

MATHEMATICAL MODELING OF TB - HIV CO INFECTION, CASE STUDY OF TIGANIA WEST SUB COUNTY, KENYA.

Abstract

TB is one the leading causes of death among individuals infected with HIV/AIDS. A deterministic model for HIV/TB co-infection is presented and analysed. The analysis of model includes determining the reproduction number, finding the local and global stability of the DFE, showing that the model has an unique endemic equilibrium point, the bifucation and the sensitivity analysis of the model. The stability of the model shows that the model is stable if $R_0 < 1$ and unstable otherwise. The research seeks to investigate the impact of HIV/AIDS on TB infections. Numerical simulation shows that HIV infection speeds the progression from exposed to infectious/active TB. The two diseases exhibit synergistic relationship where the infection of one disease accelerates the progression of the other. The model also seeks to confirm the need of HIV testing of all TB patients. From the sensitivity analysis and simulation, treatment reduces the spread of TB in the population among the TB infected and HIV/TB infected individuals. Numerical simulation is done using data from Tigania West Sub County Hospital.

Key words: Basic reproduction number, disease free equilibrium(DFE), endemic equilibrium(EEP), local and global of equilibrium points.

1 Introduction

TB is a bacterial disease caused by mycobacterial tuberculosis (*tubercle bacilli*). It was not clear how TB was transmitted until Robert koch's brilliant discovery of the *tubercle*

bacillus in 1982 [4]. The bacteria lives in the lungs of the infected host. They spread in the air when infectious individual sneeze, cough, speak or sing[4], [15]. Once infected, the person stays infected for many years, possibly latent infected for life. People with latent TB infection do not fall sick and do not have any symptoms. They are not infectious and cannot spread TB to others. TB bacteria become infectious if the immune system cannot stop them from growing.

HIV- the Human Immunodeficiency Virus, is the etiological agent responsible for the Acquired Immunodeficiency Syndrome (AIDS). HIV is transmitted either through sexual intercourse, sharing needles with HIV infected persons or via HIV contaminated blood transfusion. Also infants may acquire HIV at birth or through breast feeding if the mother is HIV positive, HIV virus infects cells of immune system, destroying or impairing their functions. As the infection progresses the immune system becomes weaker and the person becomes susceptible to infections. These infections damages the immune system which causes latent TB to develop to infectious TB. The two diseases exhibit some sort of synergistic relationship, where each accelerates the progression of the other. One third of 39.5 million HIV infected people world wide are co-infected with TB and up to fifty percent of the individuals living with HIV are expected to likely develop TB [5]. Many TB carries who are infected with HIV are 30 to 50 times more likely to develop active TB than those without HIV [5]. The HIV epidemic has significantly impacted the dynamics of TB. For individuals infected with HIV, the presence of other infectious diseases including TB tends to increase the rate of HIV replication. TB has proven to be difficult to control in regions with high prevalence of HIV. The impact of HIV prevalence on TB dynamics will be explored in this paper.

A few statistical or mathematical models of TB have been made. These include, [1], [2], [3], [7], [5], [14]. HIV is modeled mathematical by, [12], [11]. TB/HIV co infection models have also been modeled by [4], [5],[12], [11] to explore the consequences of joint dynamics at the population. Sharomi, Podder and Gumel (2008) designed and qualitatively analyzed a new and more comprehensive HIV/TB deterministic model for gaining insights to the transmission dynamics and control of the two diseases in a population. Their study showed that the prospects of effective treatment for both diseases was bright. Roger, Feng and Castillo-Chavez (2009) focused on the joint dynamics of HIV and TB in a pseudo - competitive environment at the population. The model was used to explore the impact of factors associated with co-infection on the prevalence of each of the two diseases. They found out that the progression from HIV to AIDS is the same for a person with or without latent TB infection. The focus of this study is to examine the impact of HIV on TB infection with treatment of TB and management of HIV using ART(Antiretroviral Therapy).

2 Model Description and Formulation

This model includes all sexually active human population at time t denoted by $N(t)$. This is divided into subpopulation of Susceptible individuals $S(t)$, individuals exposed to TB only (latent TB) $E_T(t)$, individuals with infectious TB $I_T(t)$, individuals treated for TB $T_T(t)$, individuals with HIV only but no clinical symptoms of AIDS $I_H(t)$, individuals infected with HIV infection with no symptoms of AIDS and exposed to TB $E_{HT}(t)$, individuals dually infected with HIV and TB, displaying symptoms of TB (infectious TB) but no AIDS symptoms $I_{HT}(t)$, HIV infected individuals displaying AIDS symptoms $A_H(t)$, individuals treated for TB and infected with HIV $T_{HT}(t)$ and individuals treated for TB and HIV $T_{TH}(t)$. So that the total population $N(t)$ is given by

$$N(t) = S(t) + E_T(t) + I_T(t) + I_H(t) + T_T(t) + E_{HT}(t) + I_{HT}(t) + A_H(t) + T_{HT}(t) \quad (1)$$

The differential equations associated with the model are

$$\begin{cases} \frac{dS}{dt} = \Lambda - (\lambda_T + \lambda_H + \mu)S, \\ \frac{dE_T}{dt} = \lambda_T S + \phi_1 T_T - (\mu + \pi + \tau)E_T, \\ \frac{dI_T}{dt} = \pi E_T - (\mu + \delta_T + \gamma + \omega)I_T, \\ \frac{dT_T}{dt} = \gamma I_T - (\phi_1 + \mu + \delta_T)T_T, \\ \frac{dI_H}{dt} = \lambda_H S - (\alpha + \psi + \mu)I_H, \\ \frac{dE_{HT}}{dt} = \tau E_T + \psi I_H + \phi_2 T_{HT} - (k + \delta_H + \mu)E_{HT}, \\ \frac{dI_{HT}}{dt} = \omega I_T + k E_{HT} - (\mu + \delta_T + \epsilon + \delta_H)I_{HT}, \\ \frac{dA_H}{dt} = \alpha I_H - (\delta_H + \mu)A_H, \\ \frac{dT_{HT}}{dt} = \epsilon I_{HT} - (\phi_2 + \mu + \delta_H)T_{HT}. \end{cases} \quad (2)$$

λ_H and λ_T are the force of infection of HIV and TB respectively given by:

$$\begin{cases} \lambda_T = \beta_T(\eta_1 I_T + \eta_2 I_{HT}) \\ \lambda_H = \beta_H(\xi_1 I_H + \xi_2 E_{HT} + \xi_3 I_{HT} + \xi_4 T_{HT}) \end{cases} \quad (3)$$

Where β_H and β_T is the effective contact rate of HIV and TB respectively.

3 Model Analysis

3.1 Invariant Region

We consider the total population given by N in equation (1). The derivatives of the equation (1) is:

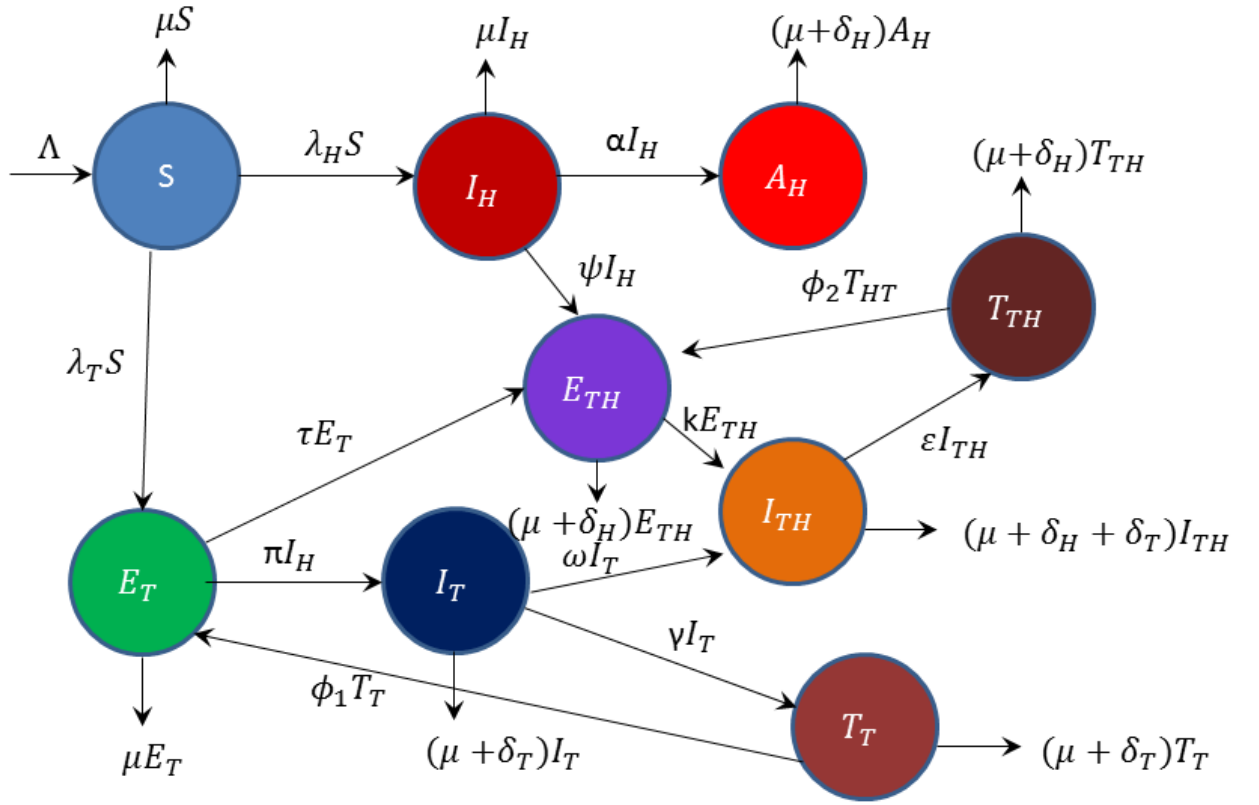


Figure 1: Flow chart of HIV/TB co-infection

$$\begin{aligned} \frac{dN}{dt} &= \frac{dS}{dt} + \frac{dE_T}{dt} + \frac{dI_T}{dt} + \frac{dT_T}{dt} + \frac{dE_{HT}}{dt} + \frac{dI_{HT}}{dt} + \frac{dA_H}{dt} + \frac{dT_{HT}}{dt}, \\ \frac{dN}{dt} &= \Lambda - N\mu - (I_T + I_{HT})\delta_T - (I_{HT} + I_H + E_{HT} + T_{HT} + A_H)\delta_H. \end{aligned}$$

In the absence of mortality rate due to TB and HIV we have

$$\frac{dN}{dt} \leq \Lambda - N\mu \quad (4)$$

Integrating both sides of (4) we have

$$\Lambda - N\mu \geq Ae^{-\mu t} \quad (5)$$

Where A is the constant of integration. Applying the initial conditions $N(0) = N_0$ at $t = 0$, i get the value of A as

$$A \leq \Lambda - N_0\mu. \quad (6)$$

Substituting the value of A into equation (5) and letting $t \rightarrow \infty$ i get,

$$N \leq \frac{\Lambda}{\mu}. \quad (7)$$

This implies that the value of N ranges from zero to $\frac{\Lambda}{\mu}$ i.e $0 \leq N \leq \frac{\Lambda}{\mu}$. Thus for all future time t , the model enters and remains in the region:

$$\Omega = \{S, E_T, I_T, T_T, T_H, E_{TH}, I_{TH}, A_H, T_{TH} \in R_+^9 : N \leq \frac{\Lambda}{\mu}\}. \quad (8)$$

Therefore the model is well posed mathematically and epidemiologically, hence i can study the dynamics of the model in Ω

3.2 Positivity of the Solutions

Assuming that the initial conditions are all nonnegative, ($S > 0, E_T > 0, I_T > 0, I_H > 0, E_{TH} > 0, I_{TH} > 0, T_T > 0, A_H > 0, T_{TH} > 0$), it is shown that the solutions of the model are also positive. Considering the system of equation (2), let us take the first equation:

$$\frac{dS}{dt} = \Lambda - (\lambda_T + \lambda_H + \mu)S, \rightarrow \frac{dS}{dt} \geq (\lambda_T + \lambda_H + \mu)S$$

Integrating both sides i get,

$$\frac{1}{(\lambda_T + \lambda_H + \mu)} \ln S \geq -t + C. \quad (9)$$

Where C is a constant of integration. Introducing the exponential and simplifying equation (9) we have:

$$S \geq Ae^{-(\lambda_T + \lambda_H + \mu)t} \quad (10)$$

Where A is a constant. Finding the value of A when $t = 0$, equation (10) becomes

$$S(t) \geq S(0)e^{-(\lambda_T + \lambda_H + \mu)t} \geq 0. \quad (11)$$

Considering the second equation of (2) which is

$$\begin{cases} \frac{dE_T}{dt} = \lambda_T S + \phi_1 T_T - (\mu + \pi + \tau)E_T, \rightarrow \\ \frac{dE_T}{dt} \geq -(\mu + \pi + \tau)E_T. \end{cases} \quad (12)$$

Integrating by separation of variables and using the initial conditions the following is obtained:

$$E_T(t) \geq E_T(0)e^{-(\mu + \pi + \tau)t} \geq 0 \quad (13)$$

Similarially the third equation of (2) is evaluated as follows:

$$\begin{cases} \frac{dI_T}{dt} = \pi E_T - (\mu + \delta_T + \gamma + \omega)I_T, \rightarrow \\ \frac{dI_T}{dt} \geq -(\mu + \delta_T + \gamma + \omega)I_T. \rightarrow \\ I_T(t) \geq I_T(0)e^{-(\mu+\delta_T+\gamma+\omega)t} \geq 0 \end{cases} \quad (14)$$

The same process is applied to the other equations of (2) and the results are:

$$\begin{cases} I_T(t) \geq I_T(0)e^{-(\phi_1+\mu+\delta_T)t} \geq 0 \\ I_H(t) \geq I_H(0)e^{-(\alpha+\psi+\mu+\pi)t} \geq 0 \\ E_{TH}(t) \geq E_{TH}(0)e^{-(k+\delta_H+\mu)t} \geq 0 \\ I_{TH}(t) \geq I_{TH}(0)e^{-(\epsilon+\delta_T+\mu+\delta_H)t} \geq 0 \\ A_H(t) \geq A_H(0)e^{-(\delta_H+\mu)t} \geq 0 \\ T_{TH}(t) \geq T_{TH}(0)e^{-(\phi_2+\delta_H+\mu)t} \geq 0 \end{cases} \quad (15)$$

Therefore all the solutions of the model are all positive.

3.3 Disease Free Equilibrium (DFE)

To evaluate the DFE, the right hand side of equation (2) is equated to zero and solving it at $E_T = I_T = T_T = I_H = E_{TH} = I_{TH} = A_H = T_{TH} = 0$. Therefore the DFE (E_0) is given by:

$$E_0 = \left\{ \frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0 \right\} \quad (16)$$

3.3.1 Basic Reproduction Number R_0 and Local Stability of DFE

Basic reproduction number R_0 is the average number of secondary cases produced by an average infectious individual in a totally susceptible population. It measures the transmission potential of infectious diseases. To estimate the basic reproduction number the next generation matrix method is used[13]. The model equations are written starting

with the newly infective classes.

$$\begin{cases} \frac{dE_T}{dt} = \lambda_T S + \phi_1 T_T - k_1 E_T, \\ \frac{dI_T}{dt} = \pi E_T - k_2 I_T, \\ \frac{dT_T}{dt} = \gamma I_T - k_3 T_T, \\ \frac{dI_H}{dt} = \lambda_H S - k_4 I_H, \\ \frac{dE_{HT}}{dt} = \tau E_T + \psi I_H + \phi_2 T_{HT} - k_5 E_{HT}, \\ \frac{dI_{HT}}{dt} = \omega I_T - k_6 I_{HT}, \\ \frac{dA_H}{dt} = \alpha I_H - k_7 A_H, \\ \frac{dT_{HT}}{dt} = \epsilon I_{HT} - k_8 T_{HT} \end{cases} \quad (17)$$

Where $k_1 = \mu + \pi + \tau$, $k_2 = \mu + \delta_T + \gamma + \omega$, $k_3 = \phi_1 + \mu + \delta_T$, $k_4 = \alpha + \psi + \mu + \pi$, $k_5 = k + \delta_H + \mu$, $k_6 = \mu + \delta_T + \epsilon + \delta_H$, $k_7 = \delta_H + \mu$, $k_8 = \phi_2 + \mu + \delta_H$.

We let F to represent the new infection and V to represent the transfer of infection. The basic reproduction number is given by the spectra radius of the matrix $F.V^{-1}$.

$$\begin{cases} F = \left\{ \frac{\partial F_i(x_0)}{\partial x_j} \right\}, \\ V = \left\{ \frac{\partial V_i(x_0)}{\partial x_j} \right\}. \\ i, j = 1, 2, 3, \dots, 8 \end{cases} \quad (18)$$

$$F = \begin{pmatrix} 0 & \frac{\Lambda \eta_1 \beta_T}{\mu} & 0 & 0 & 0 & \frac{\Lambda \beta_T \eta_2}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\Lambda \xi_1 \beta_H}{\mu} & \frac{\Lambda \xi_2 \beta_H}{\mu} & \frac{\Lambda \xi_3 \beta_H}{\mu} & 0 & \frac{\Lambda \xi_4 \beta_H}{\mu} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} k_1 & 0 & -\phi_1 & 0 & 0 & 0 & 0 & 0 \\ -\pi & k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma & k_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & k_4 & 0 & 0 & 0 & 0 \\ -\tau & 0 & 0 & -\psi & k_5 & 0 & 0 & -\phi_2 \\ 0 & -\omega & 0 & 0 & -\kappa & k_6 & 0 & 0 \\ 0 & 0 & 0 & -\alpha & 0 & 0 & k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\epsilon & 0 & k_8 \end{pmatrix}$$

The eigenvalues of the matrix $F.V^{-1}$ are: $\lambda_1 = \lambda_2 = \lambda_3 = \lambda_4 = \lambda_5 = \lambda_6 = 0$, $\lambda_7 = \frac{\Lambda \beta_H \xi_2}{\mu k_5}$, $\lambda_8 = \frac{\pi \Lambda k_3 \beta_T (k_6 \eta_1 + \omega \eta_2)}{\mu k_6 (k_1 k_2 k_3 - \pi \gamma \phi_1)}$. The reproduction number of our model is given by the largest

eigenvalue of $F.V^{-1}$. The reproduction numbers of the model (2) are:

$$R_{0H} = \frac{\Lambda\beta_H\xi_2}{\mu k_5} \quad (19)$$

$$R_{0T} = \frac{\pi\Lambda k_3\beta_T(k_6\eta_1 + \omega\eta_2)}{\mu k_6(k_1k_2k_3 - \pi\gamma\phi_1)} \quad (20)$$

Theorem 1 *The DFE point of the model is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

From equation (19) and (20), it is clear that $R_{0H} > 0$. We also know from the values of k_1, k_2, k_3 that $k_1, k_2, k_3 > \pi\gamma\phi_1$. With this information we can conclude that $R_{0H} > 1$ and $R_{0T} > 1$. Hence our model is unstable.

3.3.2 Global Stability of DFE

To investigate global stability of our model we use the method used by Castillo-Chevez and Song (2004) [?]. The theorem of [?] is as follows:

Theorem 2 *The fixed point $U_0 = (x^*, 0)$ is a globally asymptotic stable (g.a.s.) equilibrium of (2) provided that $R_0 < 1$ (l.a.s.) and that assumptions (H1) and (H2) are satisfied.*

Proof. We re-write model (2) as:

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

Where X represent the uninfected classes and Z represent the infected and infectious classes. So $X = (S)$ and $Z = (E_T, I_T, T_T, I_H, E_{TH}, I_{TH}, A_H, T_{TH})$. The DFE point of the model (2) is $U_0 = (X^*, 0) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0)$. The point $U_0 = (X^*, 0)$ is globally asymptotically stable (g.a.s) if $R_0 < 1$ (which is the condition for local stability) and the conditions $H1$ and $H2$ are:

(H1), for $\frac{dX}{dt} = F(X, 0)$, X^* is g.a.s,

(H2). $G(X, Z) = AZ - \hat{G}(X, Z)$, $\hat{G}(X, Z) \geq 0$ for $(X, Z) \in R_+^9$ where $A = D_Z G(X, Z)$ is a M-matrix (the off diagonal elements of A are nonnegative) and R_+^9 is the region where the model makes biological sense.

In our model,

$$F(X, 0) = \Lambda - (\lambda_T + \lambda_H + \mu),$$

$$A = \begin{pmatrix} -k_1 & \beta_T \eta_1 & \phi_1 & 0 & 0 & \beta_T \eta_2 & 0 & 0 \\ \pi & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma & -k_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -k_4 + \beta_H \xi_1 & \beta_H \xi_2 & \beta_H \xi_3 & 0 & \beta_H \xi_4 \\ \tau & 0 & 0 & \psi & -k_5 & 0 & 0 & \phi_2 \\ 0 & \omega & 0 & 0 & 0 & -k_6 & 0 & 0 \\ 0 & 0 & 0 & \alpha & 0 & 0 & -k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \epsilon & 0 & -k_8 \end{pmatrix}$$

The off diagonal elements of matrix A are nonnegative. $G(X, Z) = AZ - \hat{G}(X, Z)$ where

$$\hat{G}(X, Z) = \begin{pmatrix} \beta_T \eta_1 I_T (1 - \frac{S}{N}) + \beta_T \eta_2 I_{TH} (1 - \frac{S}{N}) \\ 0 \\ 0 \\ \beta_H (\xi_1 I_H + \xi_2 E_{HT} + \xi_3 I_{HT} + \xi_4 T_{HT}) (1 - \frac{S}{N}) \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Since $0 \leq S \leq N$, then $\hat{G}(X, Z) \geq 0$ and the model (2) is g.a.s.

3.4 Endemic Equilibrium Point (EEP)

The EEP of the model is denoted by $E^* = (S^*, E_T^*, I_T^*, T_T^*, I_H^*, E_{TH}^*, I_{TH}^*, A_H^*, T_{TH}^*)$, which occurs when the disease persist in the community. To find conditions necessary for the existence of the endemic equilibrium, the system of equations (2) are equated to zero and solved to obtain:

$$\begin{cases} S^* = \frac{\Lambda}{\mu + \lambda_H^* + \lambda_T^*} \\ E_T^* = \frac{\Lambda k_2 k_3 \lambda_T^*}{(\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_T^* = \frac{\pi \Lambda k_3 \lambda_T^*}{(\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ T_T^* = \frac{\pi \gamma \Lambda \lambda_T^*}{(\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_H^* = \frac{\Lambda \lambda_H^*}{k_4 (\mu + \lambda_H^* + \lambda_T^*)} \\ E_{HT}^* = \frac{\Lambda k_6 k_8 (k_2 k_3 (\psi k_1 \lambda_H^* + k_4 \lambda_T^*) - \pi \gamma \psi \lambda_H^* \phi_1 + \pi \epsilon \Lambda \omega k_3 k_4 \phi_2)}{k_4 k_5 k_6 k_8 (\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_{HT}^* = \frac{\pi \Lambda \omega k_3 \lambda_T^*}{k_6 (\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ A_H^* = \frac{\alpha \Lambda \lambda_H^*}{k_4 k_7 (\mu + \lambda_H^* + \lambda_T^*)} \\ T_{HT}^* = \frac{\pi \epsilon \Lambda \omega k_3 \lambda_T^*}{k_6 k_8 (\mu + \lambda_H^* + \lambda_T^*)(k_1 k_2 k_3 - \pi \gamma \phi_1)} \end{cases} \quad (21)$$

The force of TB infection is given by

$$\lambda_T^* = \beta_T(\eta_1 I_T^* + \eta_2 I_{HT}^*).$$

Substituting I_T^* and I_{HT}^* into λ_T^* and solving using mathematica we obtain:

$\lambda_T^* = 0$, which corresponds to DFE and

$$\lambda_T^* = -\mu - \lambda_H^* - \frac{\pi \Lambda \beta_T^* k_3 (k_6 \eta_1 + \omega \eta_2)}{k_6 (k_1 k_2 k_3 - \pi \gamma \phi_1)},$$

which corresponds to EEP. We further solve β_T^* in terms of the reproduction number R_{0T} and substitute into λ_T^* in order to find conditions necessary for $\lambda_T^* > 0$.

$$\beta_T^* = \frac{k_6 R_{0T} (\mu k_1 k_2 k_3 - \pi \gamma \mu \phi_1)}{\pi \Lambda k_3 (k_6 \eta_1 + \omega \eta_2)} \quad (22)$$

$$\lambda_T^* = \mu (R_{0T} - 1) - \lambda_H^* \quad (23)$$

Substituting λ_T^* into equation (21) we get:

$$\left\{ \begin{array}{l} S^* = \frac{\Lambda}{\mu R_{0T}} \\ E_T^* = \frac{\Lambda k_2 k_3 (\mu (R_{0T} - 1) - \lambda_H^*)}{\mu R_{0T} (k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_T^* = \frac{\Lambda \pi k_3 (\mu (R_{0T} - 1) - \lambda_H^*)}{\mu R_{0T} (k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ T_T^* = \frac{\pi \gamma \Lambda (\mu (R_{0T} - 1) - \lambda_H^*)}{\mu R_{0T} (k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_H^* = \frac{\Lambda \lambda_H}{\mu k_4 R_{0T}} \\ E_{HT}^* = \frac{\Lambda k_6 k_8 (k_2 k_3 (\tau k_4 (\mu (R_{0T} - 1) - \lambda_H) + \psi k_1 \lambda_H) - \pi \gamma \psi \lambda_H \phi_1) + \pi \epsilon \Lambda k_3 k_4 (\mu (R_{0T} - 1) - \lambda_H) \phi_2}{\mu k_4 k_5 k_6 k_8 (k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ I_{HT}^* = \frac{\pi \Lambda \omega k_3 (\mu (R_{0T} - 1) - \lambda_H)}{\mu k_6 R_{0T} (k_1 k_2 k_3 - \pi \gamma \phi_1)} \\ A_H^* = \frac{\alpha \Lambda \lambda_H}{\mu k_4 k_7 R_{0T}} \\ T_{HT}^* = \frac{\pi \epsilon \Lambda \omega k_3 (\mu (R_{0T} - 1) - \lambda_H)}{\mu k_6 k_8 R_{0T} (k_1 k_2 k_3 - \pi \gamma \phi_1)} \end{array} \right. \quad (24)$$

Theorem 3 If $R_0 > 1$, the model has an unique endemic equilibrium.

We need to show that equation (24) makes biological by having all population classes greater than zero. This will be possible if $(R_{0T} - 1) \lambda_H > 0$ and $k_1 k_2 k_3 > \pi \gamma \phi_1$. We know that $k_1 k_2 k_3 > \pi \gamma \phi_1$ from earlier definition. Inoder for $(R_{0T} - 1) \lambda_H > 0$, then $R_{0T} > 1$ and $(R_{0T} - 1) > \lambda_H$. Hence we coclude that the model has an unique endemic equilibrium.

3.5 Bifurcation of the Model

To investigate the presence of the EEP we let $S = x_1, E_T = x_2, I_T = x_3, T_T = x_4, I_H = x_5, E_{HT} = x_6, I_{HT} = x_7, A_H = x_8, T_{HT} = x_9$. Model (2) can now be written in the form

$\frac{dX}{dt} = F(X)$ where $F = (f_1, f_2, f_3, \dots, f_9)$ as shown below:

$$\begin{cases} \frac{dx_1}{dt} = \Lambda - (\lambda_T + \lambda_H + \mu)x_1, \\ \frac{dx_2}{dt} = \lambda_T x_1 + \phi_1 x_4 - (\mu + \pi + \tau)x_2, \\ \frac{dx_3}{dt} = \pi x_2 - (\mu + \delta_T + \gamma + \omega)x_3, \\ \frac{dx_4}{dt} = \gamma x_3 - (\phi_1 + \mu + \delta_T)x_4 \\ \frac{dx_5}{dt} = \lambda_H x_1 - (\alpha + \psi + \mu + \pi)x_5, \\ \frac{dx_6}{dt} = \tau x_2 + \psi x_5 + \phi_2 x_9 - (k + \delta_H + \mu)x_6, \\ \frac{dx_7}{dt} = \omega x_3 - (\mu + \delta_T + \epsilon + \delta_H)x_7, \\ \frac{dx_8}{dt} = \alpha I_H - (\delta_H + \mu)x_8, \\ \frac{dx_9}{dt} = \epsilon x_7 - (\phi_2 + \mu + \delta_H)x_9. \end{cases} \quad (25)$$

The Jacobian of (23) at DFE is given by:

$$J(E^0) = \begin{pmatrix} -\mu & 0 & -g_1 & -g_2 & -g_3 & -g_4 & -g_5 & 0 & -g_6 \\ 0 & -k_1 & 0 & \phi_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & \pi & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & -k_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -k_4 & 0 & 0 & 0 & 0 \\ 0 & \tau & 0 & 0 & \psi & -k_5 & 0 & 0 & \phi_2 \\ 0 & 0 & \omega & 0 & 0 & 0 & -k_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha & 0 & 0 & -k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \epsilon & 0 & -k_8 \end{pmatrix} \quad (26)$$

Where

$$g_1 = \frac{\Lambda \beta_T \eta_1}{\mu}, g_2 = \frac{\Lambda \beta_T \eta_2}{\mu}, g_3 = \frac{\Lambda \beta_H \xi_1}{\mu}, g_4 = \frac{\Lambda \beta_H \xi_2}{\mu}, g_5 = \frac{\Lambda \beta_H \xi_3}{\mu}, g_6 = \frac{\Lambda \beta_H \xi_4}{\mu}.$$

We now calculate the right eigenvectors of $J(E^0)$ denoted by $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9)^T$.

$$\begin{pmatrix} -\mu & 0 & -g_1 & -g_2 & -g_3 & -g_4 & -g_5 & 0 & -g_6 \\ 0 & -k_1 & 0 & \phi_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & \pi & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & -k_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -k_4 & 0 & 0 & 0 & 0 \\ 0 & \tau & 0 & 0 & \psi & -k_5 & 0 & 0 & \phi_2 \\ 0 & 0 & \omega & 0 & 0 & 0 & -k_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha & 0 & 0 & -k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \epsilon & 0 & -k_8 \end{pmatrix} \begin{pmatrix} w_1 \\ w_2 \\ w_3 \\ w_4 \\ w_5 \\ w_6 \\ w_7 \\ w_8 \\ w_9 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad (27)$$

Equation (25) can be written as

$$\begin{cases} -\mu w_1 - g_1 w_3 - g_2 w_4 - g_3 w_5 - g_4 w_6 - g_5 w_7 - g_6 w_9 = 0 \\ -k_1 w_2 + \phi_1 w_4 = 0 \\ \pi w_2 - k_2 w_3 = 0 \\ \gamma w_3 - k_3 w_4 = 0 \\ -k_4 w_5 = 0 \\ \tau w_2 + \psi w_5 - k_5 w_6 + \phi_2 w_9 = 0 \\ \omega w_3 - k_6 w_7 = 0, \\ \alpha w_5 - k_7 w_8 = 0, \\ \epsilon w_7 - k_8 w_9 = 0. \end{cases} \quad (28)$$

From (26) we obtain:

$$w_1 = \frac{-(g_1 w_3 + g_3 w_4 + g_4 w_6 + g_5 w_7 + g_6 w_9)}{\mu} < 0, w_2 > 0, w_3 > 0, w_4 > 0, w_7 > 0, w_9 > 0,$$

$$w_5 = w_8 = 0, w_6 = \frac{\gamma w_2 + \phi_2 w_9}{k_5} > 0.$$

The left eigenvectors of $J(E^0)$, denoted by $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9)^T$ is calculated as follows:

$$\begin{pmatrix} -\mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -k_1 & \pi & 0 & 0 & \tau & 0 & 0 & 0 \\ -g_1 & 0 & -k_2 & \gamma & 0 & 0 & \omega & 0 & 0 \\ \phi_1 - 2 & \phi_1 & 0 & -k_3 & 0 & 0 & 0 & 0 & 0 \\ -g_3 & 0 & 0 & 0 & -k_4 & \psi & 0 & \alpha & 0 \\ -g_4 & 0 & 0 & 0 & 0 & -k_5 & 0 & 0 & 0 \\ -g_5 & 0 & 0 & 0 & 0 & 0 & -k_6 & 0 & \epsilon \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -k_7 & 0 \\ -g_8 & 0 & 0 & 0 & 0 & \phi_2 & 0 & 0 & -k_8 \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \\ v_8 \\ v_9 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad (29)$$

Equation (28) can also be written as:

$$\begin{cases} -\mu v_1 = 0 \\ -k_1 v_2 + \pi v_3 + \tau v_6 = 0, \\ -g_1 v_1 - k_2 v_3 + \gamma v_4 + \omega v_7 = 0 \\ -g_2 v_1 + \phi_1 v_2 - k_3 v_4 = 0 \\ -g_3 v_1 - k_4 v_5 + \psi v_6 + \alpha v_8 = 0 \\ -g_4 v_1 - k_5 v_6 = 0 \\ -g_5 v_1 - k_6 v_7 + \epsilon v_9 = 0 \\ -k_7 v_8 = 0 \\ -g_6 v_1 + \phi_2 v_6 - k_8 v_9 = 0 \end{cases} \quad (30)$$

Solving equation (28) gives

$$v_1 = v_5 = v_6 = v_7 = v_8 = v_9 = 0; v_2 = \frac{\pi v_3}{k_1} > 0; v_3 = \frac{\gamma v_4}{k_2} > 0; v_4 = \frac{\phi_2 v_2}{k_3} > 0.$$

We use centre manifold theory discussed in [?] to investigate the nature of the bifurcation of model (2). The centre manifold theory is given below.

Theorem 4 Consider the following genereal systems of ordinary differential equation with parameter β^*

$$\frac{dx}{dt} = f(x, \beta^*), R^n \times R \rightarrow R \text{ and } f \in C^2(R^n \times R),$$

Where 0 is the equilibrium point of the system (that is, $f(x, \beta^*) \equiv 0$ for all β^*) and assume **A1**: $A = D_x f(0, 0) = (\frac{df_i}{dx_j}(0, 0))$ is the linearization matrix of the system (4.21) around the equilibrium 0 with β^* evaluated at 0. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts: **A2**: Matrix a has a nonnegative right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue. let f_k be the k^{th} component of f and

$$a = \sum_k v_k w_i w_j \frac{d^2 f_k}{dx_i dx_j}(0, 0)$$

$$b = \sum_k v_k w_i \frac{f^2 f_k}{dx_i d\beta^*}(0, 0)$$

The local dynamics of the system around 0 is totally determined by the signs of a and b.

- i. $a > 0, b > 0$. When $\beta^* < 0$ with $|\beta^*| \ll 1$, 0 is locally asymptotically stable and there exist a positive unstable equilibrium: when $0 < \beta^* \ll 1$, 0 is unstable and there exists a negative, locally asymptotically stable equilibrium:
- ii. $a < 0, b < 0$. When $\beta^* < 0$ with $\beta \ll 1$, 0 is unstable, when $0 < \beta^* \ll 1$, 0 is locally asymptotically stable equilibrium, and there exist a positive unstable equilibrium.
- iii. $a > 0, b < 0$. When $\beta^* < 0$ with $|\beta^*| \ll 1$, 0 is unstable, and there exist a locally asymptotically stable negative equilibrium: when $0 < \beta^* \ll 1$, 0 is stable, and a positive unstable equilibrium appears.

iv. $a < 0, b > 0$. When β^* changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

The values of a and b are as follows:

$$a = v_2 w_1 \beta_T \frac{\Delta}{\mu} (w_3 \eta_1 + w_4 \eta_2) < 0, \text{ since } w_1 < 0 \text{ and } v_2, w_3, w_4 > 0.$$

$$b = v_2 \frac{\Delta}{\mu} (w_2 \eta_1 + w_4 \eta_2) > 0.$$

Hence from theorem (4) above, item (iv), $a < 0$ and $b > 0$, β^* changes from negative to positive, 0 changes its stability from stable to unstable. Also negative unstable equilibrium becomes positive and locally asymptotically stable.

3.6 Sensitivity analysis of the model

The sensitivity analysis of the model is done to identify which parameters have great influence on the basic reproduction number (R_0). We use partial derivatives of the reproduction number with respect to treatment of TB. We vary two parameters, γ and ϵ which represent the rate of treatment of individuals infected by TB and rate of of treatment of HIV and TB infected individuals respectively.

$$\frac{\partial R_{0T}}{\partial \gamma} = \frac{\pi \Lambda k_3 \beta_T (k_6 \eta_1 + \omega \eta_2) (\pi \phi_1 - k_1 k_3)}{\mu k_6 (k_1 k_3 (\gamma + \mu + \omega + \delta_T) - \pi \gamma \phi_1)^2} < 0 \quad (31)$$

Equation (31) is less than zero because $k_1 k_3 > \pi \phi_1$. This implies that treatment of the TB infected individuals reduces the reproduction number R_{0T} , hence TB can be controlled in the presence of treatment.

$$\frac{\partial R_{0T}}{\partial \epsilon} = - \frac{\pi \Lambda k_3 \beta_T \eta_2}{\mu (\epsilon + \mu + \delta_H + \delta_T)^2 (k_1 k_2 k_3 - \pi \gamma \phi_1)} < 0 \quad (32)$$

This means that treatment of HIV/TB infected individuals reduces the reproduction number hence this is a strategy of reducing TB infections among the HIV/AIDS infected individuals.

3.7 Numerical Simulation

We carried out the simulation using parameters in Table 1 and initial values from miathene subcounty hospital. the initials values for the population are: $S = 100000, E_T = 3000, I_T = 200, T_T = 150, I_H = 260, E_{HT} = 500, I_{HT} = 100, A_H = 50, T_{HT} = 90$. The main aim of our research is to investigate the effect of TB treatment on TB infected and on the coinfected individuals. In order to achieve this we vary the parameters γ and ϵ which represent the rate of treatment of the TB infected and HIV/TB infected respectively.

Table 1: Parameters and their Description

Description	Symbol	Value	Source
Recruitment rate	Λ	1.92	[8]
Natural death rate	μ	0.02	estimate
Rate of exposed to TB infected by HIV	τ	0.004	[8]
Death rate due to TB, HIV	δ_T, δ_H	0.05, 0.04	[8]
Rate of I_T progression to I_{HT}	ω	0.001	assumed
Progression rate of E_T to I_{HT}	κ	0.03	assumed
Rate of TB infection from E_T to I_T	π	0.002	[6]
Rate of HIV transmission	λ_H	0.006	estimate
Rate of TB transmission	λ_T	0.003	estimate
Rate of I_H contacting TB	ψ	0.3	estimate
Rate of recovery of TB of T_T and T_{HT}	ϕ_1, ϕ_2	0.09, 0.002	estimate
Rate of progression from HIV to AIDS	α	0.005	estimate
Treatment rate of I_T	γ		variable
Treatment rate of I_{HT}	ϵ		variable

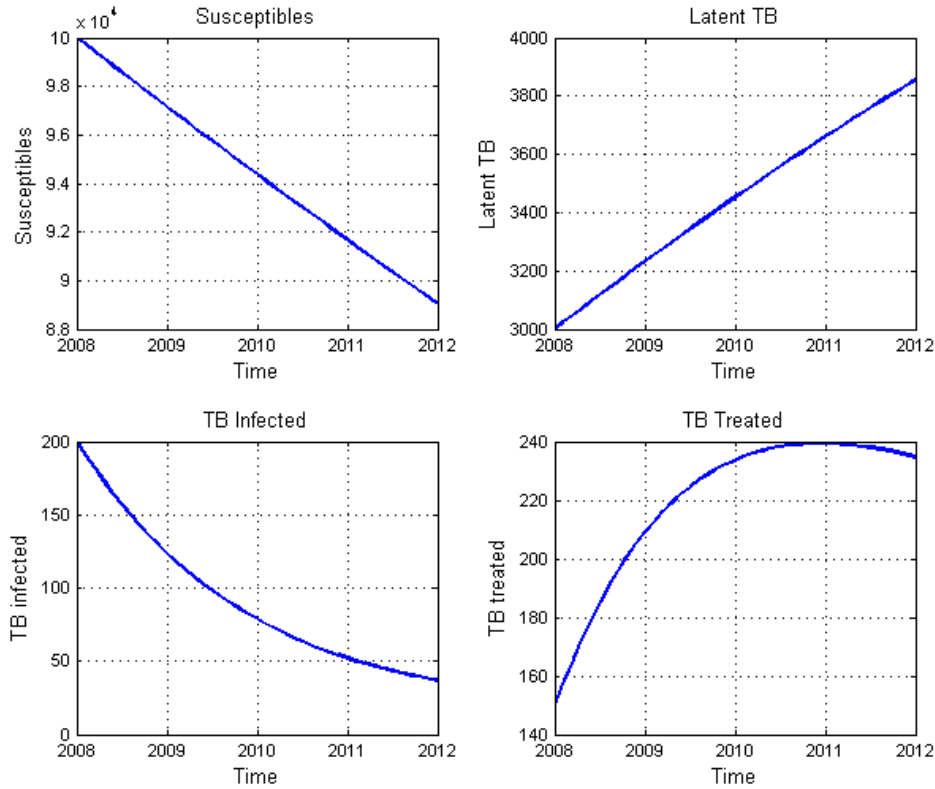


Figure 2: Subplot showing TB progression using $\gamma = 0.5$ and $\epsilon = 0.5$.

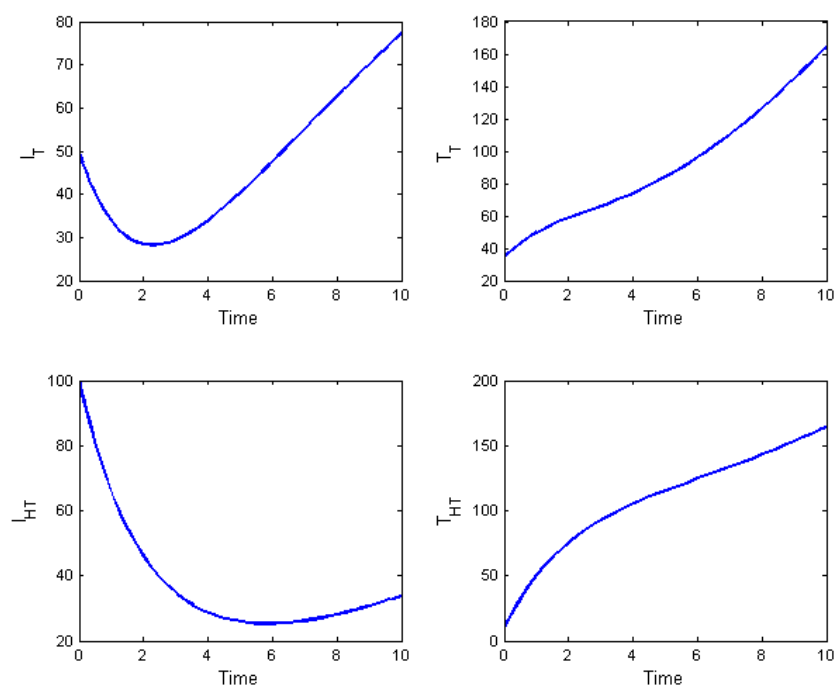


Figure 3: Subplot showing TB infected classes with $\beta = 0.5$ and $\epsilon = 0.5$. The other parameters are as in Table 1.

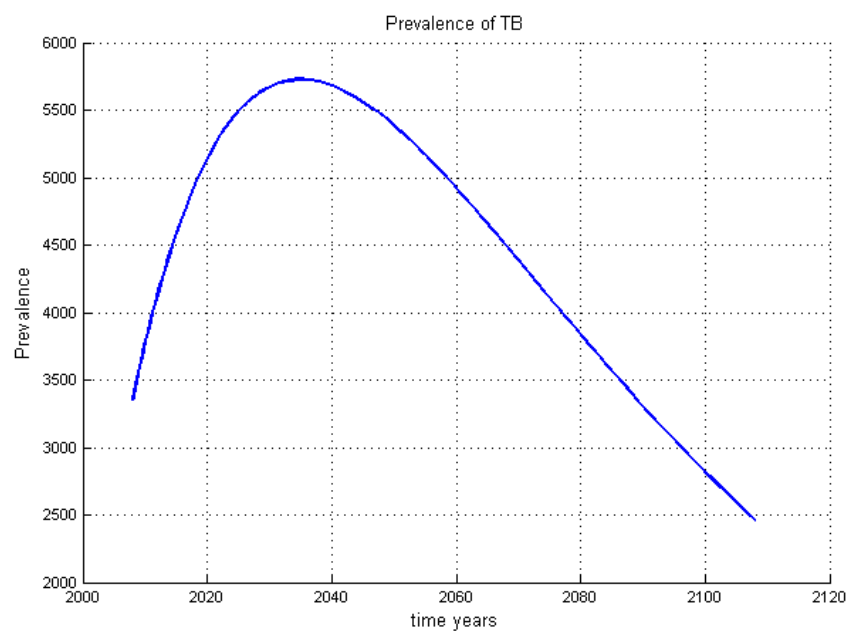


Figure 4: TB prevalence from 2008 to 2108. The prevalence reduces with time.

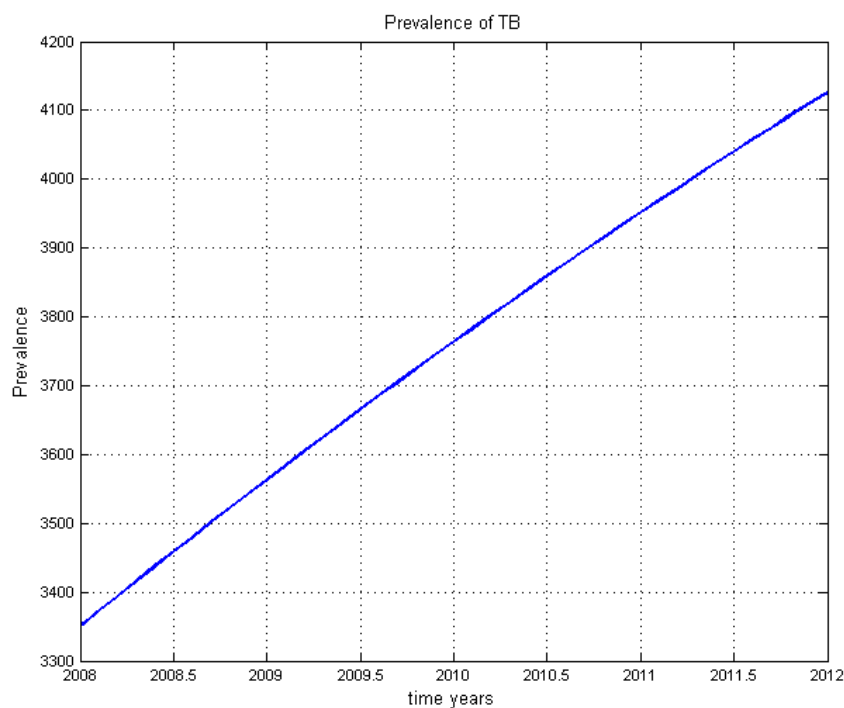


Figure 5: TB prevalence from 2008 to 2012 using $\alpha = 0.5$. The prevalence of TB increases with time. If we make projection of the next 100 years for example the rate of the prevalence will reduce as shown in the figure 4 below.

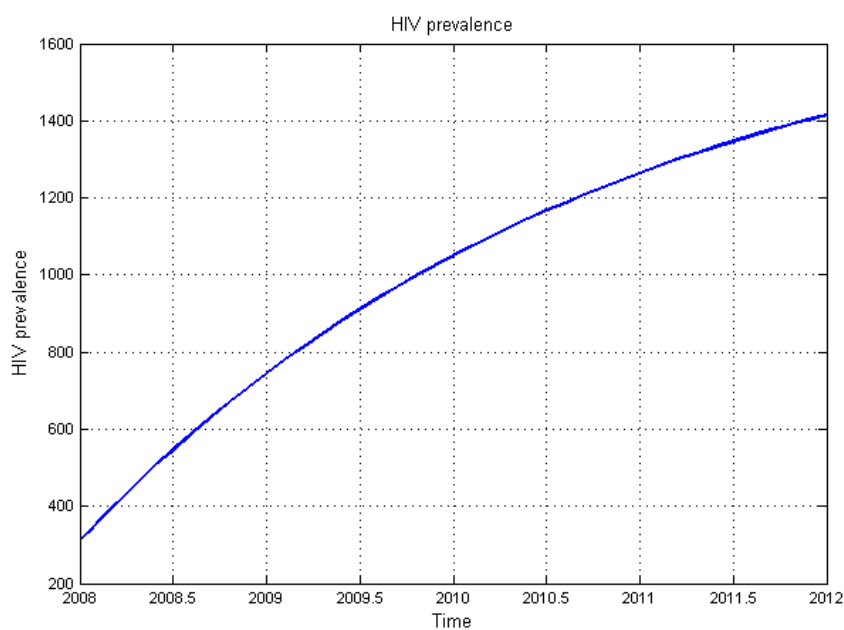


Figure 6: HIV prevalence from 2008 to 2012

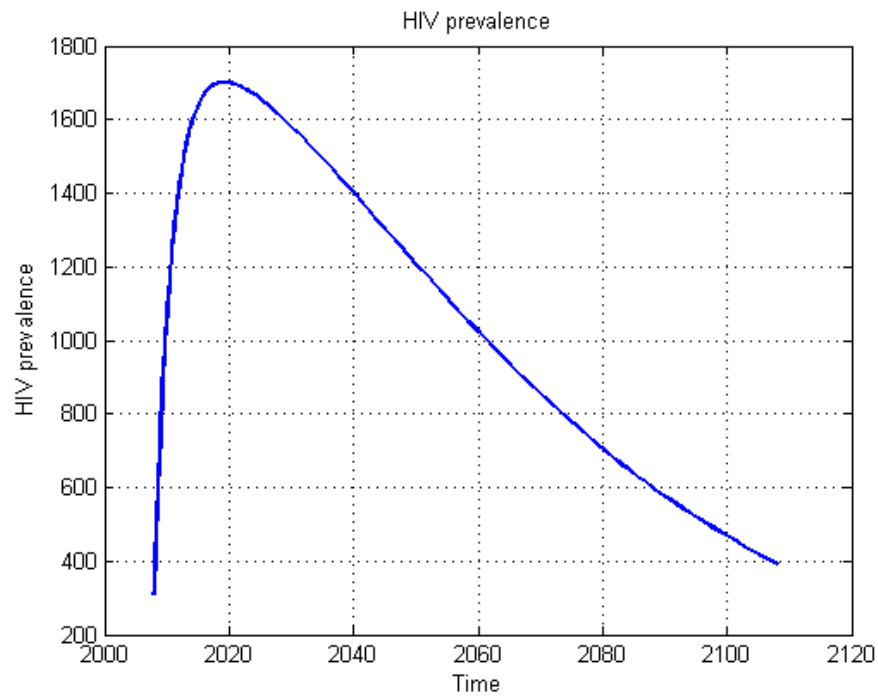


Figure 6a: HIV prevalence from 2008 to 2108. HIV prevalence also reduces within the next 100 years.

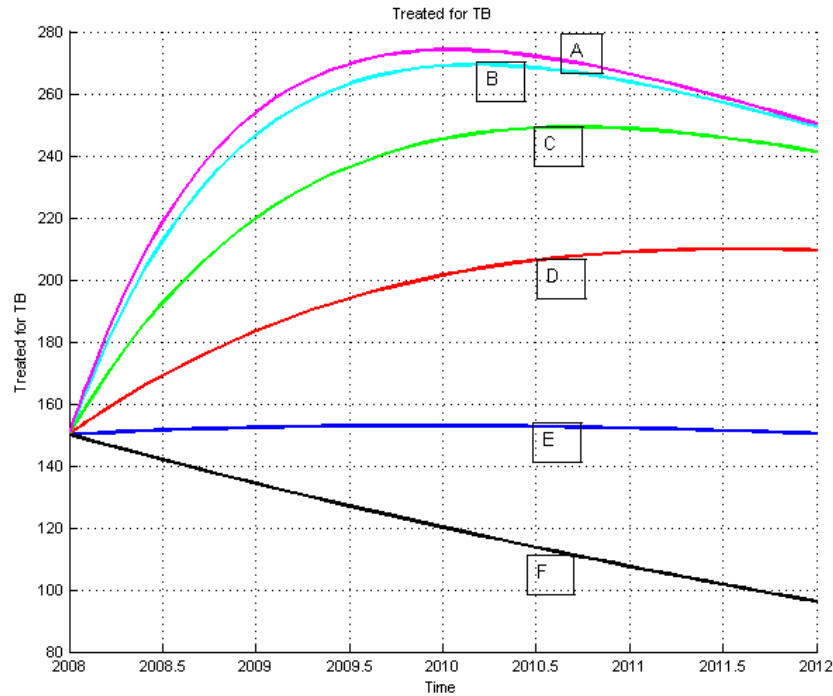


Figure 7: This show how treatment affects the treated population. The curves are labeled A to F with A, $\gamma = 1$, B, $\gamma = 0.9$, C, $\gamma = 0.6$, D, $\gamma = 0.3$, E, $\gamma = 0.1$ and F, $\gamma = 0$.

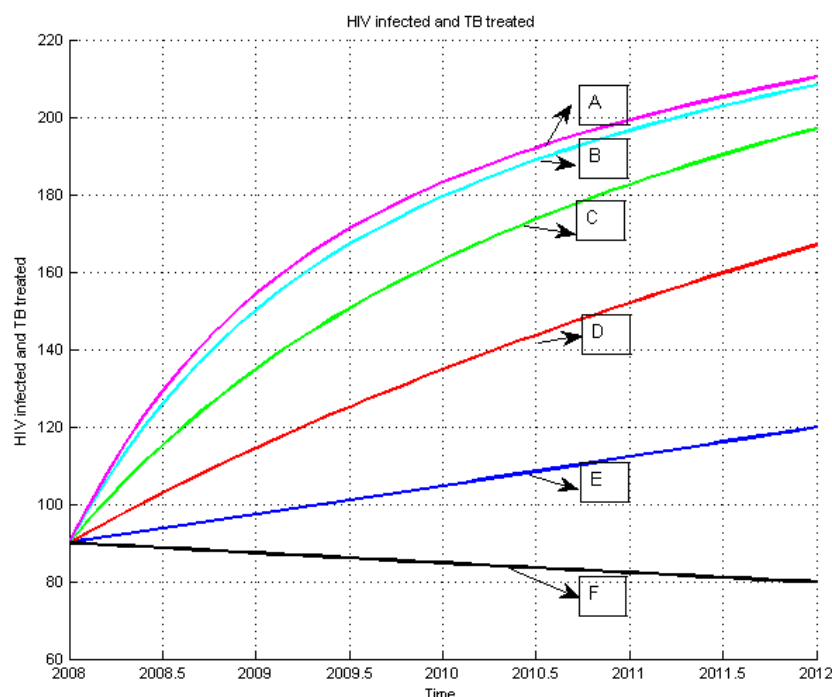


Figure 8: HIV infected and TB treated while varying ϵ from $\epsilon = 0$ to $\epsilon = 1$ with curve A, $\epsilon = 1$, F, $\epsilon = 0$.

The values of γ and ϵ are varied as shown in Figure 7 and Figure 8. When the values of γ and ϵ are increased, the rate of treatment of TB increases, which shows that treatment is a good control measure of TB. If treatment of TB is emphasized, then TB can be wiped out with time.

3.8 Discussion

Our research emphasized the need of TB testing and treatment, mostly among individuals infected by HIV. Most of the HIV/AIDS patients are vulnerable to TB infection because their immune systems is affected by the HIV virus. Also progression of TB from latent/exposed to infectious TB could be as a result of low immunity caused by HIV virus. Thus we recommend the following:

- i. Testing of latent TB be available in health centers in Kenya and treatment of latent TB be administered. ~~[10]~~
- ii. Kenyans ~~to~~ be sensitized on the need HIV/AIDS testing so as to control the spread of TB.
- iii. All TB patients ~~to~~ be tested for HIV/AIDS and all HIV/AIDS positive to be tested for TB, if positive be treated immediately.

Treating TB infection early controls its spread and also reduces the prevalence of TB in the population as evidenced in the simulations.

While carrying out our research, we encountered several challenges mostly the availability of well organized data in our health centers and hospitals for the past several years. We recommend that data be well collected and organized for all infectious diseases and be available to researchers in future. This will help them make future predictions which will help the health ministry to manage the disease in time.

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