frac{\beta_1}{R_0} & -\frac{\beta_2}{R_0} & -\frac{\beta_3}{R_0} \\ \lambda^* & \frac{\beta_1}{R_0} - (\alpha_1+\mu) & \frac{\beta_2}{R_0} & \frac{\beta_3}{R_0} \\ 0 & \alpha_1 & -(\alpha_2+\gamma_2+\mu) & 0 \\ 0 & 0 & \alpha_2 & -(\alpha_3+\gamma_3+\mu) \end{pmatrix}$$

$$\begin{aligned} r_1: &\quad \lambda^* + (\mu+\rho) > \frac{\beta_1+\beta_2+\beta_3}{R_0} \\ r_2: &\quad -\lambda^* + (\mu+\alpha_1) > \frac{\beta_1+\beta_2+\beta_3}{R_0} \\ r_3: &\quad 1 > \frac{\alpha_1}{(\alpha_2+\gamma_2+\mu)} \\ r_4: &\quad 1 > \frac{\alpha_2}{(\alpha_3+\gamma_3+\mu)} \end{aligned}$$

Adding inequalities r_1 to r_2 gives

$$(\mu+\alpha_1) + (\mu+\rho) > \frac{2}{R_0}[\beta_1+\beta_2+\beta_3]$$

Dividing through by $(\mu+\alpha_1)(\mu+\rho)$ gives

$$\frac{1}{(\mu+\rho)}+\frac{1}{(\mu+\alpha)} > \frac{2}{R_0}\left[\frac{\beta_1}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\beta_2}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\beta_3}{(\mu+\alpha_1)(\mu+\rho)}\right]$$

Multiplying the above inequality by μ gives

$$\frac{\mu}{(\mu+\rho)}+\frac{\mu}{(\mu+\alpha)} > \frac{2}{R_0}\left[\frac{\mu\beta_1}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\mu\beta_2}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\mu\beta_3}{(\mu+\alpha_1)(\mu+\rho)}\right]$$

Dividing through by 2 gives

$$1 > \frac{1}{2}\left(\frac{\mu}{(\mu+\rho)}+\frac{\mu}{(\mu+\alpha)}\right) > \frac{1}{R_0}\left[\frac{\mu\beta_1}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\mu\beta_2}{(\mu+\alpha_1)(\mu+\rho)}+\frac{\mu\beta_3}{(\mu+\alpha_1)(\mu+\rho)}\right] \tag{3.4.20}$$

$$1 > \frac{R_0(\rho)}{R_0} > \frac{1}{R_0} \tag{3.4.21}$$

Hence (3.4.20) holds provided $R_0 > 1$. We therefore conclude that the endemic equilibrium point is locally asymptotically stable. This completes the proof. □

4. Numerical simulation

4.1 Antiretroviral Treatment

Current treatment regimens have significantly improved the quality of life for those living with HIV. ARV treatment refer to the treatment administered to HIV infected individuals using the drugs known as antiretroviral drugs. These drugs are usually taken in combinations of two or more. This is so, so that it will be able to suppress the viral replication much more than when it is being administered one at a time. This is because when only one is taken, it is easier for the virus to resist than when more are taken at the same time.

4.1.1 Optimal Time for Starting ARV Treatment. The time to start Antiretroviral(ARV) Treatment has been a source of debate among the stakeholders about the control of the pandemic. A paper published by Granich et al. (2009) suggested that the ARV treatment should commence as soon as a patient is tested positive with HIV infection. A WHO 2006 guideline suggested that, in "resource-constrained settings", treatment should not commence until the $CD4^+$ T cell count < 200 cell$/mm^3$. That is, until the patient progresses to the AIDS stage.

In the Project we will be examining starting the treatment at various infection stages, except for the primary stage, because many of the patients may not even be aware that they are infected. We will then compare the overall effect on the incidence. We will then take as the *optimal stage for initiating ARV treatment*, as the starting stage which reduces the incidence fastest.

We noted that, for an infectious disease which has no cure, the key to controlling the spread lies in a rapid reduction of the incidence rate, combined with an aggressive educational campaign aimed at reducing susceptibility.

4.2 Estimation of the parameters and the initial conditions

Our case study is South Africa. This same analysis can be perform for any country by making use of their data.

4.2.1 Initial conditions. According to the South Africa Statistical release $P302$. The number of sexually active individuals age $15-49$ years was approximately 26.43 million. The number of HIV/AIDS positive individuals was 5.8 million. The numbers of individuals receiving ARV treatment was 0.8 million, this implies that $T(0) = 0.8$ million and a report stated that half of the individuals who needed the ARV treatment are being treated which implies that the AIDS sick individual is twice the treated group. Hence we take $A(0) = 1.6$ million. $I_1(0) + I_2(0) + I_3(0) + A(0) + T(0) = 5.8$ million. The data revealed that the incidence $I_1(0) = 0.4$ million, so that $I_2(0) = 2I_3(0)$, $I_3(0) = 1$ million and $I_2(0) = 2$ million. Since $N(0) = 26.43$ million, we then estimated $S(0)$ to be $S(0) = 26.43 - 5.8 = 20.63$ million SRZA.

4.2.2 Parameter estimation. *Constant recruitment rate* (Λ): this was estimated as the net births that occurred $15 - 20$ years ago plus the present migration. The net birth were calculated using the average of births in South Africa between 1993 and 2003 since this gives a good rough estimate of the group that will become sexually active after the year 2008. The birth value obtained was adjusted with the infant mortality rate over the same period. According to Statistical release P0302 SRZA, the crude births in

South Africa for the between the year $1993 - 2003$ is 25 per population while the infant mortalities were 49 per thousand live births. We use the number of people in South Africa in 1993, which was 37.474 million, to estimate the births during $1993 - 2003$. Also, the net annual migration into South Africa between 2000 - 2010 was 0.14 million WBD and SRZA. Hence, the constant recruitment rate (Λ) is calculated as follows:

$$\begin{aligned}\Lambda &= Pop. \times \text{crude birth rate} \times \text{infant survival rate} + \text{migration} \\ &= 37.474 \times 0.025 \times (1 - 0.049) + 0.14 \,\text{million} \\ &= 1.03 \,\text{million}\end{aligned}$$

Natural death rate (μ): This was estimated as the reciprocal of life expectancy for South Africa for 2009 which was estimated to be 53 by WBD. This is based on the assumption that if the population were to be normally distributed, 1 in every 53 people will die every year. Thus (μ) is estimated as $(\mu) = \frac{1}{53} = 0.0189$.

Progression rates $(\alpha_1, \alpha_2, \alpha_3)$: We assumed that it take 6 weeks which is equivalent to $\frac{3}{26}$ year for a newly infected individual to progress from primary stage to the asymptomatic stage and it takes an average of 11 years for an infected individual to progress from the asymptomatic stage to the symptomatic state, while the symptomatic stage is estimated to last for 3 years before progressing to full blown AIDS. Therefore we obtain $\alpha_1 = 12.01$, $\alpha_2 = 0.126$ and $\alpha_3 = 0.462$.

Disease induced death (δ): This is estimated to be the reciprocal of the average duration it takes an infected individual to progress from the primary stage to AIDS stage, we assumed $(\delta) = \frac{1}{15} = 0.067$.

Transmission rate β_i, $i = 1, 2, 3$: It is known that the transmission rate (β_1) of individuals in the primary stage is higher than the transmission rates (β_2) and (β_3) and the transmission rate (β_2) is the smallest. We assumed that $\beta_1 = 0.3$, $\beta_2 = 0.01$ and $\beta_3 = 0.1$

Parameter	Units	Value	Reference
Λ	Population $year^{-1}$	1.03 million	SRZA and Estimated
β_1	$year^{-1}$	0.3	Estimated
β_2	$year^{-1}$	0.01	Estimated
β_3	$year^{-1}$	0.1	Estimated
μ	$year^{-1}$	0.0189	WBD and Estimated
ρ	$year^{-1}$	$0 \leq \rho \leq 1$	Variable
α_1	$year^{-1}$	12.01	Estimated
α_2	$year^{-1}$	0.126	Estimated
α_3	$year^{-1}$	0.462	Estimated
ϵ_2	$year^{-1}$	0.4	SRZA and Estimated
ϵ_3	$year^{-1}$	0.8	SRZA and Estimated
ϵ_A	$year^{-1}$	0.5	SRZA and Estimated
δ	$year^{-1}$	0.067	Estimated

Table 4.1: Parameter values obtained from South Africa data

4.3 Sensitivity analysis of the effective reproduction number

Sensitivity analysis is used to describe the effect of changing the parameter values on the model (that is, how the model respond to change in parameter values). The sensitivity index may be computed by using the normalized forward sensitivity index method.

$$\Gamma_{\mu}^{R_0(\rho)} = \frac{\partial R_0(\rho)}{\partial \mu} \cdot \frac{\mu}{R_0(\rho)}$$

	parameter	sign	value
1	μ	$+$	0.913824268722451
2	α_1	$-$	0.399542248791919
3	α_2	$+$	0.543030417424037
4	α_3	$-$	0.112012267148297
5	β_1	$+$	0.401121764961176
6	β_2	$+$	0.288298767036728
7	β_3	$+$	0.310579468002096
8	γ_2	$-$	0.430074136473123
9	γ_3	$-$	0.193960635754627
10	ρ	$-$	0.940438871473354

Table 4.2: Table showing the sensitivity index of $R_0(\rho)$

The sensitivity analysis was commuted with each of the parameter that make up $R_0(\rho)$. The sign in front of each of the index signifies what will happened to $R_0(\rho)$ if the parameter is increased. Positive sensitivity index implies that there there will be increase the value of $R_0(\rho)$ while negative sensitivity index implies that there will be decrease in the value of $R_0(\rho)$ when the parameter is being increased. From the sensitivity index of $R_0(\rho)$, it is obvious that the parameter that affect the reduction in $R_0(\rho)$ the most is the ρ, achieving a good ratio for this parameter is therefore the key to controlling the spread of the disease.

4.4 Interpretation of the figures

In treating the infected patient, we want to concentrate all the resources made available by the government to treat each of the various stage one at a time in order to visualize the effect of treatment at each of these stages on the incidence. This will help us to come up with a reasonable conclusion on the most appropriate stage to initialise the treatment. This will also help us to verify Granich et al. (2009) suggestion and WHO in order to ascertain which of the two suggestion will be the most appropriate or maybe we have to come up with another stage for initiating the treatment for maximum reduction in the incidence of the infection. We are assuming that the educational campaign and all other awareness technique and the prevention measure made available will help to reduce the susceptible population by 30%. Presented below are the effect of concentrating all the available resources to treat each of the infection stage starting from the asymptomatic stage to the AIDS stage.

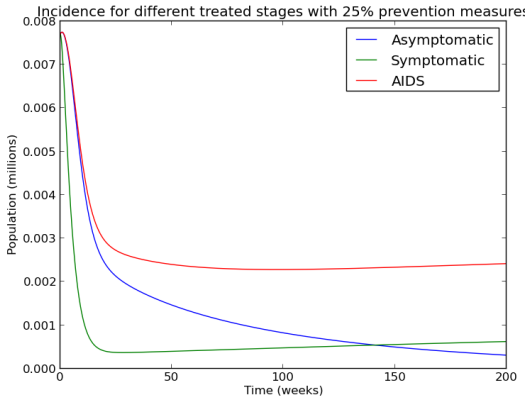

Figure 4.1: Dynamics of the incidence of the infection with 25% prevention measure

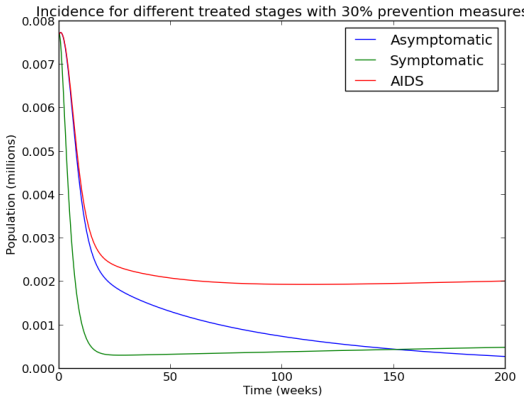

Figure 4.2: Dynamics of the incidence of the infection with 30% prevention measure

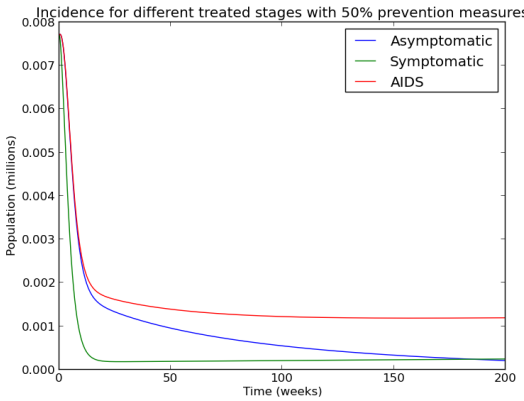

Figure 4.3: Dynamics of the incidence of the infection with 50% prevention measure

Figure (4.1), (4.2) and (4.3) represent the effect of administering treatment to the various stages and successful removal of 25%, 30% and 50% respectively from the susceptible population on the incidence of the infection. From each of these plots, it is obvious that the optimal stage to initiate the ARV treatment is the pre-AIDS (Symptomatic) stage because that is where we recorded much impart in the incidence reduction.

% removed	Weeks	Asymptomatic populatn	Symptomatic populatn	AIDS populatn
25	15	0.002898 million	0.000551 million	0.003367 million
	52	0.001048 million	0.000408 million	0.002388 million
	104	0.000776 million	0.000449 million	0.002245 million
	180	0.000367 million	0.000592 million	0.002347 million

Table 4.3: Summary of the 25% prevention measures and its effect on each of the treated group

% removed	Weeks	Asymptomatic populatn	Symptomatic populatn	AIDS populatn
30	15	0.002449 million	0.000429 million	0.002867 million
	52	0.001225 million	0.000306 million	0.002061 million
	104	0.000694 million	0.000365 million	0.001919 million
	180	0.000306 million	0.000469 million	0.001959 million

Table 4.4: Summary of the 30% prevention measures and its effect on each of the treated group

% removed	Weeks	Asymptomatic populatn	Symptomatic populatn	AIDS populatn
50	15	0.001571 million	0.000225 million	0.001857 million
	52	0.000918 million	0.000122 million	0.001388 million
	104	0.000510 million	0.000184 million	0.001186 million
	180	0.000204 million	0.000204 million	0.001142 million

Table 4.5: Summary of the 50% prevention measures and its effect on each of the treated group

Table (4.3), (4.4) and (4.5) show the summary of figure (4.1), (4.2) and (4.3) respectively. From these tables, we could observed that the higher the remove percentage, the more the reduction in the incidence of the infection. With $\rho = 0.5$, we were able to a achieve considerable reduction in the incidence.

5. Discussion and Conclusion

5.1 Discussion

The analysis of the basic SI model reveals that the only solution to prevent an *incurable* disease from a community is to find a way of reducing the incidence of the disease. The two alternatives which could be of help is finding a way of reducing the susceptibility to the infection and treating the infected individual which will help to reduce the rate at which the disease is being transmitted. The treatment is aimed at improving the health of the patients which will invariably help to minimize the morbidity related to the disease.

Having studied the within host model, it reveals that there are four different stages of HIV/AIDS infection. It becomes imperative to decide among these various stages, which will be the optimal stage to initiate ARV treatment in order to achieve the most effective reduction in the incidence of the infection. So many suggestions have been made about the stage to initiate the treatment, Granich et al. (2009) suggested that treatment should commence as soon as an individual is tested positive with HIV infection, while WHO 2006 guidelines suggested that treatment should be delayed until an individual progressed to AIDS stage (when the individual has the $CD4^+$ T cell count of < 200 cell$/mm^3$). Delaying treatment until later as proposed by WHO makes the immune system to deteriorate faster, leads to development of opportunistic infections, declining quality of life and eventually death, but starting ARV treatment too early as proposed by Granich has the disadvantages of exhausting drug options, patient's ability to tolerate drugs, it is not economically viable and also unrealistic in resources-constraint countries.

5.2 Conclusion

After simulation has been made on the various stage, we observed that the optimal stage to initiate ARV treatment in order to reduce the incidence is the Pre-AIDS stage as opposed to what was suggested by Granich and the WHO 2006 guideline which is being practised by most countries. We also observed that achieving a good ratio for the prevention measure (ρ) is therefore the key to controlling the spread of the disease.

5.2.1 Recommendation. In a situation whereby the resources made available by the government translates to treating certain number of individuals, preference should be given to the individuals at the pre-AIDS stage. Intensified effort should continue on educational campaign and voluntary testing about the infection as this will help to increase the number of the proportions removed from the susceptible population which is the key factor in controlling an incurable disease.

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To God be the glory, great things He has done. Lord, You're Awesome in my life. You lifted me out of the miry clay and set my feet upon a solid rock and put a new song in my mouth. Daddy, to you alone be all the glory.

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DEDICATION

This project is dedicated to the LORD ALMIGHTY and to my father, Late Prof J. Ola. A Adefisan. May your gentle soul rest in perfect peace. Rest on Double chief, till we meet to path no more. LORD YOU'RE FAITHFUL.

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