Mathematical Epidemiology of HIV/AIDS and Tuberculosis Co-infection

by

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Abstract

The project deals with the analysis of a general dynamical model for the spread of HIV/AIDS and tuberculosis Co-infection. We capture in the model the dynamics of HIV/AIDS infected individuals and investigate their impacts in the progression of tuberculosis with and without TB treatment. It is shown that TB-only model and HIV-only model have locally asymptotically stable disease-free equilibrium when the basic reproduction number is less than unity and a unique endemic equilibrium exists when the basic reproduction number is greater than unity. We analyze the full HIV/AIDS-TB coinfection model and incorporate treatment strategy for the exposed and active forms of TB. The stability of equilibria is derived through the use of Van den Driessche method of generational matrix and Routh Harwitz stability criterion. Numerical simulations are provided to justify the analytical results and to investigate the effect of change of certain parameters on the co-infection. Sensitivity analysis shows that reducing the most sensitive parameters β_1 and β_2 could help to lower the basic reproduction number and thereby reducing the rate of infection. From the study, we conclude that treating latent and active forms of TB reduce the rate of infection, reduce the rate of progression of individuals to AIDS stage and lowers co-infection.

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Chapter 1

Introduction

The advent of AIDS made the relationship between HIV and Tuberculosis (TB) a public health concern and the co-infection of TB and HIV exist when individuals are HIV positive and are either exposed or active to TB. Getting infected with TB bacteria is not automatic for HIV infected individuals unless in contact with infectious TB individuals. Similarly, individuals infectious to TB do not automatically get infected with HIV unless in contact with HIV positive individuals.

1.1 HIV

HIV, the Human Immunodeficiency Virus is the agent responsible for the acquired immunodeficiency syndrome (AIDS) [11, 19]. HIV is a retrovirus that destroys the human immune system by infecting the $CD4^{+}T$ cells. HIV virus attacks the normal functioning of the immune system to produce more HIV viruses [9]. Population of viruses increase as a result of decrease in the $CD4^{+}T$ cells count in the body. Individuals infected with HIV can stay with this infection for years and therefore may not be ill or show symptoms of HIV infection [11].

HIV is not known to be transmitted casually but through sexual intercourse [19]. HIV is secreted in the body fluid and therefore can be transmitted in a larger amount from semen, pre-seminal fluid, vaginal secretion, and breast feeding [25]. The modes of transmitting HIV includes but not limited to unprotected sexual contacts and non-sexual contacts (injection needles for drug use, direct blood contact,

vertical transmission) [9]. HIV is capable of suppressing the immune system when not treated, it makes individuals to be more susceptible to other infections and will at the end be diagnosed of AIDS [1, 9].

1.1.1 Stages of HIV infection

Research shows that HIV transmission rate is not consistent and therefore the transmission rate differs from different stages of infection. Progression of individuals from one stage of infection to another changes the degree of infectiousness, and therefore the transmission rate of viruses is grouped according to the stages of progression of the infection in an infected individuals [4].

HIV infection is classified into four different stages: primary infection, clinically asymptomatic stage, symptomatic HIV infection, and progression from HIV to AIDS.

- **Primary HIV infection:** This stage carries on for a few weeks and it often occur with a short flu-like illness. The immune system in the primary stage begins to react to the virus and therefore produce HIV antibodies and cytotoxic lymphocytes as a result of a large volume of HIV in the peripheral blood. This process of developing detectable antibodies due to HIV infection is called seroconversion and an incomplete seroconversion may lead to a positive HIV antibody test [4].

- **Clinically asymptomatic stage:** The stage carries on typically for of ten years, when infected individual shows no symptoms but there may be swollen glands. HIV level in the peripheral blood reduces to very low levels and HIV antibody test becomes positive since people remain infectious. Research had shown that when a viral load test (normally use to measure HIV RNA) is carried out, HIV is found to be active, but very active in the lymph nodes [4].

- **Symptomatic HIV infection:** At this stage, HIV mutates and becomes more stronger which leads to the destruction of the $CD4^{+}T$ cells. Immune system becomes damaged and the body fails to keep replacing the lost $CD4^{+}T$ cells. We can also refer to this stage as the pre-AIDS stage where individuals begin

to show symptoms of the infection. HIV-infected individuals on treatment may remain clinically asymptomatic as a result of treatment, and untreated individuals may continue to experience a deteriorating immune system with HIV symptoms getting worse.

- **Progression from HIV to AIDS:** At this stage, individuals develop other opportunistic infections (for example; Tuberculosis) and they are eventually diagnosed of AIDS as a result of the critical damage caused to the immune system [4]. Individuals with AIDS or other infections will have a reduced $CD4^{+}T$ cell usually from around $1000mm^{-3}$ to $200mm^{-3}$ or below [15]. Symptoms of full-blown AIDS appears due to an increased viral load and this stage can be classified as the progression from HIV to AIDS stage. The movement from HIV stage to AIDS stage usually lasts for $8-10$ years during which some individuals may progress much more rapidly while others progress slowly [4, 15].

1.2 Tuberculosis

Tuberculosis (TB), one of the leading cause of death from a single infectious agent, is an airborne transmitted disease caused by the releasing of Mycobacterium tuberculosis (M. tuberculosis) droplets in the air when an infectious individual coughs, sneezes [6, 12, 18] or talks [16]. TB as known to be one of the most wide spread infectious diseases caused by M. tuberculosis is one of the world's leading causes of loss of life [14, 18]. Larger number of TB cases in the United states are caused by M.tuberculosis also called tubercle bacilli [8].

M.tuberculosis can be found in airborne particles called droplet nuclei and these particles can be suspended in the air for several hours depending on the environment. M.tuberculosis is of $1-5$ microns in diameter [8].

Individuals exposed to infectious people at all time for long period of time stand a chance of being infected. According to World Health Organization (WHO), it is estimated that one third of the population of people in the world is infected with TB and as a result leads to $2-3$millions death each year [6, 13], with about $8-9$ millions developing active TB [13]. Although, $90\%-95\%$ percent of TB cases occur in developing countries and about 1.8 million new cases of tuberculosis occur

per year in India [20].

TB disease is a disease with slow dynamics and therefore the epidemics must be studied over a long window in time [6, 13, 17]. Understanding the difference between TB infection and the disease itself will be very important because an infected individual may not be infectious [9]. Infected individuals may remain in the asymptomatic stage throughout their entire lives (Exposed or Latent TB) [3, 24] since exposed periods range from months to decades depending on individuals infected and their immune system [6]. Exposed stage is a stage where individuals show no symptoms of the infection and are not infectious. Individuals progress from exposed stage to infectious or active stage and TB disease is as a result of this progression [9].

Although, the probability of progression towards active TB usually depends on age of infection [2]. Individuals in this active stage show symptoms of the infection and are infectious [9].

We can group Active TB (TB disease) as pulmonary and extra-pulmonary kinds. Pulmonary TB is often seen in adults and transmitted by M.tuberculosis, while extra-pulmonary is more frequent among women, children and in HIV infected individuals [16]. We can classified tuberculosis within the period of five years after infection as primary TB, while tuberculosis after the period of five years from initial infection can be classified as secondary TB. Only about 5% of infected individuals develop primary TB within the period of five years if there are no other conditions to accelerate the infection. Exogenous reinfection (exogenous reactivation) which is classified under secondary TB is the aggravation of an old infection [24].

Some of the factors that can affect the transmission of M.tuberculosis are the number, vitality, and exacerbation of organisms within sputum droplet nuclei, and most significantly, time spent near an infectious individual. Transmission is also affected by Socio-economic status, family size, crowding, malnutrition, and bad health care. Mathematical model for tuberculosis have been a useful tool in assessing the spread of the infection, the epidemiological results and control of the infection [6].

1.3 HIV and TB

HIV and TB accentuate the progression of each other [21]. Immunity deteriorates as HIV infection progresses and this makes infected individuals more susceptible to any opportunistic infection. Treatments of both HIV and TB in many societies have altered the co-infection of HIV and TB. One third of 39.5 million of people infected with HIV are co-infected with TB and individuals infected with HIV are expected to develop TB with probability of 0.5. Many TB and HIV co-infected individuals are at higher risk of developing active TB (30 to 50 times more) than only TB infected individuals [19]. There is always increase in the recurrence rate of TB in HIV infected individuals due to endogenous reactivation and exogenous re-infection [21].

1.3.1 Impact of HIV on TB

The HIV epidemic has significantly impacted TB dynamic. Over the last 5 years, one third of the detected increases in active TB cases can be related to the HIV epidemic [19]. How HIV increases the incidence of new M.tuberculosis infections had been described by several reports. It aggravates the degree of infectiousness of TB and re-activates latent M.tuberculosis[10].

1.3.2 Impact of TB on HIV

Immunocompromised HIV infected individuals are at higher risk of opportunistic infections like TB, TB tends to increase the HIV replication rate. Replication of HIV may lead to fast progression to AIDS [7, 19].

1.3.3 Treatment of HIV and TB

Although HIV-related TB can both be treated and prevented, co-infection is increasing in developing nations where resources are limited [16]. The combined used of highly active antiretroviral therapy (HAART) and antituberculosis treatment is the present drug regimen to treat HIV-TB co-infection [9]. Interaction between both drug regimens can sometimes cause complications, especially between protease inhibitors (antituberculosis drug) and non-nucleotide reverse transcriptase inhibitors (antiretroviral drug). Due to these complications, some protocols have

been made to treat HIV-TB co-infection: Treatment of TB comes before HIV infection treatment, HAART if already in use must be adjusted to implement the use of TB drug treatment, and treatment timing is important if an infected individual has not started HAART treatment. Drug treatment for adverse drug reactions need to be tracked. Carrying out TB test on HIV infected individuals to know a good time to start prophylactic treatment is also a preventive measure [9]. Starting prophylactic treatment can reduce the risk of progression to active TB in HIV infected and TB exposed individuals. Some developing countries still have no access to these drugs and treatments. However, mathematical modelling of the transmission dynamics of the coinfection has been in place due to public health concern [21].

In this project, we look at the possible future effect of treating TB on the co-infection of HIV and TB using a mathematical model. Chapter 1 summarizes the basic background information on HIV and TB, the rest of the thesis is therefore organized as follows:

In chapter 2, we present our motivation and review some studies done on HIV/AIDS and TB and these will be used as a basis for the formulation of our model. In chapter 3, a model for HIV/AIDS and TB co-infection is developed and allows the incorporation of both infections and TB treatment. Two sub-models of the full model are analysed and the full model is also analysed. Computation of their reproduction numbers and analysis are done. Chapter 4 highlights analytical results using selected numerical simulations. Sensitivity is conducted to identify the most sensitive parameter(s).

Chapter 2

Literature Review

Three selected studies done either on TB, HIV, and HIV/TB would be reviewed in this chapter and use them as basis for our study on HIV/AIDS-TB co-infection.

Roeger et al. [19] formulated a mathematical model and considered a simple deterministic model that includes the co-infection of HIV/TB and TB treatment. The basic reproduction numbers of each of the diseases $\mathscr{R}_1$ (TB), $\mathscr{R}_2$ (HIV) and both diseases $\mathscr{R} = \max\{\mathscr{R}_1, \mathscr{R}_2\}$ were found and the model was qualitatively analysed. They obtained limited analytical results where they found the disease free equilibrium for the full model to be locally asymptotically stable when $\mathscr{R} < 1$ and the disease free equilibrium point for TB-only model to be locally asymptotically stable when $\mathscr{R}_1 > 1$ and $\mathscr{R}_2 < 1$. Analytical results showed that $\mathscr{R}_1 < 1$ and $\mathscr{R}_2 > 1$ may not give a stable HIV-only equilibrium and there is possibility of TB coexisting with HIV when $\mathscr{R}_2 > 1$. Results of their numerical simulation show that the increased in the rate at which TB progresses from latent to active form of TB in individuals that are co-infected with both diseases contributed greatly to the prevalence of TB. Similarly, they were also able to show that increase in the rate at which HIV progresses from HIV to AIDS in co-infected individuals contributed to the prevalence of HIV and cause damped oscillations in the system. From their simulation, they found that it is possible to have co-infection of HIV and TB when $\mathscr{R}_1 < 1$ and $\mathscr{R}_2 > 1$. Their model provided general insights into the effects of HIV infection on TB and vice versa. Their numerical results suggested that investing more in reducing the prevalence of HIV could be an effective way to reduce or

control the impact of TB. Results of their model were only based on local mathematical analysis, and their deterministic model needs to be adjusted to incorporate the mode of HIV transmission and the treatment of latent and active forms of TB. We can therefore say that, the dynamics of the co-infection was still need to be well studied mathematically and theoretically.

Chowell-Puente et al. [9] developed an epidemiological model to analyse the dynamical interaction of HIV/AIDS and TB epidemic in South Africa among adults between the age of 15 to 49. Their model was analysed to determine the level to which the HIV epidemic aggravates the TB epidemic. They conducted sensitivity and uncertainty analysis to determine the effect of changing the parameter values on the model and to know the parameter value(s) that is most sensitive to the basic reproduction ($\mathscr{R}_0$). Numerical simulations were also done to know the long term effect of both epidemics. The exponential curve fit to the population data from 1970 to 2005 was done and they numerically estimated the annual growth rate of South Africa from curve fitting. The TB-free model was shown to have a globally stable disease free equilibrium when $\mathscr{R}_0^{HIV} < 1$ and a locally asymptotically stable endemic equilibrium when $\mathscr{R}_0^{HIV} > 1$ while The HIV-free model was shown to have a locally stable disease free equilibrium when $\mathscr{R}_0^{TB} < 1$. The basic reproduction number $\mathscr{R}_0$ for the full model was determined by the $\max\{\mathscr{R}_0^{TB}, \mathscr{R}_0^{TB}\}$. Their results showed that HIV-TB co-infection will eventually shift the declining trend of total TB cases in South Africa. Therefore, they suggested that treatment should be focussed on HIV-positive individuals who are latently infected with TB because they are at a higher risk of progressing to active TB.

Hussaini [15] formulated a deterministic model which incorporates public health education campaign as an intervention strategy for the prevention of HIV/AIDS. The model was analysed to know more about the epidemiological dynamics of HIV/AIDS. The study investigated when the public health education program was 100% effective. The global stability of the disease-free equilibrium of the model was done. The threshold analysis of the effective reproduction number showed that we could have a positive, no, or harmful impact when public health education campaign is used depending on the value of impact factor (Υ). Results of the numerical simulations suggested that the universal strategy is more effective than any other strategy in reducing new HIV cases and that the prospect of effective control

of HIV increases with increasing efficacy and coverage rate of the public health education campaign.

Ideas from these studies are used to formulate a general mathematical model to investigate implications of HIV/AIDS-TB co-infection and to show that increase in the spread of TB infections have been associated with the spread of HIV infection and that there would be a significant decrease in the co-infection cases if TB is treated.

Chapter 3

Mathematical Analysis of the model

3.1 Model Formulation

Mathematical model to study the dynamics of HIV/AIDS-TB co-infection is presented in this chapter. The schematic diagram of the model is shown in figure 3.1.

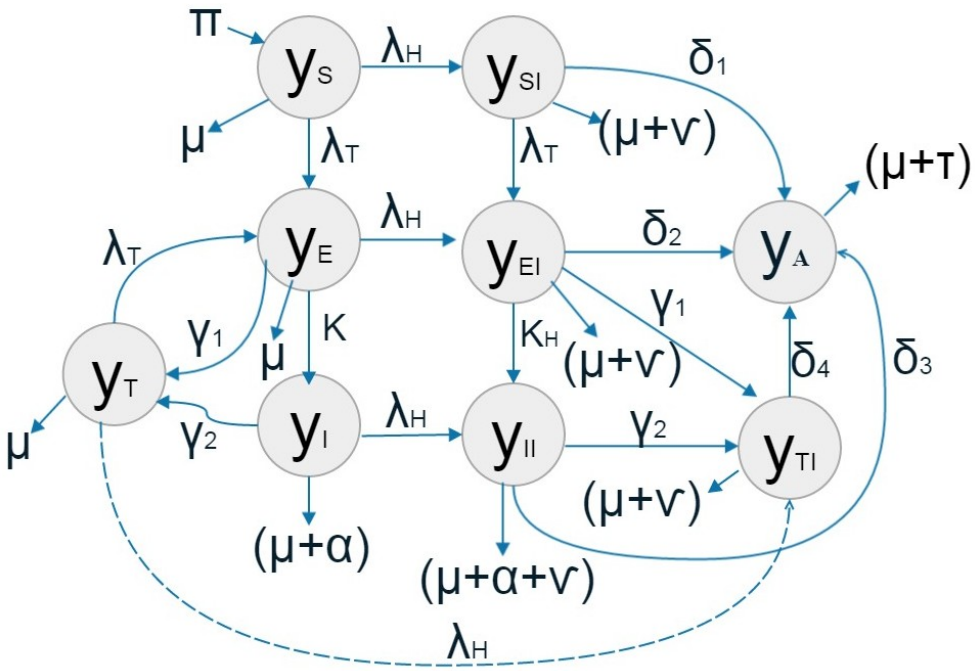

Figure 3.1: The model diagram shows how susceptible individuals are infected with TB and HIV. We see from the diagram the transmission dynamics of the two infections. The population is divided into nine epidemiological classes: Susceptible (y_S), Exposed TB (y_E), Infectious TB (y_I), HIV-positive (y_{SI}), HIV infectious and TB Exposed (y_{EI}), Infectious with both TB and HIV (y_{II}), AIDS individuals (y_A), treated individuals exposed or infected with TB (y_T), dually infected individuals with TB treatment only (y_{TI}). Classes (y_{EI}), (y_{II}), (y_{TI}) and (y_A) represent the co-infection of HIV/AIDS and TB.

From figure 3.1, we have the susceptible class (y_S) to be individuals with no infection (no TB and no HIV infection). The model is structured such that susceptible individuals can either be infected with TB by individuals in the epidemiological classes y_I or y_{II} and with HIV by individuals in the classes y_{SI}, y_{EI}, y_{II} or y_{TI} . Note that individuals with HIV can easily progress to y_{II} or y_A through TB infection and reactivation of the exposed TB infection and we can say that HIV increases the rate of progression of TB infection.

The Exposed class (y_E) are individuals with TB infection but not infectious

and they can be infected with HIV by individuals in the classes y_{SI}, y_{EI}, y_{II} or y_{TI}. The infectious TB class (y_I) are individuals with TB disease and are infectious. They can also be infected with HIV by individuals in the classes y_{SI}, y_{EI}, y_{II} or y_{TI}. The HIV-positive class y_{SI} are HIV-positive individuals and can be infected with TB infection by individuals in the classes y_I and y_{II}. The y_{EI} class are HIV-positive and exposed TB individuals. The class y_{II} are HIV-positive and infectious TB individuals. The class y_T are treated infected TB individuals. The class (y_{TI}) are treated dually infected individuals. Finally, the class y_A are AIDS individuals with either AIDS or TB and AIDS.

Parameters π denote the rate at which individuals are recruited into the susceptible class and μ denote the rate at which they can die naturally. Since TB can be spread by individuals in the classes y_I and y_{II} to susceptible individuals and HIV can be transmitted by individuals in the classes y_{SI}, y_{EI}, y_{II} or y_{TI} to susceptible individuals. Thus susceptible individuals infected with TB enter the class y_E at the rate $\beta_1 \frac{(y_I + \rho_1 y_{II})}{N}$ while susceptible individuals infected with HIV enter the class y_{SI} at the rate $\beta_2 \frac{(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})}{N}$ where β_1 and β_2 are transmission rates per year for TB and HIV respectively, the quantity $\frac{(y_I + \rho_1 y_{II})}{N}$ is the probability of having contact with an individual infected with TB out of the total population and $\frac{(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})}{N}$ is the risk measure involved with HIV levels in the population.

Parameter $\rho_1 > 1$ indicates that individuals with HIV and infectious TB are more infectious to pass TB disease compared with individuals with only infectious TB. The rates $1 \leq \eta_1 \leq \eta_2 \leq \eta_3$ indicate that becoming infected with HIV from individuals with HIV-positive and TB disease or HIV-positive and exposed TB or HIV-positive and treated TB is easier than from just HIV-positive individuals.

Exposed TB individuals can also move to HIV-positive class (y_{EI}) at the rate $\beta_2 \frac{(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})}{N}$ or progress to TB infectious class (y_I) at the rate k, where β_2 is the HIV transmission rate. Infectious TB individuals (y_I) and exposed TB individuals (y_E) can be treated and move to TB treated class (y_T) at the rate γ_2 and γ_1 respectively. Infectious TB individuals can die from TB at the rate α, or enter the class (y_{II}) at the rate $\beta_2 \frac{(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})}{N}$. Individuals who

are HIV-positive in the class y_{SI} can be infected with TB and they will enter the HIV-positive and exposed TB class (y_{EI}) at the rate $\beta_1 \frac{(y_I + \rho_1 y_{II})}{N}$ and die due to HIV at the rate ν. Otherwise, they progress to the AIDS class (y_A) at the rate δ_1.

Individuals in the class (y_{EI}) progress to the class (y_{II}) at the rate k_H or die due to HIV at the rate ν. Figure 3.1 shows that Individuals in the class (y_{EI}) can also progress to AIDS class (y_A) or treated class (y_{TI}) at the rate δ_2 and γ_1 respectively. Individuals in the class (y_{II}) progress to the treated class (y_{TI}) and AIDS class (y_A) at the rate γ_2 and δ_3 respectively. Individuals in the class (y_{II}) die from both HIV and TB disease at the rate ν and α respectively. Individuals in the class (y_A) die due to both infections at the rate τ. Individuals in the class (y_T) can be reinfected by both HIV and TB and enter the class (y_E) and (y_{TI}) at the rate $\beta_1 \frac{(y_I + \rho_1 y_{II})}{N}$ and $\beta_2 \frac{(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})}{N}$ respectively. Individuals in the class (y_{TI}) can die due to HIV at the rate ν or progress to the AIDS class (y_A) at the rate δ_4. Individuals in all the nine classes can die naturally at the rate μ.

3.2 Model Assumptions

- We can have a model with a constant or varying population, so we assume susceptible individuals are recruited into the population at a constant rate π.
- Since it is difficult to identify any symptoms clinically at the exposed level of TB, we then assume that TB exposed individuals are not infectious and can not transmit TB infection.
- TB could be spread through different means as discussed in the first chapter. We therefore assume in the model that TB infection is spread between infectious and susceptible individuals by airborne spread only.
- We have different means through which HIV could be transmitted, but the model assumes HIV is transmitted between infectious and susceptible individuals neglecting the mode of transmission.
- Since it is possible for dually infectious individuals to develop or not develop AIDS in reality and in the presence of TB treatment. Hence, we assume that Individual infectious with both diseases may or may not develop AIDS.

- Since we know that individuals infected with TB can not fully recover, then we assume that individuals would not completely recover from TB but would be exposed.
- We ignore the treatment of HIV/AIDS since it is difficult to cure or eradicate.
- Since HIV treatment is not considered in this model, we then assume that it is possible for HIV-positive individuals to die due to HIV,
- We know that most people infected with HIV at the initial stage may or may not show any symptoms of it, we therefore assume that individuals can die due to HIV but at a very low probability when not co-infected with TB.
- Susceptible individuals get infected with HIV following contact with HIV infected individuals at a rate λ_H and they acquire TB infection from individuals with active TB only at a rate λ_T.
- Individuals in the class (y_A) die due to either AIDS or TB and AIDS at the same rate τ and assume it is difficult to identify the cause of deaths in this class.
- Since the mode of transmission is neglected and it is possible for individuals in the class y_A to spread TB or HIV. We therefore assume that individuals in the class (y_A) are too weak to transmit any disease or infect others outside the class.
- We assume that individuals in the class y_A can either remain in this class or die. We assume they will not recover from this class because the immune system will not be strong enough to fight against infections.
- Since it is possible for infectious TB individuals to transmit infection, we therefore assume that treated TB individuals (y_T) may not transmit infection since they are on treatment, but could be reinfected since they would not fully recover.
- Co-infected individuals on TB treatment may also not transmit TB infection, but can transmit HIV infection since they are not on HIV treatment.

- We assume that $\kappa_H \geq \kappa$ since it is easier to be TB infectious when one is co-infected with HIV, i.e. we assume it is faster to move from class y_{EI} to class y_{II} than from the class y_E to class y_I.

Based on the assumptions above and the model diagram, the model representing the dynamics of HIV/AIDS and tuberculosis is given by a system of non-linear ordinary differential equation 3.1, and table 3.1 gives the description of the variables and parameters in the model.

$$\begin{aligned}
\dot{y}_S &= \pi - \lambda_T y_S - \lambda_H y_S - \mu y_S, \\
\dot{y}_E &= \lambda_T y_S - \lambda_H y_E + \lambda_T y_T - (\mu + k + \gamma_1) y_E, \\
\dot{y}_I &= k y_E - \lambda_H y_I - (\mu + \alpha + \gamma_2) y_I, \\
\dot{y}_{SI} &= \lambda_H y_S - \lambda_T y_{SI} - (\mu + \nu + \delta_1) y_{SI}, \\
\dot{y}_{EI} &= \lambda_H y_E + \lambda_T y_{SI} - (\mu + \nu + k_H + \delta_2 + \gamma_1) y_{EI}, \\
\dot{y}_{II} &= k_H y_{EI} + \lambda_H y_I - (\mu + \gamma_2 + \delta_3 + \alpha + \nu) y_{II}, \\
\dot{y}_A &= \delta_1 y_{SI} + \delta_2 y_{EI} + \delta_3 y_{II} - (\mu + \tau) y_A + \delta_4 y_{TI}, \\
\dot{y}_T &= \gamma_1 y_E + \gamma_2 y_I - \lambda_T y_T - \lambda_H y_T - \mu y_T, \\
\dot{y}_{TI} &= \gamma_1 y_{EI} + \gamma_2 y_{II} + \lambda_H y_T - (\mu + \nu + \delta_4) y_{TI}.
\end{aligned} \tag{3.1}$$

where

$$\lambda_T = \frac{\beta_1}{N}(y_I + \rho_1 y_{II})$$

and

$$\lambda_H = \frac{\beta_2}{N}(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})$$

The total population $N(t)$ is given by

$$N(t) = y_S(t) + y_E(t) + y_I(t) + y_{SI}(t) + y_{EI}(t) + y_{II}(t) + y_A(t) + y_T(t) + y_{TI}(t)$$

and it satisfies

$$\frac{dN}{dt} = \pi - \mu N - \alpha(y_I + y_I I) - \nu(y_{SI} + y_{EI} + y_{II} + y_{TI}) - \tau y_A$$

where π is the recruitment rate, $\beta_i, i = 1,2$ is the transmission rate, μ is the natural death rate, $\gamma_i, i = 1,2$ is the progression rate from infected stage to treated stage, $\delta_i, i = 1,2,3,4$ is the progression rate from HIV infected stage to AIDS stage, α and ν are disease induced death rates for TB and HIV respectively. Table 3.1 gives the detailed definitions.

Table 3.1: Model variables, parameters and their descriptions

Variable	Description
$y_S(t)$	Susceptible individuals
$y_E(t)$	Latent TB individuals
$y_I(t)$	Infectious(Active) TB individuals
$y_{SI}(t)$	HIV-positive individuals
$y_{EI}(t)$	HIV infectious and TB latent individuals
$y_{II}(t)$	Individuals Infectious with both TB and HIV
$y_A(t)$	Individuals with AIDS
$y_T(t)$	Treated individuals with TB
$y_{TI}(t)$	Dually infected individuals treated of TB
Parameter	Description
π	Recruitment rate of susceptible individuals
β_1	probability of TB transmission to a susceptible per contact with an infectious TB individual
β_2	probability of HIV transmission to a susceptible per contact with an HIV individual
μ	natural death rate
τ	death rate due to AIDS
ν	death rate due to HIV
α	death rate due to TB
k	rate of progression of y_E to y_I
k_H	rate of progression of y_{EI} to y_{II}
δ_1	rate of progression of y_{SI} to y_A
δ_2	rate of progression of y_{EI} to y_A
δ_3	rate of progression of y_{II} to y_A
δ_4	rate of progression of y_{TI} to y_A
γ_1	Treatment rate of latent TB individuals
γ_2	Treatment rate of infectious TB individuals
ρ_1	coefficient of infectiousness of y_{II} to transmit TB disease
η_1	coefficient of infectiousness of y_{EI} to transmit HIV-positive disease
η_2	coefficient of infectiousness of y_{II} to transmit HIV-positive disease
η_3	coefficient of infectiousness of y_{TI} to transmit HIV-positive disease

We will study the dynamics of the system 3.1 based on biological consideration in the region

$$\Theta = \left\{ (y_S + y_E + y_I + y_{SI} + y_{EI} + y_{II} + y_A + y_T + y_{TI}) \in \mathscr{R}_+^9 : N \leq \frac{\pi}{\mu} \right\}, \quad (3.2)$$

which is positively invariant with respect to the model system 3.1. We need to show that all variables and parameters of model system 3.1 are all positive for all time since the model is for human populations.

Lemma 3.2.1. *The region $\mathscr{R}_+^9$ is positive everywhere for model 3.1 which establishes that our model does not predict negative values for the state variables at any future time.*

Proof.

Let $t_1 = sup\{t > 0 : y_S \geq 0, y_E \geq 0, y_I \geq 0, y_{SI} \geq 0, y_{EI} \geq 0, y_{II} \geq 0, y_A \geq 0, y_T \geq 0, y_{TI} \geq 0 \in [0,t]\}$.

From the first equation in the model 3.1, we have

$$\dot{y}_S = \pi - \lambda_T y_S - \lambda_H y_S - \mu y_S$$

where $\lambda_T = \frac{\beta_1}{N}(y_I + \rho_1 y_{II})$ and $\lambda_H = \frac{\beta_2}{N}(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})$.

$$\Rightarrow \dot{y}_S + (\lambda_T + \lambda_H) y_S + \mu y_S = \pi$$

$$\Rightarrow \frac{d}{dt}\left(y_S(t) exp\left\{ \mu t + \int_0^t (\lambda_T(\xi) + \lambda_H(\xi)) d\xi \right\} \right) = \pi exp\left\{ \mu t + \int_0^t (\lambda_T(\xi) + \lambda_H(\xi)) d\xi \right\}.$$

Then we have,

$$y_S(t_1) exp\left\{ \mu t_1 + \int_0^{t_1} (\lambda_T(\xi) + \lambda_H(\xi)) d\xi \right\} - y_S(0) = \int_0^{t_1} \pi exp\left\{ \mu\varphi + \int_0^{\varphi} (\lambda_T(\rho) + \lambda_H(\rho)) d\rho \right\} d\varphi.$$

Hence,

$$y_S(t_1) = y_S(0) exp\left\{ -\left(\mu t_1 + \int_0^{t_1} (\lambda_T(\xi) + \lambda_H(\xi)) d\xi \right) \right\}$$

$$+ exp\left\{ -\left(\mu t_1 + \int_0^{t_1} (\lambda_T(\xi) + \lambda_H(\xi)) d\xi \right) \right\} \times \int_0^{t_1} \pi exp\left\{ \mu\varphi + \int_0^{\varphi} (\lambda_T(\rho) + \lambda_H(\rho)) d\rho \right\} d\varphi \geq 0.$$

This can also be shown for other compartments. □

Lemma 3.2.2. *Every solutions in* Θ *remain in* Θ *for all time.*

Proof. We know that the rate of change of the total population $N(t)$ gotten by adding equations in 3.1 is given by

$$\frac{dN}{dt} = \pi - \mu N - \alpha(y_I + y_I I) - \nu(y_{SI} + y_{EI} + y_{II} + y_{TI}) - \tau y_A.$$

Considering initial conditions in $\mathscr{R}^9_+$ and $t \geq 0$, we have

$$\frac{dN}{dt} \leq \pi - \mu N \Rightarrow \frac{d}{dt}(Ne^{\mu t}) \leq \pi e^{\mu t}$$

$$\Rightarrow N(t)e^{\mu t} - N(0) \leq \frac{\pi}{\mu}(e^{\mu t} - 1) \leq \frac{\pi}{\mu}e^{\mu t}.$$

And for $t \geq 0$,

$$N(t) \leq N(0)e^{-\mu t} + \frac{\pi}{\mu}. \tag{3.3}$$

If $(y_S^*, y_E^*, y_I^*, y_{SI}^*, y_{EI}^*, y_{II}^*, y_A^*, y_T^*, y_{TI}^*)$ is an Θ limit point of a region in $\mathscr{R}^9_+$, such that there exist a subsequence $t_i \to \infty$ and

$$\lim_{t\to\infty}(y_S(t_i), y_E(t_i), y_I(t_i), y_{SI}(t_i), y_{EI}(t_i), y_{II}(t_i), y_A(t_i), y_T(t_i), y_{TI}(t_i)) = (y_S^*, y_E^*, y_I^*, y_{SI}^*, y_{EI}^*, y_{II}^*, y_A^*, y_T^*, y_{TI}^*).$$

$$\text{Therefore,} \quad \lim_{t\to\infty} N(t_i) = N^* = y_S^*, y_E^*, y_I^*, y_{SI}^*, y_{EI}^*, y_{II}^*, y_A^*, y_T^*, y_{TI}^*.$$

If we evaluate $t = t_i$ at $i \to \infty$, we have $N^* \leq \frac{\pi}{\mu}$ and we can say that $(y_S^*, y_E^*, y_I^*, y_{SI}^*, y_{EI}^*, y_{II}^*, y_A^*, y_T^*, y_{TI}^*) \in \Theta$.

Thus, for initial values $(y_S(0), y_E(0), y_I(0), y_{SI}(0), y_{EI}(0), y_{II}(0), y_A(0), y_T(0), y_{TI}(0)) \in \mathscr{R}^9_+$, the trajectory lies within Θ and we consider the model to be well posed mathematically and epidemiologically. □

3.3 Model analysis

Gaining insights into the dynamics of the models for HIV sub-model(HIV-only model) and TB sub-model(TB-only model) will be a first step to understanding more about the co-infection.

3.3.1 HIV sub-model

We have the model with HIV only by setting $y_E = y_I = y_{EI} = y_{II} = y_T = y_{TI} = 0$ in 3.1 and it is given by

$$\begin{aligned} \dot{y}_S &= \pi - \lambda_H y_S - \mu y_S, \\ \dot{y}_{SI} &= \lambda_H y_S - (\mu + \nu + \delta_1) y_{SI}, \\ \dot{y}_A &= \delta_1 y_{SI} - (\mu + \tau) y_A, \end{aligned} \tag{3.4}$$

$$\text{where} \quad \lambda_H = \frac{\beta_2}{N}(y_{SI}) \quad \text{and now we have} \quad N = y_S + y_{SI} + y_A.$$

We can show for this model that the region

$$\Theta_1 = \left\{ (y_S, y_{SI}, y_A) \in \mathscr{R}^3_+ : N \leq \frac{\pi}{\mu} \right\},$$

is positively invariant and solutions starting in Θ_1 approach, enter or stay in Θ_1

Disease free equilibrium point

Disease-free equilibrium point is a steady state solution where there is no HIV infection and AIDS disease in the population.

When there are no diseases in the population, the non-negative population values are

$$y_{SI} = y_A = 0. \tag{3.5}$$

Set the right hand side of the second and third equation in 3.4 to zero and apply equation 3.5, then the HIV sub-model has a disease-free equilibrium point (DFE) of

$$E_{0H} = \left(\frac{\pi}{\mu},\ 0,\ 0 \right).$$

Reproduction Number $\mathscr{R}_0$

The basic reproduction number $\mathscr{R}_0$ is defined as the number of secondary infections produced by an infectious individual introduced during the period of infectiousness into a totally susceptible population [24]. We can distinguish new infections

from all other changes in population so as to find $\mathscr{R}_0$. Let $\mathscr{F}_i$ be the vector rates of appearance of new infections in each compartment i ($i = 1,2$), $\mathscr{V}_i^+(x)$ be the vector rates of transfer of individuals into the particular compartment of i by all other means, $\mathscr{V}_i^-(x)$ be the vector rates of transfer of individuals out of particular compartment of i. We can find $\mathscr{R}_0 = \rho(FV^{-1})$ [24]. In this case, we have the reproduction number $\mathscr{R}_H$ as the number of HIV infections produced by HIV positive cases.

Note that we have two infectious classes y_{SI}, y_A, and the matrix showing the rate of appearance of new infections in compartment i is given by

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

The matrix showing the rate of transfer of individuals in and out of compartments i is

$$\mathscr{V} = \mathscr{V}^- - \mathscr{V}^+ = \begin{pmatrix} (\mu+\nu+\delta_1)y_{SI} \\ (\mu+\tau)y_A - \delta_1 y_{SI} \end{pmatrix}$$

$$\text{where} \quad \mathscr{V}^+ = \begin{pmatrix} 0 \\ \delta_1 y_{SI} \end{pmatrix} \quad \text{and} \quad \mathscr{V}^- = \begin{pmatrix} (\mu+\nu+\delta_1)y_{SI} \\ (\mu+\tau)y_A \end{pmatrix}.$$

The Jacobian matrix of $\mathscr{F}$ evaluated at the disease free equilibrium point, DFE=$\left(\frac{\pi}{\mu}, 0, 0\right)$ is given by

$$F = \frac{\partial \mathscr{F}(E_{0H})}{\partial x_j} = \begin{pmatrix} \beta_2 & 0 \\ 0 & 0 \end{pmatrix} \quad \text{where} \quad x_j = y_{SI}, y_A \quad \text{for} \quad j = 1,2.$$

The Jacobian matrix of $\mathscr{V}$ evaluated at the disease free equilibrium point DFE is

$$V = \frac{\partial \mathscr{V}(E_{0H})}{\partial x_j} = \begin{pmatrix} (\mu+\nu+\delta_1) & 0 \\ -\delta_1 & (\mu+\tau) \end{pmatrix}.$$

The next generation matrix FV^{-1} is given by

$$\begin{pmatrix} \frac{\beta_2}{(\mu+\nu+\delta_1)} & 0 \\ 0 & 0 \end{pmatrix}.$$

The dominant eigenvalues of FV^{-1} which is the spectral radius of the matrix FV^{-1} gives the basic reproduction number for HIV/AIDS from the model (3.4) as;

$$\mathscr{R}_H = \rho(FV^{-1}) = \frac{\beta_2}{(\mu+\nu+\delta_1)},$$

where

• $\mathscr{R}_H$ is the reproduction number for HIV/AIDS dynamics given by the product of the probability of HIV infection β_2 for susceptible per contact with an HIV individual and the probability that an infective progresses from HIV-positive to AIDS stage $\frac{1}{(\mu+\nu+\delta_1)}$.

Stability analysis of disease-free equilibrium point

The Jacobian matrix of the system of equations 3.4 is given by

$$J = \begin{pmatrix} -(\mu+\lambda_H) & \frac{-\beta_2}{N} y_S & 0 \\ \lambda_H & -(\mu+\nu+\delta_1)+\frac{\beta_2}{N} y_S & 0 \\ 0 & \delta_1 & -(\mu+\tau) \end{pmatrix}.$$

Theorem 3.3.2. *The disease free equilibrium E_{0H} point of HIV-only model is locally asymptotically stable (LAS) if $\mathscr{R}_H < 1$ and unstable, if $\mathscr{R}_H > 1$.*

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

$$J_{0H} = \begin{pmatrix} -\mu & -\beta_2 & 0 \\ 0 & -(\mu+\nu+\delta_1)+\beta_2 & 0 \\ 0 & \delta_1 & -(\mu+\tau) \end{pmatrix}.$$

To determine the stability of disease-free equilibrium point, we use $|J_{0H} - \lambda I| = 0$

to obtain eigenvalues of J_{0H}.

$$\begin{vmatrix} -\mu-\lambda & -\beta_2 & 0 \\ 0 & -(\mu+\nu+\delta_1)+\beta_2-\lambda & 0 \\ 0 & \delta_1 & -(\mu+\tau)-\lambda \end{vmatrix} = 0, \tag{3.6}$$

We can factor out $-(\mu+\tau)-\lambda$ from 3.6 to have

$$\lambda_1 = -(\mu+\tau) < 0,$$

which reduces 3.6 to

$$\begin{vmatrix} -\mu-\lambda & -\beta_2 \\ 0 & -(\mu+\nu+\delta_1)+\beta_2-\lambda \end{vmatrix} = 0,$$

whose eigenvalues are the diagonal elements

$$\lambda_2 = -\mu < 0 \quad \text{and} \quad \lambda_3 = \beta_2 - (\mu+\nu+\delta_1).$$

We can write $\lambda_3 = \beta_2 - (\mu+\nu+\delta_1)$ in terms of $\mathscr{R}_H$ as

$$\lambda_3 = (\mathscr{R}_H - 1)(\mu+\nu+\delta_1)$$

The eigenvalue λ_3 is negative or have negative when $\mathscr{R}_H - 1 < 0$ or when $1-\mathscr{R}_H > 0$ i.e. when $\mathscr{R}_H < 1$.

Since $\lambda_1,\ \lambda_2,\ \lambda_3$ are all negative or have negative real parts when $\mathscr{R}_H < 1$, we say the disease free equilibrium point is locally asymptotically stable when $\mathscr{R}_H < 1$. This completes the proof. □

We can rewrite model 3.4 as,

$$\begin{aligned} \frac{dU}{dt} &= F(U,V), \\ \frac{dV}{dt} &= G(U,V), \quad G(U,0)=0, \end{aligned} \tag{3.7}$$

where $U = y_S$ and $V = (y_{SI}, y_A)$, with $U \in \mathscr{R}^1_+$ denoting the number of susceptible individuals and $V \in \mathscr{R}^2_+$ denoting the number of infected individuals.

We now denote the disease free equilibrium by,

$$E_{0H} = (U^*, 0), \quad \text{where} \quad U^* = \left(\frac{\pi}{\mu}\right). \tag{3.8}$$

Conditions $S1$ and $S2$ in equation 3.9 must be satisfied to guarantee local asymptotic stability.

$$\begin{aligned} S1 : \frac{dU}{dt} &= F(U,0), \quad U^* \quad \text{is globally asymptotic stable (g.a.s)} \\ S2 : G(U,V) &= AV - \widehat{G}(U,V), \quad \widehat{G}(U,V) \geq 0 \quad \text{for} \quad (U,V) \in \Theta_1, \end{aligned} \tag{3.9}$$

where $A = D_V G(U^*, 0)$ denotes the M-matrix (the off diagonal elements of A are non-negative) and Θ_1 denotes the region where the model makes biological sense. Theorem 3.3.3 holds if system 3.7 satisfies the conditions in 3.9.

Theorem 3.3.3. *The disease free equilibrium point E_{0H} of HIV-only model is globally asymptotically stable if $\mathscr{R}_H < 1$ and conditions in 3.9 are satisfied.*

Proof. We have from theorem 3.3.2 that E_{0H} is locally asymptotically stable if $\mathscr{R}_H < 1$. Now consider

$$F(U,0) = [\pi - \mu y_S], \tag{3.10}$$

$$G(U,V) = AV - \widehat{G}(U,V), \quad A = \begin{pmatrix} \beta_2 - (\mu + \nu + \delta_1) & 0 \\ \\ \delta_1 & -(\mu + \tau) \end{pmatrix}. \tag{3.11}$$

$$\widehat{G}(U,V) = \begin{pmatrix} \widehat{G_1}(U,V) \\ \\ \widehat{G_2}(U,V) \end{pmatrix} = \begin{pmatrix} \beta_2 \left(1 - \frac{1}{N}\right)(y_{SI}) \\ \\ 0 \end{pmatrix}. \tag{3.12}$$

We have the conditions in 3.9 satisfied since $\widehat{G_1}(U,V) \geq 0$ and $\widehat{G_2}(U,V) = 0 \Rightarrow \widehat{G}(U,V) \geq 0$. And therefore we can conclude that E_{0H} is globally asymptotically stable for $\mathscr{R}_H < 1$. This completes the proof. □

Endemic equilibrium points

We can solve equations in 3.4 in terms of the force of infection $\lambda_H^* = \frac{\beta_2}{N^*}(y_{SI}^*)$ to find the conditions for the existence of an equilibrium for which HIV/AIDS is endemic in the population.

Equating the right-hand side of equations 3.4 to zero, we have

$$\begin{aligned} \pi - \lambda_H^* y_S^* - \mu y_S &= 0, && (3.13)\\ \lambda_H^* y_S^* - (\mu + \nu + \delta_1) y_{SI}^* &= 0, && (3.14)\\ \delta_1 y_{SI}^* - (\mu + \tau) y_A^* &= 0. && (3.15) \end{aligned}$$

From equation 3.13 to 3.15, we have

$$\begin{aligned} y_S^* &= \frac{\pi}{(\mu + \lambda_H^*)}, && (3.16)\\ y_{SI}^* &= \frac{\lambda_H^* y_S^*}{(\mu + \nu + \delta_1)}, && (3.17)\\ y_A^* &= \frac{\delta_1 y_{SI}^*}{(\mu + \tau)}. && (3.18) \end{aligned}$$

And the endemic equilibrium is given by

$$E_H^* = (y_S^*,\ y_{SI}^*,\ y_A^*),$$

$$\text{where} \quad \lambda_H^* = \frac{\beta_2 y_{SI}^*}{N^*}.$$

From equation 3.17, we have

$$\begin{aligned}
\frac{y_{SI}^*}{y_S^*} &= \frac{\lambda_H^*}{(\mu+\nu+\delta_1)}, \\
\frac{y_{SI}^*}{y_S^*} &= \frac{1}{(\mu+\nu+\delta_1)}\left(\frac{\beta_2 y_{SI}^*}{N^*}\right), \\
\frac{N^*}{y_S^*} &= \frac{1}{(\mu+\nu+\delta_1)}\left(\frac{\beta_2 y_{SI}^*}{y_{SI}^*}\right), \\
\frac{N^*}{y_S^*} &= \frac{\beta_2}{(\mu+\nu+\delta_1)}, \\
\frac{N^*}{y_S^*} &= \mathscr{R}_H, \\
\mathscr{R}_H &= \frac{N^*}{y_S^*}, \\
&= \frac{y_S^*+y_{SI}^*+y_A^*}{y_S^*}, \\
&= 1+\frac{y_{SI}^*}{y_S^*}+\frac{y_A^*}{y_S^*}, \\
\mathscr{R}_H &= 1+\frac{\lambda_H^*}{(\mu+\nu+\delta_1)}+\frac{\lambda_H^*\delta_1}{(\mu+\tau)(\mu+\nu+\delta_1)}, \\
\mathscr{R}_H-1 &= \frac{\lambda_H^*}{(\mu+\nu+\delta_1)}\left(1+\frac{\delta_1}{(\mu+\tau)}\right), \\
\mathscr{R}_H-1 &= \lambda_H^*\Pi, \\
\lambda_H^* &= \frac{(\mathscr{R}_H-1)}{\Pi},
\end{aligned}$$

where Π is denoted as the mean infective period which is given by

$$\Pi = \frac{1}{(\mu+\nu+\delta_1)}\left(1+\frac{\delta_1}{(\mu+\tau)}\right).$$

When λ_H^* is substituted into the endemic equilibrium point in 3.16 to 3.18, we will

obtain the endemic equilibrium point in terms of $\mathscr{R}_H$ as

$$\begin{aligned} y_S^* &= \frac{\pi\Pi}{\mu\Pi+(\mathscr{R}_H-1)}, \\ y_{SI}^* &= \frac{(\mathscr{R}_H-1)y_S^*}{\Pi(\mu+\nu+\delta_1)}, \\ y_A^* &= \frac{\delta_1(\mathscr{R}_H-1)y_S^*}{\Pi(\mu+\tau)(\mu+\nu+\delta_1)}. \end{aligned} \tag{3.19}$$

Theorem 3.3.4. *The endemic equilibrium E_H^* point of HIV-only model is locally asymptotically stable (LAS) if $\mathscr{R}_H > 1$.*

Proof. The Jacobian matrix J evaluated at the endemic equilibrium E_H^* point is given as

$$J_H^* = \begin{pmatrix} -(\mu+\lambda_H^*) & \frac{-\beta_2}{\mathscr{R}_H} & 0 \\ \lambda_H^* & \frac{\beta_2}{\mathscr{R}_H}-(\mu+\nu+\delta_1) & 0 \\ 0 & \delta_1 & -(\mu+\tau) \end{pmatrix},$$

where $\mathscr{R}_H = \dfrac{N^*}{y_S^*}$ and $\lambda_H^* = \dfrac{(\mathscr{R}_H-1)}{\Pi}$.

To determine the stability of endemic equilibrium point, we use $|J_H^* - \lambda I| = 0$ to obtain eigenvalues of J_H^*.

$$|J_H^* - \lambda I| = \begin{vmatrix} -(\mu+\lambda_H^*)-\lambda & \frac{-\beta_2}{\mathscr{R}_H} & 0 \\ \lambda_H^* & \frac{\beta_2}{\mathscr{R}_H}-(\mu+\nu+\delta_1)-\lambda & 0 \\ 0 & \delta_1 & -(\mu+\tau)-\lambda \end{vmatrix} = 0,$$

$$\lambda_1 = -(\mu+\tau) \quad \text{and} \quad \left(-(\mu+\lambda_H^*)-\lambda\right)\left(\frac{\beta_2}{\mathscr{R}_H}-(\mu+\nu+\delta_1)-\lambda\right)+\frac{\beta_2\lambda_H^*}{\mathscr{R}_H},$$

whose characteristic equation is given by

$$A\lambda^2 + B\lambda + C = 0.$$

Coefficients A B and C can be written in form of $\mathscr{R}_H$ as

$$\begin{aligned} A &= 1, \\ B &= (\mu + \lambda_H^*), \\ C &= \frac{\beta_2 \lambda_H^*}{\mathscr{R}_H}. \end{aligned}$$

We use the Routh-Hurwitz stability criterion for second order polynomial so as to be sure that all eigenvalues of J_H^* are either negative or have negative real parts. The following conditions must hold for stability:

$$A > 0, \quad B > 0 \quad \text{and} \quad C > 0.$$

Clearly, $A > 0$, $B > 0$ and $C > 0$ when $\lambda_H^* > 0$, i.e when $\mathscr{R}_H > 1$.

All the Routh-Hurwitz criterion conditions are satisfied when $\mathscr{R}_H > 1$. Hence E_H^* is asymptotically stable when $\mathscr{R}_H > 1$. □

3.3.5 TB Sub-model

We have the model with TB only by setting $y_{SI} = y_{EI} = y_{II} = y_A = y_{TI} = 0$ in equation 3.1 and it is given by

$$\begin{aligned} \dot{y}_S &= \pi - \lambda_T y_S - \mu y_S, \\ \dot{y}_E &= \lambda_T y_S + \lambda_T y_T - (\mu + \kappa + \gamma_1) y_E, \\ \dot{y}_I &= \kappa y_E - (\mu + \alpha + \gamma_2) y_I, \\ \dot{y}_T &= \gamma_1 y_E + \gamma_2 y_I - \lambda_T y_T - \mu y_T, \end{aligned} \tag{3.20}$$

$$\text{where} \quad \lambda_T = \frac{\beta_1 y_I}{N} \quad \text{and now we have} \quad N = y_S + y_E + y_I + y_T.$$

We can show for this model that the region

$$\Theta_2 = \left\{ (y_S, y_E, y_I, y_T) \in \mathscr{R}_+^4 : N \leq \frac{\pi}{\mu} \right\},$$

is positively invariant and solutions starting in Θ_2 approach, enter or stay in Θ_2

Disease free equilibrium point

When there is no TB disease in the population, the non-negative population values are

$$y_E = y_I = y_T = 0. \tag{3.21}$$

Set the right hand side of equation 3.20 to zero and apply 3.21, then our model has a disease-free equilibrium point (DFE) of

$$E_{0T} = \left(\frac{\pi}{\mu},\ 0,\ 0,\ 0\right).$$

Reproduction Number $\mathscr{R}_0$

In this case, we have the reproduction number $\mathscr{R}_T$ as the number of TB infections produced by infectious TB cases.

Note that we have three infectious classes y_E, y_I, y_T, and the matrix showing the rate of appearance of new infections in compartment i is given by

$$\mathscr{F} = \begin{pmatrix} \lambda_T y_S + \lambda_T y_T \\ 0 \\ 0 \end{pmatrix}.$$

The matrix showing the rate of transfer of individuals in and out of compartments i is

$$\mathscr{V} = \mathscr{V}^- - \mathscr{V}^+ = \begin{pmatrix} (\mu + \kappa + \gamma_1) y_E \\ (\mu + \alpha + \gamma_2) y_I - \kappa y_E \\ \lambda_T y_T + \mu y_T - \gamma_1 y_E - \gamma_2 y_I \end{pmatrix}$$

The jacobian matrix of $\mathscr{F}$ evaluated at the disease free equilibrium point, DFE=$\left(\frac{\pi}{\mu}, 0, 0, 0\right)$ is given by

$$F = \frac{\partial \mathscr{F}(E_{0T})}{\partial x_j} = \begin{pmatrix} 0 & \beta_1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{where} \quad x_j = y_E, y_I, y_T \quad \text{for} \quad j = 1, 2, 3.$$

The jacobian matrix of $\mathscr{V}$ evaluated at the disease free equilibrium point DFE is

$$V = \frac{\partial \mathscr{V}(E_{0T})}{\partial x_j} = \begin{pmatrix} (\mu+\kappa+\gamma_1) & 0 & 0 \\ -\kappa & (\mu+\alpha+\gamma_2) & 0 \\ -\gamma_1 & -\gamma_2 & \mu \end{pmatrix}$$

The dominant eigenvalues of FV^{-1} which is the spectral of the matrix FV^{-1} gives the basic reproduction number for TB from the model 3.20 as;

$$\mathscr{R}_T = \rho(FV^{-1}) = \frac{\beta_1 \kappa}{(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)} = \left(\frac{\beta_1}{(\mu+\alpha+\gamma_2)}\right)\left(\frac{\kappa}{(\mu+\kappa+\gamma_1)}\right),$$

where

• $\mathscr{R}_T$ is the reproduction number for TB dynamics given by the product of the probability of TB infection β_1 for susceptible per contact with an infectious TB individual and the average time $\left(\frac{1}{(\mu+\alpha+\gamma_2)}\right)$ an individual spends in an infectious class times the product of the rate κ at which a latent TB individual becomes infectious and the average time $\left(\frac{1}{(\mu+\kappa+\gamma_1)}\right)$ an individual spends in the latent class.

Stability analysis of disease-free equilibrium point

The Jacobian matrix of the system of equations 3.20 is given by

$$J = \begin{pmatrix} -(\mu+\lambda_T) & 0 & \frac{-\beta_1}{N} y_S & 0 \\ \lambda_T & -(\mu+\kappa+\gamma_1) & \frac{\beta_1}{N}(y_S+y_T) & \lambda_T \\ 0 & \kappa & -(\mu+\alpha+\gamma_2) & 0 \\ 0 & \gamma_1 & \gamma_2 - \frac{\beta_1}{N} y_T & -(\mu+\lambda_T) \end{pmatrix}.$$

Theorem 3.3.6. *The disease free equilibrium E_{0T} point of TB-only model is locally asymptotically stable (LAS) if $\mathscr{R}_T < 1$ and unstable, if $\mathscr{R}_T > 1$.*

Proof. The Jacobian matrix J evaluated at the disease free equilibrium DFE E_{0T}

point is given as

$$J_{0T} = \begin{pmatrix} -\mu & 0 & -\beta_1 & 0 \\ 0 & -(\mu+\kappa+\gamma_1) & \beta_1 & 0 \\ 0 & \kappa & -(\mu+\alpha+\gamma_2) & 0 \\ 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix}.$$

To determine the stability of disease-free equilibrium point, we use $|J_{0T} - \lambda I| = 0$ to obtain eigenvalues of J_{0T}.

$$|J_{0T} - \lambda I| = \begin{vmatrix} -\mu-\lambda & 0 & -\beta_1 & 0 \\ 0 & -(\mu+\kappa+\gamma_1)-\lambda & \beta_1 & 0 \\ 0 & \kappa & -(\mu+\alpha+\gamma_2)-\lambda & 0 \\ 0 & \gamma_1 & \gamma_2 & -\mu-\lambda \end{vmatrix} = 0$$

$$\lambda_1 = -\mu < 0, \quad \lambda_2 = -\mu < 0$$

and

$$\begin{vmatrix} -(\mu+\kappa+\gamma_1)-\lambda & \beta_1 \\ \kappa & -(\mu+\alpha+\gamma_2)-\lambda \end{vmatrix} = 0,$$

which gives

$$\Big(-(\mu+\kappa+\gamma_1)-\lambda\Big)\Big(-(\mu+\alpha+\gamma_2)-\lambda\Big) - \Big(\beta_1\kappa\Big) = 0. \tag{3.22}$$

From equation 3.22 we have;

$$\lambda^2 + \Big((\mu+\kappa+\gamma_1)+(\mu+\alpha+\gamma_2)\Big)\lambda + \Big((\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2) - \beta_1\kappa\Big) = 0,$$

which can be written in terms of $\mathscr{R}_T$ as

$$\lambda^2 + \Big((\mu+\kappa+\gamma_1)+(\mu+\alpha+\gamma_2)\Big)\lambda + (1-\mathscr{R}_T)(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2) = 0 \tag{3.23}$$

The eigenvalues $\lambda_{3,4}$ of 3.23 are negative or have negative real parts when $1-\mathscr{R}_T > 0$ i.e. when $\mathscr{R}_T < 1$.

Since $\lambda_1,\ \lambda_2,\ \lambda_3,\ \lambda_4$ are all negative or have negative real parts when $\mathscr{R}_T < 1$, we say the disease free equilibrium point is locally asymptotically stable when $\mathscr{R}_T < 1$. This completes the proof. □

We can rewrite model 3.20 as,

$$\begin{aligned} \frac{dU}{dt} &= F(U,V), \\ \frac{dV}{dt} &= G(U,V), \quad G(U,0) = 0, \end{aligned} \tag{3.24}$$

where $U = (y_S, y_T)$ and $V = (y_E, y_I)$, with $U \in \mathscr{R}^2_+$ denoting the number of uninfected individuals and $V \in \mathscr{R}^2_+$ denoting the number of infected individuals.

We now denote the disease free equilibrium by,

$$E_{0T} = (U^*, 0), \quad \text{where} \quad U^* = \left(\frac{\pi}{\mu}, 0\right). \tag{3.25}$$

Conditions $S1$ and $S2$ in equation 3.26 must be satisfied to guarantee local asymptotic stability.

$$\begin{aligned} S1 : \frac{dU}{dt} &= F(U,0), \quad U^* \quad \text{is globally asymptotic stable (g.a.s)} \\ S2 : G(U,V) &= BV - \widehat{G}(U,V), \quad \widehat{G}(U,V) \geq 0 \quad \text{for} \quad (U,V) \in \Theta_2, \end{aligned} \tag{3.26}$$

where $B = D_V G(U^*, 0)$ denotes the M-matrix (the off diagonal elements of B are non-negative) and Θ denotes the region where the model makes biological sense. Theorem 3.3.7 holds if system 3.24 satisfies the conditions in 3.26.

Theorem 3.3.7. *The disease free equilibrium point E_{0T} of HIV-only model is globally asymptotically stable if $\mathscr{R}_T < 1$ and conditions in 3.26 are satisfied.*

Proof. We have from theorem 3.3.6 that E_{0T} is locally asymptotically stable if $\mathscr{R}_T < 1$. Now consider

$$F(U,0) = \begin{pmatrix} \pi - \mu y_S \\ \\ 0 \end{pmatrix}, \tag{3.27}$$

$$G(U,V) = BV - \widehat{G}(U,V), \quad B = \begin{pmatrix} -(\mu+\kappa+\gamma_1) & \beta_1 \\ \\ \kappa & -(\mu+\alpha+\gamma_2) \end{pmatrix}. \tag{3.28}$$

$$\widehat{G}(U,V) = \begin{pmatrix} \widehat{G_1}(U,V) \\ \\ \widehat{G_2}(U,V) \end{pmatrix} = \begin{pmatrix} \beta_1 y_I \left(1 - \frac{y_S + y_T}{N}\right) \\ \\ 0 \end{pmatrix}. \tag{3.29}$$

We have the conditions in 3.26 satisfied since $\widehat{G_1}(U,V) \geq 0$ and $\widehat{G_2}(U,V) = 0 \Rightarrow \widehat{G}(U,V) \geq 0$. And therefore we can conclude that E_{0T} is globally asymptotically stable for $\mathscr{R}_T < 1$. This completes the proof. □

Endemic equilibrium points

We can solve equations in 3.20 in terms of the force of infection $\lambda_T^* = \dfrac{\beta_1}{N^*}(y_I^*)$ to find the conditions for the existence of an equilibrium for which TB is endemic in the population.

Equating the right-hand side of equations 3.20 to zero, we have

$$\begin{aligned} \pi - \lambda_T y_S - \mu y_S &= 0, \\ \lambda_T y_S + \lambda_T y_T - (\mu+\kappa+\gamma_1) y_E &= 0, \\ \kappa y_E - (\mu+\alpha+\gamma_2) y_I &= 0, \\ \gamma_1 y_E + \gamma_2 y_I - \lambda_T y_T - \mu y_T &= 0. \end{aligned} \tag{3.30}$$

From (3.30), we have

$$y_S^* = \frac{\pi}{(\mu+\lambda_T^*)}, \tag{3.31}$$

$$y_E^* = \frac{(\mu+\alpha+\gamma_2)y_I^*}{\kappa}, \tag{3.32}$$

$$y_T^* = \frac{(\mu+\kappa+\gamma_1)y_E^*}{\lambda_T^*} - y_S^*, \tag{3.33}$$

$$y_I^* = \frac{\lambda_T^*\kappa(\mu+\lambda_T^*)y_S^*}{(\mu+\alpha+\gamma_2)\{(\mu+\lambda_T^*)(\mu+\kappa+\gamma_1)-\gamma_1\lambda_T^*\}-\gamma_2\kappa\lambda_T^*}. \tag{3.34}$$

And the endemic equilibrium is given by

$$E_T^* = (y_S^*, y_E^*, y_T^*, y_I^*),$$

$$\text{where} \quad \lambda_T^* = \frac{\beta_1 y_I^*}{N^*}$$

From equation 3.33 we have

$$
\begin{aligned}
y_T^* + y_S^* &= \frac{(\mu+\kappa+\gamma_1)y_E^*}{\lambda_T^*}, \\
\frac{y_T^* + y_S^*}{y_E^*} &= \frac{(\mu+\kappa+\gamma_1)}{\lambda_T^*}, \\
\frac{y_E^*}{y_T^* + y_S^*} &= \frac{\lambda_T^*}{(\mu+\kappa+\gamma_1)}, \\
\frac{y_E^*}{y_T^* + y_S^*} &= \frac{1}{(\mu+\kappa+\gamma_1)}\left(\frac{\beta_1 y_I^*}{N^*}\right), \\
\frac{N^*}{y_T^* + y_S^*} &= \frac{1}{(\mu+\kappa+\gamma_1)}\left(\frac{\beta_1 y_I^*}{y_E^*}\right), \\
\frac{N^*}{y_T^* + y_S^*} &= \frac{1}{(\mu+\kappa+\gamma_1)}\left(\frac{\beta_1 \kappa}{(\mu+\alpha+\gamma_2)}\right), \\
\frac{N^*}{y_T^* + y_S^*} &= \left(\frac{\beta_1 \kappa}{(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)}\right), \\
\frac{N^*}{y_T^* + y_S^*} &= \mathscr{R}_T, \\
\mathscr{R}_T &= \frac{N^*}{y_T^* + y_S^*}, \\
&= \frac{y_S^* + y_E^* + y_T^* + y_I^*}{y_T^* + y_S^*}, \\
&= 1 + \frac{y_E^*}{y_T^* + y_S^*} + \frac{y_I^*}{y_T^* + y_S^*}, \\
\mathscr{R}_T &= 1 + \frac{\lambda_T^*}{(\mu+\kappa+\gamma_1)} + \frac{\lambda_T^* \kappa}{(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)}, \\
\mathscr{R}_T - 1 &= \frac{\lambda_T^*}{(\mu+\kappa+\gamma_1)}\left(1 + \frac{\kappa}{(\mu+\alpha+\gamma_2)}\right), \\
\mathscr{R}_T - 1 &= \lambda_T^* \Omega, \\
\lambda_T^* &= \frac{(\mathscr{R}_T - 1)}{\Omega},
\end{aligned}
\tag{3.35}
$$

where Ω is denoted as the mean infective period for TB which is given by

$$
\Omega = \frac{1}{(\mu+\kappa+\gamma_1)}\left(1 + \frac{\kappa}{(\mu+\alpha+\gamma_2)}\right).
$$

When λ_T^* is substituted into the endemic equilibrium point in 3.31 to 3.34, we will obtain the endemic equilibrium point in terms of $\mathscr{R}_T$ as

$$\begin{aligned} y_S^* &= \frac{\pi\Omega}{\mu\Omega+(\mathscr{R}_T-1)}, \\ y_E^* &= \frac{(\mu+\alpha+\gamma_2)y_I^*}{\kappa}, \\ y_T^* &= \frac{(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)\Omega y_I^*}{\kappa(\mathscr{R}_T-1)} - y_S^*, \\ y_I^* &= \frac{(\pi\kappa(\mathscr{R}_T-1)}{(\mu\Omega+(\mathscr{R}_T-1))(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)-(\mathscr{R}_T-1)(\gamma_1+\kappa\gamma_2(\mu+\alpha+\gamma_2))}. \end{aligned} \tag{3.36}$$

Theorem 3.3.8. *The endemic equilibrium E_T^* point of TB-only model is locally asymptotically stable (LAS) if $\mathscr{R}_T > 1$.*

Proof. The Jacobian matrix J evaluated at the endemic equilibrium E_T^* point is given as

$$J_T^* = \begin{pmatrix} -(\mu+\lambda_T^*) & 0 & \frac{-\beta_1}{N*}y_S^* & 0 \\ \lambda_T^* & -(\mu+\kappa+\gamma_1) & \frac{\beta_1}{\mathscr{R}_T} & \lambda_T^* \\ 0 & \kappa & -(\mu+\alpha+\gamma_2) & 0 \\ 0 & \gamma_1 & \gamma_2-\frac{\beta_1}{N^*}y_T^* & -(\mu+\lambda_T^*) \end{pmatrix}.$$

where $\mathscr{R}_T = \dfrac{N^*}{y_S^*+y_T^*}$ and $\lambda_T^* = \dfrac{(\mathscr{R}_T-1)}{\Omega}$.

To determine the stability of endemic equilibrium point, we use $|J_T^* - \lambda I| = 0$

to obtain eigenvalues of J_T^*.

$$|J_T^* - \lambda I| = \begin{vmatrix} -(\mu+\lambda_T^*)-\lambda & 0 & \frac{-\beta_1}{N*}y_S^* & 0 \\ \lambda_T^* & -(\mu+\kappa+\gamma_1)-\lambda & \frac{\beta_1}{\mathscr{R}_T} & \lambda_T^* \\ 0 & \kappa & -(\mu+\alpha+\gamma_2)-\lambda & 0 \\ 0 & \gamma_1 & \gamma_2 - \frac{\beta_1}{N^*}y_T^* & -(\mu+\lambda_T^*)-\lambda \end{vmatrix} = 0,$$

We have that $\lambda_1 = -(\mu+\lambda_T^*) < 0$ and the characteristic equation is given by

$$\lambda^3 + D\lambda^2 + E\lambda + F = 0.$$

Coefficients D, E and F can be written in form of $\mathscr{R}_T$ as

$$\begin{aligned} D &= (\mu+\kappa+\gamma_1)+(\mu+\alpha+\gamma_2)+(\mu+\lambda_T^*), \\ E &= (\mu+\lambda_T^*)\left((\mu+\kappa+\gamma_1)+(\mu+\alpha+\gamma_2)\right)-\lambda_T^*\gamma_1, \\ &= (\mu+\lambda_T^*)\left((\mu+\kappa)+(\mu+\alpha+\gamma_2)\right)+\mu\gamma_1, \\ F &= \lambda_T^*\left(\frac{\beta_1\kappa}{\mathscr{R}_T}-\gamma_1(\mu+\alpha+\gamma_2)-\kappa\gamma_2\right), \\ &= \lambda_T^*\left((\mu+\kappa)(\mu+\alpha)+\mu\gamma_2\right). \end{aligned}$$

We use the Routh-Hurwitz stability criterion for third order polynomial so as to be sure that all eigenvalues of J_T^* are either negative or have negative real parts. The following conditions must hold for stability:

$$D>0, \quad F>0 \quad \text{and} \quad DE-F>0.$$

Clearly, $D>0$ and $F>0$ when $\mathscr{R}_T>1$.

Now

$$DE-F = \{(\mu+\kappa+\gamma_1)+(\mu+\lambda_T^*)\}\{(\mu+\lambda_T^*)[(\mu+\kappa)+(\mu+\alpha+\gamma_2)]+\mu\gamma_1\}$$

$$+(\mu+\alpha+\gamma_2)\{(\mu+\lambda_T^*)(\mu+\alpha+\gamma_2)+\mu\gamma_1+\mu(\mu+\kappa)\}+\lambda_T^*\gamma_2\kappa>0, \quad \text{when} \quad \lambda_T^*>0 \quad \text{i.e when} \quad \mathscr{R}_T>1.$$

All the Routh-Hurwitz criterion conditions are satisfied when $\mathscr{R}_T > 1$. Hence E_T^* is asymptotically stable when $\mathscr{R}_T > 1$. □

3.3.9 Analysis of the full model

In this section, we will analyse the full model 3.1.

Disease free equilibrium point

Disease-free equilibrium point is a steady state solution where there is no disease in the whole population.

When there are no diseases in the population, the non-negative population values are

$$y_E = y_I = y_{SI} = y_{EI} = y_{II} = y_A = y_T = y_{TI} = 0. \tag{3.37}$$

Set the right hand side of (3.1) to zero and apply 3.37, then our full model has a disease-free equilibrium point (DFE) of

$$E_0 = \left(\frac{\pi}{\mu},\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0\right). \tag{3.38}$$

Reproduction Number $\mathscr{R}_0$

In this case, we have the reproduction number $\mathscr{R}_0$ as the number of HIV/AIDS or TB infections produced by a single TB infective or single HIV/AIDS positive individual.

Note that we have eight infectious classes $y_E, y_I, y_{SI}, y_{EI}, y_{II}, y_A, y_T, y_{TI}$, and the matrix showing the rate of appearance of new infections in compartment i is given

by

$$\mathscr{F} = \begin{pmatrix} \lambda_T(y_S + y_T) \\ 0 \\ \lambda_H y_S \\ \lambda_H y_E + \lambda_T y_{SI} \\ \lambda_H y_I \\ 0 \\ 0 \\ \lambda_H y_T \end{pmatrix}.$$

The matrix showing the rate of transfer of individuals in and out of compartments i is

$$\mathscr{V} = \mathscr{V}^- - \mathscr{V}^+ = \begin{pmatrix} \lambda_H y_E + (\mu + \kappa + \gamma_1) y_E \\ (\mu + \alpha + \gamma_2) y_I + \lambda_H y_I - \kappa y_E \\ \lambda_T y_{SI} + (\mu + \nu + \delta_1) y_{SI} \\ (\mu + \nu + \kappa_H + \delta_2 + \gamma_1) y_{EI} \\ (\mu + \gamma_2 + \delta_3 + \alpha + \nu) y_{II} - k_H y_{EI} \\ (\mu + \tau) y_A - \delta_4 y_{TI} - \delta_1 y_{SI} - \delta_2 y_{EI} - \delta_3 y_{II} \\ (\mu + \lambda_T + \lambda_H) y_T - \gamma_1 y_E - \gamma_2 y_I \\ (\mu + \nu + \delta_4) y_{TI} - \gamma_1 y_{EI} - \gamma_2 y_{II} \end{pmatrix}$$

where

$$\lambda_T = \frac{\beta_1}{N}(y_I + \rho_1 y_{II}) \quad \text{and} \quad \lambda_H = \frac{\beta_2}{N}(y_{SI} + \eta_1 y_{EI} + \eta_2 y_{II} + \eta_3 y_{TI})$$

The Jacobian matrix of $\mathscr{F}$ evaluated at the disease free equilibrium E_0 point, is

given by

$$F = \frac{\partial \mathscr{F}(E_0)}{\partial x_j} = \begin{pmatrix} 0 & \beta_1 & 0 & 0 & \beta_1\rho_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 & \beta_2\eta_1 & \beta_2\eta_2 & 0 & 0 & \beta_2\eta_3 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where $x_j = y_E, y_I, y_{SI}, y_{EI}, y_{II}, y_A, y_T, y_{TI}$ for $j = 1, \ldots, 8$. Let

$$\begin{aligned} a_1 &= \mu + \kappa + \gamma_1, \\ a_2 &= \mu + \alpha + \gamma_2, \\ a_3 &= \mu + \nu + \delta_1, \\ a_4 &= \mu + \nu + \kappa_H + \delta_2 + \gamma_1, \\ a_5 &= \mu + \gamma_2 + \delta_3 + \alpha + \nu, \\ a_6 &= \mu + \tau, \\ a_7 &= \mu + \nu + \delta_4, \end{aligned}$$

so that the Jacobian matrix of $\mathscr{V}$ evaluated at the disease free equilibrium E_0 point is

$$V = \frac{\partial \mathscr{V}(E_0)}{\partial x_j} = \begin{pmatrix} a_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\kappa & a_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & a_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\kappa_H & a_5 & 0 & 0 & 0 \\ 0 & 0 & -\delta_1 & -\delta_2 & -\delta_3 & a_6 & 0 & -\delta_4 \\ -\gamma_1 & -\gamma_2 & 0 & 0 & 0 & 0 & \mu & 0 \\ 0 & 0 & 0 & -\gamma_1 & -\gamma_2 & 0 & 0 & a_7 \end{pmatrix}.$$

The dominant eigenvalues of FV^{-1} which is the spectral of the matrix FV^{-1} gives

the basic reproduction number for TB and HIV/AIDS from the model 3.1 as;

$$\mathscr{R}_0 = \rho(FV^{-1}) = \max\{\mathscr{R}_H, \mathscr{R}_T\},$$

$$\text{where} \quad \mathscr{R}_H = \frac{\beta_2}{(\mu+\nu+\delta_1)},$$

$$\mathscr{R}_T = \left(\frac{\beta_1}{(\mu+\alpha+\gamma_2)}\right)\left(\frac{\kappa}{(\mu+\kappa+\gamma_1)}\right),$$

and these correspond to the reproduction number for HIV sub-model and TB sub-model respectively.

Stability analysis of disease-free equilibrium point

Theorem 3.3.10. *The disease free equilibrium E_0 point of the full model is locally asymptotically stable (LAS) if $\mathscr{R}_0 < 1$ and unstable, if $\mathscr{R}_0 > 1$.*

Proof. The Jacobian matrix of the system of equations (3.1) evaluated at E_0 is given by

$$J = \begin{pmatrix} -\mu & 0 & -\beta_1 & -\beta_2 & -\beta_2\eta_1 & -\beta_1\rho_1 - \beta_2\eta_2 & 0 & 0 & -\beta_2\eta_3 \\ 0 & -a_1 & \beta_1 & 0 & 0 & \beta_1\rho_1 & 0 & 0 & 0 \\ 0 & \kappa & -a_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_2 - a_3 & \beta_2\eta_1 & \beta_2\eta_2 & 0 & 0 & \beta_2\eta_3 \\ 0 & 0 & 0 & 0 & -a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \kappa_H & -a_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & \delta_3 & -a_6 & 0 & \delta_4 \\ 0 & \gamma_1 & \gamma_2 & 0 & 0 & 0 & 0 & -\mu & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & \gamma_2 & 0 & 0 & -a_7 \end{pmatrix}.$$

To determine the stability of disease-free equilibrium point, we use $|J_0 - \lambda I| = 0$

to obtain eigenvalues of J_0.

$$\begin{vmatrix} -\mu-\lambda & 0 & -\beta_1 & -\beta_2 & -\beta_2\eta_1 & -\beta_1\rho_1-\beta_2\eta_2 & 0 & 0 & -\beta_2\eta_3 \\ 0 & -a_1-\lambda & \beta_1 & 0 & 0 & \beta_1\rho_1 & 0 & 0 & 0 \\ 0 & \kappa & -a_2-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_2-a_3-\lambda & \beta_2\eta_1 & \beta_2\eta_2 & 0 & 0 & \beta_2\eta_3 \\ 0 & 0 & 0 & 0 & -a_4-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \kappa_H & -a_5-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & \delta_3 & -a_6-\lambda & 0 & \delta_4 \\ 0 & \gamma_1 & \gamma_2 & 0 & 0 & 0 & 0 & -\mu-\lambda & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & \gamma_2 & 0 & 0 & -a_7-\lambda \end{vmatrix} = 0,$$

$$\lambda_{1,2} = -\mu < 0,$$

and the matrix reduces to

$$\begin{vmatrix} -a_1-\lambda & \beta_1 & 0 & 0 & \beta_1\rho_1 & 0 & 0 \\ \kappa & -a_2-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2-a_3-\lambda & \beta_2\eta_1 & \beta_2\eta_2 & 0 & 0 \\ 0 & 0 & 0 & -a_4-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & \kappa_H & -a_5-\lambda & 0 & 0 \\ 0 & 0 & \delta_1 & \delta_2 & \delta_3 & -a_6-\lambda & 0 \\ \gamma_1 & \gamma_2 & 0 & 0 & 0 & 0 & -\mu-\lambda \end{vmatrix} = 0.$$

We have $\lambda_3 = -(\mu+\nu+\kappa_H+\delta_2+\gamma_1) < 0$, $\lambda_4 = -(\mu+\gamma_2+\delta_3+\alpha+\nu) < 0$ and $\lambda_5 = -(\mu+\nu+\delta_4) < 0$,

so that either

$$\Big(\beta_2 - (\mu+\nu+\delta_1) - \lambda\Big)\Big(-(\mu+\tau)-\lambda\Big) = 0. \tag{3.39}$$

or

$$\Big(-(\mu+\kappa+\gamma_1)-\lambda\Big)\Big(-(\mu+\alpha+\gamma_2)-\lambda\Big) - \beta_1\kappa = 0. \tag{3.40}$$

From equation (3.39) we have;

$$\lambda^2 + \Big((\mu+\nu+\delta_1)+(\mu+\tau)-\beta_2\Big)\lambda + \Big((\mu+\nu+\delta_1)(\mu+\tau) - \beta_2(\mu+\tau)\Big) = 0,$$

which can be written in terms of $\mathscr{R}_H$ as

$$\lambda^2 + \Big((\mu+\tau)+(\mu+\nu+\delta_1)(1-\mathscr{R}_H)\Big)\lambda + (1-\mathscr{R}_H)(\mu+\tau)(\mu+\nu+\delta_1) = 0 \tag{3.41}$$

The eigenvalues of 3.41 are negative or have negative real parts when $1-\mathscr{R}_H > 0$ i.e. when $\mathscr{R}_H < 1$. Equation 3.40 can also be written in terms of $\mathscr{R}_T$ as;

$$\lambda^2 + \Big((\mu+\kappa+\gamma_1)+(\mu+\alpha+\gamma_2)\Big)\lambda + (1-\mathscr{R}_T)(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2), \tag{3.42}$$

The eigenvalues of (3.42) are negative or have negative real parts when $1-\mathscr{R}_T > 0$ i.e. when $\mathscr{R}_T < 1$ Since all eigenvalues are negative or have negative real parts when $\mathscr{R}_H < 1$ and when $\mathscr{R}_T < 1$, we say the disease free equilibrium point is locally asymptotically stable when $\mathscr{R}_H < 1$ and when $\mathscr{R}_T < 1$. And the disease dies out. The basic reproduction number $\mathscr{R}_0 = \max\{\mathscr{R}_H, \mathscr{R}_T\} < 1$. Hence, we say that the disease free equilibrium point E_0 is locally asymptotically stable whenever $\mathscr{R}_0 < 1$. This completes the proof. □

We can rewrite model 3.1 as,

$$\begin{aligned} \frac{dU}{dt} &= F(U,V), \\ \frac{dV}{dt} &= G(U,V), \quad G(U,0) = 0, \end{aligned} \tag{3.43}$$

where $U = (y_S, y_T)$ and $V = (y_E, y_I, y_{SI}, y_{EI}, y_{II}, y_A, y_{TI})$, with $U \in \mathscr{R}^2_+$ denoting the number of uninfected individuals and $V \in \mathscr{R}^7_+$ denoting the number of infected individuals.

We now denote the disease free equilibrium by,

$$E_0 = (U^*, 0), \quad \text{where} \quad U^* = \left(\frac{\pi}{\mu}, 0\right). \tag{3.44}$$

Conditions $S1$ and $S2$ in equation 3.45 must be satisfied to guarantee local asymp-

totic stability.

$$\begin{aligned} S1: \frac{dU}{dt} &= F(U,0), \quad U^* \quad \text{is globally asymptotic stable (g.a.s)} \\ S2: G(U,V) &= CV - \widehat{G}(U,V), \quad \widehat{G}(U,V) \geq 0 \quad \text{for} \quad (U,V) \in \Theta, \end{aligned} \tag{3.45}$$

where $C = D_V G(U^*, 0)$ denotes the M-matrix (the off diagonal elements of C are non-negative) and Θ denotes the region where the model makes biological sense. Theorem 3.3.11 holds if system 3.43 satisfies the conditions in 3.45.

Theorem 3.3.11. *The disease free equilibrium point E_0 of the full model is globally asymptotically stable if $\mathscr{R}_0 < 1$ and conditions in 3.45 are satisfied.*

Proof. We have from theorem 3.3.10 that E_0 is locally asymptotically stable if $\mathscr{R}_0 < 1$. Now consider

$$F(U,0) = \begin{pmatrix} \pi - \mu y_S \\ \\ -\mu y_T \end{pmatrix}, \tag{3.46}$$

$$G(U,V) = CV - \widehat{G}(U,V), \tag{3.47}$$

$$C = \begin{pmatrix} -a_1 & \beta_1 & 0 & 0 & \beta_1\rho_1 & 0 & 0 \\ \kappa & -a_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 - a_3 & \beta_2\eta_1 & \beta_2\eta_2 & 0 & \beta_2\eta_3 \\ 0 & 0 & 0 & -a_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & \kappa_H & -a_5 & 0 & 0 \\ 0 & 0 & \delta_1 & \delta_2 & \delta_3 & -a_6 & \delta_4 \\ 0 & 0 & 0 & \gamma_1 & \gamma_2 & 0 & -a_7 \end{pmatrix}. \tag{3.48}$$

$$\widehat{G}(U,V)=\begin{pmatrix}\widehat{G_1}(U,V)\\ \widehat{G_2}(U,V)\\ \widehat{G_3}(U,V)\\ \widehat{G_4}(U,V)\\ \widehat{G_5}(U,V)\\ \widehat{G_6}(U,V)\\ \widehat{G_7}(U,V)\end{pmatrix}=\begin{pmatrix}\beta_1\left(1-\frac{y_S+y_T}{N}\right)(y_I+\rho_1 y_{II}+\rho_2 y_A)+\lambda_H y_E\\ \lambda_H y_I\\ \beta_2\left(1-\frac{1}{N}\right)(y_{SI}+\eta_1 y_{EI}+\eta_2 y_{II}+\eta_3 y_{TI}+\eta_4 y_A)+\lambda_T y_{SI}\\ -\lambda_H y_E-\lambda_T y_{SI}\\ -\lambda_H y_I\\ 0\\ -\lambda_H y_T\end{pmatrix}. \tag{3.49}$$

We have the condition $(S2)$ in 3.45 not satisfied since $\widehat{G_4}(U,V)<0$, $\widehat{G_5}(U,V)<0$ and $\widehat{G_7}(U,V)<0$. And therefore we can conclude that E_0 may not be globally asymptotically stable for $\mathscr{R}_0<1$. This completes the proof. □

Endemic equilibrium points

The computation of the endemic equilibrium of the full model (co-infection model) is difficult analytically, and therefore the model 3.1 endemic equilibria corresponds to,

1. $E_1=(y_{S1},0,0,y_{SI1},0,0,y_{A1},0,0)$

$$(y_{S1},0,0,y_{SI1},0,0,y_{A1},0,0)=\left(\frac{\pi\Pi}{\mu\Pi+(\mathscr{R}_H-1)},0,0,\frac{(\mathscr{R}_H-1)y_{S1}}{\Pi(\mu+\nu+\delta_1)},0,0,\frac{\delta_1(\mathscr{R}_H-1)y_{S1}}{\Pi(\mu+\tau)(\mu+\nu+\delta_1)}\right), \tag{3.50}$$

the TB free equilibrium. This exists when $\mathscr{R}_H>1$. The analysis of the equilibria E_1 is similar to the endemic equilibria E_H^* in equation 3.19.

2. $E_2 = (y_{S2}, y_{E2}, y_{I2}, 0, 0, 0, 0, y_{T2}, 0)$, the HIV free equilibrium, where

$$\begin{aligned} y_{S2} &= \frac{\pi\Omega}{\mu\Omega + (\mathscr{R}_T - 1)}, \\ y_{E2} &= \frac{(\mu+\alpha+\gamma_2)y_{I2}}{\kappa}, \\ y_{T2} &= \frac{(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2)\Omega y_{I2}}{\kappa(\mathscr{R}_T - 1)} - y_{S2}, \\ y_{I2} &= \frac{\pi\kappa(\mathscr{R}_T - 1)}{(\mu\Omega + (\mathscr{R}_T - 1))(\mu+\kappa+\gamma_1)(\mu+\alpha+\gamma_2) - (\mathscr{R}_T - 1)(\gamma_1 + \kappa\gamma_2(\mu+\alpha+\gamma_2))}. \end{aligned} \tag{3.51}$$

   This exists when $\mathscr{R}_T > 1$. The analysis of the equilibria E_2 is similar to the endemic equilibria E_T^* in equation 3.36.

3. $E_3 = (y_{S3}, y_{E3}, y_{I3}, y_{SI3}, y_{EI3}, y_{II3}, y_{A3}, y_{T3}, y_{TI3})$, the HIV-TB co-infection equilibrium. This exists when each component of E_3 is positive.

We summarize the existence of the disease free equilibrium points in the following theorem:

Theorem 3.3.12. *The system of equations 3.1 has the following disease free equilibrium points:*

1. *E_{0H} which exist when $\mathscr{R}_H < 1$.*
2. *E_{0T} which exist when $\mathscr{R}_T < 1$.*
3. *E_0 which exists when $\mathscr{R}_H < 1$ and $\mathscr{R}_T < 1$, i.e. $\mathscr{R}_0 < 1$.*

And summarize the existence of the endemic equilibrium points in the following theorem:

Theorem 3.3.13. *The system of equations in 3.1 has the following endemic equilibrium points:*

1. *E_H^* or E_1 which exist when $\mathscr{R}_H > 1$.*
2. *E_T^* or E_2 which exist when $\mathscr{R}_T > 1$.*

3. *E_3 which exists when $\mathscr{R}_H > 1$ and $\mathscr{R}_T > 1$, i.e. $\mathscr{R}_0 > 1$. We will give a detailed explanation of E_3 in our numerical simulations.*

Remarks:

The model revealed the following scenarios regarding the effects of HIV/AIDS and Tuberculosis in an endemic section:

1. A scenario where we have population of individuals infected with only TB (TB sub-model).

2. A scenario where we have population of individuals infected with only HIV (HIV sub-model).

3. A scenario where there are individuals with both infection (co-infection model).

We shall also explore the impact of these scenarios on the progression of HIV and TB infection using numerical simulations.

In summary, we have been able to show the mathematical analysis for TB sub-model, HIV sub-model and the full co-infection model. We show that the basic reproduction number $\mathscr{R}_0$ determines the dynamics of the model. Disease free equilibrium point E_0 is also shown to be locally asymptotically stable when $\mathscr{R}_0 < 1$ and unstable if $\mathscr{R}_0 > 1$, we therefore have that solutions converge to E_0 and diseases die out. We show that the Endemic equilibrium point E^* is locally asymptotically stable if $\mathscr{R}_0 > 1$ and unstable if $\mathscr{R}_0 < 1$, we then have that solutions converge to E^* and any initial epidemics of TB and HIV/AIDS will become endemic in the population. Our analytical results will be justified by our numerical simulations.

Chapter 4

Numerical Simulations and Sensitivity analysis

Results of the numerical simulation are given in this section and the set of parameters used are given in table 4.1. Initial values used for different values of β_1 and β_2 is also given in table 4.2.

Table 4.1: Parameter values and their sources

Symbol	Value	References	Symbol	Value	References
$N(0)$	$500,000$		δ_1	$0.1\ yr^{-1}$	[22, 23]
π	7142		δ_2	$0.102\ yr^{-1}$	[5]
μ	$1/70\ yr^{-1}$	[9, 22, 23]	δ_3	$0.25\ yr^{-1}$	[5]
β_1	Variable		δ_4	$0.125\ yr^{-1}$	[21]
β_2	Variable		γ_1	$1\ yr^{-1}$	[22]
τ	$0.33\ yr^{-1}$	[5, 23]	γ_2	$2\ yr^{-1}$	[22]
ν	$0.01\ yr^{-1}$	[21]	ρ_1	100	[20]
α	$0.02\ yr^{-1}$	[21]	η_1	1	
κ	$1\ yr^{-1}$	[22]	η_2	1	
κ_H	1.3κ	[22]	η_3	1	

Table 4.2: Initial values for different values of β_1 and β_2.

β_1	β_2	$y_S(0)$	$y_E(0)$	$y_I(0)$	$y_{SI}(0)$	$y_{EI}(0)$	$y_{II}(0)$	$y_A(0)$	$y_T(0)$	$y_{TI}(0)$
2.5	0.03	$\frac{60N}{100}$	$\frac{15N}{100}$	$\frac{2N}{100}$	$\frac{4N}{100}$	$\frac{14N}{100}$	$\frac{4N}{100}$	$\frac{N}{100}$	0	0
5.2	0.3	$\frac{60N}{100}$	$\frac{15N}{100}$	$\frac{2N}{100}$	$\frac{4N}{100}$	$\frac{14N}{100}$	$\frac{4N}{100}$	$\frac{N}{100}$	0	0
5.2	0.03	$\frac{60N}{100}$	$\frac{15N}{100}$	$\frac{2N}{100}$	$\frac{4N}{100}$	$\frac{14N}{100}$	$\frac{4N}{100}$	$\frac{N}{100}$	0	0
0.4	0.8	$\frac{60N}{100}$	$\frac{15N}{100}$	$\frac{2N}{100}$	$\frac{4N}{100}$	$\frac{14N}{100}$	$\frac{4N}{100}$	$\frac{N}{100}$	0	0
7	0.6	$\frac{60N}{100}$	$\frac{15N}{100}$	$\frac{2N}{100}$	$\frac{4N}{100}$	$\frac{14N}{100}$	$\frac{4N}{100}$	$\frac{N}{100}$	0	0
5.2	0.03	$\frac{99N}{100}$	$\frac{N}{100}$	0	0	0	0	0	0	0
2.5	0.03	0	N	0	0	0	0	0	0	0
0.4	0.8	$\frac{99N}{100}$	0	0	$\frac{N}{100}$	0	0	0	0	0
2.5	0.03	0	0	0	N	0	0	0	0	0

4.1 Sensitivity Analysis

We are able to know how important each parameter is to the spread of the disease through sensitivity indices of $\mathscr{R}_0$ to all different parameters. This is helpful in assigning the correct and appropriate parameter for making an endemic scenario [20].

Sensitivity analysis in this section describes the effect of changes in the parameter values on the model. Now we will let ε be any of the non-negative parameters that make up $\mathscr{R}_0$ in the model. A small perturbation in ε by $\Delta\varepsilon$ will also cause a perturbation in $\mathscr{R}_0$ by $\Delta\mathscr{R}_0$. We define the normalized sensitivity index by Υ_ε (the ratio of the corresponding normalized changes[9]). Therefore, the sensitivity index Υ_ε is computed by using the normalized forward sensitivity index method:

$$\Upsilon_\varepsilon = \frac{\Delta\mathscr{R}_0}{\mathscr{R}_0} \Big/ \frac{\Delta\varepsilon}{\varepsilon} = \frac{\varepsilon}{\mathscr{R}_0} \cdot \frac{\partial\mathscr{R}_0}{\partial\varepsilon}. \tag{4.1}$$

We can calculate the sensitivity index in terms of $\mathscr{R}_H$ and $\mathscr{R}_T$ since $\mathscr{R}_0 = \max\{\mathscr{R}_H, \mathscr{R}_T\}$.
The sensitivity indices in terms of $\mathscr{R}_H = \dfrac{\beta_2}{(\mu+\nu+\delta_1)}$ is given as

$$\Upsilon_{\beta_2} = 1, \quad \Upsilon_\mu = \frac{-\mu}{(\mu+\nu+\delta_1)}, \quad \Upsilon_\nu = \frac{-\nu}{(\mu+\nu+\delta_1)}, \quad \Upsilon_{\delta_1} = \frac{-\delta_1}{(\mu+\nu+\delta_1)}.$$

The sensitivity indices of $\mathscr{R}_T = \left(\dfrac{\beta_1}{(\mu+\alpha+\gamma_2)}\right)\left(\dfrac{\kappa}{(\mu+\kappa+\gamma_1)}\right)$ is given as

$$\Upsilon_{\beta_1} = 1, \quad \Upsilon_{\gamma_2} = \frac{-\gamma_2}{(\mu+\alpha+\gamma_2)}, \quad \Upsilon_\alpha = \frac{-\alpha}{(\mu+\alpha+\gamma_2)}, \quad \Upsilon_{\gamma_1} = \frac{-\gamma_1}{(\mu+\kappa+\gamma_1)}, \quad \Upsilon_\kappa = \frac{\mu+\gamma_1}{(\mu+\kappa+\gamma_1)},$$

$$\Upsilon_{\mu} = -\frac{\mu}{(\mu+\alpha+\gamma_2)} - \frac{\mu}{(\mu+\kappa+\gamma_1)}$$

Most parameter values used were gotten from previous HIV-TB model manuscripts [5, 9, 20–23]. Using the parameter values in table 4.1, the sensitivity indexes are computed in table 4.3 and 4.4 as

Table 4.3: Sensitivity analysis of $\mathscr{R}_H$.

Sensitivity index	Value
Υ_{β_2}	1
Υ_{μ}	-0.0141
Υ_{ν}	-0.0805
Υ_{δ_1}	-0.8046

Table 4.4: Sensitivity analysis of $\mathscr{R}_T$.

Sensitivity index	Value
Υ_{β_1}	1
Υ_{γ_2}	-0.9831
Υ_{α}	-0.0098
Υ_{γ_1}	-0.4965
Υ_{κ}	0.5035
Υ_{μ}	-0.0141

The sign in front of each of the values in tables 4.3 and 4.4 shows what will happen to $\mathscr{R}_0$ if the parameter is increased or decreased. $\mathscr{R}_0(\mathscr{R}_H$ or $\mathscr{R}_T)$ increases when sensitivity indeces with positive signs increase, while $\mathscr{R}_0(\mathscr{R}_H$ or $\mathscr{R}_T)$ decreases when sensitivity indeces with negative signs increase and vice versa.

The most sensitive parameters to $\mathscr{R}_H$ and $\mathscr{R}_T$ are found to be β_2 and β_1 respectively. Sensitivity indeces $\Upsilon_{\beta_1} = 1$ and $\Upsilon_{\beta_2} = 1$ mean that $\mathscr{R}_H$ or $\mathscr{R}_T$ approximately decreases by 1% when either β_1 or β_2 is decreased by 1%.

Since decrease in β_1 and β_2 is the possible intervention strategy for the reduction of $\mathscr{R}_0$. We will consider changes of parameters β_1 and β_2 and see their effects on $\mathscr{R}_T$ and $\mathscr{R}_H$.

4.2 Numerical simulations for different values of β_1, β_2 and discussion of results

All parameter values used in the simulations are given in table 4.1. Table 4.2 shows different initial conditions for different values of β_1 and β_2. It shows the effect of β_1 on $\mathscr{R}_T$ and the effect of β_2 on $\mathscr{R}_H$.

In general, 500 years from our figures may not be a reasonable timescale from the model to be predictive, but we have decided to use it as an illustration to show that TB infection persists for decades.

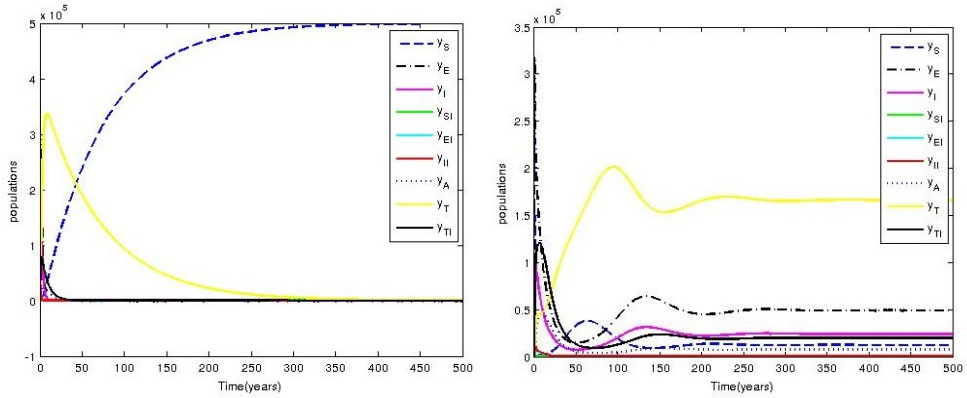

Figure 4.1: The left panel shows the plot of the stability analysis of the disease free equilibrium at $\beta_1 = 2.5$ and $\beta_2 = 0.03$ while the right panel shows the plot of the stability analysis of the endemic equilibrium at $\beta_1 = 5.2$ and $\beta_2 = 0.3$

From the left panel figure of figure 4.1, we considered initial conditions from table 4.2 and $\mathscr{R}_0 < 1$ ($\mathscr{R}_T < 1$ and $\mathscr{R}_H < 1$) to establish the stability of the disease free equilibrium E_0 given by 3.38. It is shown numerically that y_S converges to N as $t \to \infty$, and every other disease in the population dies out. From the right panel figure of figure 4.1, we considered initial conditions from table 4.2 and $\mathscr{R}_0 > 1$ ($\mathscr{R}_T > 1$ or $\mathscr{R}_H > 1$) to establish the stability of the endemic equilibrium E^*. We have shown numerically that for $\mathscr{R}_0 > 1$ and as t$\to \infty$, the state variables converge to E^* and the endemic equilibrium exist.

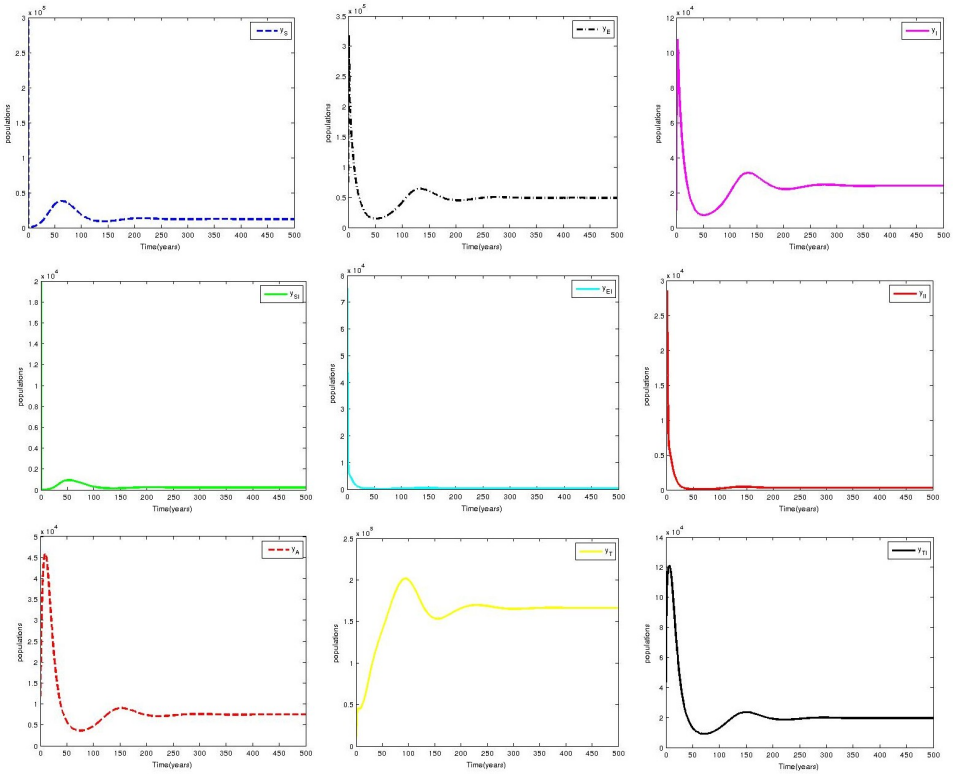

Figure 4.2: Graphs showing the susceptibles y_S, exposed to TB y_E, infectious to TB y_I, the HIV positive y_{SI}, HIV positive exposed to TB y_{EI}, HIV positive suffering from TB y_{II}, those suffering from AIDS y_A, singly infected treated of TB y_T and dually infected treated of TB y_{TI}. These are simulations in different compartments with $\beta_1 = 5.2$ and $\beta_2 = 0.3$

Figure 4.2 represents the behaviour of individuals in various stages of the co-infection of HIV/AIDS and TB over a period of 500 years in which treatment of latent and active TB treatment is incorporated.

Left panel figure on the first row shows that treatment of TB reduces the susceptible population to a stable state and remains constant. It shows that when $t \to \infty$, susceptible does not go to zero due to TB treatment.

Middle panel figure on the third row shows the behaviour of individuals infected with TB and on TB. Individuals on TB treatment increase with respect to decrease in all other TB infected individuals and we can see from middle panel

figure on the first row that untreated TB infection leads to increase in the number of infected individuals.

Middle and right panel figures on the first row, and, left and right panel figures on the third row show that treatment of TB result in their decrease to low levels. These imply that the population of TB individuals decrease up to a certain stage and become constant as $t \to \infty$ and does not go to zero due to TB treatment. Left panel figure on the second row shows that the population drops and starts increasing due to some AIDS individuals recovering from TB for the dually infected individuals. Middle and right panel figures on the second row show a decrease in the number of dually infected individuals to almost zero where they remain constant due to the number of those entering the AIDS class, those on TB treatment and due to deaths (natural and disease deaths).

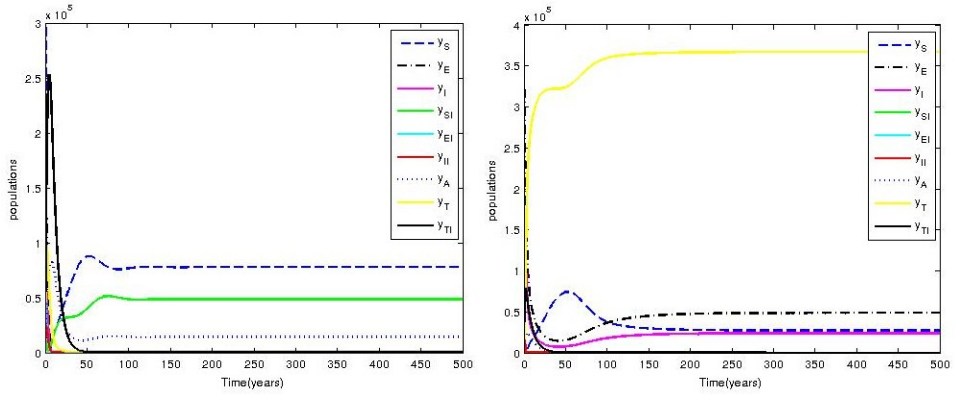

Figure 4.3: The left panel shows the plot of the stability of TB free equilibrium E_H^* at $\beta_1 = 0.4$ and $\beta_2 = 0.8$ while the right panel shows the plot of the stability of HIV free equilibrium E_T^* at $\beta_1 = 5.2$ and $\beta_2 = 0.03$

The left panel figure of figure 4.3 shows the stability of TB free equilibrium E_H^*. It shows that HIV/AIDS persist in the society while other disease dies out. The population has a higher number of susceptible individuals exposing the population to a slower progression towards AIDS due to TB treatment. The model responds to changing β_1 and β_2 to 0.4 and 0.8 respectively. It means TB free equilibrium occurs when β_1 is very low and β_2 is very high i.e when $\mathscr{R}_T < 1$ and $\mathscr{R}_H > 1$ and this represents TB-only model. The right panel figure of figure 4.3 shows the

stability of HIV free equilibrium E_T^*. This shows that TB persists in the society while the other disease dies out. The model responds to changing β_1 and β_2 to 5.2 and 0.03 respectively. It means HIV free equilibrium occurs when β_1 is very high and β_2 is very low i.e when $\mathscr{R}_T > 1$ and $\mathscr{R}_H < 1$ and this represents HIV-only model.

Figure 4.4 shows the effect and impact of treating and not treating TB on the model. Comparing figure on the right and left panel where TB is treated and not treated respectively, we see that latent TB y_E decreases faster in the right panel making TB infectious y_I and HIV positive with TB disease y_{II} increase and exposing the population to a faster progression towards the AIDS class within the period of 15 years. While this is the other way in left panel due to TB treatment. TB treatment lowers the rate of progression of the exposed individuals and this leads to increase in dually infected individuals on TB treatment. We can say that TB treatment at the exposed and infectious stage may prevent or reduce co-infection.

From the right panel of figure 4.4, we observe that after 3 years, individuals infected with TB disease and HIV reduce than in the left panel. This happens because TB is treated in the left panel and untreated in the right panel. The decrease in the population of y_{II} in the right panel is because co-infection triggers the symptoms of AIDS and therefore decrease in y_{II} would lead to increase in y_A.

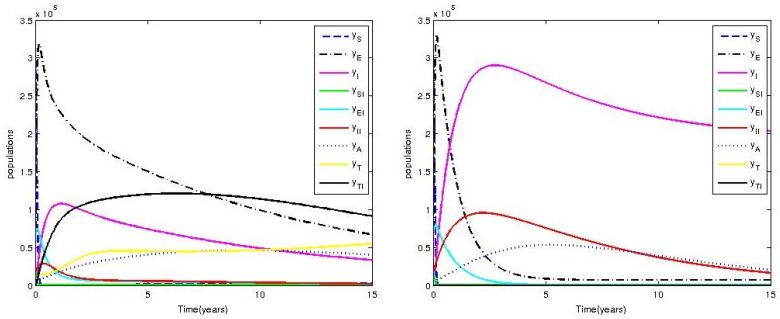

Figure 4.4: The behaviour of the model for the period of 15 years with and without TB treatment γ_1 and γ_2 at $\beta_1 = 7, \beta_2 = 0.6$ and with disease induced death. The left panel shows the impact of TB treatment ($\gamma_1 = 1$ and $\gamma_2 = 2$) on the model, while the right panel shows the behaviour of the model without TB treatment ($\gamma_1 = 0$ and $\gamma_2 = 0$).

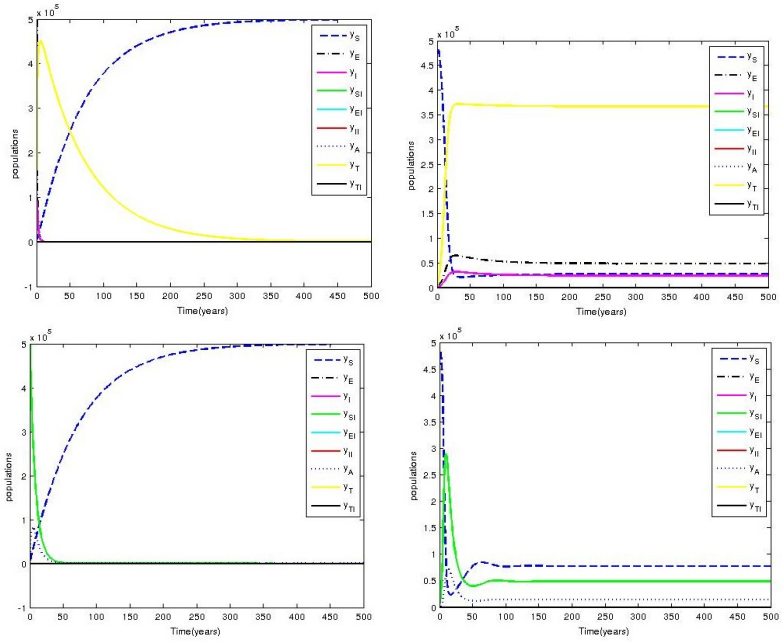

Figure 4.5: Graphs showing the behaviour of the model to changes in initial conditions. The plot of the stability of equilibria E_{0T}, E_{0H}, E_T^* and E_H^*

Figure 4.5 shows the behaviour and response of the model to different initial conditions. The left panel figure on the first row is the disease free E_{0T} for TB-sub model and it shows that TB infection dies out while susceptible goes to N as $t \to \infty$. The left panel figure on the second row is the disease free E_{0H} for HIV-sub model and it shows that HIV infection dies out while susceptible goes to N as $t \to \infty$. Figures on the right panel of the first and second row are respectively similar to figure 4.3 and their descriptions follow from figure 4.3.

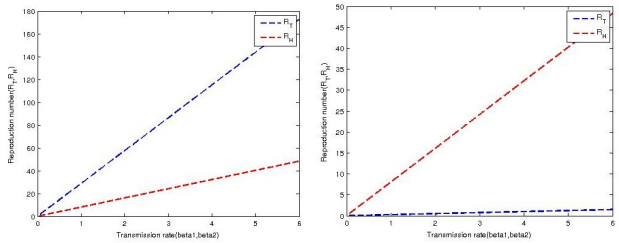

Figure 4.6: Graphs showing different values of the basic reproduction numbers $\mathscr{R}_T$ and $\mathscr{R}_H$ at different values of β_1 and β_2 respectively, with and without TB treatment

Figure 4.6 can be explained from the analytical solution that $\mathscr{R}_0$ from the interaction of two diseases (HIV/AIDS and TB) is illustrated as $\max\{\mathscr{R}_H, \mathscr{R}_T\}$ and this is shown in figure 4.6. We have the left panel figure in 4.6 by varying β_1 and β_2 from 0 to 6 with no TB treatment while we have the right panel figure in 4.6 by varying β_1 and β_2 from 0 to 6 with TB treatment . The disease threshold is determined by the value of our parameters. Varying β_1 and β_2 with TB treatment and using the parameter values from table 4.1, we find from the right panel of figure 4.6 that $\mathscr{R}_H$ is greater than $\mathscr{R}_T$ and therefore $\mathscr{R}_H$ is the epidemic threshold value when TB is treated. Also,varying β_1 and β_2 without TB treatment and using the parameter values from table 4.1, we find from the left panel of figure 4.6 that $\mathscr{R}_T$ is greater than $\mathscr{R}_H$ and therefore $\mathscr{R}_T$ is the epidemic threshold value when TB is not treated. These mean that it is possible for the disease threshold to change if we increase or decrease β_1 or β_2 and with or without TB treatment, e.g. $\gamma_1 = 0, \gamma_2 = 0$ as in the left panel changes $\mathscr{R}_0$ to $\mathscr{R}_T$ while $\gamma_1 = 1, \gamma_2 = 2$ as in the right panel changes $\mathscr{R}_0$ to $\mathscr{R}_H$.

4.3 Conclusion

We considered a general mathematical model of nine nonlinear differential equations on HIV/AIDS and TB co-infection. We denoted the population of susceptible individuals by y_S, the population of latent TB individuals by y_E, the population of infectious (active) TB individuals by y_I, the population of HIV-positive individuals by y_{SI}, the population of HIV-positive and latent TB individuals by y_{EI}, the

population of HIV-positive and infectious TB individuals by y_{II}, the population of AIDS individuals by y_A, the population of treated individuals with TB by y_T and the population of dually infected individuals treated of TB by y_{TI}.

The threshold parameter $\mathscr{R}_0$ was calculated and used to determined the conditions under which the HIV/AIDS and TB could be transmitted and remained endemic in the population. We analyzed the model to know the level at which the HIV/AIDS epidemic aggravates the spread of Tuberculosis (TB) and vice versa. We thus showed that three disease-free equilibrium points E_{0H}, E_{0T}, E_0 respectively for HIV-sub model, TB-sub model and the full model are locally asymptotically stable when $\mathscr{R}_0 < 1$ i.e. $\mathscr{R}_T < 1$ and $\mathscr{R}_H < 1$. We also showed that the population with both HIV and TB infection have three endemic equilibrium points E_H^*, E_T^*, E^* respectively for HIV-sub model, TB-sub model and the full model which are locally asymptotically stable when $\mathscr{R}_0 > 1$ i.e. $\mathscr{R}_T > 1$ or $\mathscr{R}_H > 1$. Global stability analysis of the three disease-free equilibrium points was established. We found the most sensitive parameters to be β_1 and β_2 and showed how changes to these parameters with or without TB treatment affect the basic reproduction number.

Numerical simulations were used to compare the endemic scenarios revealed by analytical results. Simulations were purely hypothetical since the data used are not for a particular community but the qualitative features that revealed the impact of each of the scenarios on HIV/AIDS and TB transmission were shown. Figure 4.6 gave a linear relationship between the two reproduction number, and this showed that $\mathscr{R}_T$ gave the epidemic threshold value when TB was not treated, while $\mathscr{R}_H$ gave the epidemic threshold value with TB treatment. Our results suggested that the better scenarios are where some of the individuals (the right panel of figure **??**) have lower infection levels i.e. when TB was treated, and the worst scenarios are where there are co-infection of both HIV/AIDS and TB (the left panel of figure **??**) without TB treatment.

Thus, we can interpret the situation in an epidemiological manner that a society with some individuals infected with TB and without TB treatment is at the worst risk of being co-infected with HIV which in turn creates socio-economic effects if no intervention is implemented in time for either or both HIV/AIDS and TB infection. We conclude that TB treatment for individuals with TB infections results in a significant reduction (as in the left panel of figure 4.4) of the number of individuals

progressing to active TB, reduction of the co-infected individuals and reduction of the disease induced death. Also, effective treatment of TB for the co-infected individuals also reduced the number of individuals that progress to AIDS class. Thus in a situation where treatment of HIV is not readily available, we can therefore advise public health authorities that treating both the exposed and active form of TB in both singly and dually TB infected individuals could be a good public health measure to improve life for HIV-positive individuals.

As part of future work to improve the model in question, restructuring of the model to include HIV/AIDS treatment for only HIV/AIDS individuals (HIV-sub model) and co-infected individuals could be a better approach to studying the dynamics of HIV/AIDS and TB, and could be the best measure to reduce $\mathscr{R}_0$ and co-infection. We also wish to find the global stability of the endemic equilibrium points in the future work and a nonlinear relationship between $\mathscr{R}_T$ and $\mathscr{R}_H$. Despite all its limitations, the model provided useful information and insights into the potential impact of treating Tuberculosis on the dynamics of HIV/AIDS and TB co-infection.

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