ANALYSIS OF A TB/HIV CO-INFECTION MODEL WITH VERTICAL TRANSMISSION AND TREATMENT

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Abstract

In this mini thesis, we developed a new mathematical model for the dynamics of HIV/TB co-infection in a population with treatment and vertical transmission. TB and HIV sub-models are derived from the full model and analyzed separately. The aim was to use mathematical modeling to find favorable conditions under which the diseases can be stopped from spreading further in the population. The models are built with a motive to study the dynamic behavior of the trajectories which has the potentials to guide TB and HIV control. The study used the Routh-Hurwitz criteria to conclude on the stability of the system. The basic reproduction numbers for TB ($\mathcal{R}_T$) and HIV ($\mathcal{R}_H$) are computed using the next generation matrix method, and the basic reproduction number $\mathcal{R}_0 = \max\{\mathcal{R}_T, \mathcal{R}_H\}$ of the full model is also provided. From the study, it was established that if $\mathcal{R}_0 < 1$ then the disease-free equilibrium is stable, and the disease dies out; if $\mathcal{R}_T < 1$ and $\mathcal{R}_H > 1$, then the HIV is endemic and TB dies out; however if $\mathcal{R}_H < 1$ and $\mathcal{R}_T > 1$, then TB is endemic and HIV dies out; in addition, if $\mathcal{R}_T > 1$ and $\mathcal{R}_H > 1$, the two diseases persist in the population. Sensitivity analysis of the basic reproduction number for TB-only model with respect to the model parameters was carried out. Results from quantitative analysis revealed that, increasing treatment rate for both HIV and T-B significantly reduces the values of the basic reproduction number. The study concluded that, decreasing the probability rate of transmission of HIV/AIDS and TB leads to the decrease of the population of infectives. Furthermore, by controlling the probability rate of transmission, the spread of the disease can be reduced significantly. Effective treatment for TB breaks the cycle of transmission. TB individuals must be identified and treated in order to reduce further spread of TB in human population.

Keywords: Next-Generation matrix method, Basic reproduction number, Routh-Hurwitz criteria, Disease-free equilibrium, Sensitivity analysis, HIV/TB co-infection.

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LIST OF ABBREVIATIONS

AIDS - Acquired Immunodeficiency Syndrome

ART - Antiretroviral Treatment

DFE - Disease Free Equilibrium

HIV - Human Immunodeficiency Virus

ODEs - Ordinary Differential Equations

PDEs - Partial Differential Equations

TB - Tuberculosis

WHO - World Health Organization

LIST OF SYMBOLS

$\mathcal{R}_0$ - Basic Reproduction Number for HIV/TB co-infection model

$\mathcal{R}_H$ - Basic Reproduction Number for HIV - only model

$\mathcal{R}_T$ - Basic Reproduction Number for TB - only model

E_0^T - Disease Free Equilibrium point for TB - only model

E_0^H - Disease Free Equilibrium point for HIV - only model

E_0^{TH} - Disease Free Equilibrium point for HIV/TB co-infection model

E_T^* - Endemic Equilibrium point for TB - only model

E_H^* -Endemic Equilibrium point for HIV - only model

E_{TH}^* -Endemic Equilibrium point for HIV/TB co-infection model

N - Total population for the HIV/TB model

N_T - Total population for TB-only model

N_H - Total population for HIV-only model

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DECLARATION

I, Maria Mesias Shaale, hereby declare that this study, **Analysis of a TB/HIV co-infection model with vertical transmission and treatment**, is my own work and is a true reflection of my research, and that this work, or any part thereof has not been submitted for a degree at any other institution.

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Chapter 1

Introduction

In this chapter, we present, the background of the HIV/TB co-infection and other related models, followed by the statement of the problem, objectives of the study and finally we layout the thesis organization.

1.1 Background of the study

Mathematical modeling of infectious diseases was initiated by Daniel Bernoulli in 1760 to model epidemics of infectious diseases, and computer simulations have become useful in analyzing the spread and control of infectious diseases. In 1927 W. O. Kermack and A. W. McKendrick developed a simple mathematical epidemic model for the transmission dynamics of viral and bacterial infectious agents within the population of hosts [29].

Tuberculosis (TB) is a bacterial disease caused by *Mycobacterium tuberculosis*. According to the World Health Organization (WHO) reports, TB remains one of the top 10 deadly diseases of recent decades in the world [15]. It is transmitted through the inhalation of droplets containing the bacillus, which typically affects the lungs, but can affect other parts as well [27]. TB is a type of disease which increases due to environmental factors such as open drainage of sewage in residential areas or open water storage tanks [30]. WHO declared TB a global emergency in 1993. The disease is responsible for many deaths in most parts of the world, specifically among groups with a high prevalence rate of Human Immunodeficiency Virus (HIV) and those living in crowded conditions (see [26, 4]). However, it is preventable and curable.

The 2018 WHO report shows that nearly a third of the worlds population is infected with tuberculosis, with millions of deaths as well as millions of new cases of infection each year. The report confirms that tuberculosis is one of the top 10 causes of death worldwide. For example in 2015, 10.4 million people contracted TB and more than 1.5 million died from the disease, including 0.4 million among people with HIV [15].

Highly contagious, COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been proven to spread easily when cold winter conditions are met. COVID-19 mostly kills people with pre-existing diseases such as diabetes, high blood pressure, tuberculosis and also HIV [13].

Acquired Immunodeficiency Syndrome (AIDS), which is caused by HIV, is a pandemic that has accounted for over 30 million deaths since the first reported death in 1981. The estimated number of persons living with HIV worldwide in 2008 was 33.4 millions, and the number of newly infected with HIV in 2008 was 2.7 million [32].

Co-infection of TB and HIV is when someone has both HIV and TB infections. When someone has HIV and TB, HIV infection accelerates the activation of tuberculosis, and tuberculosis increases the rate at which HIV infection develops into AIDS. Globally, one-third of the 34 million people living with HIV are infected with TB [20].

According to the WHO, HIV and TB are the first and second cause of death from a single infectious agent, respectively [35]. HIV infection is the most powerful risk factor for progression from TB infection to disease [10]. As HIV infection progresses, immunity declines and patients tend to become more susceptible to common or even rare infections. Therefore, individuals infected with HIV are more likely to develop TB because of their immunodeficiency. In 2012, 1.1 million of 8.6 million people who developed TB worldwide were HIV-positive [35]. This acceleration may result in higher levels of infection and rapid HIV progression to the AIDS stage. In 2014, about 400000 people who had both TB and HIV were estimated to have died, whereas 1.1 million people died due to TB alone and 80000 deaths were recorded from HIV alone [36].

Diseases can be transmitted in different ways, some of which can be classified as either horizontal or vertical [33]. Vertical transmission of HIV results from direct transfer of the disease from an infected mother to an unborn or newborn offspring. Makinde *et al.* [33] further added that, vertical transmission of HIV can occur during pregnancy, delivery or breastfeeding, and is influenced by many factors, including maternal viral load and the type of delivery, while TB is transmitted through the inhalation of droplets containing the *bacillus*.

Namibia faces a high burden of TB and HIV-infection. HIV associated tuberculosis in Namibia has actuated around 58% over the past five years. It was 59% in 2008 and 58% in 2009, as reported in [19]. In addition, in 2011, 50% of the TB patients were co-infected with HIV. While all patients co-infected with TB and HIV are eligible for antiretroviral treatment (ART), only 54% were reported to have received ART according to national data [19]. However, in 2012 an estimated 13% of the 8.6 million new TB patients worldwide were co-infected with HIV [31].

In 2013, Namibia was ranked fourth in the world in terms of high number of cases per population TB incidence, after Swaziland, Lesotho and South Africa. In the 2008/2009 Ministry of Health and Social Services Annual Report, the Erongo region, along with Khomas, Ohangwena and Kavango, had the highest numbers of TB cases in the country, while Walvis Bay and Swakopmund towns hosted the highest numbers of TB patients [8]. TB is one of the most common opportunistic infections observed in patients already infected with HIV and one of the earliest to appear [19]. In addition, it was reported at the end of 2019 that 200 000 Namibians are living with HIV [23]. In 2016, Namibia had 230 000 people living with HIV and 9154 new TB cases, including 4310 (38%) co-infected cases [28]. The negative impact of the synergetic interaction between TB and HIV has caused worldwide concern. However, only few mathematical models have been used to explore the consequences of their joint dynamics at the population level [27]. Examples of HIV/TB mathematical models can be found in ([9, 12, 27]).

The specific aims of this study are to determine the conditions under which HIV/TB co-infection epidemic will cease or occur by carefully analyzing the calculated reproduction number.

1.2 Statement of the problem

TB and HIV each has its own way of operating in the human system. Feng *et al.* [27] studied a TB/HIV co-infection model without considering the effect of vertical transmission and treatment. Furthermore, models for HIV/AIDS (only) infection, taking into account the effect of vertical transmission and treatment have been studied by Golarin [12] and by Kgosimore and Lungu [16]. However, the dynamics of a TB/HIV co-infection model with vertical transmission and in the presence of treatment, to the best of our knowledge, have not been explored before. People who are infected with both diseases suffer most, as these diseases can lead to huge epidemic, which might in turn lead to a big loss of population.

Therefore, our purpose is to use mathematical modeling to find conditions under which the diseases can be stopped from spreading further in the population, taking into account vertical transmission and treatment.

1.3 Objectives of the study

The main goal of this study is to analyze a TB/HIV co-infection model with vertical transmission and treatment. The specific objectives are:

a) to derive a simplified deterministic model, and check if it is well-posed with positive solutions;

b) to determine the equilibrium point(s) (for disease-free, HIV-free, TB-free and TB/HIV endemic) and to perform local and global stability analysis;

c) to compute the basic reproduction number of the model;

d) to conduct sensitivity analysis of the equilibrium points (as well as the reproduction number(s)) with respect to the parameters of the model;

e) to present numerical solutions of the plausible model.

1.4 Thesis organisation

This mini-thesis is organized as follows: The next chapter, which is the second chapter presents the literature review pertaining to HIV/TB co-infection and mathematical model is given. Third chapter presents preliminaries on mathematical analysis, where the definitions, prior results and notations are provided. The fourth chapter presents the formulation of the HIV and TB co-infection model, as well as the TB and HIV sub-models and the co-infection model, with analysis. In chapter five, we conduct quantitative analysis of TB and HIV sub-models, as well as the HIV/TB co-infection model and finally we present summary and concluding remarks.

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Chapter 2

Literature Review

In this chapter, we present the literature review pertaining to HIV/TB co-infection model as well as other related models.

A large volume of great work has been done in the mathematical modelling of HIV/TB co-infection. In 2009, Roeger *et al.* [27] developed a mathematical model of HIV/TB co-infection. They computed independent reproduction numbers for TB (R_1) and HIV (R_2) and the overall reproduction number for the system, $R = \max\{R_1, R_2\}$. They concluded that, if $R < 1$, the disease-free equilibrium is locally asymptotically stable, the HIV-free equilibrium with only TB present is stable if $R_1 > 1$ and $R_2 < 1$. The TB-free equilibrium will not be stable if $R_1 < 1$ and $R_2 > 1$, thus the co-existence of both diseases is possible when $R_1 < 1$ and $R_2 > 1$.

Moreover, an extension of HIV/TB co-infection was further addressed by Bolari in 2016 [12], who developed and analyzed a mathematical model of HIV/TB co-infection. He concluded that, whenever HIV is present, the patient may likely be infected with TB if proper and timely care is not given. He finally stated that early detection of HIV and TB cases and provision of early treatment can help to control the diseases. Furthermore, Carla [25] addressed the idea of integer order and fractional order versions of an HIV and TB co-infection model. The reproduction number was computed and the stability analysis conducted for the integer order model. The results unraveled new types of transients and an interesting fact, namely, the order of the fractional derivative might be seen as a bifurcation parameter for the model. Carla *et al.* [25] then concluded that the dynamics of integer and fractional order versions of the model are very rich and that together these versions may provide a better understanding of the dynamics of HIV and TB co-infection.

West and Thompson [34] developed models which reflect the transmission dynamics of both TB and HIV, and discussed the magnitude and duration of the effect that the HIV epidemic may have on TB. They found the effect that HIV will have on the general population to be dependent on the contact structure between the general population and the HIV risk groups, as well as a possible shift in the dynamics associated with TB transmission. A simulation model as studied in [26] predicts the effects of HIV on TB outbreaks. This simulation revealed that HIV epidemic can significantly increase the frequency and severity of TB outbreaks. However, the amplification effect of HIV can be substantially reduced by extremely high TB treatments rates. It was suggested therein that WHO should significantly increase their target treatment levels for TB in countries with high TB and HIV burden. They strongly advocated for controlling TB epidemic in developing countries with severe HIV through chemoprophylaxis treatment and through treatment of HIV infected individuals.

Ghosh *et al.* [11] used a deterministic non-linear mathematical model to determine the effect of screening and treatment on the transmission dynamics of HIV and TB co-infection. Qualitative analysis and simulation results showed that screening with proper counseling of HIV infectives caused a significant reduction in the progression of HIV to AIDS. Similarly, TB screening resulted in the reduction of TB infection prevalence. They suggested that effective control measures that put screening with proper counseling into account must be taken.

Goufo [15] presented the modeling analysis and simulation of a mathematical model of TB transmission in a population incorporating several factors and study their impact on the disease dynamics. The spread of TB is modeled by eight compartments including different groups, which are too often not taken into account in the projections of tuberculosis incidence. The rigorous mathematical analysis of this model is provided, the basic reproduction number is obtained and used for TB dynamics control. The results obtained show that lost to follow-up and transferred individuals constitute a risk, but less than the cases carrying germs. Rapidly evolving latent/exposed cases are responsible for the incidence increasing in the short and medium term, while slower evolving latent/exposed cases will be responsible for the persistent long-term incidence and maintenance of TB and delay elimination in the population. The numerical simulations of the model show that, with certain parameters, TB will die out or sensibly reduce in the entire Democratic Republic of the Congo (DRC) population. But monitoring contact, detection of latent individuals and their treatment are actions to be taken to reduce the incidence of the disease and thus effectively control it in the population.

An epidemic model with fractional derivatives and nonlinear incidence model of the Kermack-McKendrick [14] with zero immunity was investigated, where the authors studied the existence of equilibrium points in terms of the nonlinear incidence function. The authors [14] also established the condition for the disease free equilibrium to be asymptotically stable and provide the expression of the basic reproduction number. The existence of equilibrium points and the stability of the disease free equilibrium both depend on the nonlinear incidence function and the expression of the basic reproduction number for the fractional model was provided.

Seeling *et al.* [31] explored the perspective of health-care profession on barriers to antiretroviral treatment (ART) for HIV-positive TB patients in Windhoek, Namibia. Nine semi-structured qualitative interviews were conducted with health care professionals from TB and HIV services in Windhoek in 2012 to investigate access barriers to ART for HIV-positive TB patients. Results of the study identified access barriers to ART for HIV-positive TB patients and their relevance in Namibia. The findings provide evidence for tailored interventions to increase ART-uptake among HIV-positive TB patients.

However, none of the above reviewed literature considered treatment and vertical transmission in the TB/HIV co-infection model.

Chapter 3

Preliminaries

In this chapter, we will recall a few definitions and theorems that will be used in the analysis of our models.

3.1 Basic definitions

The following definitions can be found, among others, in [18], and will be useful in the model analysis.

Consider a dynamical system of the form:

$$\dot{\mathbf{X}}(t) = f(\mathbf{X}(t), t) \tag{3.1}$$

where $\mathbf{X} = [x_1, x_2, x_3, ..., x_n]^T$ and $\mathbf{f} = [f_1, f_2, f_3, ..., f_n]^T$ and for all i, $x_i : \mathbf{R} \to \mathbf{R}$, $f_i : \mathbf{R}^{n+1} \to \mathbf{R}$ and $X : \mathbf{R} \to \mathbf{R}^n$ are continuously differentiable; T being the notation for matrix transpose.

Definition 1. A vector $\bar{\mathbf{X}}$ is an equilibrium point for the dynamical system (3.1) if once the state vector is equal to $\bar{\mathbf{X}}$, it remains equal to $\bar{\mathbf{X}}$ for all future time. That is, if

$$\dot{\mathbf{X}}(t) = f(\mathbf{X}(t), t) \tag{3.2}$$

then an equilibrium point is a state $\bar{\mathbf{X}}$ satisfying

$$f(\bar{\mathbf{X}}, t) = 0 \tag{3.3}$$

In other words, an equilibrium point is a solution that does not change with time. If the system starts at an equilibrium, it remains at that equilibrium forever.

Definition 2. The basic reproduction number, denoted by R_0, is the expected number of secondary infectives produced by an index case in a completely susceptible population.

Definition 3. The disease-free equilibrium (DFE), denoted by E_0, is an equilibrium state of an epidemiological model when there is no disease strain present in the population.

Definition 4. The endemic equilibrium is an equilibrium state of the epidemiological model where the disease is present in the population.

To elaborate on the concept of stability, which is explored in the next three definitions, we first introduce $D(\bar{X}, \rho)$ to denote a spherical region in the state space with center at $\bar{X}$ and radius ρ

Definition 5. An equilibrium point $\bar{X}$ is stable if there is a $\rho_0 > 0$ such that for every $\rho < \rho_0$, there exist m, where $0 < m < \rho$, such that if $X(0)$ is inside $D(\bar{X}, m)$, then $X(t)$ is inside $D(\bar{X}, \rho)$ for all $t > 0$.

Definition 6. An equilibrium point $\bar{X}$ is asymptotically stable if it is stable, and in addition there is an $\bar{\rho} > 0$ such that whenever the state is initiated inside $D(\bar{X}, \bar{\rho})$, it tends to $\bar{X}$ as time increases.

Definition 7. An equilibrium point $\bar{X}$ is unstable if it is not stable. Equivalently, $\bar{X}$ is unstable if for some $\rho_0 > 0$ and any $m > 0$ there is a point in the spherical region $D(\bar{X}, m)$ such that if initiated there, the system state will eventually move outside of $D(\bar{X}, \rho_0)$.

Definition 8. Let $\mathbf{X} = (x_1, x_2, ..., x_n)^T$ and $\mathbf{f} = (f_1, f_2, ..., f_n)^T$, where for all i, $x_i : \mathbf{R} \to \mathbf{R}$ and $f_i : \mathbf{R}^n \to \mathbf{R}$ are continuously differentiable. The *Jacobian matrix* of the system $\dot{\mathbf{X}} = \mathbf{f}(\mathbf{X}(t))$ is defined as:

$$J = \begin{pmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \cdots & \frac{\partial f_1}{\partial x_n} \\ \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \cdots & \frac{\partial f_2}{\partial x_n} \\ \vdots & \vdots & \vdots & \vdots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_n} \end{pmatrix}.$$

3.2 Stability criteria

In this section, we will look at three results, that if met, they guarantee the global and local asymptotic stability of the disease-free equilibrium point respectively. A common approach in studying the global stability of the DFE is to construct a Lyapunov function. However, in this work, we will apply the following result, as establised in [1]. We list two conditions that, if met, it guarantees the global asymptotic stability of the disease-free state for the TB-only model, HIV-only model and for the full HIV/TB co-infection model.

Theorem 1. Consider a model system written in the form:

$$\begin{aligned} \frac{dX}{dt} &= F(X, Z), \\ \frac{dZ}{dt} &= G(X, Z), \; G(X, 0) = 0 \end{aligned}$$

where $X \in \mathbf{R}^n_+$ denotes (its components) the number of uninfected individuals and $Z \in \mathbf{R}^m_+$ denotes (its components) the number of infected individuals capable of transmitting the disease.

Let's suppose the disease-free equilibrium point is denoted by:

$Q_0 = (X^*, 0)$.

Also further assume that the conditions (TH1) and (TH2) below are satisfied

(TH1) For $\frac{dX}{dt} = F(X, 0)$, X^* are globally asymptotically stable;

(TH2) $G(X,Z) = AZ - \tilde{G}(X,Z), \quad \tilde{G}(X,Z) \geq 0$ for $(X,Z) \in \Omega$

where $A = D_Z G(X^*, 0)$ is a matrix whose off diagonal entries are non-negative and Ω is the region where the model makes biological sense. Then the DFE

$$Q_0 = (X^*, 0), \tag{3.4}$$

is globally asymptotically stable provided that $\mathcal{R}_0 < 1$ and the conditions (TH1) and (TH2) are satisfied.

We use the Routh-Hurwitz criteria to analyze the asymptotic stability of an equilibrium point for the dynamic system. Linear stability of the system of ordinary differential equations is determined by the roots of a polynomial. The necessary and sufficient conditions for this to hold are the *Routh-Hurwitz conditions.*

Theorem 2. (Routh-Hurwitz stability criteria [21]**)**

Given the characteristic equation in the general form,

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + \cdots + a_n = 0, \tag{3.5}$$

where the coefficients a_i are all real constants, $i = 0, 1, ..., n$ defines the n Hurwitz matrices using the coefficients a_i of the polynomial (3.5) as:

$$D_1 = a_1 > 0, \; D_2 = \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix} > 0, \; D_3 = \begin{vmatrix} a_1 & a_3 & a_5 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{vmatrix} > 0,$$

$$D_k = \begin{vmatrix} a_1 & a_3 & a_5 & \cdots \\ 1 & a_2 & a_4 & \cdots \\ 0 & a_1 & a_3 & \cdots \\ \vdots & \vdots & \vdots & \\ 0 & 0 & \cdots & a_k \end{vmatrix} > 0, \; k = 1, 2, 3, \cdots, n.$$

All of the roots of (3.5) are negative or have negative real parts if and only if the determinants of the Hurwitz matrices are positive, i.e.,

$$\det(D_k) > 0,$$

$k = 0, 1, 2, ..., n.$

Remark 1. The roots of the quadratic equation $\lambda^2 + a_1\lambda + a_2 = 0$ have negative real parts whenever all the coefficients are positive, that is $a_1 > 0$ and $a_2 > 0$. The roots of the cubic equation $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, has negative real parts whenever we have the following:

$$\begin{aligned} a_1 &> 0, \\ a_3 &> 0, \\ a_1a_2 - a_3 &> 0. \end{aligned}$$

Corollary 1. If the characteristic equation of the Jacobian matrix satisfies the conditions of the Routh-criteria, i.e, the determinants of all of the Hurwitz matrices are positive, $det(D_k) > 0$, $k = 1, 2, 3, ..., n$, then the disease-free equilibrium is locally asymptotically stable. If the $det(D_k) < 0$ for some $k = 1, 2, ..., n$ then the disease-free equilibrium point is unstable.

We list 5 conditions $(A1) - (A5)$, as established in [5] that, if met, it guarantees the local asymptotic stability if $\mathcal{R}_0 < 1$, and non stable if $\mathcal{R}_0 > 1$ at the disease-free equilibrium point. In the theorem below, we have $\mathbf{X}_s$ which defines the set of all disease-free states, that is ($\mathbf{X}_s = \{x \geqslant 0 | x_i = 0,\ i = 1, ..., m\}$); x_0 is the DFE; $x = (x_1, ..., x_n)^T$, with each $x_i \geqslant 0$, be the number of individuals in each compartment; $F_i(x)$ is the rate of appearance of new infections in the infected states; V_i^+ is the rate of transfer of individuals into the infected states and V_i^+ is the rate of transfer of individuals out of compartment of infectives. Hence, the disease transmission model consists of the following system of equations

$\dot{x}_i = f_i(x) = F_i(x) - V_i(x)$, $i = 1, ..., n$

where $V_i = V_i^- - V_i^+$. $(A1)$ hold since each function represents a direct transfer of individuals, then they are all non-negative. If the compartment is empty, then there can be no transfer of individuals out of the compartment by death or infection, thus $(A2)$ hold. Condition $(A3)$ arises from the fact that the incidence of infection for uninfected compartment is zero. If the population is free of disease, then the population will remain free of disease. That is, there is no immigration of infectives, hence $(A4)$ holds. The remaining condition $(A5)$ is based on the derivatives of f near a DFE. Therefore, we have the following Theorem:

Theorem 3. Consider the disease transmission model, with $f(x)$ satisfying the following conditions $(A1) - (A5)$

(A1) If $x \geq 0$, then F_i, V_i^+, $V_i^- \geq 0$ for $i = 1, ..., n$.

(A2) If $x_i = 0$, then $V_i^- = 0$. In particular, if $x \in \mathbf{X}_s$, then $V_i^- \geq 0$ for $i = 1, ..., m$.

(A3) $F_i = 0$ if $i > m$.

(A4) If $x \in \mathbf{X}_s$, then $F_i(x) = 0$ and $V_i^+ \geq 0$ for $i = 1, ..., m$.

(A5) If $F(x)$ is set to zero, than all eigenvalues of $J(x_0)$ have negative real parts.

If x_0 is a DFE of the model, then x_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$, but unstable if $\mathcal{R}_0 > 1$, where $\mathcal{R}_0$ is the basic reproduction number

These are some of the definitions and results that we will be using. Otherwise, we might state more if and when the need arise.

Chapter 4

Model Formulation and Qualitative Analysis

In this chapter, we present the formulation of HIV/TB co-infection model, and explain with the help of flow diagram how susceptible individuals, upon being infected with TB and HIV progress through various stages. We than analyze the models for TB only, HIV only, as well as the full model. The non-linear systems of TB-only model and HIV-only model will be qualitatively analyzed to find the conditions for existence and stability of disease-free equilibrium point. We then discuss the local and global stability of the disease-free equilibrium for each model. The basic reproduction numbers will be found and discussed. Endemic equilibrium point of TB only and HIV only will also be derived.

4.1 Formulation of a HIV/TB co-infection model with vertical transmission and treatment

In this section, a non linear mathematical model is proposed to study the dynamics of HIV/TB co-infection model that incorporates vertical transmission and treatment of HIV and TB infected individuals. In the modelling dynamics, the total population $N(t)$ at time t is divided into nine epidemiological subgroups: susceptible denoted by S; infectious with TB denoted by I; HIV infectious denoted by J_1; infectious with both TB and HIV denoted by J_2; full blown AIDS denoted by A; successfully recovered from TB denoted by T_T; individuals that are on treatment for HIV denoted by T_H; infectious with both AIDS and TB denoted by A_c; and individuals that are on treatment for both TB and HIV denoted by T_c.

The interactions between the classes are assumed as follows: the susceptible get HIV infected via sexual contacts with infectives, which may also lead to the birth of infected children. A fraction of newborn children are infected during birth and hence are directly recruited into the infective class with the rate $(1-\varepsilon)\theta$, with $(0 \leq \varepsilon \leq 1)$ and others die effectively at birth. Here ε is the fraction of newborns infected with HIV who die immediately after birth and θ is the rate of newborns infected with HIV.

We do not consider direct recruitment of infected persons but by vertical transmission only. It is assumed that the AIDS patients also infected with TB are isolated and sexually inactive, and therefore they are not capable of producing children. However, since a woman can develop AIDS or be infected with both AIDS and TB when she is already pregnant, then we are also assuming that $(1-\varepsilon)\theta A_c$ and $(1-\varepsilon)\theta A$ are to be considered in the dynamics.

The susceptibles can only get TB through interaction with TB infectious individuals (I, J_2 and A_c). All individuals in different human subgroups can die from natural causes (at a constant rate μ), while J_1, J_2, A, A_c and I classes can die from natural causes as well as from the diseases at rates μ_1, μ_2, μ_A, μ_C and μ_I respectively.

We derive our system of *Ordinary Differential Equations* (ODEs) from the flowchart below

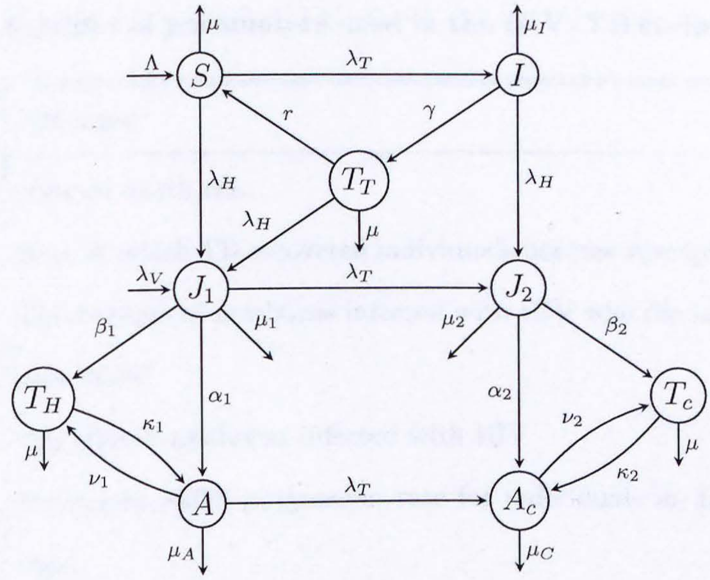

Figure 4.1: Flow diagram of the TB/HIV co-infection Model.

The model parameters are defined as follows:

Table 4.1: Definitions of parameters used in the HIV/TB co-infection model

Parameter	Definition
μ	Natural death rate
r	Rate at which TB recovered individuals become susceptible to TB
ε	The fraction of newborns infected with HIV who die immediately after birth
θ	The rate of newborns infected with HIV
α_i	Per-capita AIDS progression rate for individuals in J_i $(i = 1, 2)$ class
γ	Treatment rate of active TB individuals
β_1	Treatment rate of HIV individuals
Λ	Recruitment rate into susceptible
ν_1	The rate at which AIDS patients get treatment
d_T	Death rate due to TB
d_H	Death rate due to HIV
d_{HT}	Death rate due to TB and HIV
d_A	Death rate due to AIDS
d_{AT}	Death rate due to AIDS and TB
κ_1	The rate at which HIV recovered individuals develop HIV
β_2	The rate at which patients with both HIV and TB get treatment
ν_2	The rate at which AIDS with TB recovered get treatment
κ_2	The rate at which AIDS with TB recovered individuals develop AIDS and TB
C_T	Per capita contact rate for TB
C_H	Per capita contact rate for HIV
δ_T	Probability of transmission of TB infection from an active to a susceptible per contact unit time
δ_H	Probability of transmission of HIV infection from an infected person to an uninfected person per contact unit time.

From the flowchart (see page 19), we then get the following system of nine *Ordinary Differential Equations* (ODEs).

$$\begin{cases} \dfrac{dS}{dt} &= \Lambda + rT_T - (\lambda_T + \lambda_H + \mu)S \\ \dfrac{dI}{dt} &= \lambda_T S - (\lambda_H + \mu_I + \gamma)I \\ \dfrac{dT_T}{dt} &= \gamma I - (\lambda_H + r + \mu)T_T \\ \dfrac{dJ_1}{dt} &= \lambda_H S + \lambda_H T_T + \lambda_V - (\beta_1 + \mu_1 + \alpha_1 + \lambda_T)J_1 \\ \dfrac{dJ_2}{dt} &= \lambda_H I + \lambda_T J_1 - (\beta_2 + \mu_2 + \alpha_2)J_2 \\ \dfrac{dT_H}{dt} &= \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1)T_H \\ \dfrac{dA}{dt} &= \kappa_1 T_H + \alpha_1 J_1 - (\mu_A + \nu_1 + \lambda_T)A \\ \dfrac{dA_c}{dt} &= \kappa_2 T_c + \alpha_2 J_2 + \lambda_T A - (\mu_C + \nu_2)A_c \\ \dfrac{dT_c}{dt} &= \beta_2 J_2 + \nu_2 A_c - (\kappa_2 + \mu)T_c. \end{cases} \tag{4.1}$$

The total population size $N(t)$ at any time t is given by

$$N(t) = S(t) + I(t) + T_T(t) + J_1(t) + J_2(t) + A(t) + T_H(t) + A_c(t) + T_c(t).$$

The model has initial conditions given by:

$S(0) = S_0 \geq 0$; $I(0) = I_0 \geq 0$; $T_T(0) = T_{T_0} \geq 0$; $J_1(0) = J_{1_0} \geq 0$; $J_2(0) = J_{2_0} \geq 0$; $A(0) = A_0 \geq 0$; $T_H(0) = T_{H_0} \geq 0$; $A_c(0) = A_{c_0} \geq 0$ and $T_c(0) = T_{c_0} \geq 0$.

The force of infection λ_T, associated with TB infection is given as:

$$\lambda_T = \delta_T C_T \left(\frac{I + J_2 + A_c}{N} \right),$$

the force of infection associated with HIV infection given as:

$$\lambda_H = \delta_H C_H \left(\frac{J_1 + J_2}{N}\right),$$

and, the vertical transmission rate for HIV is given by:

$$\lambda_V = (1 - \varepsilon)\theta(J_1 + J_2 + A + A_c).$$

With,

$$\begin{aligned}
\mu_I &= \mu + d_T \\
\mu_1 &= \mu + d_H \\
\mu_2 &= \mu + d_{HT} \qquad (4.2) \\
\mu_A &= \mu + d_A \\
\mu_C &= \mu + d_{AT}.
\end{aligned}$$

4.1.1 Positivity and boundedness analysis

The model system (4.1) considers human populations, and variables describing human population or population dynamics in general can not be negative, and therefore it is necessary to show that our model (4.1) is epidemiologically meaningful by demonstrating that all their state variables used in the model formulation are non-negative for all $t \geq 0$. We also need to establish that solutions of the model system (4.1) with positive initial data remains positive for all time $t > 0$. This will be done in Theorem 4 below.

We consider a biologically-feasible region:

$$\mho_{TH} = \left\{(S, I, T_T, J_1, J_2, T_H, A, A_c, T_c) \in \mathbf{R}^9_+ | N(t) \leq \frac{\Lambda}{\mu}\right\}.$$

All solutions starting in $\mho_{TH}$ approach, enter or stay in $\mho_{TH}$. Using the Standard Comparison Theorem [17], it is possible to show the boundedness of $N(t)$ as given below:

$$N(t) = S(t) + I(t) + T_T(t) + J_1(t) + J_2(t) + A(t) + T_H(t) + A_c(t) + T_c(t),$$

which gives the rate of change of the total population considered in (4.1) as

$$\frac{dN(t)}{dt} = \Lambda - \mu S - \mu_I I - \mu T_T - \lambda_V - \mu_1 J_1 - \mu_2 J_2 - \mu T_H - \mu_A A - \mu_C A_c - \mu T_c.$$

Since $\mu_I = \mu + d_T$, $\mu_1 = \mu + d_H$, $\mu_2 = \mu + d_{HT}$, $\mu_A = \mu + d_A$ and $\mu_C = \mu + d_{AT}$, then we have the following:

$$\begin{aligned}\frac{dN(t)}{dt} &= \Lambda - \mu N(t) - (d_T I + \lambda_V + d_H J_1 + d_{HT} J_2 + d_A A + d_{AT} A_c)\\ &\leq \Lambda - \mu N(t),\end{aligned}$$

hence

$$\frac{dN(t)}{dt} \leq \Lambda - \mu N(t).$$

Separating the variables and integrating both sides we have,

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

with the initial time $t = 0$.

Since $e^{-\mu t} \geq 0$ for all $t \geq 0$, then if $N(0) \leq \frac{\Lambda}{\mu}$, then $N \leq \frac{\Lambda}{\mu}$. Which implies that $N(t)$ is bounded and all the solutions starting in $\mho_{TH}$ approach, enter or remain in $\mho_{TH}$ for $t > 0$.

This result is summarized in the following.

Theorem 4. Consider the model system (4.1). If $S(0) \geq 0$, $I(0) \geq 0$, $T_T(0) \geq 0$, $J_1(0) \geq 0$, $J_2(0) \geq 0$, $A(0) \geq 0$, $T_H(0) \geq 0$, $A_c(0) \geq 0$, and $T_c(0) \geq 0$, then $S(t)$, $I(t)$, $T_T(t)$, $J_1(t)$, $J_2(t)$, $A(t)$, $T_H(t)$, $A_c(t)$, and $T_c(t)$ are positive for all $t \geq 0$.

Proof. We prove this Theorem by contradiction, assuming that the total population $N(t) \neq 0$ for all $t \geq 0$.

We assume that there exists a first time t_1 such that

$$S(t_1) = 0, S^{'}(t_1) < 0, I(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0, \tag{4.3}$$

for $0 \leq t \leq t_1$,

or there exists a first time t_2 such that:

$$I(t_2) = 0, I'(t_2) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.4}$$

for $0 \leq t \leq t_2$,

or there exists a first time t_3 such that:

$$T_T(t_3) = 0, T_T'(t_3) < 0, S(t) \geq 0, I(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.5}$$

for $0 \leq t \leq t_3$,

or there exists a first time t_4 such that:

$$J_1(t_4) = 0, J_1'(t_4) < 0, S(t) \geq 0, T_T(t) \geq 0, I(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.6}$$

for $0 \leq t \leq t_4$,

or there exists a first time t_5 such that:

$$J_2(t_5) = 0, J_2'(t_5) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, I(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.7}$$

for $0 \leq t \leq t_5$,

or there exists a first time t_6 such that:

$$A(t_6) = 0, A'(t_6) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, I(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.8}$$

for $0 \leq t \leq t_6$,

or there exists a first time t_7 such that:

$$T_H(t_7) = 0, T_H'(t_7) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.9}$$

for $0 \leq t \leq t_7$,

or there exists a first time t_8 such that:

$$A_c(t_8) = 0, A_c^{'}(t_8) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., T_c(t) \geq 0 \tag{4.10}$$

for $0 \leq t \leq t_8$,

or there exists a first time t_9 such that:

$$T_c(t_9) = 0, T_c^{'}(t_9) < 0, S(t) \geq 0, T_T(t) \geq 0, J_1(t) \geq 0, J_2(t) \geq 0, A(t) \geq 0, ..., I(t) \geq 0 \tag{4.11}$$

for $0 \leq t \leq t_9$.

From (4.3), we have

$$S^{'}(t_1) = \Lambda + rT_T(t_1) > 0,$$

which is a contradiction, meaning that $S(t)$, $t \geq 0$ remains positive.

From (4.4), we have

$$I^{'}(t_2) = \delta_T C_T \left(\frac{J_2(t_2) + A_c(t_2)}{N} \right) S(t_2) \geq 0,$$

which is again a contradiction, meaning that $I(t) \geq 0$, $t \geq 0$.

Again from (4.5), we get

$$T_T^{'}(t_3) = \gamma I(t_3) \geq 0$$

which is a contradiction, implying that $T_T(t)$, $t \geq 0$ remains positive.

From (4.6), we have

$$J_1^{'}(t_4) = \delta_H C_H J_2(t_4) \left(\frac{S(t_4) + T_T(t_4)}{N} \right) + (1 - \epsilon)\theta(J_2(t_4) + A(t_4) + A_c(t_4)) \geq 0$$

which is a contradiction, meaning that J_1 remains positive.

Similarly, using the assumptions in equations (4.7)-(4.11), we get the following contradictions respectively:

$$\begin{aligned} J_2^{'}(t_5) &= \delta_T C_T \left(\frac{I(t_5) + A_c(t_5)}{N} \right) + \delta_H C_H \frac{J_2(t_5)}{N} \geq 0 \\ A_c^{'}(t_8) &= \kappa_2 T_c(t_8) + \alpha_2 J_2(t_8) + \delta_T C_T \frac{I(t_8) + J_2(t_8)}{N} \geq 0 \end{aligned}$$

$$
\begin{aligned}
T_H'(t_7) &= \beta_1 J_1(t_7) + \nu_1 A(t_7) \geq 0 \\
A'(t_6) &= \kappa_1 T_H(t_6) + \alpha_1 J_1(t_6) \geq 0 \\
T_c'(t_9) &= \beta_2 J_2(t_9) + \nu_2 A_c(t_9) \geq 0.
\end{aligned}
$$

Therefore we can conclude that in all cases, $J_2(t) \geq 0$, $T_H(t) \geq 0$, $A(t) \geq 0$, $A_c(t) \geq 0$ and $T_c(t) \geq 0$ for $t \geq 0$. Hence, the solutions $S(t)$, $I(t)$, $T_T(t)$, $J_1(t)$, $J_2(t)$, $A(t)$, $T_H(t)$, $A_c(t)$, and $T_c(t)$ are positive for all $t \geq 0$.

□

Model equation (4.1) describe human population and therefore it was shown that all the state variable are non-negative for all time t. This has ensured that the model is well posed and it is realistic in representing the human populations with no negative values.

4.2 Qualitative Analysis of the models

In this section, we analyze the models for TB only, HIV only, as well as the full model. The non-linear systems of TB-only model and HIV-only model will be qualitatively analyzed to find the conditions for existence and stability of disease-free equilibrium point. We then discuss the local and global stability of the disease-free equilibrium for each model. The basic reproduction numbers will be found and discussed. Endemic equilibrium point of TB only and HIV only will also be derived.

4.2.1 TB-only model

The sub-model of (4.1) with no HIV/AIDS disease is obtained as given in (4.12) by setting $J_1(t) = J_2(t) = A(t) = T_H(t) = A_c(t) = T_c(t) = 0)$ is given by the following system of equations:

$$\begin{cases} \dfrac{dS}{dt} &= \Lambda + rT_T - (\lambda_T + \mu)S \\ \\ \dfrac{dI}{dt} &= \lambda_T S - (\mu_I + \gamma)I \\ \\ \dfrac{dT_T}{dt} &= \gamma I - (r + \mu)T_T \end{cases} \qquad (4.12)$$

with non-negative initial conditions. The force of infection is given by

$$\lambda_T = \delta_T C_T \frac{I}{N_T}.$$

Where $N_T(t)$ is the total population for the system (4.12) and is given by

$$N_T(t) = S(t) + I(t) + T_T(t),$$

so that

$$\frac{dN_T}{dt} = \Lambda - \mu S - \mu T_T - \mu_I I.$$

Following a similar reasoning as Theorem 4, it can be proved that the region

$$\mho_2 = \left\{ (S, I, T_T) \in \mathbf{R}^3_+ | N_T(t) \leq \frac{\Lambda}{\mu} \right\}$$

is positively invariant. Therefore, the dynamics of the TB - only model will be considered in $\mho_2$.

The disease-free equilibrium

We start this subsection by finding the disease-free equilibrium point of the dynamical system (4.12).

An equilibrium point of the model (4.12) is obtained by setting

$$\frac{dS(t)}{dt} = \frac{dI(t)}{dt} = \frac{dT_T(t)}{dt} = 0.$$

At the disease-free state, we have $I^* = 0$, therefore $T_T^* = 0$ and hence,

$$S^* = \frac{\Lambda}{\mu}$$

where S^* is the first component of the disease-free equilibrium, when the disease has not yet invaded the population. Therefore, the DFE state of the model is given by:

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

The basic reproduction number and the local stability of the DFE

We start this subsection by finding the basic reproduction number using the next generation matrix method. We than analyze the local stability at the disease-free equilibrium.

The disease-free equilibrium's stability is discussed in terms of the basic reproduction number. The basic reproduction number, $\mathcal{R}_T$, for this model (4.12) is defined as the number of secondary TB cases produced by one infective individual during his/her entire lifetime in the system. We will find the basic reproduction number using the next generation method [6]. For this model, the matrix F representing the rates of appearance of new infections in the infected states I is given by:

$$F = \begin{pmatrix} \lambda_T S \end{pmatrix}.$$

The matrix V, representing the net outflow of infection from compartment I is given by

$$V = \begin{pmatrix} (\mu_I + \gamma) I \end{pmatrix}.$$

The Jacobian of the matrices F and V about the disease-free equilibrium, are given by

$$\mathcal{F} = \begin{pmatrix} \delta_T C_T \end{pmatrix},$$

and

$$\mathcal{V} = \begin{pmatrix} \mu_I + \gamma \end{pmatrix},$$

whose inverse is given by:

$$\mathcal{V}^{-1} = \left(\frac{1}{\mu_I + \gamma}\right).$$

The next generation matrix for this model is therefore found to be

$$\mathcal{F}\mathcal{V}^{-1} = \left(\frac{\delta_T C_T}{\mu_I + \gamma}\right).$$

The eigenvalue of $\mathcal{F}\mathcal{V}^{-1}$ is

$$\lambda_1 = \frac{\delta_T C_T}{\mu_I + \gamma}.$$

Thus, the TB-only reproduction number, is given by the spectral radius (the dominant eigenvalue) of the next generation matrix $\mathcal{F}\mathcal{V}^{-1}$, and is found to be

$$\mathcal{R}_T = \frac{\delta_T C_T}{\mu_I + \gamma}.$$

We therefore have the following theorem.

Theorem 5. The disease-free equilibrium of the model (4.12), E_0^T is locally asymptotically stable when $\mathcal{R}_T < 1$, and unstable when $\mathcal{R}_T > 1$.

Proof. The Jacobian matrix of this model is given by

$$J = \begin{pmatrix} -\mu & -\dfrac{\delta_T C_T S^2}{N_T^2} & r \\ 0 & -(\mu_I + \gamma) + \dfrac{\delta_T C_T S^2}{N_T^2} & 0 \\ 0 & \gamma & -(r + \mu) \end{pmatrix}.$$

We look at the linear stability of the equilibrium point by evaluating the Jacobian matrix J at $E_0^T = \left(\dfrac{\Lambda}{\mu}, 0, 0\right)$.

$$J(E_0^T) = \begin{pmatrix} -\mu & -\delta_T C_T & r \\ 0 & -(\mu_I + \gamma) + \delta_T C_T & 0 \\ 0 & \gamma & -(r + \mu) \end{pmatrix}.$$

The characteristic equation corresponding to the disease free equilibrium point is

$$0 = \begin{vmatrix} -\mu - \lambda & -\delta_T C_T & r \\ 0 & -(\mu_I + \gamma - \delta_T C_T) - \lambda & 0 \\ 0 & \gamma & -(r + \mu) - \lambda \end{vmatrix}.$$

which gives the eigenvalues: $\lambda_1 = -\mu$; $\lambda_2 = -(r+\mu)$ and $\lambda_3 = -(\mu_I+\gamma)+\delta_T C_T$.

Here, $\lambda_1 < 0$ and $\lambda_2 < 0$.

Considering λ_3,

$$\begin{aligned}\mathcal{R}_T < 1 \;&\Leftrightarrow\; \frac{\delta_T C_T}{\mu_I+\gamma} < 1\\ &\Leftrightarrow\; \delta_T C_T < \mu_I+\gamma\\ &\Leftrightarrow\; -(\mu_I+\gamma)+\delta_T C_T < 0,\end{aligned}$$

thus $\lambda_3 < 0$, and therefore, E_0^T is stable. If $\mathcal{R}_T > 1$, then $\lambda_3 > 0$, and E_0^T is a saddle point, thus unstable. □

Global stability analysis

Theorem 6. The point $E_0^T = \left(\frac{\Lambda}{\mu}, 0, 0\right)$ is a globally asymptotically stable equilibrium of the system (4.12) provided that $\mathcal{R}_T < 1$.

Proof. According to Theorem 1, we need to show that the conditions $(TH1)$ and $(TH2)$ are satisfied when $\mathcal{R}_T < 1$. But, it will shortly be established that $(TH1)$ and $(TH2)$ are always satisfied. In Theorem 5 we have proved that for $\mathcal{R}_T < 1$, E_0^T is locally asymptotically stable.

Considering the system (4.12), we let $X = (S, T_T)$, $Z = I$ with $X \in \mathbf{R}_+^2$ and $Z \in \mathbf{R}_+^1$ and disease-free equilibrium is now denoted by

$$E_0^T = (X_T^*, 0) = \left(\frac{\Lambda}{\mu}, 0, 0\right).$$

where

$$X_T^* = \left(\frac{\Lambda}{\mu}, 0\right).$$

For $(TH1)$, we have

$$\frac{dX}{dt} = F(X,Z) = \begin{bmatrix} \Lambda + rT_T - (\lambda_T+\mu)S \\ \gamma I - (r+\mu)T_T \end{bmatrix},$$

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where

$$\frac{dZ}{dt} = G(X, Z) = \left[\lambda_T S - (\mu_I + \gamma) I\right],$$

and,

$$F(X, 0) = \begin{pmatrix} \Lambda + rT_T - \mu S \\ -(r + \mu) T_T \end{pmatrix}.$$

Since $\frac{dX}{dt} = F(X, 0)$ is a linear equation, X_T^* is globally stable. Hence, $(TH1)$ holds.

For $(TH2)$, we have

$$G(X, Z) = AZ - \tilde{G}(X, Z),$$

and

$$A = \left[\delta_T C_T - (\mu_I + \gamma)\right]$$

whose off diagonal entries are non-negative. We then find that

$$AZ = \left[\delta_T C_T I - (\mu_I + \gamma) I\right].$$

We get

$$\tilde{G}(X, Z) = AZ - G(X, Z),$$

$$\tilde{G}(X, Z) = \left[\delta_T C_T I - (\mu_I + \gamma) I\right] - \left[\frac{\delta_T C_T}{N_T} IS - (\mu_I + \gamma) I\right]$$

$$\tilde{G}(X, Z) = \left[\tilde{G}_1(X, Z)\right] = \left[\delta_T C_T I \left(1 - \frac{S}{N_T}\right)\right].$$

Since S is always less than or equal to N_T, $\frac{S}{N_T} \leq 1$, so that $\tilde{G}_1(X, Z) \geq 0$. Thus, $\tilde{G}(X, Z) \geq 0$. That is, conditions in Theorem 1 are satisfied. Therefore, E_0^T is globally asymptotically stable for $\mathcal{R}_T < 1$. □

The endemic equilibrium

To obtain an endemic equilibrium, denoted by E_T^*, we set each equation in the model (4.12) equal to zero. Solving the system while expressing each equilibrium point in terms of I^* at steady state, we get S^*, I^* and T_T^* as components of endemic equilibrium point. Thus

$$E_T^* = (S^*, I^*, T_T^*)$$

is an endemic equilibrium, obtained as follows:

$$0 = \Lambda + rT_T^* - (\lambda_T + \mu)S^* \tag{4.13}$$

$$0 = \lambda_T S^* - (\mu_I + \gamma)I^* \tag{4.14}$$

$$0 = \gamma I^* - (r + \mu)T_T^* \tag{4.15}$$

where

$$\lambda_T = \frac{\delta_T C_T}{N_T^*} I^*,$$

with $N_T^* = S^* + I^* + T_T^*$.

Using equation (4.15), to find T_T^*, we have:

$$\begin{aligned} 0 &= \gamma I^* - (r + \mu)T_T^* \\ \gamma I^* &= (r + \mu)T_T^* \\ \Rightarrow T_T^* &= \frac{\gamma}{r + \mu} I^* \\ T_T^* &= a_0 I^* \end{aligned}$$

where $a_0 = \dfrac{\gamma}{r + \mu}$.

Add equation (4.13) and (4.14) (i.e (4.13) + (4.14)) from the system of equations to get;

$$
\begin{aligned}
\Lambda + rT_T^* - (\lambda_T + \mu)S^* + \lambda_T S^* - (\mu_I + \gamma)I^* &= 0 \\
\Rightarrow \Lambda + ra_0 I^* - \mu S^* - (\mu_I + \gamma)I^* &= 0 \\
\Lambda + (ra_0 - (\mu_I + \gamma))I^* &= \mu S^* \\
S^* &= \frac{1}{\mu}(\Lambda + (ra_0 - (\mu_I + \gamma))I^*) \\
S^* &= \frac{1}{\mu}(\Lambda + a_1 I^*)
\end{aligned}
$$

where

$$a_1 = ra_0 - (\mu_I + \gamma).$$

Using (4.13) to find I^*, we have;

$$0 = \lambda_T S^* - (\mu_I + \gamma)I^*$$

where λ_T is given by:

$$
\begin{aligned}
\lambda_T &= \frac{\delta_T C_T}{N_T^*} I^* \\
&= \frac{\delta_T C_T}{S^* + I^* + T_T^*} I^* \\
&= \frac{\delta_T C_T}{\frac{\Lambda}{\mu} + a_1 I^* + I^* + a_0 I^*} I^* \\
&= \frac{\delta_T C_T}{\frac{\Lambda}{\mu} + (a_1 + 1 + a_0)I^*} I^*.
\end{aligned}
$$

Then equation (4.13) becomes

$$
\begin{aligned}
\frac{\delta_T C_T}{\frac{\Lambda}{\mu} + (a_1 + 1 + a_0)I^*} I^* \left\{ \frac{1}{\mu}(\Lambda + a_1 I^*) \right\} - (\mu_I + \gamma)I^* &= 0 \\
\frac{\delta_T C_T}{\Lambda + \mu(1 + a_0 + \frac{a_1}{\mu})I^*} I^* \left\{ \Lambda + a_1 I^* \right\} - (\mu_I + \gamma)I^* &= 0.
\end{aligned}
$$

Let $a_2 = \mu(1 + a_0 + \dfrac{a_1}{\mu})$. Then we have

$$\begin{aligned}
\frac{\delta_T C_T}{\Lambda + a_2 I^*} I^* \{\Lambda + a_1 I^*\} - (\mu_I + \gamma) I^* &= 0 \\
\delta_T C_T \Lambda I^* + \delta_T C_T a_1 {I^*}^2 - \mu_I \Lambda I^* - \mu_I a_2 {I^*}^2 - \gamma \Lambda I^* - \gamma a_2 {I^*}^2 &= 0 \\
(\delta_T C_T a_1 - a_2(\mu_I + \gamma)) {I^*}^2 &= \Lambda(\mu_I + \gamma - \delta_T C_T) I^*.
\end{aligned}$$

Then we have the following:

$$I^* = 0$$

or,

$$I^* = \Lambda \frac{(\mu_I + \gamma - \delta_T C_T)}{(\delta_T C_T a_1 - a_2(\mu_I + \gamma))}.$$

Since in Endemic equilibrium point I^* (infected) is non-zero, then $I^* = 0$ is discarded. Therefore

$$I^* = \Lambda \frac{(\mu_I + \gamma - \delta_T C_T)}{(\delta_T C_T a_1 - a_2(\mu_I + \gamma))}.$$

Therefore S^*, I^* and T_T^* are given by:

$$\begin{aligned}
S^* &= \frac{1}{\mu}(\Lambda + a_1 I^*) \\
I^* &= \Lambda \frac{(\mu_I + \gamma - \delta_T C_T)}{(\delta_T C_T a_1 - a_2(\mu_I + \gamma))} \\
T_T^* &= a_0 I^*.
\end{aligned}$$

We note that S^*, I^* and T_T^* are always positive whenever we have the following: It can be seen that $a_0 = \frac{\gamma}{r+\mu}$ is positive, since all the parameter values are positive.

Claim: $a_1 < 0$

$$
\begin{aligned}
a_1 &< 0 \\
&\Leftrightarrow a_1(r+\mu) < 0 \\
&\Leftrightarrow r\left(\frac{\gamma}{r+\mu}\right)(r+\mu) - (\mu_I+\gamma)(r+\mu) < 0 \\
&\Leftrightarrow r\gamma - (\mu_I+\gamma)(r+\mu) < 0 \\
&\Leftrightarrow r\gamma - [\mu_I r + \mu_I\mu + r\gamma + \gamma\mu] < 0 \\
&\Leftrightarrow -[\mu_I r + \mu_I\mu + \gamma\mu] < 0.
\end{aligned}
$$

Hence $a_1 < 0$.

- For S^* to be positive, we have

$$
\begin{aligned}
S^* &> 0 \\
&\Leftrightarrow \frac{1}{\mu}(\Lambda + a_1 I^*) > 0 \\
&\Leftrightarrow \frac{\Lambda}{\mu} + \frac{a_1 I^*}{\mu} > 0 \\
&\Leftrightarrow \Lambda + a_1 I^* > 0 \\
&\Leftrightarrow a_1 I^* > -\Lambda \\
&\Leftrightarrow I^* < \frac{-\Lambda}{a_1}
\end{aligned}
$$

thus, S^* is positive if $I^* < \frac{-\Lambda}{a_1}$.

- $T_T^* = a_0 I^*$ is positive whenever $I^* > 0$, since $a_0 > 0$.

- For $I^* = \Lambda \dfrac{(\mu_I + \gamma - \delta_T C_T)}{(\delta_T C_T a_1 - a_2(\mu_I + \gamma))} > 0$, we have two conditions:

a) Both numerator and denominator must be positive

$$\begin{aligned}
\Lambda(\mu_I + \gamma - \delta_T C_T) &> 0 \\
&\Leftrightarrow \mu_I + \gamma - \delta_T C_T > 0 \\
&\Leftrightarrow \mu_I + \gamma > \delta_T C_T \\
&\Leftrightarrow 1 > \frac{\delta_T C_T}{\mu_I + \gamma} \\
&\Leftrightarrow 1 > \mathcal{R}_T
\end{aligned}$$

thus, the numerator is positive whenever $\mathcal{R}_T < 1$.

$$\begin{aligned}
\delta_T C_T a_1 - a_2(\mu_I + \gamma) &> 0 \\
&\Leftrightarrow \delta_T C_T a_1 > a_2(\mu_I + \gamma) \\
&\Leftrightarrow \frac{\delta_T C_T}{\mu_I + \gamma} a_1 > a_2 \\
&\Leftrightarrow \mathcal{R}_T a_1 > a_2 \\
&\Leftrightarrow \mathcal{R}_T < \frac{a_2}{a_1}
\end{aligned}$$

thus, the denominator is positive whenever $\mathcal{R}_T < \dfrac{a_2}{a_1}$.

b) Both numerator and denominator negative

$$\begin{aligned}
\Lambda(\mu_I + \gamma - \delta_T C_T) &< 0 \\
&\Leftrightarrow \mu_I + \gamma - \delta_T C_T < 0 \\
&\Leftrightarrow \mu_I + \gamma < \delta_T C_T \\
&\Leftrightarrow 1 < \frac{\delta_T C_T}{\mu_I + \gamma} \\
&\Leftrightarrow 1 < \mathcal{R}_T
\end{aligned}$$

thus, the numerator is positive whenever $\mathcal{R}_T > 1$.

$$
\begin{aligned}
\delta_T C_T a_1 - a_2(\mu_I + \gamma) &< 0 \\
&\Leftrightarrow \delta_T C_T a_1 < a_2(\mu_I + \gamma) \\
&\Leftrightarrow \frac{\delta_T C_T}{\mu_I + \gamma} a_1 < a_2 \\
&\Leftrightarrow \mathcal{R}_T a_1 < a_2 \\
&\Leftrightarrow \mathcal{R}_T > \frac{a_2}{a_1}
\end{aligned}
$$

thus, the denominator is positive whenever $\mathcal{R}_T > \frac{a_2}{a_1}$.

Therefore, we can conclude that, the components of TB endemic equilibrium points are positive whenever:

i) $0 < I^* < \frac{-\Lambda}{a_1}$

ii) $\mathcal{R}_T < \min\left\{1, \frac{a_2}{a_1}\right\}$ or $\mathcal{R}_T > \max\left\{1, \frac{a_2}{a_1}\right\}$.

4.2.2 HIV-only model

The sub-model of (4.1) with no TB infection is obtained by setting $I(t) = T_T(t) = J(t)_2 = A_c(t) = T_c(t) = 0$ to get the following system of equations,

$$
\begin{cases}
\frac{dS}{dt} = \Lambda - (\lambda_H + \mu)S \\
\frac{dJ_1}{dt} = \lambda_H S + \lambda_V - (\beta_1 + \mu_1 + \alpha_1)J_1 \\
\frac{dA}{dt} = \kappa_1 T_H + \alpha_1 J_1 - (\mu_A + \nu_1)A \\
\frac{dT_H}{dt} = \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1)T_H
\end{cases}
\tag{4.16}
$$

with non-negative initial conditions. The force of infection for HIV is given by:

$$
\lambda_H = \delta_H C_H \frac{J_1}{N_H},
$$

and the vertical transmission rate for HIV is given by:

$$\lambda_V = (1 - \varepsilon)\theta(J_1 + A).$$

Where $N_H(t)$ is the total population for the sub-model (4.16) and is given by:

$$N_H(t) = S(t) + J_1(t) + A(t) + T_H(t),$$

and

$$\frac{dN_H}{dt} = \Lambda - \mu S + \lambda_V - \mu_1 J_1 - A\mu_A - \mu T_H.$$

Following a similar reasoning as Theorem 4, it can be shown that the solutions S, J_1, A, T_H of the sub-model (4.16) are positive for $t > 0$ and that the region

$$\mho_H = \left\{(S, J_1, T_H, A) \in \mathbf{R}^4_+ | N_H(t) \leq \frac{\Lambda}{\mu}\right\}$$

is positively invariant. Therefore, the dynamics of the HIV - only model will be considered in $\mho_H$.

The disease-free equilibrium

An equilibrium point of the model (4.16) is obtained by setting

$$\frac{dS(t)}{dt} = \frac{dJ_1(t)}{dt} = \frac{dA(t)}{dt} = \frac{dT_H(t)}{dt} = 0.$$

At the disease-free equilibrium, we have $J_1^* = A^* = 0$ therefore $T_H^* = 0$, hence

$$S^* = \frac{\Lambda}{\mu}$$

where S^* is the first component of the disease-free equilibrium, when the disease has not yet invaded the population. Therefore, the DFE point of the model (4.16) is given by

$$E_0^H = (S^*, J_1^*, T_H^*, A^*) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right).$$

The basic reproduction number and the local stability of the DFE

We start this subsection by finding the basic reproduction number using the next generation matrix method. We than analyze the local stability at the disease-free equilibrium.

The disease-free equilibrium's stability is discussed in terms of the basic reproduction number, which is given by the spectral radius of the next generation matrix [6]. The reproduction number $\mathcal{R}_H$, is defined as the number of HIV infections produced by one infective HIV case during his/her lifetime in the system. For this model, the matrix F representing the rates of appearance of new infections in the infected states J_1, A and T_H is given by:

$$F = \begin{pmatrix} \lambda_H S \\ 0 \\ 0 \end{pmatrix}.$$

The matrix V, representing the net outflow of infections from compartments J_1, A and T_H is given by

$$V = \begin{pmatrix} (\beta_1 + \mu_1 + \alpha_1)J_1 - \lambda_V \\ (\mu_A + \nu_1)A - \kappa_1 T_H - \alpha_1 J_1 \\ (\mu + \kappa_1)T_H - \nu_1 A - \beta_1 J_1 \end{pmatrix}.$$

The Jacobian of the matrices F and V about the disease-free equilibrium, are given by

$$\mathcal{F} = \begin{pmatrix} \delta_H C_H & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$\mathcal{V} = \begin{pmatrix} \beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta & -(1-\epsilon)\theta & 0 \\ -\alpha_1 & \mu_A + \nu_1 & -\kappa_1 \\ -\beta_1 & -\nu_1 & (\mu + \kappa_1) \end{pmatrix},$$

so that the inverse of $\mathcal{V}$ is given by:

$$\mathcal{V}^{-1} = \frac{1}{\mathcal{M}} \begin{pmatrix} \mathcal{A}_1 & (1-\epsilon)\theta(\mu+\kappa_1) & \kappa_1(1-\epsilon)\theta \\ \alpha_1(\mu+\kappa_1)+\beta_1\kappa_1 & \mathcal{A}_2 & \mathcal{A}_5 \\ \alpha_1\nu_1+\beta_1(\mu_A+\nu_1) & \mathcal{A}_3 & \mathcal{A}_4 \end{pmatrix}$$

where,

$$\begin{aligned}
\mathcal{A}_1 &= \mu_A(\mu+\kappa_1)+\mu\nu_1 \\
\mathcal{A}_2 &= (\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta)(\mu+\kappa_1) \\
\mathcal{A}_3 &= (\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta)\nu_1+\beta_1(1-\epsilon)\theta \\
\mathcal{A}_4 &= (\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta)(\mu_A+\nu_1)-\alpha_1(1-\epsilon)\theta \\
\mathcal{A}_5 &= (\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta)\kappa_1 \\
\mathcal{M} &= [\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta]\left\{\mu_A(\mu+\kappa_1)+\mu\nu_1\right\} \\
&\quad -(1-\epsilon)\theta\left\{(\mu+\kappa_1)\alpha_1+\beta_1\kappa_1\right\}.
\end{aligned}$$

The next generation matrix for this model is therefore given as

$$\mathcal{F}\mathcal{V}^{-1} = \begin{pmatrix} \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}} & \frac{\delta_H C_H (1-\epsilon)\theta(\mu+\kappa_1)}{\mathcal{M}} & \frac{\kappa_1(1-\epsilon)\theta\delta_H C_H}{\mathcal{M}} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

The eigenvalues of $\mathcal{F}\mathcal{V}^{-1}$ are

$$\begin{aligned}
\lambda_1 &= \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}}, \\
\lambda_2 &= 0, \\
\lambda_2 &= 0.
\end{aligned}$$

Therefore, the HIV induced reproduction number, is given by the spectral radius (the dominant eigenvalue) of the next generation matrix $\mathcal{F}\mathcal{V}^{-1}$, and is found to be

$$\mathcal{R}_H = \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}}.$$

We therefore have the following theorem

Theorem 7. The equilibrium point E_0^H is locally asymptotically stable provided that $\mathcal{R}_H < 1$.

Proof. Using Theorem 3, it is sufficient to show that $(A1) - (A5)$ are satisfied.

(A1) If S, J_1 ,A, $T_H \geq 0$, then

$$F_i = \begin{pmatrix} \lambda_H S \\ 0 \\ 0 \end{pmatrix} ; \; V_i^+ = \begin{pmatrix} \lambda_V \\ \kappa_1 T_H + \alpha_1 J_1 \\ \nu_1 A + \beta_1 J_1 \end{pmatrix} ; \; V_i^- = \begin{pmatrix} (\beta_1 + \mu_1 + \alpha_1) J_1 \\ (\mu_A + \nu_1) A \\ (\mu + \kappa_1) T_H \end{pmatrix} \text{ are}$$

always greater than or equal to zero.

(A2) If the compartment is empty, then there are no infected individuals in the population, thus

$$V_i^- = \begin{pmatrix} (\beta_1 + \mu_1 + \alpha_1) J_1 \\ (\mu_A + \nu_1) A \\ (\mu + \kappa_1) T_H \end{pmatrix} = 0.$$

(A3) This condition arises from the simple fact that the incidence of infection for uninfected compartment is zero. That is

$$F_i(x) = \begin{pmatrix} \lambda_H S \\ 0 \\ 0 \end{pmatrix} = 0 \text{ for } i > m.$$

(A4) If the population is free of disease then the population will remain free of disease, thus if $x \in E_0^H$, then $F_i(x) = \begin{pmatrix} \lambda_H S \\ 0 \\ 0 \end{pmatrix} = 0$; and $V_i^+(x) =$

$$\begin{pmatrix} \lambda_V \\ \kappa_1 T_H + \alpha_1 J_1 \\ \nu_1 A + \beta_1 J_1 \end{pmatrix} = 0, \text{ for } i = 1, ..., m.$$

(A5) If $F(x)$ is set to zero, that is there is no new infection, than all eigenvalues of $J(E_0^H)$ have negative real parts.

The Jacobian matrix of this model is given by:

$$J = \begin{pmatrix} \dfrac{-\delta_H C_H J_1(J_1 + A + T_H)}{N_H^2} - \mu & \mathcal{Z}' & 0 & 0 \\ \dfrac{\delta_H C_H J_1(J_1 + A + T_H)}{N_H^2} & \mathcal{Z} & (1-\epsilon)\theta & 0 \\ 0 & \alpha_1 & -(\mu_A + \nu_1) & \kappa_1 \\ 0 & \beta_1 & \nu_1 & -(\mu + \kappa_1) \end{pmatrix},$$

where,

$$\begin{aligned} \mathcal{Z} &= \frac{\delta_H C_H S^2}{N_H^2} + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1) \\ \mathcal{Z}' &= -\frac{\delta_H C_H S^2}{N_H^2}. \end{aligned}$$

We look at the linear stability of the equilibrium point by evaluating the Jacobian matrix at $E_0^H = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$.

$$J(E_0^H) = \begin{pmatrix} -\mu & -\delta_H C_H & 0 & 0 \\ 0 & \mathcal{K}_{11} & (1-\epsilon)\theta & 0 \\ 0 & \alpha_1 & -(\mu_A + \nu_1) & \kappa_1 \\ 0 & \beta_1 & \nu_1 & -(\mu + \kappa_1) \end{pmatrix}.$$

where $\mathcal{K}_{11} = \delta_H C_H + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1)$.

The characteristic equation is given by

$$\begin{aligned} 0 &= (\lambda + \mu)[\lambda^3 + \lambda^2[(\mu_A + \nu_1 + \mu + \kappa_1) - \mathcal{D}] + \lambda[\mu_A(\mu + \kappa_1) + \mu\nu_1 \\ &\quad -\mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] + [-\mathcal{D}((\mu + \kappa_1)\mu_A + \nu_1\mu) \\ &\quad -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1)]] \end{aligned}$$

where $\mathcal{D} = (\delta_H C_H + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1))$.

The first factor is linear, which gives the eigenvalue $\lambda = -\mu$, which has a negative real part. For the remaining cubic factor, we use Routh-Hurwitz stability criteria to determine the conditions under which the λ's will have negative real parts.

The remaining cubic factor can be written as $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where

$$\begin{aligned}
a_1 &= \mu_A + \nu_1 + \mu + \kappa_1 - \mathcal{D} \\
a_2 &= \mu_A(\mu + \kappa_1) + \mu\nu_1 - \mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1 \\
a_3 &= -\mathcal{D}((\mu + \kappa_1)\mu_A + \nu_1\mu) - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1).
\end{aligned}$$

The roots of the cubic polynomial have negative real parts if and only if $a_1 > 0$, $a_3 > 0$ and $a_1a_2 - a_3 > 0$.

$$\begin{aligned}
a_3 > 0 \;\Leftrightarrow\;& -\mathcal{D}((\mu + \kappa_1)\mu_A + \nu_1\mu) - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > 0 \\
\Leftrightarrow\;& ((\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)) - \delta_H C_H)[\mu + \kappa_1)\mu_A + \nu_1\mu] \\
& -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > 0 \\
\Leftrightarrow\;& -\delta_H C_H((\mu + \kappa_1)\mu_A + \nu_1\mu) + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)) \\
& [(\mu + \kappa_1)\mu_A + \nu_1\mu] - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > 0 \\
\Leftrightarrow\;& (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta))[(\mu + \kappa_1)\mu_A + \nu_1\mu] \\
& -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > \delta_H C_H((\mu + \kappa_1)\mu_A + \nu_1\mu) \\
\Leftrightarrow\;& 1 > \frac{\delta_H C_H((\mu + \kappa_1)\mu_A + \nu_1\mu)}{\mathcal{M}} = \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}} = \mathcal{R}_H \\
\Leftrightarrow\;& \mathcal{R}_H < 1
\end{aligned}$$

recall that

$$\begin{aligned}
\mathcal{M} &= [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) \\
\mathcal{D} &= (\delta_H C_H + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1)) \\
\mathcal{A}_1 &= (\mu + \kappa_1)\mu_A + \nu_1\mu.
\end{aligned}$$

$$
\begin{aligned}
a_1 > 0 &\Leftrightarrow \mu_A + \nu_1 + \mu + \kappa_1 - \mathcal{D} > 0 \\
&\Leftrightarrow \mu_A + \nu_1 + \mu + \kappa_1 + \beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta - \delta_H C_H > 0 \\
&\Leftrightarrow \mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta) > \delta_H C_H \\
&\Leftrightarrow [\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\frac{\mathcal{A}_1}{\mathcal{M}} > \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}} = \mathcal{R}_H \\
&\Leftrightarrow \mathcal{R}_H < [\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\frac{\mathcal{A}_1}{\mathcal{M}}.
\end{aligned}
$$

Let's check if $[\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\frac{\mathcal{A}_1}{\mathcal{M}} > 1$. That is, if $[\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 > \mathcal{M}$, then $\mathcal{R}_H < 1$ is sufficient for $a_1 > 0$. Hence, we have the following workings:

$$
\begin{aligned}
1 &< [\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\frac{\mathcal{A}_1}{\mathcal{M}} \\
&\Leftrightarrow [\mu_A + \nu_1 + \mu + \kappa_1 + (\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 > \mathcal{M} \\
&\Leftrightarrow [\mu_A + \nu_1 + \mu + \kappa_1]\mathcal{A}_1 + [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 > \mathcal{M} \\
&\Leftrightarrow [\mu_A + \nu_1 + \mu + \kappa_1]\mathcal{A}_1 > -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) \\
&\Leftrightarrow [\mu_A + \nu_1 + \mu + \kappa_1]\mathcal{A}_1 + (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > 0.
\end{aligned}
$$

Since $a_3 > 0$ whenever $\mathcal{R}_H < 1$, we can conclude that $\mathcal{R}_H < 1$ is sufficient to conclude that $a_1 > 0$.

$$
\begin{aligned}
a_1a_2 - a_3 > 0 \;&\Leftrightarrow\; a_1a_2 > a_3 \\
&\Leftrightarrow\; [\mu_A + \nu_1 + \mu + \kappa_1 - \mathcal{D}] \\
&\quad [\mu_A(\mu + \kappa_1) + \mu\nu_1 - \mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\quad > -\mathcal{D}((\mu + \kappa_1)\mu_A + \nu_1\mu) - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) \\
&\Leftrightarrow\; [\mu_A + \nu_1 + \mu + \kappa_1] \\
&\quad [\mu_A(\mu + \kappa_1) + \mu\nu_1 - \mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\quad -\mathcal{D}[-\mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\quad > -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) \\
&\Leftrightarrow\; [(\mu_A + \nu_1 + \mu + \kappa_1) - \mathcal{D}][-\mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\quad +(\mu_A + \nu_1 + \mu + \kappa_1)(\mu_A(\mu + \kappa_1) + \mu\nu_1) \\
&\quad +(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) > 0.
\end{aligned}
$$

We have shown that $a_1 = [\mu_A + \nu_1 + \mu + \kappa_1 - \mathcal{D}]$ is positive whenever $\mathcal{R}_H < 1$ (see page 44). If we can show that $[-\mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1]$ is positive, then it is sufficient for $a_1a_2 - a_3 > 0$.

$$
\begin{aligned}
0 \;&<\; [-\mathcal{D}(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\Leftrightarrow\; [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta - \delta_H C_H](\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1 > 0 \\
&\Leftrightarrow\; [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta](\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1 \\
&\quad > \delta_H C_H(\mu_A + \nu_1 + \mu + \kappa_1) \\
&\Leftrightarrow\; [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta](\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1\frac{\mathcal{A}_1}{\mathcal{M}} \\
&\quad > \delta_H C_H\frac{\mathcal{A}_1}{\mathcal{M}}(\mu_A + \nu_1 + \mu + \kappa_1) = \mathcal{R}_H(\mu_A + \nu_1 + \mu + \kappa_1).
\end{aligned}
$$

Let's check if $[[\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta](\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1]\frac{\mathcal{A}_1}{\mathcal{M}} > 1$. That is, if

$[(\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1]\mathcal{A}_1 > \mathcal{M}(\mu_A + \nu_1 + \mu + \kappa_1)$, then $\mathcal{R}_H < 1$ is sufficient (but not necessary) to $a_1a_2 - a_3 > 0$. Hence, we have the following workings:

$$
\begin{aligned}
& [(\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1]\mathcal{A}_1 \\
& > \mathcal{M}(\mu_A + \nu_1 + \mu + \kappa_1) \\
\Leftrightarrow\ & [(\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)(\mu_A + \nu_1 + \mu + \kappa_1) - (1-\epsilon)\theta\alpha_1]\mathcal{A}_1 \\
& > [[\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 \\
& -(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1)](\mu_A + \nu_1 + \mu + \kappa_1) \\
\Leftrightarrow\ & -(1-\epsilon)\theta\alpha_1\mathcal{A}_1 + [(1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1)](\mu_A + \nu_1 + \mu + \kappa_1) > 0 \\
\Leftrightarrow\ & (1-\epsilon)\theta[\beta_1\kappa_1(\mu_A + \nu_1 + \mu + \kappa_1) + \kappa_1\alpha_1(\nu_1 + \mu + \kappa_1)) + \mu\alpha_1(\mu + \kappa_1))] > 0.
\end{aligned}
$$

Since $a_3 > 0$ whenever $\mathcal{R}_H < 1$, we can conclude that $\mathcal{R}_H < 1$ is sufficient to conclude that $a_1a_2 - a_3 > 0$.

Hence, we can conclude that, the disease - free equilibrium point is locally asymptotically stable as all eigenvalues of $J(E_0^H)$ have negative real parts.

□

Remark 2. If $\mathcal{R}_H > 1$, then a_3 is no longer positive, and in that case the Routh-Hurwitz criteria fail to apply, thus the DFE is unstable.

Global stability analysis

Theorem 8. The fixed point $E_0^H = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$ is a globally asymptotically stable equilibrium of the system (4.16) provided that $\mathcal{R}_H < 1$.

Proof. According to Theorem 1, we need to show that the conditions (TH1) and (TH2) are satisfied when $\mathcal{R}_H < 1$. But, it will shortly be established that (TH1) and (TH2) are always satisfied. In Theorem 7 we have proved that for $\mathcal{R}_H < 1$,

E_0^H is locally asymptotically stable.

Consider the system (4.16), $X = S$ and $Z = (J_1, A, T_H)$, with $X \in \mathbf{R}_+$ and $Z \in \mathbf{R}_+^3$ and the disease-free equilibrium is now denoted by

$$E_0^* = (X_H^*, 0, 0, 0),$$

where

$$X_H^* = \left(\frac{\Lambda}{\mu}\right),$$

and 0 is a three-dimensional zero vector. For $(TH1)$, we have

$$\frac{dX}{dt} = F(X, Z) = \left[\Lambda - (\mu + \lambda_H)S\right],$$

where

$$\frac{dZ}{dt} = G(X, Z) = \begin{bmatrix} \lambda_H S + \lambda_V - (\beta_1 + \mu_1 + \alpha_1)J_1 \\ \kappa_1 T_H + \alpha_1 J_1 - (\mu_A + \nu_1)A \\ \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1)T_H \end{bmatrix},$$

and,

$$F(X, 0) = \left(\Lambda - \mu S\right).$$

Since $\frac{dX}{dt} = F(X, 0)$ is a linear equation, X_H^* is globally stable. Hence, (TH1) holds.

For (TH2), we have

$$G(X, Z) = BZ - \tilde{G}(X, Z),$$

and,

$$B = \begin{pmatrix} \delta_H C_H + (1-\varepsilon)\theta - (\beta_1 + \mu_1 + \alpha_1) & (1-\epsilon)\theta & 0 \\ \alpha_1 & -(\mu_A + \nu_1) & \kappa_1 \\ \beta_1 & \nu_1 & -(\mu + \kappa_1) \end{pmatrix}$$

whose off diagonal entries are non-negative, so that,

$$BZ = \begin{pmatrix} (\delta_H C_H + (1-\varepsilon)\theta - (\beta_1 + \mu_1 + \alpha_1)) J_1 + (1-\epsilon)\theta A \\ \alpha_1 J_1 - (\mu_A + \nu_1)A + \kappa_1 T_H \\ \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1) T_H \end{pmatrix}.$$

We get

$\tilde{G}(X,Z) = BZ - G(X,Z)$,

$$= \begin{pmatrix} (\delta_H C_H + (1-\varepsilon)\theta - (\beta_1 + \mu_1 + \alpha_1)) J_1 + (1-\epsilon)\theta A \\ \alpha_1 J_1 - (\mu_A + \nu_1)A + \kappa_1 T_H \\ \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1) T_H \end{pmatrix} - \begin{pmatrix} \lambda_H S + \lambda_V - (\beta_1 + \mu_1 + \alpha_1) J_1 \\ \kappa_1 T_H + \alpha_1 J_1 - (\mu_A + \nu_1) A \\ \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1) T_H \end{pmatrix},$$

$$\tilde{G}(X,Z) = \begin{pmatrix} \tilde{G}_1(X,Z) \\ \tilde{G}_2(X,Z) \\ \tilde{G}_3(X,Z) \end{pmatrix} = \begin{pmatrix} \delta_H C_H J_1 \left(1 - \dfrac{S}{N_H}\right) \\ 0 \\ 0 \end{pmatrix}.$$

Since S is always less than or equal to N_H, $\dfrac{S}{N_H} \leq 1$, so that $\tilde{G}_1(X,Z) \geq 0$; and $\tilde{G}_2(X,Z) = \tilde{G}_3(X,Z) = 0$. Thus, we can conclude that $\tilde{G}(X,Z)$ is greater than or equal to zero. This implies that DFE point is globally asymptotically stable. □

The endemic equilibrium

To obtain an endemic equilibrium, denoted by E_H^*, we set each equation in the model (4.16) equal to zero. Solving the system while expressing each component in terms of A^* at steady state, we get S^*, J_1^* , A^* and T_H^* as components of an endemic equilibrium point. Therefore,

$$E_H^* = (S^*, J_1^*, A^*, T_H^*)$$

is an endemic equilibrium, obtained as follows:

Set each equation in the model (4.16) to zero

$$0 = \Lambda - (\lambda_H^* + \mu)S^* \tag{4.17}$$

$$0 = \lambda_H^* S^* + \lambda_V^* - (\beta_1 + \mu_1 + \alpha_1) J_1^* \tag{4.18}$$

$$0 = \kappa_1 T_H^* + \alpha_1 J_1^* - (\mu_A + \nu_1) A^* \tag{4.19}$$

$$0 = \beta_1 J_1^* + \nu_1 A^* - (\mu + \kappa_1) T_H^* \tag{4.20}$$

where

$\lambda_V^* = (1-\epsilon)\theta(J_1^* + A^*)$, and $\lambda_H^* = \dfrac{\delta_H C_H}{N_H^*} J_1^*$, with $N_H^* = S^* + J_1^* + A^* + T_H^*$.

To obtain T_H^*, we multiply equation (4.19) with β_1 and equation (4.20) with α_1.

$$\begin{aligned}
\beta_1(4.19) - \alpha_1(4.20) &= 0 \\
\beta_1\kappa_1 T_H^* + \beta_1\alpha_1 J_1^* - \beta_1(\mu_A + \nu_1)A^* - \alpha_1\beta_1 J_1^* - \alpha_1\nu_1 A^* + \alpha_1(\mu + \kappa_1)T_H^* &= 0 \\
\beta_1\kappa_1 T_H^* - \beta_1(\mu_A + \nu_1)A^* - \alpha_1\nu_1 A^* + \alpha_1(\mu + \kappa_1)T_H^* &= 0
\end{aligned}$$

$$\begin{aligned}
(\beta_1\kappa_1 + \alpha_1(\mu + \kappa_1))T_H^* &= (\beta_1(\mu_A + \nu_1) + \alpha_1\nu_1)A^* \\
T_H^* &= \frac{(\beta_1(\mu_A + \nu_1) + \alpha_1\nu_1)}{(\beta_1\kappa_1 + \alpha_1(\mu + \kappa_1))}A^* \\
T_H^* &= b_0 A^*
\end{aligned}$$

where $b_0 = \dfrac{(\beta_1(\mu_A + \nu_1) + \alpha_1\nu_1)}{(\beta_1\kappa_1 + \alpha_1(\mu + \kappa_1))}$.

To obtain J_1^*, we substitute T_H^* in (4.20) to get

$$\begin{aligned}
0 &= \beta_1 J_1^* + \nu_1 A^* - (\mu + \kappa_1) b_0 A^* \\
\beta_1 J_1^* &= (\mu + \kappa_1) b_0 A^* - \nu_1 A^* \\
J_1^* &= \frac{1}{\beta_1}\left\{(\mu + \kappa_1) b_0 - \nu_1\right\} A^* \\
J_1^* &= b_1 A^*
\end{aligned}$$

where $b_1 = \dfrac{1}{\beta_1}((\mu + \kappa_1) b_0 - \nu_1)$.

Add equation (4.17) and (4.18) to obtain S^*

$$
\begin{aligned}
(4.17) + (4.18) \Rightarrow \Lambda - (\lambda_H^* + \mu)S^* + \lambda_H^* S^* + \lambda_V^* - (\beta_1 + \mu_1 + \alpha_1)J_1^* &= 0 \\
\Lambda - \mu S^* + \lambda_V^* - (\beta_1 + \mu_1 + \alpha_1)J_1^* &= 0
\end{aligned}
$$

where λ_V^* and λ_H^* will be given as:

$$
\begin{aligned}
\lambda_V^* &= (1-\epsilon)\theta(J_1^* + A^*) \\
\lambda_V^* &= (1-\epsilon)\theta(b_1 A^* + A^*) \\
\lambda_V^* &= (1-\epsilon)\theta(b_1 + 1)A^*.
\end{aligned}
$$

Then we have the following

$$
\begin{aligned}
\Lambda - \mu S^* + (1-\epsilon)\theta(b_1+1)A^* - (\beta_1 + \mu_1 + \alpha_1)b_1 A^* &= 0 \\
\Lambda + (1-\epsilon)\theta(b_1+1)A^* - (\beta_1 + \mu_1 + \alpha_1)b_1 A^* &= \mu S^*
\end{aligned}
$$

$$
\begin{aligned}
S^* &= \frac{\Lambda}{\mu} + \frac{1}{\mu}\left\{(1-\epsilon)\theta(b_1+1) - (\beta_1 + \mu_1 + \alpha_1)b_1\right\} A^* \\
S^* &= \frac{\Lambda}{\mu} + b_2 A^*
\end{aligned}
$$

where $b_2 = \frac{1}{\mu}\{(1-\epsilon)\theta(b_1+1) - (\beta_1 + \mu_1 + \alpha_1)b_1\}$.

Substitute S^*, J_1^* and T_H^* and work on λ_V in equation (4.17), to get A^*

$$
\begin{aligned}
\lambda_H^* &= \frac{\delta_H C_H J_1^*}{N_H^*} \\
\lambda_H^* &= \frac{\delta_H C_H J_1^*}{S^* + J_1^* + T_H^* + A^*} \\
\lambda_H^* &= \frac{\delta_H C_H b_1 A^*}{\frac{\Lambda}{\mu} + b_2 A^* + b_0 A^* + b_1 A^* + A^*} \\
\lambda_H^* &= \frac{\delta_H C_H b_1 A^*}{\frac{\Lambda}{\mu} + (b_2 + b_0 + b_1 + 1)A^*}.
\end{aligned}
$$

So that:

$$\Lambda - \frac{\delta_H C_H b_1 A^*}{\frac{\Lambda}{\mu} + (b_2 + b_0 + b_1 + 1)A^*}\left\{\frac{\Lambda}{\mu} + b_2 A^*\right\} - \mu\left\{\frac{\Lambda}{\mu} + b_2 A^*\right\} = 0$$

$$\Lambda - \delta_H C_H b_1 A^*\left\{\frac{\Lambda}{\mu} + b_2 A^*\right\} - \mu\left\{\frac{\Lambda}{\mu} + b_2 A^*\right\}(\frac{\Lambda}{\mu} + (b_2 + b_0 + b_1 + 1)A^*) = 0$$

$$(\delta_H C_H b_1 b_2 + \mu b_2(b_2 + b_0 + b_1 + 1))A^{*^2} = \frac{-\Lambda}{\mu}\left(\delta_H C_H b_1 + \mu b_2\right) A^*.$$

Therefore,

$$A^* = 0$$

or,

$$A^* = \frac{\frac{-\Lambda}{\mu}\left(\delta_H C_H b_1 + \mu b_2\right)}{b_2[\delta_H C_H b_1 + \mu(b_2 + b_0 + b_1 + 1)]}.$$

Since in Endemic equilibrium point A^* (infected) is non-zero, then $A^* = 0$ is discarded. Hence

$$A^* = \frac{\frac{-\Lambda}{\mu}\left(\delta_H C_H b_1 + \mu b_2\right)}{b_2[\delta_H C_H b_1 + \mu(b_2 + b_0 + b_1 + 1)]}.$$

Therefore, the components of the endemic equilibrium S^*, J_1^*, A^* and T_H^* are given by

$$\begin{aligned} S^* &= \frac{\Lambda}{\mu} + b_2 A^* \\ J_1^* &= b_1 A^* \\ T_H^* &= b_0 A^* \\ A^* &= \frac{\frac{-\Lambda}{\mu}\left(\delta_H C_H b_1 + \mu b_2\right)}{b_2[\delta_H C_H b_1 + \mu(b_2 + b_0 + b_1 + 1)]}. \end{aligned}$$

.

As we will explore in quantitative analysis, it can be established that with a specific set of parameters, the endemic equilibrium point is feasible.

4.2.3 HIV/TB co-infection model

In this section, we carry out the mathematical analysis for HIV/TB co-infection with treatment and vertical transmission. The non-linear system (4.1) will be qualitatively analyzed to find the conditions for existence and stability of disease-free equilibrium point. We then discuss the local and global stability of the disease-free equilibrium for the model.

The disease- free equilibrium

We consider the system of nonlinear equations (4.1), and an equilibrium point of the model is obtained by setting

$$\begin{aligned}\frac{dS(t)}{dt} &= \frac{dI(t)}{dt} = \frac{dT_T(t)}{dt} = \frac{dJ_1(t)}{dt} = \frac{dJ_2(t)}{dt} = \frac{dA(t)}{dt} = \frac{dT_H(t)}{dt} = \frac{dA_c(t)}{dt} \\ &= \frac{dT_c(t)}{dt} = 0.\end{aligned}$$

The disease-free state is found by letting $I(t)^* = J_2(t)^* = J_1(t)^* = A(t)^* = A_c(t)^* = 0$, therefore $T_H(t)^* = T_c(t)^* = 0$.

Then we have

$$S^* = \frac{\Lambda}{\mu},$$

where S^* is the first component of the disease-free state, when the disease has not yet invaded the population. Therefore, the DFE state of the model is given by

$$\begin{aligned}E_0^{TH} &= (S(t)^*, I^*(t), T_c^*(t), J_1^*(t), J_2^*(t), A^*(t), T_H^*(t), A_c^*(t), T_T^*(t)) \\ &= \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0\right).\end{aligned}$$

The basic reproduction number and the local stability of the DFE

We start this subsection by finding the basic reproduction number using the next generation matrix method. We than analyze the local stability at the disease-free equilibrium.

For this model, the matrix F representing the rates of appearance of new infections in the infected states I, J_1, J_2, T_H, A, A_c and T_c is given by:

$$F = \begin{pmatrix} \lambda_T S \\ \lambda_H S + \lambda_H T_T \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

The matrix V, representing the net outflow of infections from compartments I, J_1, J_2, T_H, A, A_c and T_c is given by:

$$V = \begin{pmatrix} (\lambda_H + \mu_I + \gamma)I \\ (\beta_1 + \mu_1 + \alpha_1 + \lambda_T)J_1 - \lambda_V \\ (\beta_2 + \mu_2 + \alpha_2)J_2 - \lambda_H I - \lambda_T J_1 \\ (\mu + \kappa_1)T_H - \beta_1 J_1 - \nu_1 A \\ (\mu_A + \nu_1 + \lambda_T)A - \kappa_1 T_H - \alpha_1 J_1 \\ (\mu_C + \nu_2)A_c - \kappa_2 T_c - \alpha_2 J_2 - \lambda_T A \\ (\kappa_2 + \mu)T_c - \beta_2 J_2 - \nu_2 A_c \end{pmatrix}.$$

The Jacobian of the matrices F and V about the disease-free equilibrium, are given by

$$\mathcal{F} = \begin{pmatrix} \delta_T C_T & 0 & \delta_T C_T & 0 & 0 & \delta_T C_T & 0 \\ 0 & \delta_H C_H & \delta_H C_H & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$
\mathcal{V}=\begin{pmatrix}
\mu_I+\gamma & 0 & 0 & 0 & 0 & 0 & 0\\
0 & \mathcal{A}_3 & -(1-\epsilon)\theta & 0 & -(1-\epsilon)\theta & -(1-\epsilon)\theta & 0\\
0 & 0 & \beta_2+\mu_2+\alpha_2 & 0 & 0 & 0 & 0\\
0 & -\beta_1 & 0 & \mu+\kappa_1 & -\nu_1 & 0 & 0\\
0 & -\alpha_1 & 0 & -\kappa_1 & \mu_A+\nu_1 & 0 & 0\\
0 & 0 & -\alpha_2 & 0 & 0 & \mu_C+\nu_2 & -\kappa_2\\
0 & 0 & -\beta_2 & 0 & 0 & -\nu_2 & (\kappa_2+\mu)
\end{pmatrix}
$$

where $\mathcal{A}_3=\beta_1+\mu_1+\alpha_1-(1-\epsilon)\theta$, so that the inverse of $\mathcal{V}$ is given by:

$$
\mathcal{V}^{-1}=\begin{pmatrix}
\frac{1}{\mu_I+\gamma} & 0 & 0 & 0 & 0 & 0 & 0\\
0 & \frac{\mathcal{A}_1}{\mathcal{M}} & \frac{\mathcal{S}_2}{\mathcal{BMY}} & \frac{(1-\epsilon)\theta\kappa_1}{\mathcal{M}} & \mathcal{K}_5 & \frac{\mathcal{L}_1}{\mathcal{MY}} & \frac{\mathcal{L}_2}{\mathcal{MY}}\\
0 & 0 & \frac{1}{\mathcal{B}} & 0 & 0 & 0 & 0\\
0 & \frac{\mathcal{S}_3}{\mathcal{M}} & \frac{\mathcal{N}}{\mathcal{BMY}} & -\frac{\mathcal{K}}{\mathcal{Z}} & \frac{\mathcal{U}}{\mathcal{M}} & -\frac{\mathcal{D}_1}{\mathcal{MY}} & -\frac{\mathcal{D}_2}{\mathcal{ZY}}\\
0 & \frac{\mathcal{S}_4}{\mathcal{M}} & \frac{\mathcal{N}_1}{\mathcal{BZY}} & \frac{\kappa_1\mathcal{T}}{\mathcal{M}} & \frac{(\mu+\kappa_1)\mathcal{T}}{\mathcal{Z}} & -\frac{\mathcal{K}_1}{\mathcal{MY}} & -\frac{\mathcal{K}_2}{\mathcal{MY}}\\
0 & 0 & \mathcal{K}_4 & 0 & 0 & -\frac{\kappa_2+\mu}{\mathcal{Y}} & -\frac{\kappa_2}{\mathcal{Y}}\\
0 & 0 & \mathcal{K}_3 & 0 & 0 & -\frac{\nu_2}{\mathcal{Y}} & -\frac{(\mu_C+\nu_2)}{\mathcal{Y}}
\end{pmatrix}
$$

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where

$$\begin{aligned}
\mathcal{M} &= [\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta)]\mathcal{A}_1 - (1-\epsilon)\theta((\mu + \kappa_1)\alpha_1 + \beta_1\kappa_1) \\
\mathcal{A}_1 &= \mu_A(\mu + \kappa_1) + \mu\nu_1 \\
\mathcal{S}_2 &= -(1-\epsilon)\theta\mathcal{A}_1[\kappa_2\nu_2 - \alpha_2(\kappa_2 + \mu) - \beta_2\kappa_2 - (\mu_C + \nu_2)(\kappa_2 + \mu)] \\
\mathcal{S}_3 &= \alpha_1\nu_1 + \beta_1(\mu_A + \nu_1) \\
\mathcal{S}_4 &= \alpha_1(\mu + \kappa_1) + \beta_1\kappa_1 \\
\mathcal{B} &= \beta_2 + \mu_2 + \alpha_2 \\
\mathcal{Y} &= \kappa_2\nu_2 - (\mu_C + \nu_2)(\kappa_2 + \mu) \\
\mathcal{N} &= (1-\epsilon)\theta[\alpha_1\nu_1 + \beta_1(\mu_A + \nu_1)][\kappa_2\nu_2 - \alpha_2(\kappa_2 + \mu) - \beta_2\kappa_2] \\
\mathcal{N}_1 &= (1-\epsilon)\theta[\alpha_1(\mu + \kappa_1) + \beta_1\kappa_1)][\kappa_2\nu_2 - \alpha_2(\kappa_2 + \mu) - \beta_2\kappa_2 - (\mu_C + \nu_2)(\kappa_2 + \mu)] \\
\mathcal{K} &= (1-\epsilon)\theta\alpha_1 - (\mu_A + \nu_1)(\beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta) \\
\mathcal{T} &= \beta_1 + \mu_1 + \alpha_1 - (1-\epsilon)\theta \\
\mathcal{U} &= (\beta_1 + \mu_1 + \alpha_1)\nu_1 - (1-\epsilon)\theta[\nu_1 - \beta_1] \\
\mathcal{L}_1 &= (1-\epsilon)\theta(\kappa_2 + \mu)[\kappa_1\nu_1 - (\mu + \kappa_1)(\mu_A + \nu_1)] \\
\mathcal{L}_2 &= (1-\epsilon)\theta\kappa_2[\kappa_1\nu_1 - (\mu + \kappa_1)(\mu_A + \nu_1)] \\
\mathcal{D}_1 &= (1-\epsilon)\theta(\kappa_2 + \mu)[\alpha_1\nu_1 + \beta_1(\mu_A + \nu_1)] \\
\mathcal{D}_2 &= (1-\epsilon)\theta\alpha_2[\alpha_1\nu_1 + \beta_1(\mu_A + \nu_1)] \\
\mathcal{K}_1 &= (1-\epsilon)\theta(\kappa_2 + \mu)[\alpha_1(\mu + \kappa_1) + \beta_1\kappa_1] \\
\mathcal{K}_2 &= (1-\epsilon)\theta\kappa_2[\alpha_1(\mu + \kappa_1 + \beta_1\kappa_1)] \\
\mathcal{K}_3 &= -\frac{\alpha_2\nu_2 + \beta_2(\mu_c + \nu_2)}{\mathcal{B}\mathcal{Y}} \\
\mathcal{K}_4 &= -\frac{(\kappa_2 + \mu)\alpha_2 + \beta_2\kappa_2}{\mathcal{B}\mathcal{Y}} \\
\mathcal{K}_5 &= \frac{(\mu + \kappa_1)(1-\epsilon)\theta}{\mathcal{Z}}.
\end{aligned}$$

The next generation matrix for this model is therefore found as

$$
\mathcal{FV}^{-1} = \begin{pmatrix}
\frac{\delta_T C_T}{\mu_I+\gamma} & 0 & \mathcal{K}_6 & 0 & 0 & -\frac{\delta_T C_T(\kappa_2+\mu)}{\mathcal{Y}} & -\delta_T C_T\frac{\kappa_2}{\mathcal{Y}} \\
0 & \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}} & \mathcal{K}_7 & \mathcal{K}_9 & -\mathcal{K}_8 & \frac{\delta_H C_H \mathcal{L}_1}{\mathcal{MY}} & \frac{\delta_H C_H \mathcal{L}_2}{\mathcal{MY}} \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix}.
$$

where

$$
\begin{aligned}
\mathcal{K}_6 &= \frac{\delta_T C_T}{\mathcal{B}}\left(1-\frac{(\kappa_2+\mu)\alpha_2+\beta_2\kappa_2}{\mathcal{Y}}\right) \\
\mathcal{K}_7 &= \frac{\delta_H C_H}{\mathcal{B}}\left(1+\frac{\mathcal{S}_2}{\mathcal{MY}}\right) \\
\mathcal{K}_8 &= \frac{\delta_H C_H(\mu+\kappa_1)(1-\epsilon)\theta\kappa_1}{\mathcal{M}} \\
\mathcal{K}_9 &= \frac{\delta_H C_H(1-\epsilon)\theta\kappa_1}{\mathcal{M}}.
\end{aligned}
$$

The eigenvalues of $\mathcal{FV}^{-1}$ are

$$
\begin{aligned}
\lambda_1 &= \frac{\delta_T C_T}{\mu_I+\gamma}, \\
\lambda_2 &= \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}}, \\
\lambda_3 &= 0, \\
\lambda_4 &= 0, \\
\lambda_5 &= 0, \\
\lambda_6 &= 0, \\
\lambda_7 &= 0.
\end{aligned}
$$

λ_1 and λ_2 correspond to the reproduction numbers for the TB transmission model and the HIV transmission model respectively. Therefore, the basic reproduction number, $\mathcal{R}_0$ for the whole model is defined as

$$
\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} \tag{4.21}
$$

where,

$$\mathcal{R}_H = \frac{\delta_H C_H \mathcal{A}_1}{\mathcal{M}}$$

and

$$\mathcal{R}_T = \frac{\delta_T C_T}{\mu_I + \gamma}.$$

The following theorem is on the stability analysis of the DFE for the system (4.1)

Theorem 9. The equilibrium point E_0^{TH} is locally asymptotically stable provided that $\mathcal{R}_0 < 1$, and unstable when $\mathcal{R}_0 > 1$.

Proof. Using Theorem 3, it is sufficient to show that the dynamical system (4.1) satisfies the conditions $(A1) - (A5)$.

(A1) If I, J_2, A_c, T_c, T_T, S, J_1, A, $T_H \geq 0$, then

$$F_i = \begin{pmatrix} \lambda_T S \\ (S+T_T)\lambda_H \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}; \quad V_i^+ = \begin{pmatrix} 0 \\ \lambda_V \\ \lambda_H I + \lambda_T J_1 \\ \beta_1 J_1 + \nu_1 A \\ \kappa_1 T_H + \alpha_1 J_1 \\ \kappa_2 T_c + \alpha_2 J_2 + \lambda_T A \\ \beta_2 J_2 + \nu_2 A_c \end{pmatrix};$$

$$V_i^- = \begin{pmatrix} (\lambda_H + \mu_I + \gamma)I \\ (\beta_1 + \mu_1 + \alpha_1 + \lambda_T)J_1 \\ (\beta_2 + \mu_2 + \alpha_2)J_2 \\ (\mu + \kappa_1)T_H \\ (\mu_A + \nu_1 + \lambda_T)A \\ (\mu_C + \nu_2)A_c \\ (\kappa_2 + \mu)T_c \end{pmatrix}$$ are always greater than or equal to zero, since all the parameter values are positive.

(A2) If the compartment is empty, then there are no infected individuals in the population. That is $I = J_1 = J_2 = T_H = A = A_c = T_c = 0$. Therefore,

$$V_i^- = \begin{pmatrix} (\lambda_H + \mu_I + \gamma)I \\ (\beta_1 + \mu_1 + \alpha_1 + \lambda_T)J_1 \\ (\beta_2 + \mu_2 + \alpha_2)J_2 \\ (\mu + \kappa_1)T_H \\ (\mu_A + \nu_1 + \lambda_T)A \\ (\mu_C + \nu_2)A_c \\ (\kappa_2 + \mu)T_c \end{pmatrix} = 0.$$

(A3) This condition arises from the simple fact that the incidence of infection for uninfected compartment is zero. That is

$$F_i = \begin{pmatrix} \lambda_T S \\ (S + T_T)\lambda_H \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = 0 \text{ for } i > m.$$

(A4) If the population is free of disease then the population will remain free of disease, thus if $x \in E_0^{TH}$, then $F_i = \begin{pmatrix} \lambda_T S \\ (S + T_T)\lambda_H \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = 0$ for $i > m$; and

$$V_i^+ = \begin{pmatrix} \lambda_V \\ \lambda_H I + \lambda_T J_1 \\ \beta_1 J_1 + \nu_1 A \\ \kappa_1 T_H + \alpha_1 J_1 \\ \kappa_2 T_c + \alpha_2 J_2 + \lambda_T A \\ \beta_2 J_2 + \nu_2 A_c \end{pmatrix} = 0, \text{ for } i = 1, ..., m.$$

(A5) If $F(x)$ is set to zero, that is there is no new infection, then all eigenvalues of $J(E_0^{TH})$ have negative real parts.

The Jacobian matrix evaluated at the disease-free equilibrium point is given by:

$$J(E_0^{TH}) = \begin{bmatrix} -\mu & \mathcal{P}_6 & r & -\delta_H C_H & -\mathcal{P}_4 & 0 & 0 & -\delta_T C_T & 0 \\ 0 & \mathcal{P}_5 & 0 & 0 & \delta_T C_T & 0 & 0 & \delta_T C_T & 0 \\ 0 & \gamma & \mathcal{P}_7 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \mathcal{P}_1 & \mathcal{P}_2 & 0 & (1-\epsilon)\theta & (1-\epsilon)\theta & 0 \\ 0 & 0 & 0 & 0 & -\mathcal{P}_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_1 & 0 & \mathcal{P}_8 & \nu_1 & 0 & 0 \\ 0 & 0 & 0 & \alpha_1 & 0 & \kappa_1 & -(\mu_A + \nu_1) & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha_2 & 0 & 0 & -(\mu_C + \nu_2) & \kappa_2 \\ 0 & 0 & 0 & 0 & \beta_2 & 0 & 0 & \nu_2 & \mathcal{P}_9 \end{bmatrix}$$

where;

$$
\begin{aligned}
\mathcal{P}_1 &= \delta_H C_H + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1) \\
\mathcal{P}_4 &= \delta_T C_T + \delta_H C_H \\
\mathcal{P}_2 &= \delta_H C_H + (1-\epsilon)\theta \\
\mathcal{P}_3 &= \beta_2 + \mu_2 + \alpha_2 \\
\mathcal{P}_5 &= -(\mu_I + \gamma) + \delta_T C_T \\
\mathcal{P}_6 &= -\delta_T C_T \\
\mathcal{P}_7 &= -(r + \mu) \\
\mathcal{P}_8 &= -(\mu + \kappa_1) \\
\mathcal{P}_9 &= -(\kappa_2 + \mu).
\end{aligned}
$$

The characteristic equation of the co-infection model is given by the following:

$$
\begin{aligned}
0 &= (-r-\mu-\lambda)(-\alpha_2-\beta_2-\mu_2-\lambda)(-\lambda-\gamma-\mu_I+\delta_T C_T)(-\lambda-\mu) \\
&\quad [\lambda^2 + \lambda(\kappa_2+\mu+\mu_C+\nu_2) + \kappa_2\mu_C + \mu(\mu_C+\nu_2)] \\
&\quad [\lambda^3 + \lambda^2[(\mu_A+\nu_1+\mu+\kappa_1) - \mathcal{D}] + \\
&\quad \lambda[\mu_A(\mu+\kappa_1) + \mu\nu_1 - \mathcal{D}(\mu_A+\nu_1+\mu+\kappa_1) - (1-\epsilon)\theta\alpha_1] \\
&\quad +[-\mathcal{D}((\mu+\kappa_1)\mu_A + \nu_1\mu) - (1-\epsilon)\theta((\mu+\kappa_1)\alpha_1 + \beta_1\kappa_1)]],
\end{aligned}
$$

where $\mathcal{D} = (\delta_H C_H + (1-\epsilon)\theta - (\beta_1+\mu_1+\alpha_1))$.

The factors in the characteristic equation gives the following eigenvalues

$$\begin{aligned}
\lambda_1 &= -(r+\mu) < 0 \\
\lambda_2 &= -(\alpha_2+\beta_2+\mu_2) < 0 \\
\lambda_3 &= -\mu < 0 \\
\lambda_4 &= -(\gamma+\mu_I)+\delta_T C_T
\end{aligned}$$

considering λ_4,

$$\begin{aligned}
\mathcal{R}_T < 1 &\Leftrightarrow \frac{\delta_T C_T}{\mu_I+\gamma} < 1 \\
&\Leftrightarrow \delta_T C_T < \mu_I + \gamma \\
&\Leftrightarrow -(\mu_I+\gamma)+\delta_T C_T < 0,
\end{aligned}$$

thus $\lambda_4 < 0$. If $\mathcal{R}_T > 1$, then $\lambda_4 > 0$.

For the remaining factors, we use Routh-Hurwitz stability criteria to determine the conditions under which the $\lambda^{'}$s will have negative real parts.

For the quadratic factor $(\lambda^2+\lambda(\kappa_2+\mu+\mu_C+\nu_2)+\mu(\mu_C+\nu_2)+\kappa_2\mu_C)$, since all the model parameters are positive, it can be seen that all the coefficients of quadratic polynomial are positive, which means that the $\lambda^{'}$s will have negative real parts.

For the cubic factor

$$\begin{aligned}
&[\lambda^3+\lambda^2[(\mu_A+\nu_1+\mu+\kappa_1)-\mathcal{D}]+ \\
&\lambda[\mu_A(\mu+\kappa_1)+\mu\nu_1-\mathcal{D}(\mu_A+\nu_1+\mu+\kappa_1)-(1-\epsilon)\theta\alpha_1] \\
&+[-\mathcal{D}((\mu+\kappa_1)\mu_A+\nu_1\mu)-(1-\epsilon)\theta((\mu+\kappa_1)\alpha_1+\beta_1\kappa_1)]],
\end{aligned}$$

it was shown (see page 43) that the $\lambda^{'}$s will have negative real parts whenever $\mathcal{R}_H < 1$.

E_0^{TH} is locally asymptotically stable if $\mathcal{R}_T < 1$ and $\mathcal{R}_H < 1$; thus the diseases (TB and HIV) die out. Therefore, we can conclude that, the disease

- free equilibrium point is locally asymptotically stable whenever $\mathcal{R}_0 < 1$ and unstable if either $\mathcal{R}_T > 1$ or $\mathcal{R}_H > 1$.

□

Remark 3. If $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} > 1$, then we have the following

i) If $\mathcal{R}_H > 1$ and $\mathcal{R}_T < 1$, then the HIV is endemic and TB dies out.

ii) If $\mathcal{R}_H < 1$ and $\mathcal{R}_T > 1$, then the HIV dies out, while TB is endemic.

iii) If $\mathcal{R}_H > 1$ and $\mathcal{R}_T > 1$, then the two diseases are endemic.

Global stability analysis

We noticed that, for the global stability to be guaranteed, the conditions (TH1) and (TH2) in Theorem 1 must be met, provided that $\mathcal{R}_0 < 1$.
We must show that condition (TH1) hold, however (TH2) fails to hold. In Theorem 7 we have proved that for $\mathcal{R}_0 < 1$, E_0^{TH} is locally asymptotically stable.

Consider the system (4.1), $X = (S, T_T)$ and $Z = (I, J_1, J_2, A, A_c, T_H, T_c)$, with $X \in \mathbf{R}_+^2$ and $Z \in \mathbf{R}_+^7$. The disease-free equilibrium is denoted by

$$E_0^{TH} = (X_{TH}^*, 0, 0, 0, 0, 0, 0, 0),$$

where

$$X_{TH}^* = \left(\frac{\Lambda}{\mu}, 0\right).$$

For $(TH1)$, we have

$$\begin{aligned} \frac{dX}{dt} &= F(X, Z) = \begin{bmatrix} \Lambda + rT_T - (\lambda_T + \lambda_H + \mu)S \\ \gamma I - (\lambda_H + r + \mu)T_T \end{bmatrix}, \\ \frac{dZ}{dt} &= G(X, Z) \end{aligned}$$

where

$$\frac{dZ}{dt} = G(X,Z) = \begin{bmatrix} \lambda_T S - (\lambda_H + \mu_I + \gamma)I \\ \lambda_H S + \lambda_H T_T + \lambda_V - (\beta_1 + \mu_1 + \alpha_1 + \lambda_T)J_1 \\ \lambda_H I + \lambda_T J_1 - (\beta_2 + \mu_2 + \alpha_2)J_2 \\ \beta_1 J_1 + \nu_1 A - (\mu + \kappa_1)T_H \\ \kappa_1 T_H + \alpha_1 J_1 - (\mu_A + \nu_1 + \lambda_T)A \\ \kappa_2 T_c + \alpha_2 J_2 + \lambda_T A - (\mu_C + \nu_2)A_c \\ \beta_2 J_2 + \nu_2 A_c - (\kappa_2 + \mu)T_c \end{bmatrix},$$

and,

$$F(X,0) = \begin{bmatrix} \Lambda + rT_T - \mu S \\ -(\mu + r)T_T \end{bmatrix}.$$

Since $\frac{dX}{dt} = F(X,0)$ is a linear equation, X^*_{TH} is globally stable. Hence (TH1) holds.

For (TH2), we have

$$G(X,Z) = AZ - \tilde{G}(X,Z),$$

and,

$$A = \begin{bmatrix} \mathcal{B}_2 & 0 & \delta_T C_T & 0 & 0 & \delta_T C_T & 0 \\ 0 & \mathcal{B}_1 & \delta_T C_T + (1-\epsilon)\theta & 0 & (1-\epsilon)\theta & (1-\epsilon)\theta & 0 \\ 0 & 0 & -(\beta_2 + \mu_2 + \alpha_2) & 0 & 0 & 0 & 0 \\ 0 & \beta_1 & 0 & -(\mu + \kappa_1) & \nu_1 & 0 & 0 \\ 0 & \alpha_1 & 0 & \kappa_1 & -(\mu_A + \nu_1) & 0 & 0 \\ 0 & 0 & \alpha_2 & 0 & 0 & -(\mu_C + \nu_2) & \kappa_2 \\ 0 & 0 & \beta_2 & 0 & 0 & \nu_2 & -(\kappa_2 + \mu) \end{bmatrix}$$

whose off diagonal entries are non-negative, where

$$\begin{aligned} \mathcal{B}_1 &= \delta_T C_T + (1-\epsilon)\theta - (\beta_1 + \mu_1 + \alpha_1) \\ \mathcal{B}_2 &= \delta_T C_T - (\mu_I + \gamma) \end{aligned}$$

so that

$$AZ = \begin{bmatrix} \delta_T C_T I - (\mu_I + \gamma)I + \delta_T C_T J_2 + \delta_T C_T A_c \\ \mathcal{B}_5 \\ -(\beta_2 + \mu_2 + \alpha_2)J_2 \\ \beta_1 J_1 - (\mu + \kappa_1)T_H + \nu_1 A \\ \alpha_1 J_1 + \kappa_1 T_H - (\mu_A + \nu_1)A \\ \alpha_2 J_2 - (\mu_C + \nu_2)A_c + \kappa_2 T_c \\ \beta_2 J_2 + \nu_2 A_c - (\kappa_2 + \mu)T_c \end{bmatrix}$$

where $\mathcal{B}_5 = (\delta_H C_H + (1-\epsilon)\theta - (\beta_1 + \alpha_1 + \mu_1))\, J_1 + (\delta_T C_T + (1-\epsilon)\theta)J_2 + (1-\epsilon)\theta A + (1-\epsilon)\theta A_c$.

We get

$$\tilde{G}(X,Z) = AZ - G(X,Z),$$

$$\tilde{G}(X,Z) = \begin{pmatrix} \tilde{G}_1(X,Z) \\ \tilde{G}_2(X,Z) \\ \tilde{G}_3(X,Z) \\ \tilde{G}_4(X,Z) \\ \tilde{G}_5(X,Z) \\ \tilde{G}_6(X,Z) \\ \tilde{G}_7(X,Z) \end{pmatrix} = \begin{pmatrix} \delta_T C_T (I + J_2 + A_c)\left[1 - \frac{1}{N}\right] \\ \delta_T C_T \left[J_2 + \left(\frac{J_1 + J_2}{N}\right)(S + T_T)\right] \\ -(\lambda_H I + \lambda_T J_1) \\ 0 \\ \lambda_T A \\ -\lambda_T A \\ 0 \end{pmatrix}.$$

Thus $\tilde{G}_3(X,Z) < 0$ and $\tilde{G}_6(X,Z) < 0$ and this implies that $\tilde{G}(X,Z)$ is not greater than or equal to zero. (TH2) in Theorem 1 is not satisfied, and thus E_0^{TH} may not be globally asymptotically stable.

For any infectious disease, one of the most important concerns is its ability to invade a population. This can be expressed by a threshold parameter $\mathcal{R}_0$. The infected individual in its entire period of infectivity will produce less than one infected individual on average if $\mathcal{R}_0 < 1$. The disease-free equilibrium point is locally asymptotically stable. This shows that the disease will be wiped out of the population.

Chapter 5

Quantitative analysis of the models

In this chapter, we use the fourth order Runge-Kutta method to provide numerical solutions to our systems of ODEs. More generally, we use MATLAB to perform various numerical simulations to demonstrate agreement of the numerical results with the theoretical results derived in Chapter 4. The values of the parameters that we use mostly come from literature.
The phase portraits in this chapter, demonstrate how the trajectories behave depending on the initial conditions.

We consider parameter values in Tables 5.1 and 5.2 with a total initial population of $N_0 = 500$. Some of the parameters were not available, therefore we assumed them and obtained the rest from the papers we reviewed. The table below shows the set of parameter values which were used.

Table 5.1: Values of parameters used in the TB, HIV and HIV/TB models

Parameter	Definition	Value	Source
μ	Natural death rate	1/70	[7]
d_T	Death rate due to TB	0.1	[27]
r	Rate at which TB recovered individuals become susceptible to TB	3	[27]
γ	Treatment rate of active TB individuals	1	[27]
Λ	Contact recruitment rate into susceptible	0.4×500	[33]
C_T	Per capita contact rate for TB	50	[27]
δ_T	Probability of transmission of TB infection from an active to a susceptible per contact rate	0.2	[27]
d_H	Death rate due to HIV	0.2	[27]
d_A	Death rate due to AIDS	0.5	[27]
ν_1	The rate at which AIDS patients get treatment	0.1	[33]
k_1	The rate at which HIV individuals developed AIDS	0.08	[33]
α_1	Per-capita AIDS progression rate	0.1	[27]
ε	The fraction of newborns infected with HIV	0.2	[33]
θ	The rate of newborns infected with HIV	0.3	[33]
β_1	HIV treatment rate	0.1	Assumed
C_H	Per capita contact rate for HIV	4	[27]
δ_H	Probability of transmission of HIV infection from an active to a susceptible per contact rate	0.1	[27]

5.1 Simulation for TB-only model

In this section, we conduct sensitivity analysis and illustrate the behavior of our model with graphs. Sensitivity is defined as a way of quantifying how a small change in parameters used in a model affects state variables over time [2]. It is thus important in determining how easily affected the equilibrium is by small changes in parameters [24]. Sensitivity analysis is conducted to determine the parameters or changes in the model structure that have the most impact on model outputs. It is therefore helping in identifying components of the system that should be targeted for possible control measures. In this analysis, we will focus on only one parameter at a time.

$$\text{sensitivity index} = \frac{\partial \mathcal{R}_T}{\partial p_i}.\frac{p_i}{\mathcal{R}_T}$$

where

$\mathcal{R}_T = \dfrac{\delta_T C_T}{\mu + d_T + \gamma}$ and

p_i (where $i = 1, 2, 3, 4, 5$) represents each parameter in $\mathcal{R}_T$, i.e., $p_1 = \delta_T$; $p_2 = C_T$; $p_3 = \mu$; $p_4 = d_T$ and $p_5 = \gamma$.

$$\begin{aligned} \frac{\partial \mathcal{R}_T}{\partial \delta_T}.\frac{\delta_T}{\mathcal{R}_T} &= \frac{C_T}{\mu + d_T + \gamma}.\frac{\delta_T(\mu + d_T + \gamma)}{\delta_T C_T} \\ &= 1; \end{aligned}$$

$$\begin{aligned} \frac{\partial \mathcal{R}_T}{\partial C_T}.\frac{C_T}{\mathcal{R}_T} &= \frac{\delta_T}{\mu + d_T + \gamma}.\frac{C_T(\mu + d_T + \gamma)}{\delta_T C_T} \\ &= 1; \end{aligned}$$

$$\begin{aligned} \frac{\partial \mathcal{R}_T}{\partial \mu}.\frac{\mu}{\mathcal{R}_T} &= -\frac{\delta_T C_T}{(\mu + d_T + \gamma)^2}.\frac{\mu(\mu + d_T + \gamma)}{\delta_T C_T} \\ &= \frac{-\mu}{(\mu + d_T + \gamma)} \\ &= -0.0128; \end{aligned}$$

therefore, $\left|\dfrac{\partial \mathcal{R}_T}{\partial \mu}.\dfrac{\mu}{\mathcal{R}_T}\right| = 0.0128;$

$$\frac{\partial \mathcal{R}_T}{\partial d_T}\cdot\frac{d_T}{\mathcal{R}_T} = -\frac{\delta_T C_T}{(\mu + d_T + \gamma)^2}\cdot\frac{\delta_T(\mu + d_T + \gamma)}{\delta_T C_T}$$

$$= \frac{-\delta_T}{(\mu + d_T + \gamma)}$$

$$= -0.0897,$$

therefore $\left|\frac{\partial \mathcal{R}_T}{\partial d_T}\cdot\frac{d_T}{\mathcal{R}_T}\right| = 0.0897;$

$$\frac{\partial \mathcal{R}_T}{\partial \gamma}\cdot\frac{\gamma}{\mathcal{R}_T} = -\frac{\delta_T C_T}{(\mu + d_T + \gamma)^2}\cdot\frac{\gamma(\mu + d_T + \gamma)}{\delta_T C_T}$$

$$= \frac{-\gamma}{(\mu + d_T + \gamma)}$$

$$= -0.8974,$$

therefore $\left|\frac{\partial \mathcal{R}_T}{\partial \gamma}\cdot\frac{\gamma}{\mathcal{R}_T}\right| = 0.8974.$

Therefore, observing from the calculations, the parameters that can be controlled, affecting the reproduction number by small changes are δ_T and γ. Other parameters, for example μ or d_T their changes in the model structure have less impact on model outputs. C_T which is the contact rate for TB has more impact, however it can not be controlled. Hence, these two parameters δ_T and γ have the highest sensitivity indices in magnitude. Therefore they have biggest impact on the basic reproduction number, and thus a slight change in any of them is expected to considerably change the overall behavior of the system. Hence we will vary them for our sensitivity analysis.

We consider parameter values in Table 5.1 and initial total population to be $N_0 = 500$ divided as follows, $S_0 = 350$, $I_0 = 150$ and $T_{T_0} = 0$ to produce various graphs.

The positive endemic equilibrium point was shown to exist and to be locally asymptotically stable whenever $\mathcal{R}_T > 1$, (see Theorem 5). Substituting the parameter values as in Table 5.1 into the basic reproduction number, we get $\mathcal{R}_T = 8.974 > 1$, establishing that TB persists in the population. In this case, as time evolves, the population approaches a fixed point $(S^*, I^*, T_T^*) = (411, 1473, 1808)$. We see in Figures 5.1 and 5.2 that the curves approach the endemic equilibrium point. Hence, the numerical results are in agreement with the results obtained from qualitative analysis.

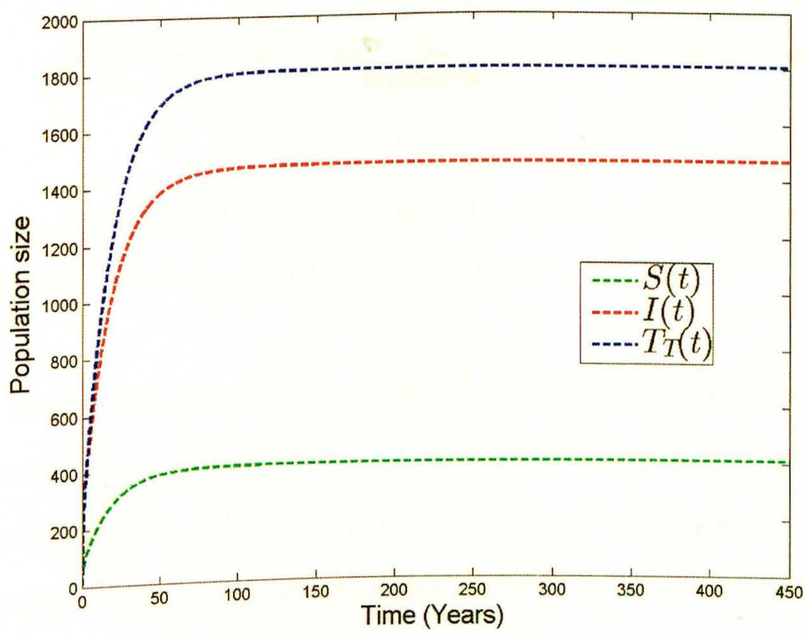

Figure 5.1: Dynamics of population in different classes, corresponding to the parameter values as in Table 5.1.

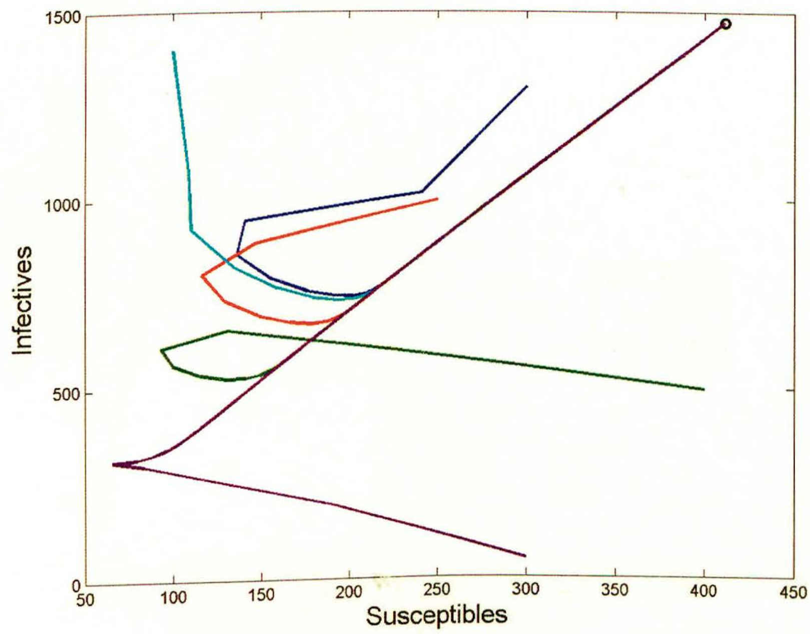

Figure 5.2: A phase portrait for the TB-only model, in a case where the disease persists, the parameter values used are as in Table 5.1.

We have proven that the DFE for the TB-only model is locally and globally asymptotically stable whenever $\mathcal{R}_T < 1$ (see Theorems 5 and 6). γ and δ_T have the highest sensitivity indices in magnitude, therefore the biggest impact on the basic reproduction number, and therefore a slight change in any of them is expected to considerably change the overall behavior of the system. Hence we will vary them for our sensitivity analysis.

If we increase treatment rate for TB, for example $\gamma = 12$, compared to the value $\gamma = 1$ used in a previous graphs (see Figures 5.1 and 5.2), we get $\mathcal{R}_T = 0.826 < 1$. The solutions are approaching the fixed point $\left(\frac{\Lambda}{\mu}, 0, 0\right)$ as given in Theorem 5, which is $(14000, 0, 0)$ as illustrated in Figures 5.3 and 5.4. Hence, the numerical results are in agreement with the results obtained from qualitative results.

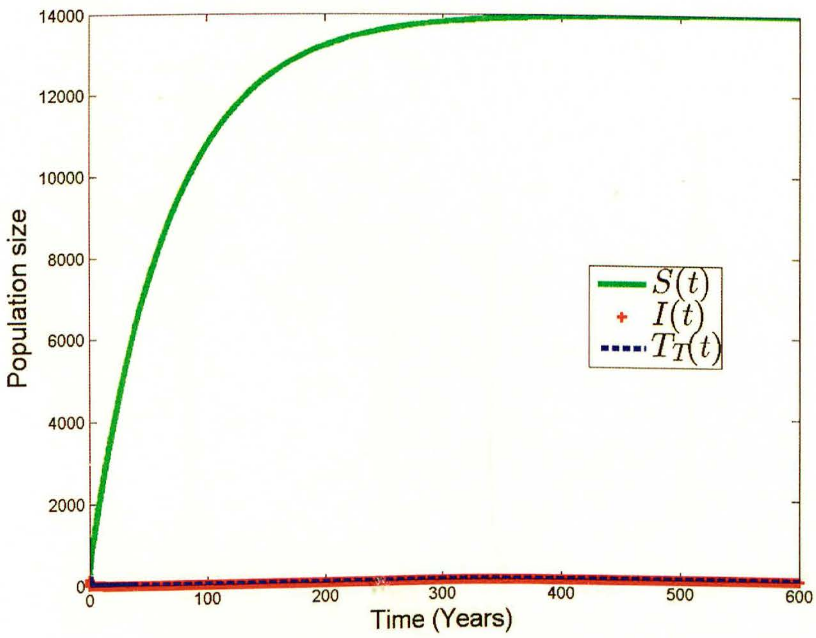

Figure 5.3: Solution trajectory corresponding to $\gamma = 12$, and all the other parameters as in Table 5.1.

Figure 5.3 is the graph of infected TB individuals only (TB-only model) against time. It is observed that the number of infected TB individuals decrease as the TB treatment parameter increases. This means, the TB can be eradicated completely in the population at t = 310 years.

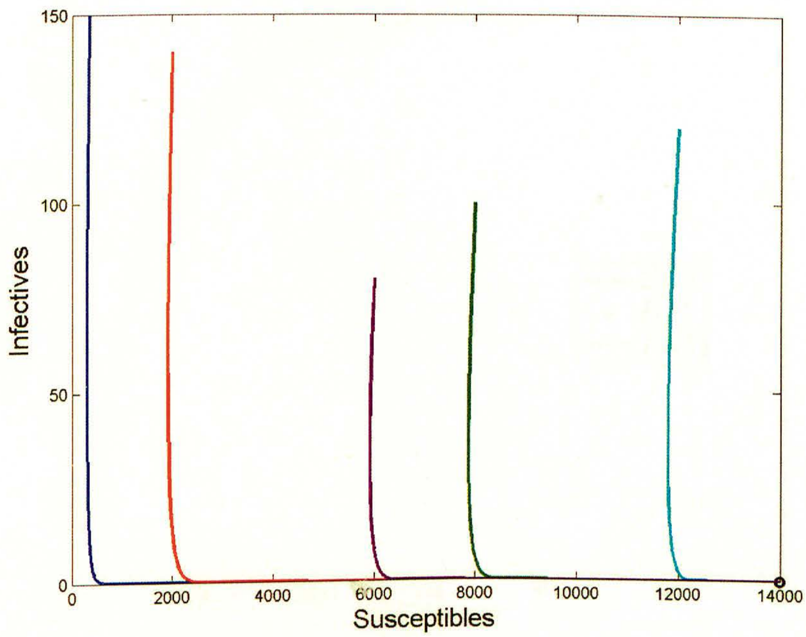

Figure 5.4: A phase portrait of the TB-only model, when the disease dies out (corresponding to $\gamma = 12$, and all the other parameters as in Table 5.1).

We also see in Figure 5.5 that if the probability of transmission of TB infection from an active to susceptible rate is decreased, for example $\delta_T = 0.01$, compared to the value $\delta_T = 0.2$ used in a previous graph (see Figure 5.1) then the HIV, AIDS and Treated populations decrease, reducing the basic reproduction number to $\mathcal{R}_H = 0.4487 < 1$. The solutions are approaching a fixed point $(14000, 0, 0, 0)$ as presented in Figures 5.5 and 5.6.

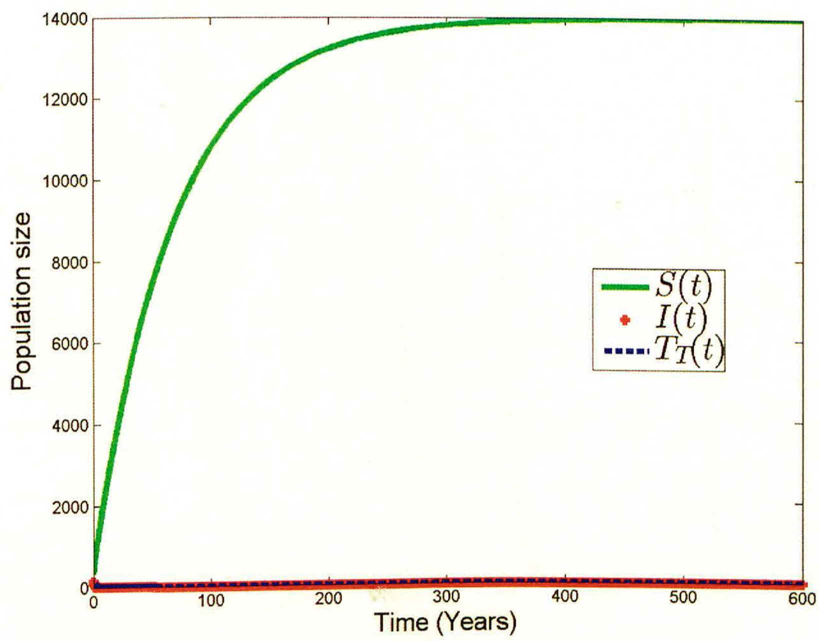

Figure 5.5: Solution trajectory corresponding to $\delta_T = 0.01$, and all the other parameters as in Table 5.1

Figure 5.5 is the graph of infected TB individuals only (TB-only model) against time. It is observed that the number of infected TB individuals decrease as the probability of transmission of TB infections parameter decreases. This means, the TB can be eradicated completely in the population at t = 350 years.

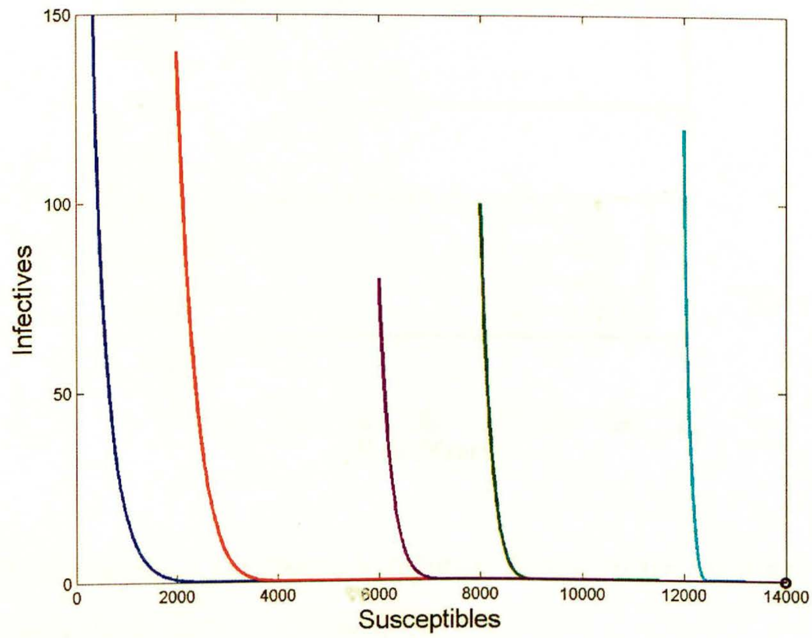

Figure 5.6: A phase portrait of the TB-only model, corresponding to $\delta = 0.01$, and all the other parameters as in Table 5.1.

5.2 Simulation for HIV-only model

We consider parameter values in Table 5.1, to produce various graphs and the initial total population as $N_0 = 500$ divided as follows $S_0 = 350$, $J_{1_0} = 150$, $A_0 = 0$ and $T_{H_0} = 0$.

The positive endemic equilibrium point was shown to exist and to be locally asymptotically stable whenever $\mathcal{R}_H > 1$, (see Theorem 7). Substituting the parameter values as in Table 5.1 into the basic reproduction number, we get $\mathcal{R}_H = 8.8406 > 1$, establishing that HIV persists in the population (see Figure 5.7 below). In this case, as time evolves, the population approaches a fixed point $(S^*, J_1^*, A^*, T_H^*) = (742, 2093, 731, 2999)$. We see in Figures 5.7, 5.8 and 5.9 that from the curves, the variables in the model approach the endemic equilibrium point. Hence, the numerical results are in agreement with findings from qualitative analysis.

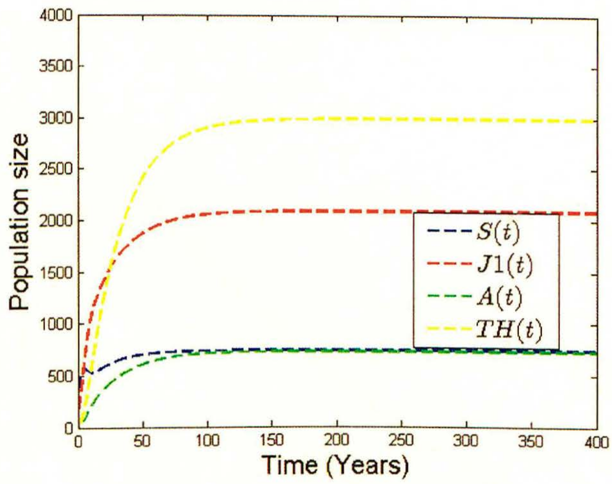

Figure 5.7: Dynamics of population in different classes, corresponding to the parameter values as in Table 5.1.

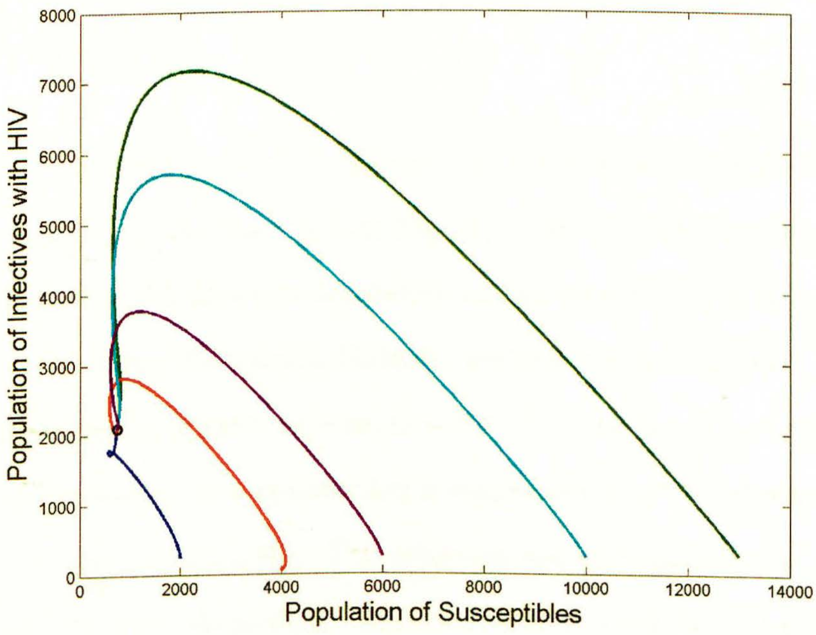

Figure 5.8: A phase portrait of the HIV-only model, corresponding to the parameter values as in Table 5.1.

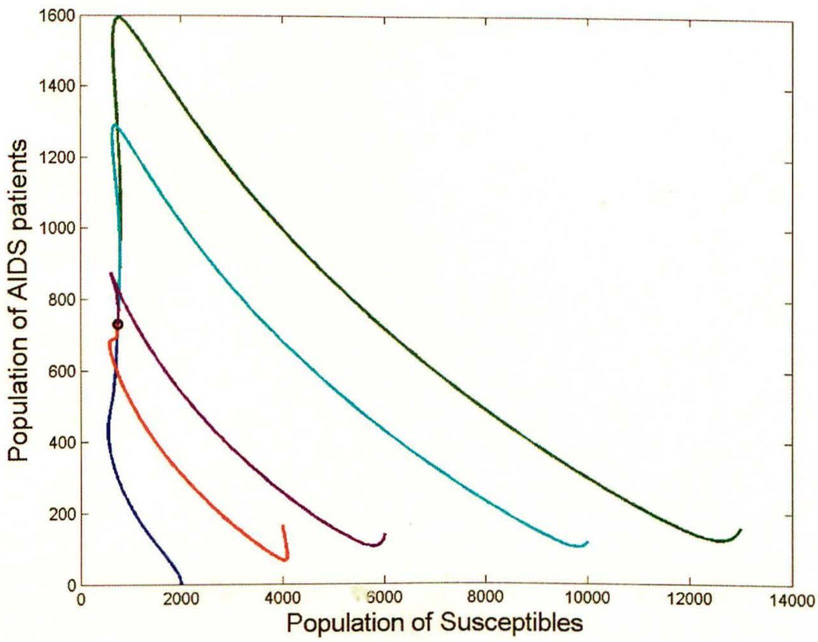

Figure 5.9: A phase portrait of the HIV-only model, corresponding to the parameter values as in Table 5.1.

We have proven that the DFE of HIV-only model is locally and globally asymptotically stable whenever $\mathcal{R}_H < 1$ (see Theorem 7 and 8). The number of infected individuals in the population is dependent on the values of β_1 and δ_H, hence we will use various values for each of them for our sensitivity analysis.

If we increase the treatment rate to $\beta_1 = 0.7$, then we get $\mathcal{R}_H = 0.8701$ which implies that the disease-free equilibrium is stable and hence the disease is expected to die out (see Figure 5.10). The solutions are approaching the stable fixed point $\left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$ as indicated in Theorem 7, which is $(14000, 0, 0, 0)$ as presented in Figures 5.10, 5.11 and 5.12. Figures 5.11 and 5.12 indicate the stability of the disease-free equilibrium. Hence, the numerical results are in agreement with findings from qualitative analysis.

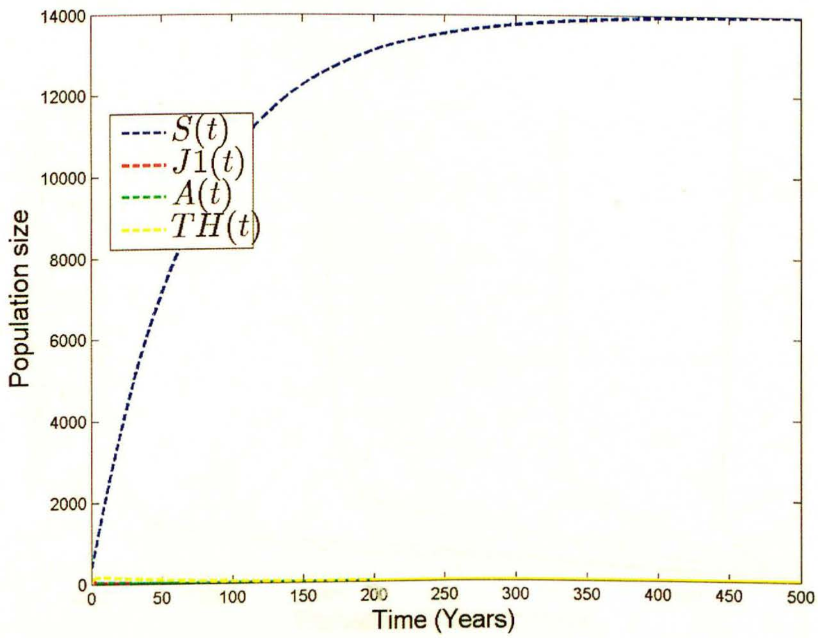

Figure 5.10: Solution trajectory for $\beta_1 = 0.7$, and all the other parameters as in Table 5.1

It can be seen that when β_1 increases, the susceptible population increases. While the susceptible population increases, the treated, HIV and AIDS populations decrease to zero, reaching its equilibrium point. This can be explained by ARV treatment and its effect in prolonging the life span.

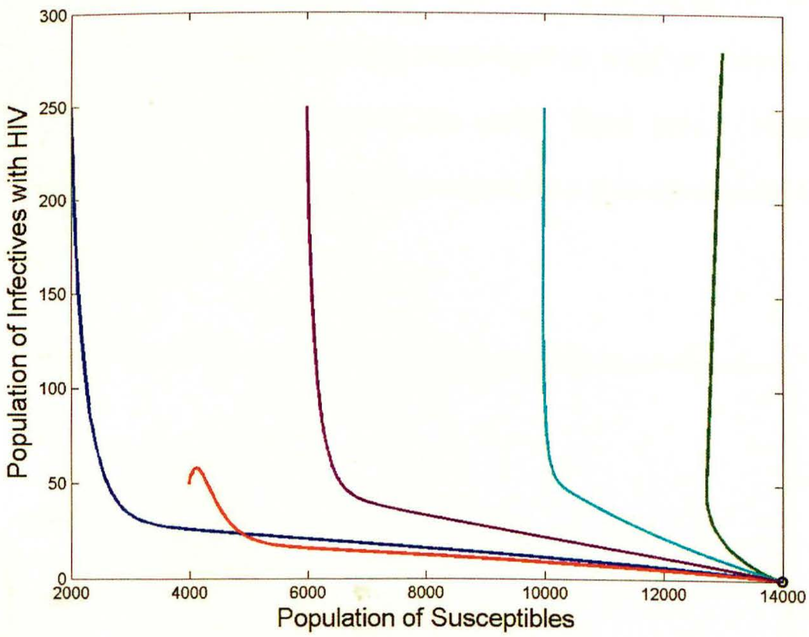

Figure 5.11: A phase portrait of the HIV-only model, corresponding to $\beta_1 = 0.7$, and all the other parameters as in Table 5.1.

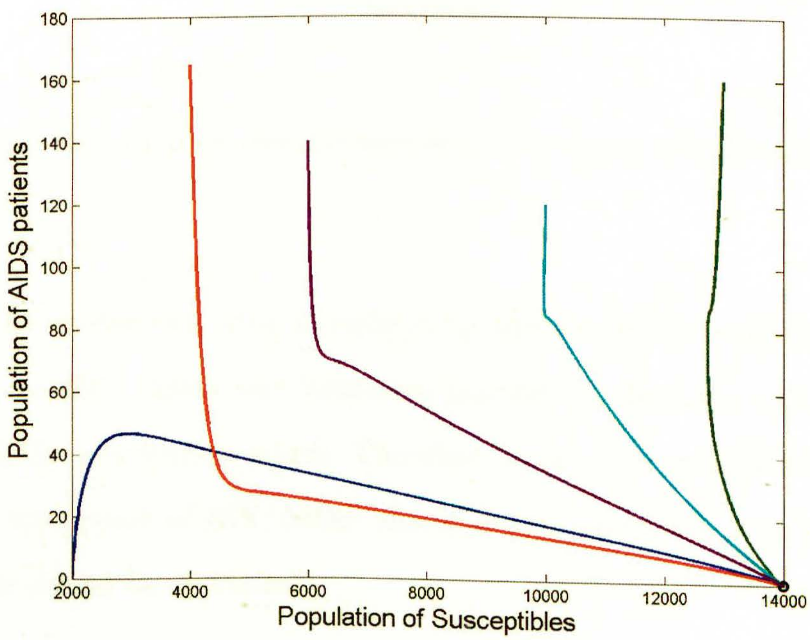

Figure 5.12: A phase portrait of the HIV-only model, corresponding to $\beta_1 = 0.7$, and all the other parameters as in Table 5.1.

If the probability of transmission of HIV infection from an active to susceptible goes down to $\delta_H = 0.01$, then the basic reproduction number decreases to $\mathcal{R}_H = 0.442$. The solutions are approaching the stable fixed point $(14000, 0, 0, 0)$ as present in Figure 5.13. Hence, the numerical results are in agreement with findings from qualitative analysis.

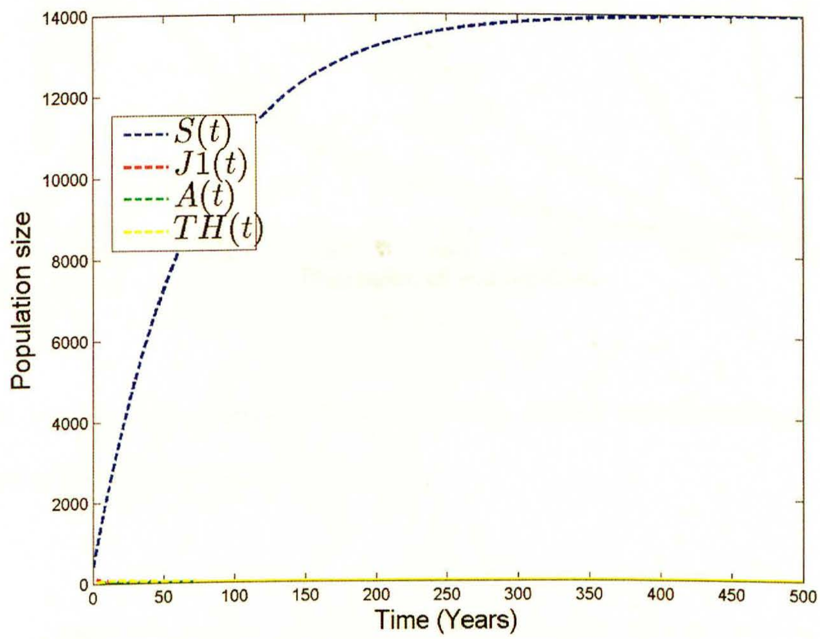

Figure 5.13: Solution trajectory corresponding to $\delta_H = 0.01$, and all other parameters as in Table 5.1.

It can be verified that with decrease in δ_H, the susceptible population increases, while the HIV, AIDS and treatment populations decrease with time until they reach the equilibrium values. Therefore, it can be concluded that in order to reduce the spread of HIV/AIDS, unsafe sexual interaction with an infective individuals should be minimized.

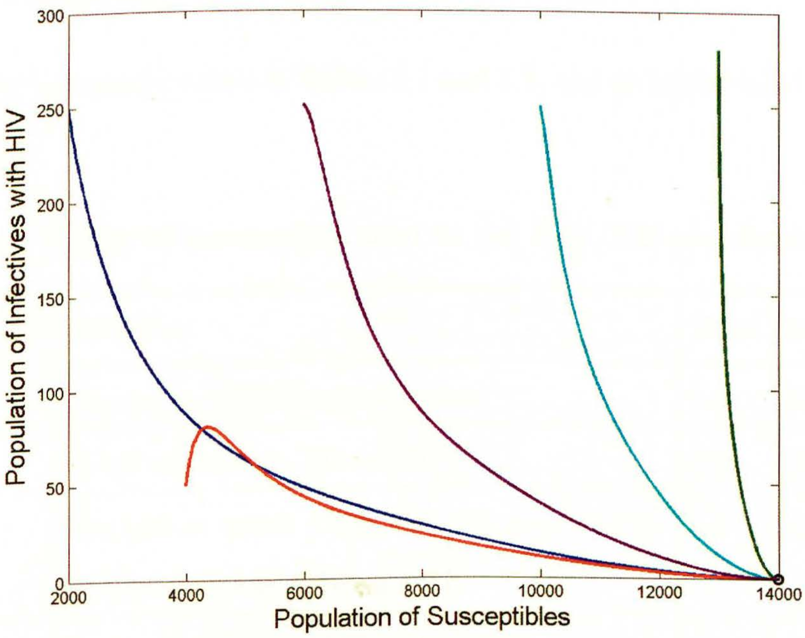

Figure 5.14: A phase portrait of the HIV-only model, corresponding to $\delta_H = 0.01$, and all other parameters as in Table 5.1.

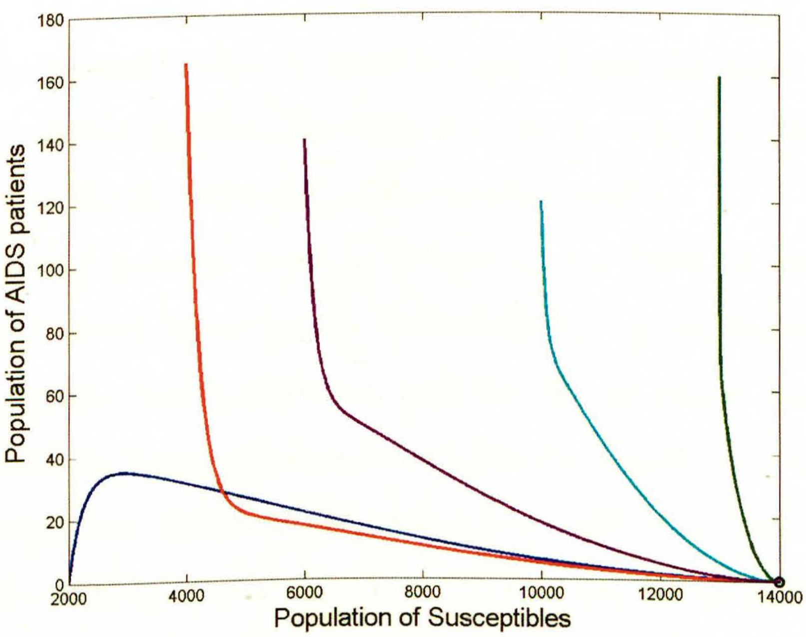

Figure 5.15: A phase portrait of the HIV-only model, corresponding to $\delta_H = 0.01$, and all other parameters as in Table 5.1.

5.3 Simulation for HIV/TB model

We consider parameter values in Tables 5.1 and 5.2, and an initial total population of $N_0 = 500$.

Table 5.2: Values of parameters used in the HIV/TB co-infection model

Parameter	Definition	Value	Source
α_2	Per-capita AIDS progression rate	0.2	[27]
d_{HT}	Death rate due to TB and HIV	0.24	[3]
κ_2	The rate at which AIDS with TB recovered individuals delelop AIDS and TB	0.3	Assumed
d_{AT}	Death rate due to AIDS and TB	0.5	Assumed
ν_2	The rate at which AIDS with TB recovered get treatment	0.1	Assumed
β_2	The rate at which patients with both HIV and TB get treatment	0.3	[3]

We consider parameter values in Tables 5.1 and 5.2, with the initial population of $N_0 = 500$ divided as follows: $S_0 = 150$, $I_0 = 100$, $T_{T_0} = 0$, $J_{1_0} = 100$, $J_{2_0} = 50$, $T_{H_0} = 0$, $A_0 = 50$, $A_{c_0} = 50$ and $T_{c_0} = 0$ to produce graphs.

Substituting the parameter values as in Table 5.1 and Table 5.2 into the basic reproduction number $\mathcal{R}_0$, we get $\mathcal{R}_H = 4.420$ and $\mathcal{R}_T = 8.974$, therefore

$\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 8.974 > 1$, both $\mathcal{R}_H$, $\mathcal{R}_T$ are greater than one, this establishes that the two diseases are endemic (see Figure 5.16), i.e., the solutions are approaching the fixed point E^*_{TH} where $S^* = 199$, $I^* = 1096$, $T^*_T = 359$, $J^*_1 = 19$, $J^*_2 = 225$, $T^*_H = 22$,$A^* = 1$, $A^*_c = 217$, $T^*_c = 284$. We see in Figures 5.16, 5.17, 5.18, 5.19, 5.20 and 5.21 that from the curve, the solution approaches the endemic equilibrium point. Hence, the numerical results are in agreement with findings from qualitative analysis.

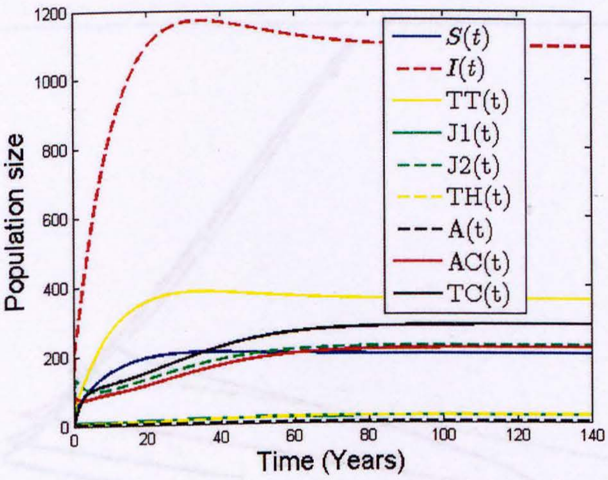

Figure 5.16: Dynamics of population in different classes, corresponding to the parameter values as in Table 5.1 and 5.2.

It can be observed that for any starting initial values, the solutions curves tend to the endemic equilibrium point. Hence, it can be concluded that the system (4.12) is globally stable about its endemic point for the parameters given in Tables 5.1 and 5.2.

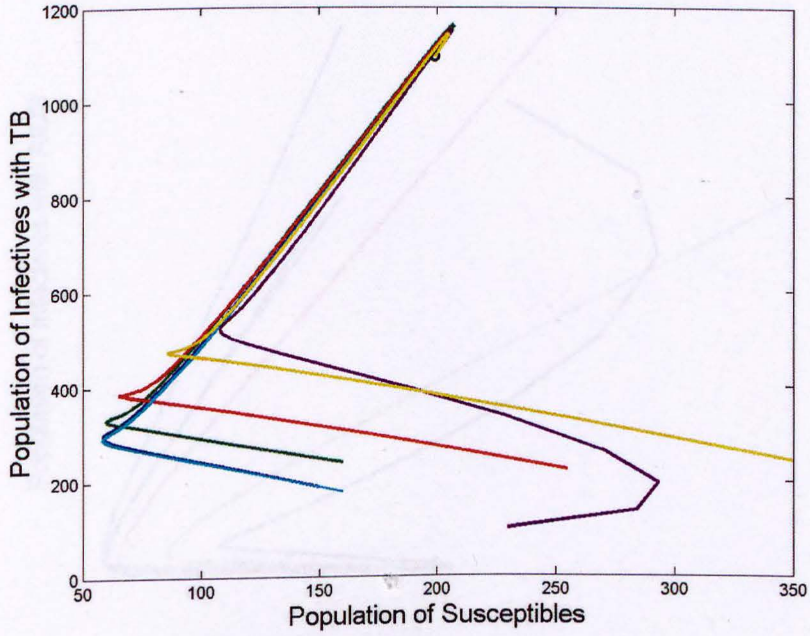

Figure 5.17: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB, corresponding to the parameter values as in Tables 5.1 and 5.2.

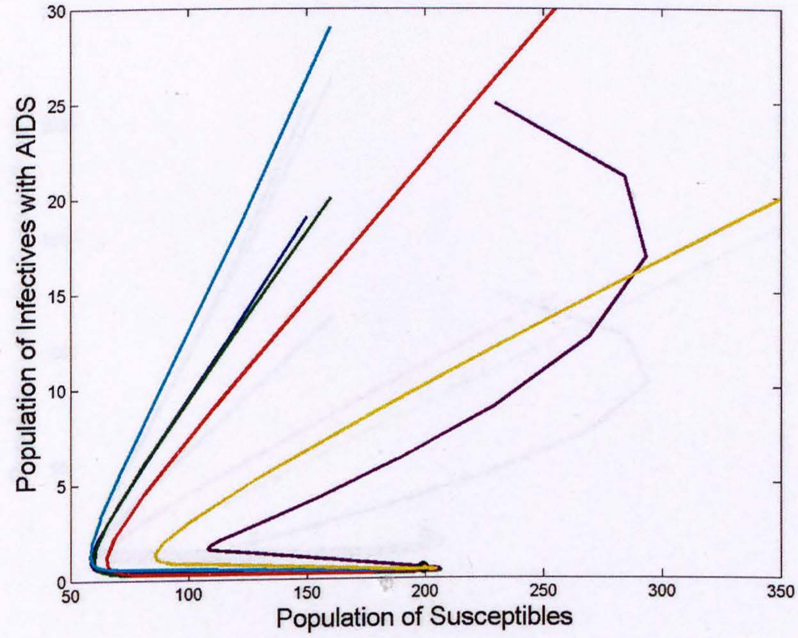

Figure 5.18: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with AIDS, corresponding to the parameter values as in Tables 5.1 and 5.2.

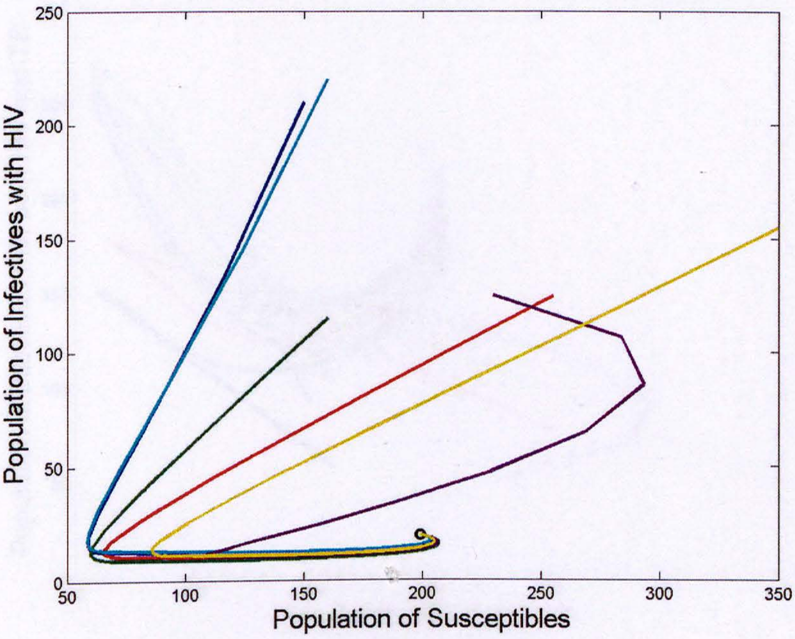

Figure 5.19: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with HIV, corresponding to the parameter values as in Tables 5.1 and 5.2.

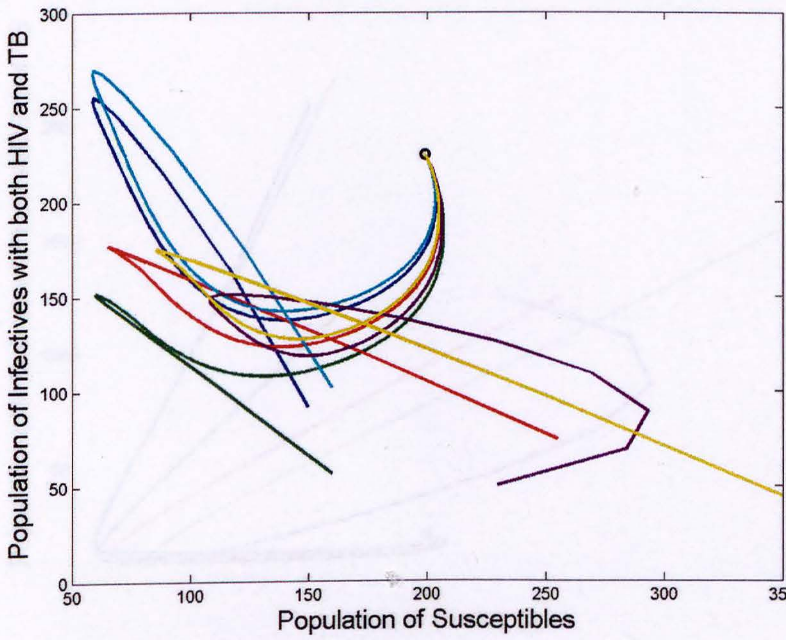

Figure 5.20: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and HIV, corresponding to the parameter values as in Tables 5.1 and 5.2.

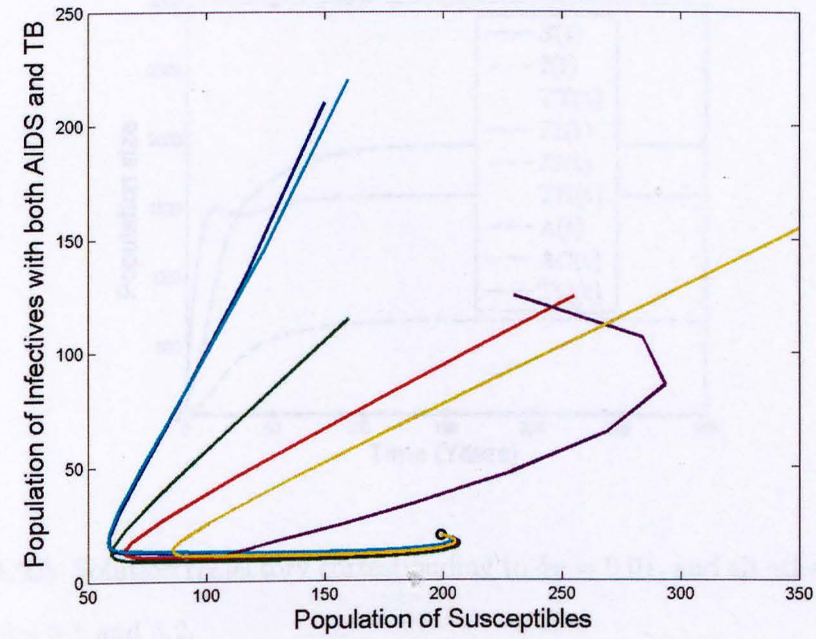

Figure 5.21: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and AIDS, corresponding to the parameter values as in Tables 5.1 and 5.2.

Now, if the probability of transmission of TB infection from an infective to susceptible is decreased, i.e., for example $\delta_T = 0.01$, we get $\mathcal{R}_H = 4.420$ and $\mathcal{R}_T = 0.449$, therefore $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 4.420 > 1$, which implies that HIV is expected to persist in the population while TB is expected to die out. The solutions are approaching a fixed point E^*_{TH}, where $S^* = 1529$, $I^* = 0$, $T^*_T = 0$, $J^*_1 = 1958$, $J^*_2 = 0$, $T^*_H = 2800$, $A^* = 683$, $A^*_c = 0$, $T^*_c = 0$, which coincides with E^*_H as illustrated in Figures 5.22, 5.23, 5.24, 5.25, 5.26 and 5.27. Hence, the numerical results are in agreement with findings from qualitative analysis.

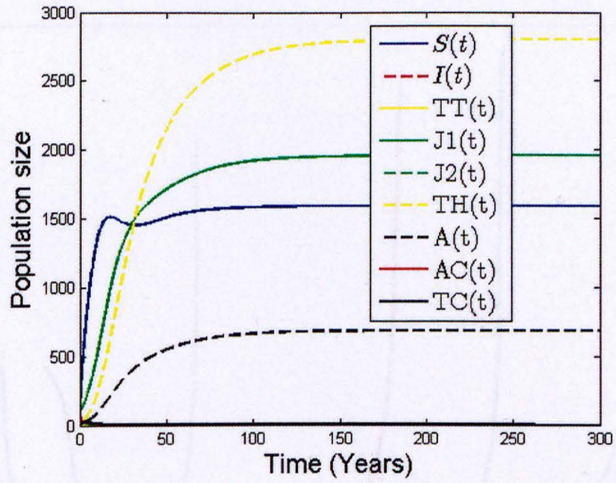

Figure 5.22: Solution trajectory corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

Figure 5.22 shows the effect of probability transmission of TB infection δ_T in HIV/TB co-infected individuals against time, with $\mathcal{R}_H = 4.420$ and $\mathcal{R}_T = 0.449$, and thus with $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 4.420$. It is observed that the number individuals infected with TB only, infected with TB and HIV, as well as infected with TB and AIDS decrease to zero as probability of transmission decrease. However, individuals infected with HIV and AIDS remains in the population.

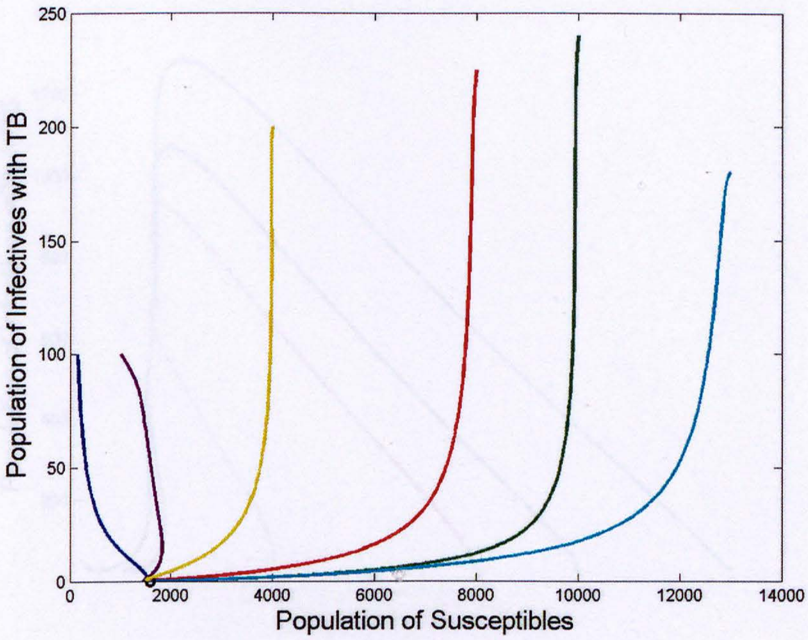

Figure 5.23: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

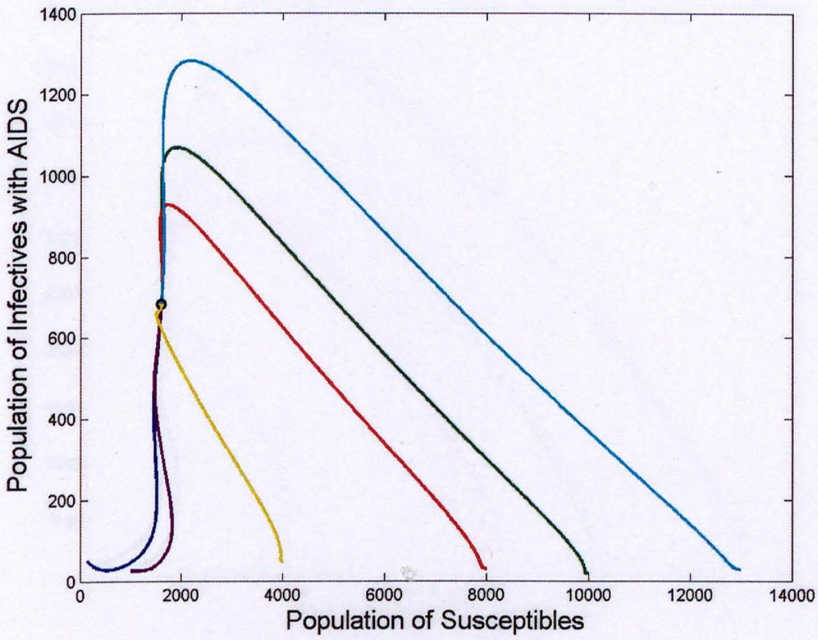

Figure 5.24: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with AIDS, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

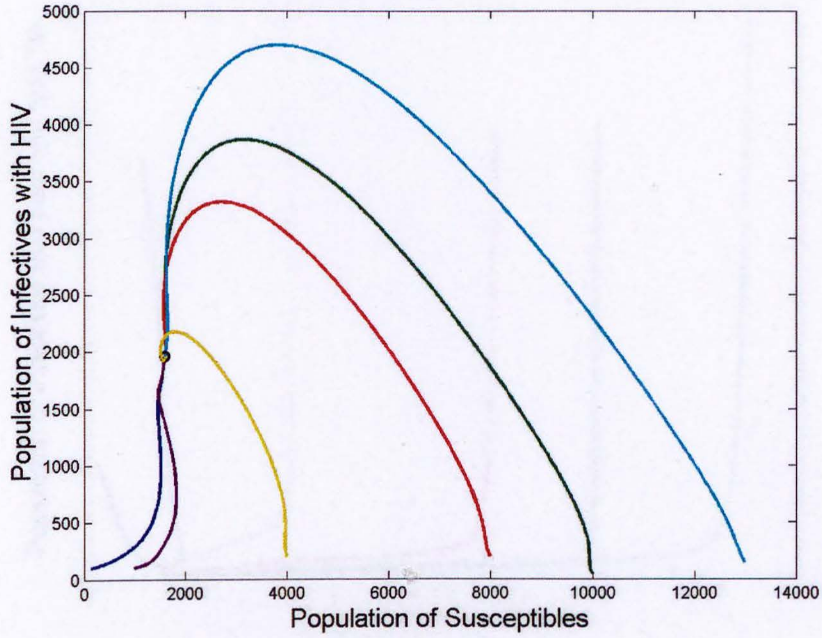

Figure 5.25: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with HIV, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

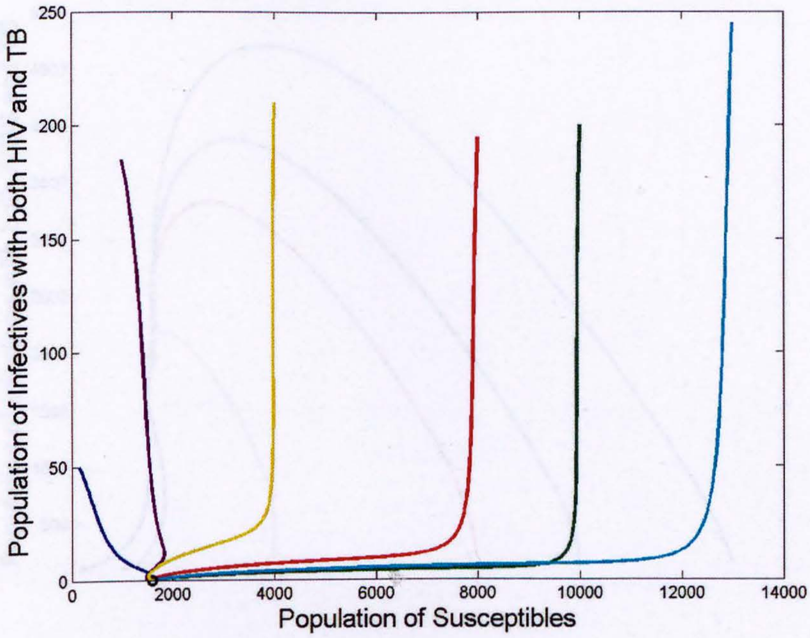

Figure 5.26: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and HIV, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

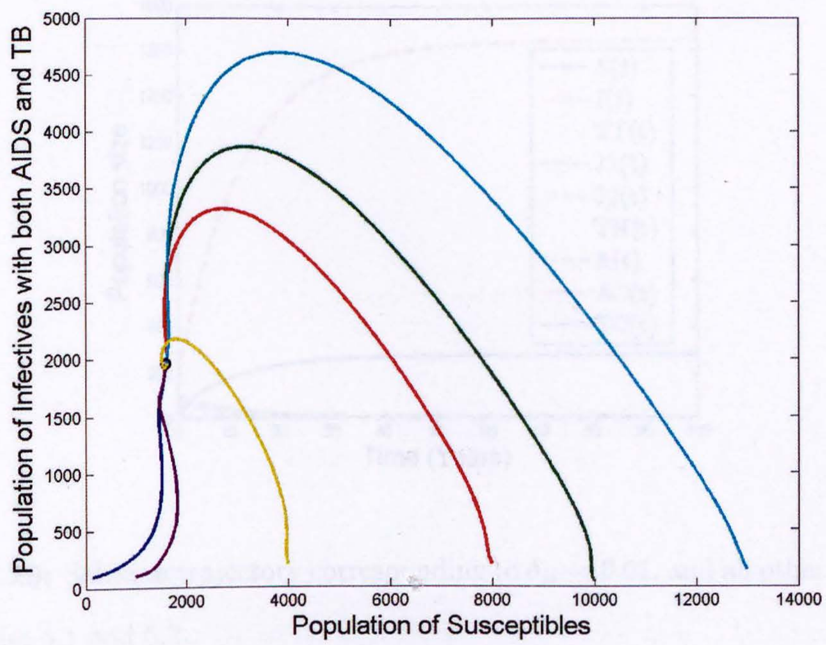

Figure 5.27: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and AIDS, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

If the probability of transmission of HIV infection from an infective to susceptible is decreased, i.e., for example $\delta_H = 0.01$, we get $\mathcal{R}_H = 0.442$ and $\mathcal{R}_T = 8.974$, therefore $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 8.974 > 1$, which implies that TB is expected to persist in the population while HIV is expected to die out. The solutions are approaching the stable fixed point E^*_{TH} where $S^* = 275$, $I^* = 1647$, $T^*_T = 547$, $J^*_1 = 0$, $J^*_2 = 0$, $T^*_H = 0$, $A^* = 0$, $A^*_c = 0$, $T^*_c = 0$ as present Figures 5.28, 5.29, 5.30, 5.31, 5.32 and 5.33. Hence, the numerical results are in agreement with findings from qualitative analysis.

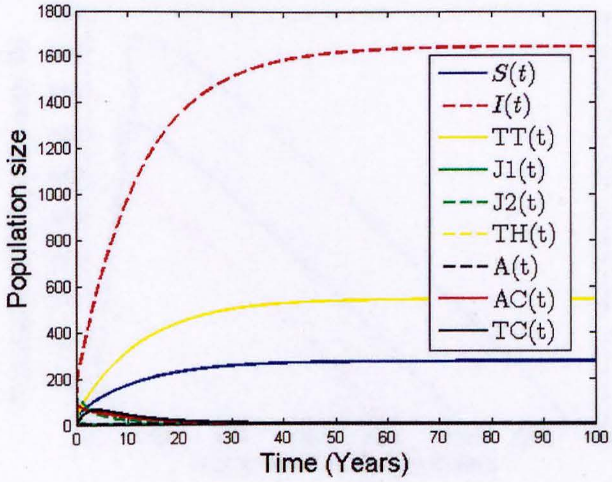

Figure 5.28: Solution trajectory corresponding to $\delta_H = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

Figure 5.28 shows the effect of probability of transmission of HIV infection δ_H in HIV/TB co-infected individuals against time, with $\mathcal{R}_H = 0.442$ and $\mathcal{R}_T = 8.974$, and thus $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 8.974$. It is observed that the number individuals infected with HIV only, AIDS only, infected with HIV and TB, as well as infected with TB and AIDS decrease to zero as probability of transmission of HIV decrease. However, individuals infected with TB remains in the population.

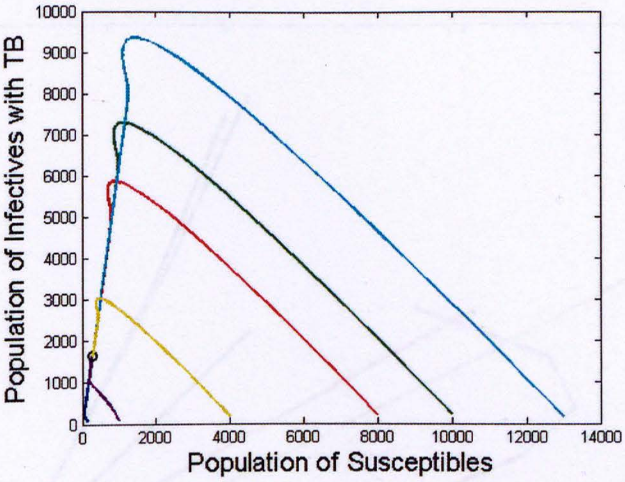

Figure 5.29: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB, corresponding to $\delta_H = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

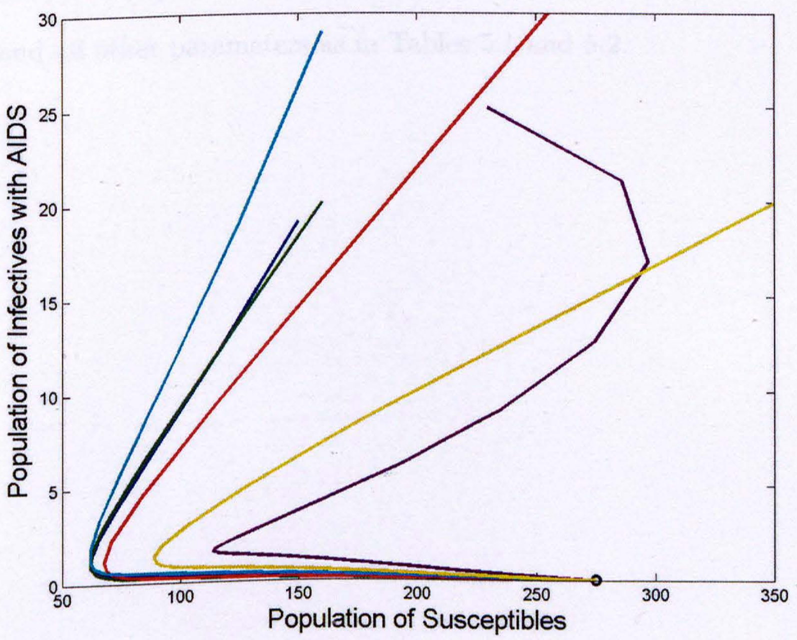

Figure 5.30: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with AIDS, corresponding to $\delta_H = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

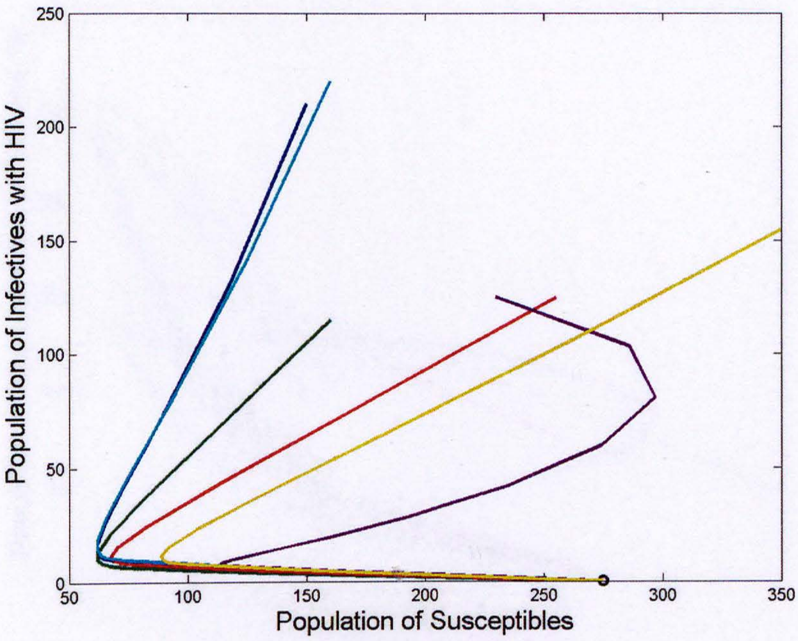

Figure 5.31: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with HIV, corresponding to $\delta_H = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

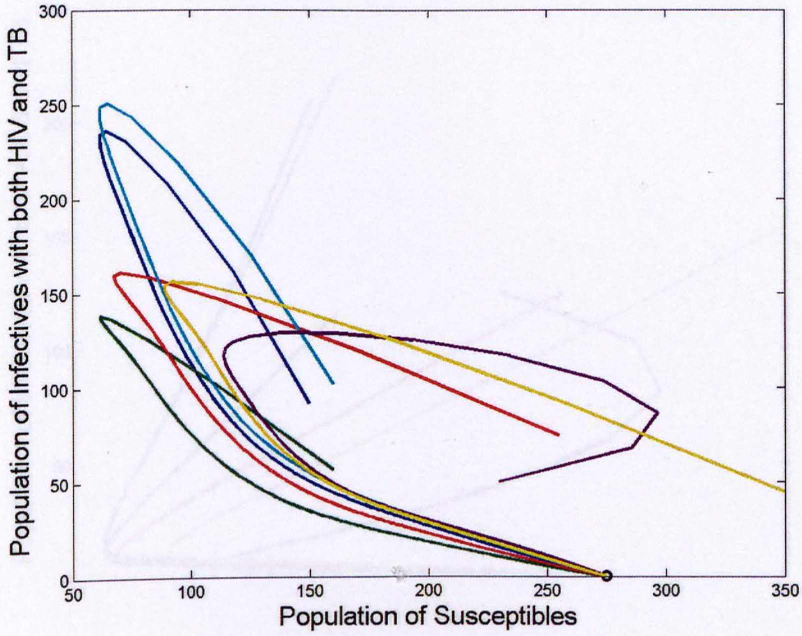

Figure 5.32: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and HIV, corresponding to $\delta_H = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

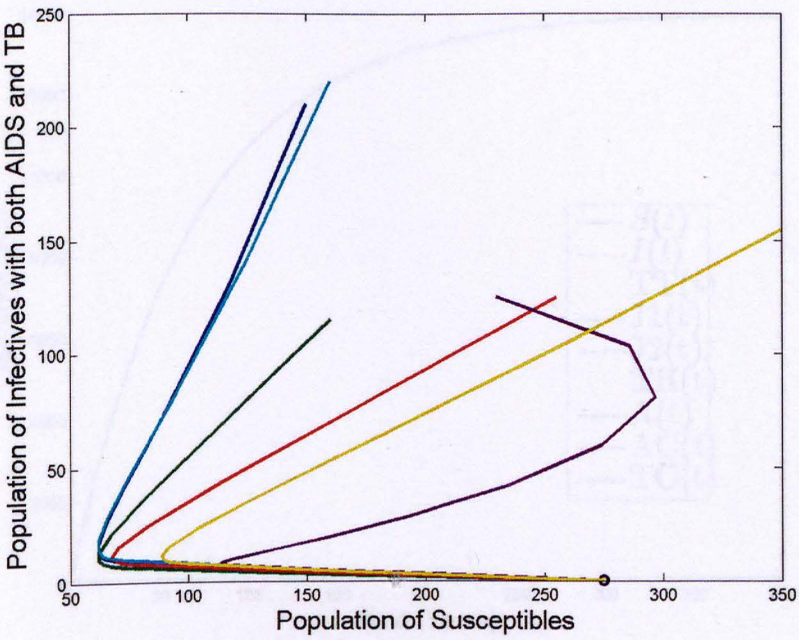

Figure 5.33: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and AIDS, corresponding to $\delta_T = 0.01$, and all other parameters as in Tables 5.1 and 5.2.

If we decrease the probability of transmission of both TB and HIV infection, i.e., for example $\delta_H = 0.01$ and $\delta_T = 0.01$, we get $\mathcal{R}_H = 0.442$ and $\mathcal{R}_T = 0.449$; therefore $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 0.449 < 1$. The solutions are approaching the stable fixed point E^*_{TH}, where $(S^*, I^*, T^*_T, J^*_1, J^*_2, T^*_H, A^*, A^*_c, T^*_c) = (14000, 0, 0, 0, 0, 0, 0, 0, 0)$ as presented in the following Figures 5.34, 5.35, 5.36, 5.37, 5.38 and 5.39, which means the DFE is stable. Hence, the numerical results are in agreement with findings from qualitative analysis.

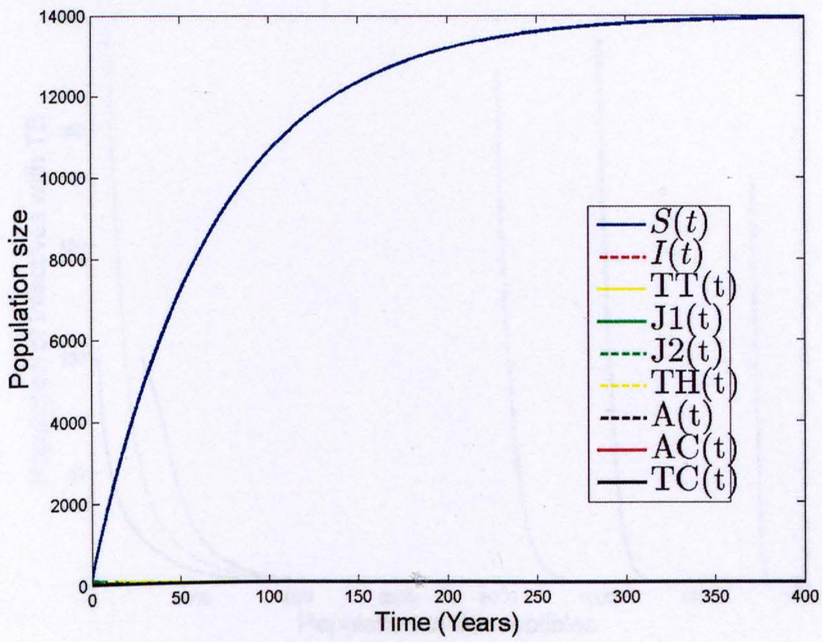

Figure 5.34: Solution trajectory corresponding to $\delta_H = 0.01$ and $\delta_T = 0.01$, and all the other parameter as in Tables 5.1 and 5.2.

Figure 5.34 shows the effects of probability of transmission of HIV and TB infection $\delta_H = 0.01$ and $\delta_T = 0.01$ of HIV/TB co-infected individuals against time. It is observed that the infected number of TB, HIV/AIDS and HIV/TB co-infected individuals decreases as the TB and HIV probability of transmission parameters δ_T and δ_H respectively decreases and brought down the number of HIV/TB infected individuals to zero. This means the HIV/TB co-infection can be eradicated completely in the population.

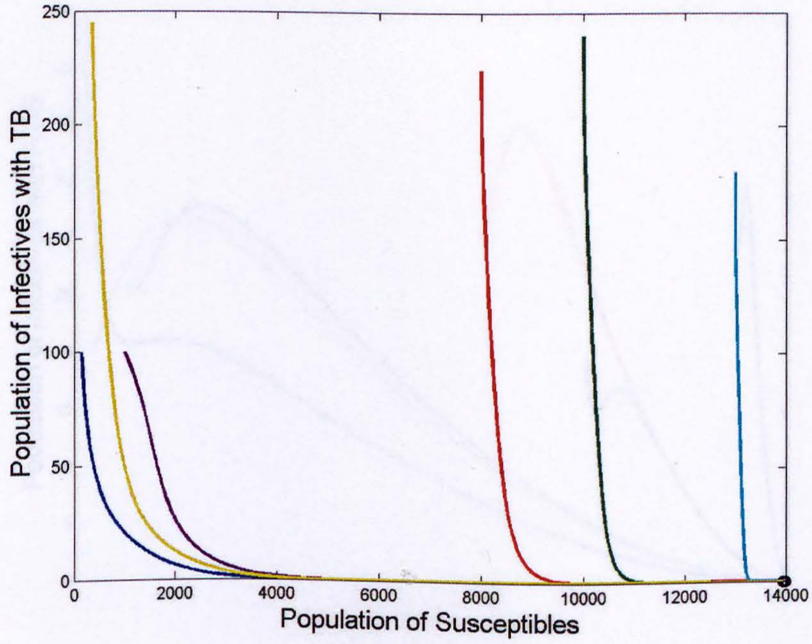

Figure 5.35: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB, corresponding to $\delta_T = 0.01$, $\delta_H = 0.01$ and all other parameters as in Tables 5.1 and 5.2.

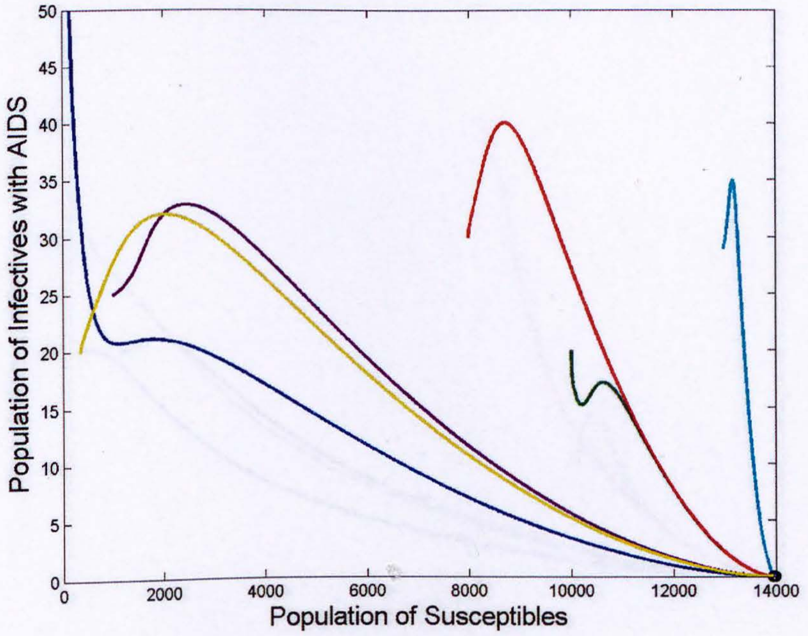

Figure 5.36: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with AIDS, corresponding to $\delta_T = 0.01$, $\delta_H = 0.01$ and all other parameters as in Tables 5.1 and 5.2.

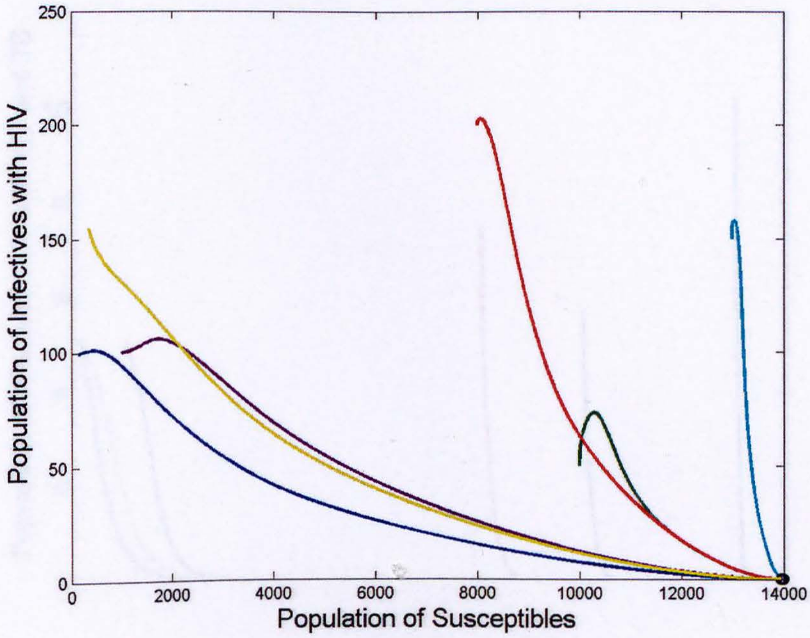

Figure 5.37: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with HIV, corresponding to $\delta_T = 0.01$, $\delta_H = 0.01$ and all other parameters as in Tables 5.1 and 5.2.

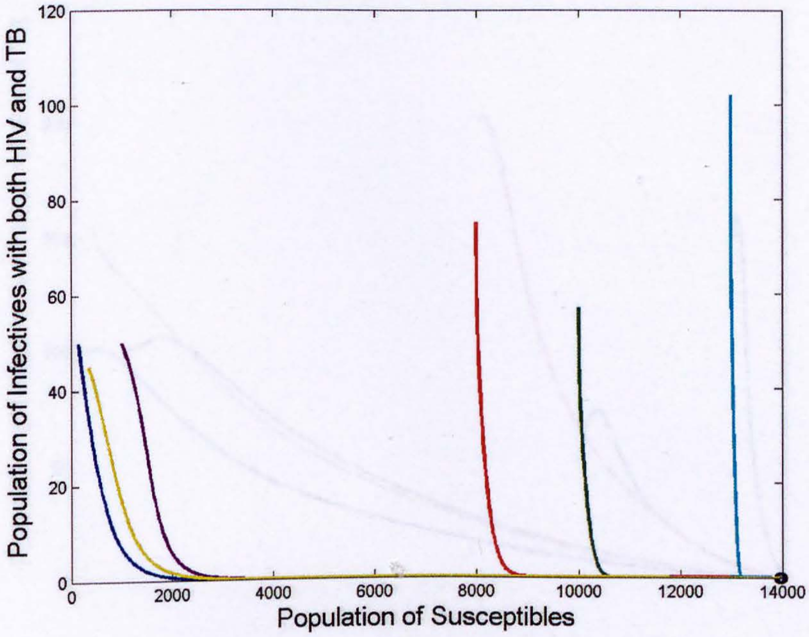

Figure 5.38: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and HIV, corresponding to $\delta_T = 0.01$, $\delta_H = 0.01$ and all other parameters as in Tables 5.1 and 5.2.

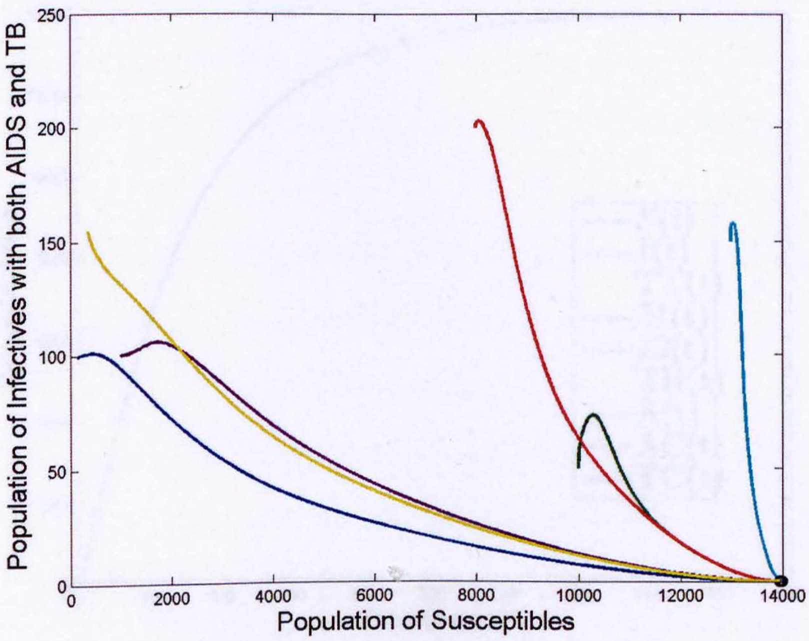

Figure 5.39: A phase portrait illustrating the behavior of solution towards the endemic equilibrium of population of Susceptible vs Infected with TB and AIDS, corresponding to $\delta_T = 0.01$, $\delta_H = 0.01$ and all the other parameters as in Tables 5.1 and 5.2.

If we increase the treatment rate for both TB and HIV i.e., for example $\gamma = 12$ and $\beta = 0.7$ we get $\mathcal{R}_H = 0.870$ and $\mathcal{R}_T = 0.825$, therefore $\mathcal{R}_0 = \max\{\mathcal{R}_H, \mathcal{R}_T\} = 0.870 < 1$, and the solutions are approaching the stable fixed point which is $(S^*, I^*, T_T^*, J_1^*, J_2^*, T_H^*, A^*, A_c^*, T_c^*) = (14000, 0, 0, 0, 0, 0, 0, 0, 0)$ as presented in Figure 5.40. Hence, the numerical results are in agreement with findings from qualitative analysis.

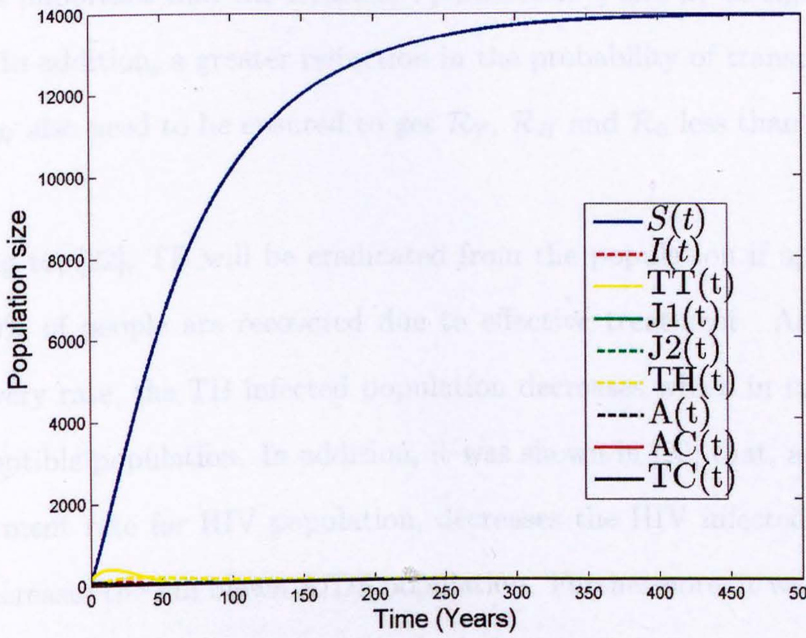

Figure 5.40: Solution trajectory corresponding to $\gamma = 12$, $\beta = 0.7$, and all the other parameters as in Tables 5.1 and 5.2.

Figure 5.40 shows the effect of treatment for HIV/TB co-infected individuals against time. It is observed that the number of TB, HIV/AIDS and HIV/TB co-infected individuals decreases as the TB and HIV treatment parameters γ and β respectively increases and brought down the number of HIV/TB infected individuals to zero at high HIV and TB treatment rates. This means the HIV/TB co-infection can be eradicated completely in the population.

5.4 Disscussion and concluding remarks

In this section, we provide discussion on the three models, i.e., TB-only model, HIV-only model and HIV/AIDS and TB co-infection model. From simulations, we noticed that an increase of treatment rates for all the models, leads to the basic reproduction number less than unity (see Figures 5.3, 5.10 and 5.40). This shows that, TB and HIV/AIDS can possibly be reduced through proper treatment and reduce the rate of progression of HIV infected individuals to AIDS. It is therefore of utmost important that the treatment parameters γ and β_1 be significantly increased. In addition, a greater reduction in the probability of transmission rates δ_T and δ_H also need to be ensured to get $\mathcal{R}_T$, $\mathcal{R}_H$ and $\mathcal{R}_0$ less than 1.

According to, [22], TB will be eradicated from the population if approximately above 90% of people are recovered due to effective treatment. An increase in the recovery rate, the TB infected population decreases which in turn increases the susceptible population. In addition, it was shown in [22] that, an increase in the treatment rate for HIV population, decreases the HIV infected population, which decreases the full blown AIDS population. Furthermore, it was established in [22] that, the number of HIV individuals in population increases rapidly due to presence of another disease that is TB. The author further concluded that, if TB in the population is effectively treated, the spread of HIV can be slowed down.

In addition, it was established in [11] that, the rates of transmission of both HIV and TB should be decreased, as an increase causes a rise in the number of infectives at the equilibrium level. Furthermore, it was shown in [11] that, when both the reproduction numbers $\mathcal{R}_T$ and $\mathcal{R}_H$ are greater than one, then there is a possibility of stability of co-infection equilibrium. The author ([11]) observed that, whenever the co-infection equilibrium exists, it is always locally asymptotically stable and in this case the other equilibrium become unstable. That means for $\mathcal{R}_T > 1$, $\mathcal{R}_H > 1$, both the diseases will exist.

Chapter 6

Conclusion

In this mini-thesis, we developed a new mathematical model for the dynamics of HIV/TB co-infection in a population that incorporate treatment and vertical transmission. Both qualitative and quantitative analysis of the model was done. The disease free equilibrium points for the models, were obtained and their stabilities were discussed. The endemic equilibrium points of TB and HIV only model were obtained from the qualitative analysis. However, the endemic equilibrium point of the co-infection model could not be obtained analytically. Local and global stability of the disease-free equilibrium of each model were discussed. The basic reproduction numbers of each model were obtained and discussed. It is noted that when $\mathcal{R}_T < 1$ and $\mathcal{R}_H < 1$, both diseases die out. However, if $\mathcal{R}_T > 1$ and $\mathcal{R}_H > 1$, then the co-infection is maintained in the population.

Numerical results revealed that, an increase in the treatment rate of all models, leads to the decrease of the population of infectives. In addition, decreasing the probability of transmission rate of both HIV and TB infection from an active to susceptible, leads to decrease in HIV/AIDS and TB infectives population. Thus for all models, TB-only model, HIV-only model and co-infection model, we suggest treatment rates to be increased, as well as decrease of probability of transmission, by involving family members and community trained health workers to ensure that all TB and HIV/AIDS patients do take and complete their medication courses especially with TB patients. This way, it helps reduce TB spreads in our communities. Early detection of HIV and TB cases and provision of early treatments can reduce the rate of infection, reduce the rate of progression of HIV infected individuals to AIDS and lower co-infection.

We recommend strengthening the work of community health workers, to educate people in their communities the importance of taking their medication, that is, to ensure that TB and HIV patients do religiously take their medications to prevent resistance especially of TB, which is costly and take even takes even longer to treat. In this way, we will not only prevent, but also reduce the spread of HIV and TB in our communities. Therefore, a strong coordination between the national of TB and HIV control programs is required for the effective management of HIV/TB patients.

For future work, the research will address a more detailed analysis by exploring the stability analysis of the endemic equilibrium point and the positivity of the endemic equilibrium point for HIV-only model, and HIV/TB co-infection model, as well as analyzing more sophisticated models such as models involving the impact of the lack of immunity after HIV treatment.

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