A MATHEMATICAL MODEL OF HIV AND TB CO-INFECTION WITH INTERVENTIONS, A CASE OF SIAYA COUNTY IN KENYA

BY

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DECLARATION

This project is entirely original and has never before been submitted to a university for a degree.

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This project has been presented for examination with my permission as the university supervisor.

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I sincerely thank the Almighty God as well as my supervisors for the opportunity and guidance to do this project.Through the research I came to know about so many new things.

DEDICATION

I dedicate the project to my parents,family and my supervisors.Special gratitude to Dr.Winfred Mutuku and Proffesor David Malonza for the push and encouragement.Special thanks to my brother Dr.George Omondi for the mentorship.I appreciate all of you for helping me.

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ABBREVIATIONS

TB: Tuberculosis

HIV: Human Immunodeficiency Virus

AIDS: Acquired Immunodeficiency Syndrome

WHO: World Health Organization

ART: Anteretroviral Therapy

ABSTRACT

In this research, we take into consideration a model of co-infection between HIV/AIDS and TB with treatment of infectious and inactive forms of TB and HIV preventive and therapeutic strategies. Specifically we consider condom use, early ART and withdrawal from sexual activities by individuals who are infected by HIV as controls. The model is positively bounded. The spectral radius of the next generation matrix has been used to determine the model's fundamental reproduction number. The model displays these equilibria: a disease free and a co-infection equilibrium. By utilizing Routh-Hurwitz standard and center manifold theory, the model has been qualitatively examined. When $R_0 < 1$,we discovered that the disease free equilibrium point was locally asymptotically stable and not globally asymptotically stable. Sensitivity analysis of R_{0T} and R_{0H} identifies ϖ_1 and ϖ_2, TB and HIV infection rates through effective contact respectively, as the main variables that if targeted, R_{0T} and R_{0T} are reduced. From numerical simulation,we show that increasing HIV interventions reduces cases of latent TB progressing to active TB and therefore is an additional strategy in the fight against TB disease.

1. INTRODUCTION

1.1 Background Information

The enormous HIV and TB related cost on public health calls for the use of Mathematical Modelling in understanding the dynamics of HIV and TB transmission. Mathematical Modelling not only helps us to comprehend the transmission dynamics of these contagious diseases but also their control strategies.A third of the millions of HIV-positive persons around the world also have TB. The remaining two thirds, who are not co-infected, are likely to have an active TB infection in 50% of them. (Castillo- Chavez et al., 2009). Individuals with both HIV and latent TB have a greater chance of developing infectious TB as in comparison to those without the HIV virus (Castillo- Chavez et al., 2009).

HIV/AIDS is an infection of the body's defence mechanism caused by the HIV virus. The disease is transmitted when one comes into contact with infected body fluids.The disease destroys the body's defence mechanism against infections. Progression of the disease makes HIV positive individuals to be immunodeficient thus susceptible to opportunistic diseases that individuals with a normal immune system can easily fend off WHO (2018). Even though HIV/AIDS has no cure, early detection and treating of infected individuals with ART drugs lowers the viral load hence prevent transmission and prolongs the life of the infected person (Ho, 1995). Although there are several proofs that ARVs are effective in curtailing the progression of HIV to AIDS, there is low access to antiretroviral treatment in scarce resource nations with higher cases of HIV/AIDS. Prevention therefore remains the only feasible option against the epidemic in the already heavily burdened societies (Nannyonga et al., 2011).

Mycobacterium tuberculosis is the source of infection known as tuberculosis.It mostly affects the lungs .The bacteria is spread to susceptible persons when those with infectious

TB releases it into the air either through cough, sneezing, speaking or singing. About a quarter of the World's population have latent TB WHO (2012). Persons with latent TB do not show any TB related signs and symptoms and cannot transmit TB.However, they are likely to develop active TB either by the disease reactivating and causing infectious TB mostly due to a compromised immune system or by exogenous reinfection in high incidence areas. Treatment of Latent TB prevents endogenous reactivation (Kruk et al., 2008). Active TB infection in an individual is characterized by; fever, unintended weight loss, cough, fatigue, night sweats and chills. TB can both be treated and prevented.Prevention of TB is done by vaccination and ART for persons with the HIV virus.

The increasing rate of HIV infection in some nations has led to the re-emergence of TB in those areas (Corbett et al., 2003). In Kenya, Siaya county records a higher HIV cases due to social cultural factors such as polygamy,low uptake of male circumcision, widow inheritance and community rites involving sex such as before planting. Control of TB has proven to be a challenge in Siaya county due to the high HIV cases. The two diseases are inextricably linked where the high prevalence of one fuels the rise in the incidence of the other (Kruk et al., 2008). In this research, we will study the effect of HIV preventive and therapeutic strategies on TB.

1.2 Statement of the Problem

Kenya is among the nations with a high TB burden according to the Global TB Report 2010. In Kenya, Siaya County is among the leading counties in new TB infection. The main factor that has led to the high incidences of TB in Kenya, and in particular Siaya County is the high HIV prevalence. Controlling the spread of TB has been a challenge in areas with high HIV cases. HIV accelerates the rate at which inactive TB infection progresses to infectious TB. TB cases are higher among the youth which is the most productive group in a nation hence has a negative impact on development since more funding is required to fight the disease. There is need therefore to address HIV and TB outbreak in Siaya County. Both HIV and TB intervention strategies are therefore crucial for the reduction of both HIV and TB in this county. The study area has a high HIV and TB prevalence with TB hotspots in the urban wards of the county. The high TB cases is attributed to both high population density and also a high HIV prevalence in those areas. This research seeks to create and analyze a model on TB-HIV/AIDS co-infection incorporating TB treatment, both latent and active TB and HIV preventive and therapeutic strategies such as condom use, early ART and withdrawal from sexual activities by HIV positive people.

1.3 Justification of the study

HIV and TB co-infection is a public health challenge in every nation. Mathematical modelling is a crucial aid to comprehension of the transmission patterns of these two diseases. Through disease modelling we are able to investigate the impact of various disease intervention strategies thus enabling us to pick on the best control strategy. Therapy for active TB alone is not sufficient in eradicating TB. To enhance the fight against TB in Siaya County, an additional strategy that will prevent the development of latent TB disease to active TB is necessary. Tuberculosis turning from latent to active as a consequence of HIV infection has to be addressed. Studies on the interactions between TB and HIV in Siaya County are few. From literature, none investigated the combined impact of treatment of both forms TB and HIV intervention strategies on the prevalence of Tuberculosis.

1.4 Objectives of the Study

1.4.1 Main Objective

The main aim of this study is to create and analyse a model of TB and HIV co-infection incorporating treatment of both inactive and infectious forms of TB and HIV preventive and therapeutic strategies using Siaya County in Kenya as a case study.

1.4.2 Specific Objectives

The particular goals of the study are to;

i create a model on HIV/TB coinfection based on a differential equation system.

ii conduct a stability study on the model's equilibrium points; endemic and disease-free .

iii investigate through numerical simulation, the role of HIV prevention and therapeutic strategies on the prevalence of infectious TB.

1.5 Significance of the Study

The goal of the study is to create and analyse a model that examines the role of HIV preventive and therapeutic strategies on the prevalence of TB in Siaya County in Kenya. The findings of this research will help policy makers in the health sector of the County to understand the importance of such HIV preventive and therapeutic strategies on reducing TB cases hence intensify campaigns on treatment of both forms of TB, HIV prevention and early anteretroviral therapy to eliminate TB in the County.

2. LITERATURE REVIEW

Mathematical models on TB have been presented and analysed. For example, Castillo-Chavez and Feng (2000) analysed a model on the external reinfection of tuberculosis. They determined that exogenous reinfection had a serious negative effect on Tuberculosis. They found out that decreasing the reproduction number to less than one was not adequate in eradicating the disease and that additional strategy aimed at reduction in reinfection was required. Adewale et al (2009)carried out a mathematical analysis of TB transmission with Directly Observed Therapy Short-course(DOTS) programme. They found out that even though exogenous reinfection resulted to new cases of TB regardless of the programme, the new cases of TB were fewer with the programme in place as compared to the many cases without the programme. Zhang and Feng (2014) analysed the global stability of a model of TB that incorporated insufficient treatment and isolation. By using Lasalle's invariant set theorem and Lyapunov stability theory,they were able to derive the disease free equilibrium. They demonstrated that, for reproduction numbers below one, the disease-free equilibrium is globally asymptotically stable. Muthuri and Malonza (2016) investigated the role of treatment of TB on the TB disease. They found out that treatment of the active disease was the best intervention to eradicate the disease in Kenya. Egonwan and Okuonghae (2018) conducted a study on the role of diagnosis and treatment of both inactive and infectious disease on the prevalence of TB. They suggested that treatment of both forms of TB and raising the rate of latent TB diagnosis and treatment effectively reduces the TB burden in a population.

Several models on HIV/AIDS have also been proposed and analysed. Nyabadza et al. (2010) analysed a model on HIV/AIDS which considered the role of public health information and individual withdrawal on the dynamics and prevalence of HIV. They concluded that increasing public awareness through campaigns on HIV prevention decreased the prevalence of the disease. They also demonstrated that withdrawal from sexual activities by persons infected with the HIV disease was key in lowering its transmission. A rise in the number of HIV-positive people quitting sexual activities was required. Mbitila and Tchuenche (2012) qualitatively investigated the role of early identification and treatment on HIV dynamics. They found out that even though case detection and treatment was critical in reducing the disease transmission, it was not sufficient and that additional control strategies were to be explored.

The co-infection of TB and HIV have also been the subject of mathematical and statistical models. Castillo- Chavez et al. (2009) in their research of the co-infection of these two diseases, found out that the rising rate of TB infection in a population was due to the higher progression rate of inactive to infectious TB in persons with the HIV virus. Bhunu et al. (2009)analysed a co-infection model that considered ART for HIV patients and treatment of both forms of TB.Their analysis showed that ART for HIV cases significantly reduced cases of dormant TB developing to infectious TB and that therapy for both TB types prevented HIV from developing into AIDS. Joyce et al. (2015) created a coinfection model that assessed the role of protection from infection for the two diseases.The cases of maximum TB protection and HIV protection were taken into consideration. Their numerical simulation showed that enhanced protection from infection has the positive impact of a decreasing the spread of each disease.Funke (2015) proposed a co-infection model to determine the role of TB treatment. Their research showed that treatment of both latent and infectious TB reduced TB in a population, reduced the rate at which HIV progresses to AIDS and also lowered co-infection. Sharomi et al. (2008) developed and qualitatively examined a comprehensive TB and HIV model to determine the best control strategies for the diseases in a community. Their model allowed for the determination of the epidemiological effect of the four treatment strategies on TB, HIV and the dual infection. Their research revealed that,more than any other technique, the successful treatment for both diseases prevented more cases of the dual infection. Lusiana et al (2017) modelled the transmission of tuberculosis in an HIV community. In their analysis,they indicated that the factors influencing the evolution of TB in a population of HIV-positive individuals included;the speed of TB's transformation from latent to active, treatment frequency of latent TB,treatment frequency of active TB and effective contact rate for TB transmission. Muthuri and Malonza (2018) designed a TB-HIV co-infection model which incorporated HIV management and TB therapy.Their focus was in the investigation of the role of HIV infection on TB.From simulation, they showed that;HIV infection increased the rate at which latent TB disease developed to infectious TB increasing TB contacts in a population. This research aims at investigating the role of HIV preventive and therapeutic strategies on HIV and infectious TB using data from Siaya County Referral Hospital.

3. MATHEMATICAL MODEL FORMULATION AND ANALYSIS

3.1 Model Formulation

The model is formulated by creating ten compartments from the human population at time t, N(t) , namely, individual vulnerable to both TB and HIV, S(t), latent TB individuals $L_T(t)$, TB Infectives $I_T(t)$, TB recovered individuals R(t), individuals who are HIV positive ,$I_H(t)$, HIV positive persons with inactive TB, $L_{HT}(t)$, HIV positive persons with active TB, $I_{HT}(t)$, AIDS individuals, $A_H(t)$, HIV infected persons treated of TB, $T_{HT(t)}$ and HIV positive persons with AIDS symptoms and have active TB ,$A_{HT}(t)$. The total population N(t) is obtained by

$$N(t) = S(t) + L_T(t) + I_T(t) + R(t) + I_H(t) + A_H(t) + L_{HT}(t) + I_{HT}(t) + T_{HT}(t) + A_{HT}(t) \tag{3.1}$$

The number of people vulnerable to TB and HIV grows at the rate Λ. All compartments experience a consistent rate of natural death, μ. Susceptible individuals become exposed to TB at a rate λ_T, given by

$$\lambda_T = (1 - \xi_1)\varpi_1(I_T(t) + I_{HT}(t) + A_{HT}(t))$$

where ϖ_1 is the TB infection rate through effective contact and $0 < \xi_1 < 1$ is the measure of interventions that reduce the transition from dormant to active tuberculosis. Individuals susceptible to HIV acquire the disease, after successful contact with HIV positive persons at a rate λ_H, as determined by

$$\lambda_H = (1 - \xi_2)\varpi_2(I_H(t) + L_{HT}(t) + I_{HT}(t) + A_H(t) + T_{HT}(t) + A_{HT}(t))$$

where ϖ_2 is the HIV transmission rate through effective contact and $0 < \xi_2 < 1$ is the measure of interventions that reduce HIV transmission. People depart from the latent TB class at a rate $\alpha\kappa_1$ and become infectious or recover with treatment at a rate,τ_1 Where $\alpha \leq 1$ is a parameter that takes into consideration the decreased possibility of progression from inactive to infectious TB due to treatment and protection from HIV infection. Infectious TB individuals recover from active TB due to treatment at a rate τ_2. Individuals who recover from TB, R, are assumed to acquire partial immunity and leave the R class at a rate of $\eta\lambda_T$ where $\eta \leq 1$. HIV positive individuals, I_H , acquire TB at the rate $\psi_1\lambda_T$, where ψ_1 is a parameter that takes into consideration the increased vulnerability to TB by HIV positive persons, with $\psi_1 \geq 1$. People with latent TB who also have HIV but displaying no AIDS symptoms depart class L_{HT} at the rate $\gamma\kappa_2$ and become infectious of TB where $\kappa_2 > \kappa_1$ and $\gamma \leq 1$ is a parameter that account for the decreased rate of progression from inactive to infectious TB due to ART. Infectious TB persons proceed to class I_{HT} at a rate $\phi\lambda_H$ where $\phi \leq 1$ is a m parameter that takes into account the fact that persons with infectious TB have decreased activity and are less susceptible due to morbidity. People in class I_{HT} advance to class A_{HT} at a rate ω or class T_{HT} at a rate τ_3 upon successful treatment of TB. The individuals in the class A_H contact TB and advance to class A_{HT} at a rate $\psi_2\lambda_T$ where $\psi_2 \geq 1$ is a parameter accounting for increased susceptibility to TB. Individuals in the class A_{HT} upon successful treatment of TB move on to the class A_H at the rate of τ_4 . HIV positive persons, I_H, move on to class A_H at the rate β while those in class T_{HT} proceed to class A_H at a rate π. HIV positive persons who show AIDS symptoms and are infected with TB , A_T, suffer from death at a rate δ_{TA} due to TB and AIDS. HIV positive persons who show AIDS symptoms, A_H, suffer from death, at a rate, δ_A due to AIDS. TB-related mortality rate is δ_T.

Table 3.1: Model Variables

Symbol	Model Variable
S	Individuals susceptible to TB and HIV
L_T	Latent TB individuals
I_T	TB Infectives
R	Individuals treated for TB
I_H	HIV cases
L_{HT}	Latent TB cases with HIV infection
I_{HT}	TB cases with HIV infection
A_H	AIDS cases
T_{HT}	HIV cases who recovered from TB
A_{HT}	AIDS cases with active TB

Table 3.2: Parameters of the model

Symbol	**Parameter description**
μ	Natural death rate
Λ	Recruitment rate into the susceptible group
λ_H	Force of infection of HIV
λ_T	Force of Infection of TB
τ_1, τ_2, τ_3 and τ_4	Rates of treatment of TB
κ_1 and κ_2	Rate of progression to active TB
β	Rate of progression from I_H to A_H
π	Rate of progression from T_{HT} to A_H
ω	Rate of progression from I_{HT} to A_{HT}
δ_A	AIDS-related mortality rate
δ_T	TB-related mortality rate
δ_{TA}	TB and AIDS induced death rate
ψ_1, ψ_2, ϕ, η, α and γ	Modification parameters

3.1.1 Model Assumptions

i The susceptible can only contact one disease at a time.

ii Human population is not constant due to the fact that birth and death occurs at different rates.

iii All identified individuals with latent and active forms of TB will be treated.

iv All identified individuals with HIV will be put under treatment.

3.1.2 Model Flow Chart and Equations

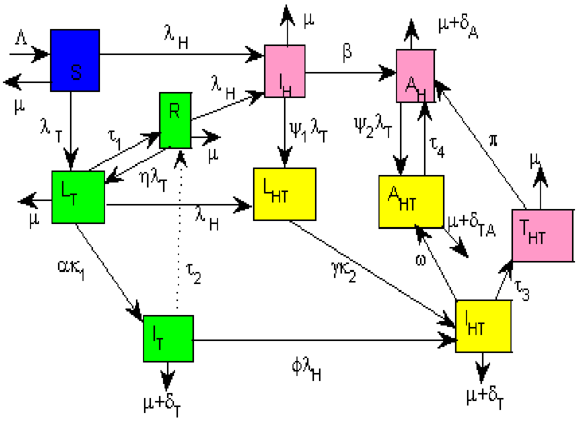

Figure 3.1: Flow chart

The following differential equations are derived from the aforementioned presumptions,flow chart and the definitions.

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - (\lambda_H + \lambda_T + \mu)S \\
\frac{dL_T}{dt} &= \lambda_T S + \eta\lambda_T R - (\mu + \alpha\kappa_1 + \tau_1 + \lambda_H)L_T \\
\frac{dI_T}{dt} &= \alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2 + \phi\lambda_H)I_T \\
\frac{dR}{dt} &= \tau_1 L_T + \tau_2 I_T - (\mu + \lambda_H + \eta\lambda_T)R \\
\frac{dI_H}{dt} &= \lambda_H S + \lambda_H R - (\mu + \beta + \psi_1\lambda_T)I_H \\
\frac{dA_H}{dt} &= \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A + \psi_2\lambda_T)A_H \\
\frac{dL_{HT}}{dt} &= \lambda_H L_T + \psi_1\lambda_T I_H - (\mu + \gamma\kappa_2)L_{HT} \\
\frac{dI_{HT}}{dt} &= \gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} + \phi\lambda_H I_T \\
\frac{dT_{HT}}{dt} &= \tau_3 I_{HT} - (\mu + \pi)T_{HT} \\
\frac{dA_{HT}}{dt} &= \omega I_{HT} + \psi_2\lambda_T A_H - (\tau_4 + \mu + \delta_{TA})A_{HT}
\end{aligned}
\qquad (3.2)
$$

We rewrite the system (3.2) described above as follows;

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - j_1 S\\
\frac{dL_T}{dt} &= \lambda_T S + \eta\lambda_T R - j_2 L_T\\
\frac{dI_T}{dt} &= \alpha\kappa_1 L_T - j_3 I_T\\
\frac{dR}{dt} &= \tau_1 L_T + \tau_2 I_T - j_4 R\\
\frac{dI_H}{dt} &= \lambda_H S + \lambda_H R - j_5 I_H\\
\frac{dA_H}{dt} &= \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - j_6 A_H\\
\frac{dL_{HT}}{dt} &= \lambda_H L_T + \psi_1\lambda_T I_H - j_7 L_{HT}\\
\frac{dI_{HT}}{dt} &= \gamma\kappa_2 L_{HT} - j_8 I_{HT} + \phi\lambda_H I_T\\
\frac{dT_{HT}}{dt} &= \tau_3 I_{HT} - j_9 T_{HT}\\
\frac{dA_{HT}}{dt} &= \omega I_{HT} + \psi_2\lambda_T A_H - j_{10} A_{HT}
\end{aligned} \tag{3.3}$$

where

$j_1 = \lambda_H + \lambda_T + \mu$ $\quad j_2 = \mu + \alpha\kappa_1 + \tau_1 + \lambda_H$ $\quad j_3 = \mu + \delta_T + \tau_2 + \phi\lambda_H$ $\quad j_4 = \mu + \lambda_H + \eta\lambda_T$ $\quad j_5 = \mu + \beta + \psi_1\lambda_T$ $\quad j_6 = \mu + \delta_A + \psi_2\lambda_T$ $\quad j_7 = \mu + \gamma\kappa_2$ $\quad j_8 = \omega + \tau_3 + \mu + \delta_T$ $\quad j_9 = \mu + \pi$ $\quad j_{10} = \tau_4 + \mu + \delta_{TA}$

3.2 Mathematical Analysis

Positiveness of solutions,the invariant region,the model's equilibrium points,and the fundamental reproduction number are all covered in this section.

3.2.1 Positivity

All initial conditions and model parameters are non-negative since the system of equations (3.2) reflects the human population.That is, $S(0) > 0$; $L_T(0), I_T(0), R(0), I_H(0), A_H(0), L_{HT}(0), I_{HT}(0$ 0. In this section we determine whether the system's solutions are positive. Considering the system equations (3.2) and expressing the systems initial equation as

$$\frac{dS}{dt} > -(\lambda_H + \lambda_T + \mu)S \tag{3.4}$$

By variable separation,we solve equation (3.4) to;

$S(t) > S(0)e^{-(\lambda_H+\lambda_T+\mu)t}$

and as $t \longrightarrow \infty$, we get

$S(t) > 0; \forall \quad t > 0$

The second equation of (3.2) can also be expressed as;

$$\frac{dL_T}{dt} \geq -(\mu + \alpha\kappa_1 + \tau_1 + \lambda_H)I_H \tag{3.5}$$

Using separation of variables, equation's (3.5) solution is given by

$L_T(t) \geq A_H(0)e^{-(\mu+\alpha\kappa_1+\tau_1+\lambda_H)t}$

which as $t \longrightarrow \infty$, yields

$L_T(t) \geq 0; \forall \quad t > 0$

Similarly the third equation of (3.2) assumes the form

$$\frac{dI_T}{dt} = -(\mu + \delta_T + \tau_2 + \phi\lambda_H)A_H \tag{3.6}$$

Applying separation of variables method in solving equation (3.6),we get

$I_T(t) \geq A_H(0)e^{-(\mu+\delta_T+\tau_2+\phi\lambda_H)t}$

Thus, as $t \longrightarrow \infty$, we have

$I_T(t) \geq 0; \forall \quad t > 0$

Applying the same procedure to the remaining equations of (3.2) we obtain:

$$\begin{cases} R(t) \geq A_H(0)e^{-(\mu+\lambda_H+\eta\lambda_T)t} \\ I_H(t) \geq I_H(0)e^{-(\mu+\beta+\psi_1\lambda_T)t} \\ A_H(t) \geq A_H(0)e^{-(\mu+\delta_A+\psi_2\lambda_T)t} \\ L_{HT}(t) \geq A_H(0)e^{-(\mu+\gamma\kappa_2)t} \\ I_{HT}(t) \geq A_H(0)e^{-(\omega+\tau_3+\mu+\delta_T)t} \\ T_{HT}(t) \geq A_H(0)e^{-(\mu+\pi)t} \\ A_{HT}(t) \geq A_H(0)e^{-(\tau_4+\mu+\delta_{TA})t} \end{cases}$$

Which as $t \longrightarrow \infty$, become

$R(t), I_H(t), A_H(t), L_{HT}(t), I_{HT}(t), T_{HT}(t), A_{HT}(t) \geq 0; \forall \quad t > 0$

As a result,the model's entire set of solutions is positive.

3.2.2 Invariant region

The derived function of equation (3.1) with respect to time;

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_H}{dt} + \frac{dA_H}{dt} + \frac{dT_{HT}}{dt} + \frac{dA_{HT}}{dt} + \frac{dI_{HT}}{dt} + \frac{dL_{HT}}{dt} + \frac{dL_T}{dt} + \frac{dI_T}{dt} + \frac{dR}{dt} \quad (3.7)$$

Now we substitute the equations of system (3.2) in equation (3.7) and simplify it to get

$$\frac{dN}{dt} = \Lambda - \mu(S + L_T + I_T + R + I_H + L_{HT} + I_{HT} + A_H + T_{HT} + A_{HT}) - \delta_A A_H - \delta_{TA} A_{HT} - \delta_T(I_T + I_{HT})$$

and it follows that

$$\frac{dN}{dt} = \Lambda - \mu N - \delta_A A_H - \delta_{TA} A_{HT} - \delta_T(I_T + I_{HT})$$

When HIV and TB are completely controlled to the the extent that there is no deaths due to HIV and TB, we have

$$\frac{dN}{dt} \leq \Lambda - \mu N$$

The above equation may be expressed be as follows.

$$\frac{dN}{dt} + \mu N \leq \Lambda \quad (3.8)$$

Equation (3.8) can be resolved by multiplying both sides by the integrating factor given by $e^{\int \mu dt} = e^{\mu t}$ to obtain

$$e^{\mu t}\frac{dN}{dt} + \mu N e^{\mu t} \leq \Lambda e^{\mu t} \quad (3.9)$$

which implies that

$$\frac{d}{dt} e^{\mu t} N \leq \Lambda e^{\mu t} \quad (3.10)$$

Upon multiplication of both sides of equation (3.10) with dt and integration, we get

$$\int de^{\mu t}N \leq \int \Lambda e^{\mu t}dt + C \tag{3.11}$$

$\Rightarrow$

$$e^{\mu t}N \leq \frac{\Lambda}{\mu}e^{\mu t} + C \tag{3.12}$$

at time $t = 0$ $C = N(0) = N_0$. Substituting C in equation (3.12) yields

$$e^{\mu t}N \leq \frac{\Lambda}{\mu}e^{\mu t} + N_0 \tag{3.13}$$

Which can be written as

$$N \leq \frac{\Lambda}{\mu} + N_0e^{-\mu t} \tag{3.14}$$

As time $t \to \infty$, equation (3.14) assumes the form

$$N \leq \frac{\Lambda}{\mu} \tag{3.15}$$

From equation (3.15)we conclude that the human population $N(t)$ ranges from 0 to $\frac{\Lambda}{\mu}$. This implies that the solution the model is bounded and the human population remain in the region: $\Omega = \left\{S, L_T, I_T, R, I_H, A_H, L_{HT}, I_{HT}, T_{HT}, A_{HT} \in \mathbb{R}^{10}_{+}\right\}$

3.2.3 Disease Free Equilibrium Point

This equilibrium is attained by setting the right side of the equations(3.2) equal to zero. We substitute $S = S^0$, $L_T = L_T^0 = 0$, $I_T = I_T^0 = 0$, $R = R^0 = 0$, $I_H = I_H^0 = 0$, $A_H = A_H^0 = 0$, $L_{HT} = L_{HT}^0 = 0$, $I_{HT} = I_{HT}^0 = 0$, $T_{HT} = T_{HT}^0 = 0$ and $A_{HT} = A_{HT}^0 = 0$. This reduces the system to one equation:

$$\Lambda - \mu S^0 = 0 \tag{3.16}$$

By solving fo S^0 in equation (3.16), we have

$S^0 = \frac{\Lambda}{\mu}$

Consequently, the disease free equilibrium is provided by

$$E^0 \begin{pmatrix} S^0 \\ L_T^0 \\ I_T^0 \\ R^0 \\ I_H^0 \\ A_H^0 \\ L_{HT}^0 \\ I_{HT}^0 \\ T_{HT}^0 \\ A_{HT}^0 \end{pmatrix} = E^0 \begin{pmatrix} \frac{\Lambda}{\mu} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

3.2.4 Basic reproduction number R_0

It is described as the typical number of secondary instances of a contagious disease that result from a single diseased person being introduced to a population where everyone is vulnerable to the disease.In order to compute R_0,we employ Van den Driessche and Watmough (2002) next generation matrix approach .The spectral radius of the matrix FV^{-1} (ρFV^{-1}) serves as the fundamental reproduction number, where $F = \frac{\partial f_i(x^0)}{\partial x_i}$ and $V = \frac{\partial v_i(x^0)}{\partial x_i}$ and f_i are new infections while v_i is the transmission of pathogens into and out of compartment i for $i = 1, 2, 3, \cdots, n$. x^0 denotes the disease free equilibrium point.

In writing the system equations (3.2) we begin with the newly infectious classes.

$$
\begin{aligned}
\frac{dL_T}{dt} &= \lambda_T S + \eta\lambda_T R - (\mu + \alpha\kappa_1 + \tau_1 + \lambda_H)L_T \\
\frac{dI_T}{dt} &= \alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2 + \phi\lambda_H)I_T \\
\frac{dR}{dt} &= \tau_1 L_T + \tau_2 I_T - (\mu + \lambda_H + \eta\lambda_T)R \\
\frac{dI_H}{dt} &= \lambda_H S + \lambda_H R - (\mu + \beta + \psi_1\lambda_T)I_H \\
\frac{dA_H}{dt} &= \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A + \psi_2\lambda_T)A_H \\
\frac{dL_{HT}}{dt} &= \lambda_H L_T + \psi_1\lambda_T I_H - (\mu + \gamma\kappa_2)L_{HT} \\
\frac{dI_{HT}}{dt} &= \gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} + \phi\lambda_H I_T \\
\frac{dT_{HT}}{dt} &= \tau_3 I_{HT} - (\mu + \pi)T_{HT} \\
\frac{dA_{HT}}{dt} &= \omega I_{HT} + \psi_2\lambda_T A_H - (\tau_4 + \mu + \delta_{TA})A_{HT}
\end{aligned}
\tag{3.17}
$$

From the system (3.17) we have

$$
f_i = \begin{bmatrix} \lambda_T S + \eta\lambda_T R \\ 0 \\ 0 \\ \lambda_H S + \lambda_H R \\ 0 \\ \lambda_H L_T + \psi_1\lambda_T I_H \\ \phi\lambda_H I_T \\ 0 \\ \psi_2\lambda_T A_H \end{bmatrix}
$$

Substituting $\lambda_T = (1-\xi_1)\varpi_1(I_T + I_{HT} + A_{HT})$ and

$\lambda_H = (1-\xi_2)\varpi_2(I_H + L_{HT} + I_{HT} + A_H + T_{HT} + A_{HT})$ in matrix f_i we obtain

$$
f_i = \begin{bmatrix} (1-\xi_1)\varpi_1(I_T + I_{HT} + A_{HT})(S + \eta R) \\ 0 \\ 0 \\ (1-\xi_2)\varpi_2(I_H + L_{HT} + I_{HT} + A_H + T_{HT} + A_{HT})(S + R) \\ 0 \\ (1-\xi_1)\varpi_2(I_H + L_{HT} + I_{HT} + A_H + T_{HT} + A_{HT})L_T + \psi_1(1-\xi_1)\varpi_1(I_T + I_{HT} + A_{HT})I_H \\ \phi(1-\xi_2)\varpi_2(I_H + L_{HT} + I_{HT} + A_H + T_{HT} + A_{HT})I_T \\ 0 \\ \psi_2(1-\xi_1)\varpi_1(I_T + I_{HT} + A_{HT})A_H \end{bmatrix}
$$

Also, from the system (3.17) we have

$$v_i = \begin{bmatrix} (\mu+\alpha\kappa_1+\tau_1+\lambda_H)L_T \\ -\alpha\kappa_1 L_T + (\mu+\delta_T+\tau_2+\phi\lambda_H)I_T \\ -\tau_1 L_T - \tau_2 I_T + (\mu+\lambda_H+\eta\lambda_T)R \\ (\mu+\beta+\psi_1\lambda_T)I_H \\ -\beta I_H - \pi T_{HT} - \tau_4 A_{HT} + (\mu+\delta_A+\psi_2\lambda_T)A_H \\ (\mu+\gamma\kappa_2)L_{HT} \\ -\gamma\kappa_2 L_{HT} + (\omega+\tau_3+\mu+\delta_T)I_{HT} \\ -\tau_3 I_{HT} + (\mu+\pi)T_{HT} \\ -\omega I_{HT} + (\tau_4+\mu+\delta_{TA})A_{HT} \end{bmatrix}$$

By definition of F and V, we have

$$F = \begin{bmatrix} 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & 0 & 0 & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and $V = \begin{bmatrix} c_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ c_2 & c_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ c_4 & c_5 & c_6 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & c_7 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & c_8 & c_9 & 0 & 0 & c_{10} & c_{11} \\ 0 & 0 & 0 & 0 & 0 & c_{12} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & c_{13} & c_{14} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & c_{15} & c_{16} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & c_{17} & 0 & c_{18} \end{bmatrix}$

where

$c_1 = \mu+\alpha\kappa_1+\tau_1 \quad c_2 = -\alpha\kappa_1 \quad c_3 = \mu+\delta_T+\tau_2 \quad c_4 = -\tau_1 \quad c_5 = -\tau_2 \quad c_6 = \mu$

$c_7 = \mu+\beta \quad c_8 = -\beta \quad c_9 = \mu+\delta_A \quad c_{10} = -\pi \quad c_{11} = -\tau_4 \quad c_{12} = (\mu+\gamma\kappa_2)$

$c_{13} = -\gamma\kappa_2 \quad c_{14} = \omega+\tau_3+\mu+\delta_T \quad c_{15} = -\tau_3 \quad c_{16} = \mu+\pi \quad c_{17} = -\omega \quad c_{18} = \tau_4+\mu+\delta_{TA}$

Using Mathematica software, the inverse of V is given by

$$V^{-1} = \begin{bmatrix} \frac{1}{c_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\frac{c_2}{c_1c_3} & \frac{1}{c_3} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{-c_3c_4+c_2c_5}{c_1c_3c_6} & -\frac{c_5}{c_3c_6} & \frac{1}{c_6} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{c_7} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\frac{c_8}{c_7c_9} & \frac{1}{c_9} & \frac{-c_{11}c_{13}c_{16}c_{17}-c_{10}c_{13}c_{15}c_{18}}{c_9c_{12}c_{14}c_{16}c_{18}} & \frac{c_{11}c_{16}c_{18}+c_{10}c_{15}c_{18}}{c_9c_{14}c_{16}c_{18}} & -\frac{c_{10}}{c_9c_{16}} & -\frac{c_{11}}{c_9c_{18}} \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{c_{12}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\frac{c_{13}}{c_{12}c_{14}} & \frac{1}{c_{14}} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{c_{13}c_{15}}{c_{12}c_{14}c_{16}} & -\frac{c_{15}}{c_{14}c_{16}} & \frac{1}{c_{16}} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{c_{13}c_{17}}{c_{12}c_{14}c_{18}} & -\frac{c_{17}}{c_{14}c_{18}} & 0 & \frac{1}{c_{18}} \end{bmatrix}$$

Thus $FV^{-1} = \begin{bmatrix} b_1 & b_2 & 0 & 0 & 0 & b_3 & b_4 & 0 & b_5 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b_6 & b_7 & b_8 & b_9 & b_{10} & b_{11} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$

where

$b_1 = -\frac{(1-\xi_1)\varpi_1\Lambda c_2}{\mu c_1 c_3} = -\frac{(1-\xi_1\varpi_1\Lambda(-\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)} = \frac{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}$

$b_2 = \frac{(1-\xi_1)\varpi_1\Lambda}{\mu c_3}$

$b_3 = \frac{(1-\xi_1)\varpi_1\Lambda}{\mu}(\frac{c_{13}c_{17}}{c_{12}c_{14}c_{18}} - \frac{c_{13}}{c_{12}c_{14}})$

$b_4 = \frac{(1-\xi_1)\varpi_1\Lambda}{\mu}(\frac{1}{c_{14}} - \frac{c_{17}}{c_{14}c_{18}})$

$b_5 = (1-\xi_1)\varpi_1\frac{\Lambda}{\mu}\frac{1}{c_{18}}$

$b_6 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}(\frac{1}{c_7} - \frac{c_8}{c_7c_9}) = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}(\frac{c_9-c_8}{c_7c_9}) = \frac{(1-\xi_2)\varpi_2\Lambda(c_9-c_8)}{\mu c_7 c_9} = \frac{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)}$

$b_7 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu c_9}$

$b_8 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}\frac{-c_{11}c_{13}c_{16}c_{17}-c_{10}c_{13}c_{15}c_{18}+c_9c_{14}c_{16}c_{18}-c_9c_{13}c_{16}c_{18}+c_9c_{13}c_{15}c_{18}+c_9c_{13}c_{16}c_{17}}{c_9c_{12}c_{14}c_{16}c_{18}}$

$b_9 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}\frac{c_{11}c_{16}c_{18}+c_{10}c_{15}c_{18}+c_9c_{16}c_{18}-c_9c_{15}c_{18}-c_9c_{16}c_{17}}{c_9c_{14}c_{16}c_{18}}$

$b_{10} = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}\frac{c_9-c_{10}}{c_9c_{16}}$

$b_{11} = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu c_{18}}$

The matrix FV^{-1} has eigen values given by $\{0, 0, 0, 0, 0, 0, 0, b_1, b_6\}$. Hence the dominant eigenvalues of FV^{-1} are

$R_{0T} = b_1 = \frac{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}$

$R_{0H} = b_6 = \frac{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)}$

and these match the reproduction rates for the models of TB and HIV transmissions respectively. Therefore, the models's basic reproduction number, R_0,is;

$R_0 = \max[R_{0T}, R_{0H}]$

3.2.5 Local stability of Disease free equilibrium (DFE)

Theorem 1. *When $R_0 < 1$,the disease-free equilibrium E^0 is locally asymptotically stable;nevertheless when $R_0 > 1$,it is unstable.*

Proof.

The Jacobian of system (3.2) at the DFE is;

$$J(E^0) = \begin{bmatrix} -\mu & 0 & -f_1 & 0 & -f_2 & -f_2 & -f_2 & f_3 & -f_2 & f_3 \\ 0 & -g_1 & f_1 & 0 & 0 & 0 & 0 & f_1 & 0 & f_1 \\ 0 & \alpha\kappa_1 & -g_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau_1 & \tau_2 & -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & g_3 & f_2 & f_2 & f_2 & f_2 & f_2 \\ 0 & 0 & 0 & 0 & \beta & -g_4 & 0 & 0 & \pi & \tau_4 \\ 0 & 0 & 0 & 0 & 0 & 0 & -g_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \gamma\kappa_2 & -g_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_3 & -g_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \omega & 0 & -g_8 \end{bmatrix}$$

where

$f_1 = \frac{(1-\xi_1)\varpi_1\Lambda}{\mu}$ $\quad f_2 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu}$ $\quad f_3 = \frac{-((1-\xi_1)\varpi_1+(1-\xi_2)\varpi_2)\Lambda}{\mu}$ $\quad g_1 = \mu + \alpha\kappa_1 + \tau_1$

$g_2 = \mu+\delta_T+\tau_2$ $\quad g_3 = \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} - (\mu+\beta)$ $\quad g_4 = \mu+\delta_A$ $\quad g_5 = \mu+\gamma\kappa_2$ $\quad g_6 = \omega+\tau_3+\mu+\delta_T$

$g_7 = \mu + \pi$ $\quad g_8 = \tau_4 + \mu + \delta_{TA}$

The determinant of $J(E^0)$ is;

$$\begin{aligned} Det(J(E^0)) = g_5g_6g_7g_8\,&((\mu+\beta)(\mu+\delta_A)\mu(-(1-\xi_1)\varpi_1\Lambda\alpha\kappa_1+(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\mu) \\ &+(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)((1-\xi_1)\varpi_1\Lambda\alpha\kappa_1-(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\mu)) \end{aligned} \tag{3.18}$$

$$\begin{aligned} Det(J(E^0)) = g_5g_6g_7g_8\,&((\mu+\beta)(\mu+\delta_A)\mu(-(1-\xi_1)\varpi_1\Lambda\alpha\kappa_1+(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\mu) \\ &-(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)(-(1-\xi_1)\varpi_1\Lambda\alpha\kappa_1+(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\mu)) \end{aligned} \tag{3.19}$$

$$\begin{aligned} Det(J(E^0)) = g_5g_6g_7g_8&((\mu+\beta)(\mu+\delta_A)\mu \\ &-(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta))((\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\mu-(1-\xi_1)\varpi_1\Lambda\alpha\kappa_1) \end{aligned} \tag{3.20}$$

And the trace of $J(E^0)$ is;

$Tr(J(E^0)) = -2\mu - g_1 - g_2 + g_3 - g_4 - g_5 - g_6 - g_7 - g_8$

$Tr(J(E^0)) = -(2\mu + g_1 + g_2 + g_4 + g_5 + g_6 + g_7 + g_8) + g_3$ $Tr(J(E^0)) = -(2\mu + g_1 + g_2 + g_4 + g_5 + g_6 + g_7 + g_8) + (\frac{(1-\xi_2)\varpi_2\Lambda}{\mu} - (\mu + \beta))$

Clearly $Det(J(E^0)) > 0$ if

$R_{0T} = \frac{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)} < 1$ and

$R_{0H} = \frac{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)} < 1$

and $Tr(J(E^0)) < 0$ for $\frac{(1-\xi_2)\varpi_2\Lambda}{\mu} < (\mu + \beta)$

Applying Routh Hurwitz conditions for all roots of the characteristic polynomial $J(E^0)$ to have negative parts as applied by Enagi et al. (2017), since $Det(J(E^0)) > 0$ provided that $R_{0T} < 1$ and $R_{0H} < 1$ and $Tr(J(E^0)) < 0$ if $\frac{(1-\xi_2)\varpi_2\Lambda}{\mu} < (\mu + \beta)$, the DFE of the model is locally asymptotically stable. □

3.2.6 Global stability conditions for the disease-free equilibrium when $R_0 < 1$

Here, we mention two conditions which, if fulfilled, wil guarantee HIV-TB coinfection model's global asymptotic stability of the disease free equilibrium system (3.2) as

$$\begin{aligned} \frac{dX}{dt} &= F(X, Z), \\ \frac{dZ}{dt} &= G(X, Z), \quad G(X, 0) = 0 \end{aligned} \tag{3.21}$$

Where $X = (S, R)$ and $Z = (L_T, I_T, I_H, A_H, L_{HT}, I_{HT}, T_{HT}, A_{HT})$.The components of $X \in \mathbb{R}^2_+$ and $Z \in \mathbb{R}^8_+$ represents classes of individuals who are infection free and the infected respectively. The disease-free equilibrium point is represented as;

$$U^0 = (X^0, 0) \quad \text{where} \quad X^0 = \left(\frac{\Lambda}{\mu}, 0\right) \tag{3.22}$$

The requirements (L1) and (L2) in equation (3.23) has to be fulfilled for the system (3.2) to be globally asymptotically stable.

$$
\begin{aligned}
(L1)\ \text{For}\ \frac{dX}{dt} &= F(X,0), \quad X^0 \ \text{is globally asymptotically stable (g.a.s)} \\
(L2)\ G(X,Z) &= AZ - \widehat{G}(X,Z), \ \ \widehat{G}(X,Z) \geq 0 \ \ \forall \ \ X,Z \in \Omega
\end{aligned}
\tag{3.23}
$$

where Ω is the region where the model makes biological sense and $A = D_Z G(X^0, 0)$ is an M-matrix whose off diagonal elements are non-negative. Theorem 2 will hold if the system (3.21) meets the requirements set out in (3.23).

Theorem 2. *The equilibrium point $U^0 = (X^0, 0)$ is a globally asymptotically stable equilibrium of the system (3.21) given that $R_0 < 1$ and that the conditions in (3.23) are satisfied*

Proof.

From the system (3.2),G(X,Z) and F(X, Z)are obtained as follows ;

$$
F(X,Z) = \begin{bmatrix} \Lambda - (\lambda_H + \lambda_T + \mu)S \\ \tau_1 L_T + \tau_2 I_T - (\mu + \lambda_H + \eta\lambda_T)R \end{bmatrix}
$$

$$
G(X,Z) = \begin{bmatrix}
\lambda_T S + \eta\lambda_T R - (\mu + \alpha\kappa_1 + \tau_1 + \lambda_H)L_T \\
\alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2 + \phi\lambda_H)I_T \\
\lambda_H S + \lambda_H R - (\mu + \beta + \psi_1\lambda_T)I_H \\
\beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A + \psi_2\lambda_T)A_H \\
\lambda_H L_T + \psi_1\lambda_T I_H - (\mu + \gamma\kappa_2)L_{HT} \\
\gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} + \phi\lambda_H I_T \\
\tau_3 I_{HT} - (\mu + \pi)T_{HT} \\
\omega I_{HT} + \psi_2\lambda_T A_H - (\tau_4 + \mu + \delta_{TA})A_{HT}
\end{bmatrix}
$$

when $Z = 0$, $F(X,Z)$ assumes the form

$$
F(X,0) = \begin{bmatrix} \Lambda - \mu S \\ 0 \end{bmatrix}
$$

$\Rightarrow$

$$
\frac{dS}{dt} = \Lambda - \mu S \tag{3.24}
$$

Solving (3.24), we obtain

$S = \frac{\Lambda}{\mu} + (S(0) - \frac{\Lambda}{\mu})S^{-\mu t}$

which as $t \to \infty$, we get

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

Thus $U^0 = (X^0, 0)$ is a globally asymptotically stable.

We calculate A by expressing the Z derivative of $G(X,Z)$ at $U^0 = (X^0, 0)$. Thus

$$A = D_Z G(X^0, 0)$$

$$= \begin{bmatrix} -g_1 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & 0 & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} \\ \alpha\kappa_1 & -g_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & g_3 & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} \\ 0 & 0 & \beta & -g_4 & 0 & 0 & \pi & \tau_4 \\ 0 & 0 & 0 & 0 & -g_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma\kappa_2 & -g_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_3 & -g_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & 0 & -g_8 \end{bmatrix}$$

where

$g_1 = \mu + \alpha\kappa_1 + \tau_1 \quad g_2 = \mu + \delta_T + \tau_2 \quad g_3 = (1-\xi_2)\varpi_2\frac{\Lambda}{\mu} - (\mu + \beta) \quad g_4 = \mu + \delta_A$

$g_5 = \mu + \gamma\kappa_2 \quad g_6 = \omega + \tau_3 + \mu + \delta_T \quad g_7 = \mu + \pi \quad g_8 = \tau_4 + \mu + \delta_{TA}$

multiplying Z with A, we get

$$AZ = \begin{bmatrix} -g_1 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & 0 & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} & 0 & \frac{(1-\xi_1)\varpi_1\Lambda}{\mu} \\ \alpha\kappa_1 & -g_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & g_3 & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} & \frac{(1-\xi_2)\varpi_2\Lambda}{\mu} \\ 0 & 0 & \beta & -g_4 & 0 & 0 & \pi & \tau_4 \\ 0 & 0 & 0 & 0 & -g_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma\kappa_2 & -g_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_3 & -g_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & 0 & -g_8 \end{bmatrix} \begin{bmatrix} L_T \\ I_T \\ I_H \\ A_H \\ L_{HT} \\ I_{HT} \\ T_{HT} \\ A_{HT} \end{bmatrix}$$

$$= \begin{bmatrix} \lambda_T\frac{\Lambda}{\mu} - (\mu + \alpha\kappa_1 + \tau_1)L_T \\ \alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2)I_T \\ \lambda_H\frac{\Lambda}{\mu} - (\mu + \beta)I_H \\ \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A)A_H \\ \lambda_H L_T - (\mu + \gamma\kappa_2)L_{HT} \\ \gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} \\ \tau_3 I_{HT} - (\mu + \pi)T_{HT} \\ \omega I_{HT} - (\tau_4 + \mu + \delta_{TA})A_{HT} \end{bmatrix}$$

From second condition (L2) in (3.23), we have

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

$$= \begin{bmatrix} \lambda_T \frac{\Lambda}{\mu} - (\mu + \alpha\kappa_1 + \tau_1)L_T \\ \alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2)I_T \\ \lambda_H \frac{\Lambda}{\mu} - (\mu + \beta)I_H \\ \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A)A_H \\ \lambda_H L_T - (\mu + \gamma\kappa_2)L_{HT} \\ \gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} \\ \tau_3 I_{HT} - (\mu + \pi)T_{HT} \\ \omega I_{HT} - (\tau_4 + \mu + \delta_{TA})A_{HT} \end{bmatrix} - \begin{bmatrix} \lambda_T S + \eta\lambda_T R - (\mu + \alpha\kappa_1 + \tau_1 + \lambda_H)L_T \\ \alpha\kappa_1 L_T - (\mu + \delta_T + \tau_2 + \phi\lambda_H)I_T \\ \lambda_H S + \lambda_H R - (\mu + \beta + \psi_1\lambda_T)I_H \\ \beta I_H + \pi T_{HT} + \tau_4 A_{HT} - (\mu + \delta_A + \psi_2\lambda_T)A_H \\ \lambda_H L_T + \psi_1\lambda_T I_H - (\mu + \gamma\kappa_2)L_{HT} \\ \gamma\kappa_2 L_{HT} - (\omega + \tau_3 + \mu + \delta_T)I_{HT} + \phi\lambda_H I_T \\ \tau_3 I_{HT} - (\mu + \pi)T_{HT} \\ \omega I_{HT} + \psi_2\lambda_T A_H - (\tau_4 + \mu + \delta_{TA})A_{HT} \end{bmatrix}$$

$$= \begin{bmatrix} \lambda_T(\frac{\Lambda}{\mu} - S) - \eta\lambda_T R \\ \phi\lambda_H I_T \\ \lambda_H(\frac{\Lambda}{\mu} - S) - \lambda_H R + \psi_1\lambda_T I_H \\ \psi_2\lambda_T A_H \\ -\lambda_H L_T - \psi_1\lambda_T I_H \\ -\phi\lambda_H I_T \\ 0 \\ -\psi_2\lambda_T A_H \end{bmatrix}$$

Therefore

$$\widehat{G}(X,Z) = \begin{bmatrix} \widehat{G}_1(X,Z) \\ \widehat{G}_2(X,Z) \\ \widehat{G}_3(X,Z) \\ \widehat{G}_4(X,Z) \\ \widehat{G}_5(X,Z) \\ \widehat{G}_6(X,Z) \\ \widehat{G}_7(X,Z) \\ \widehat{G}_8(X,Z) \end{bmatrix} = \begin{bmatrix} \lambda_T(\frac{\Lambda}{\mu} - S) - \eta\lambda_T R \\ \phi\lambda_H I_T \\ \lambda_H(\frac{\Lambda}{\mu} - S) - \lambda_H R + \psi_1\lambda_T I_H \\ \psi_2\lambda_T A_H \\ -\lambda_H L_T - \psi_1\lambda_T I_H \\ -\phi\lambda_H I_T \\ 0 \\ -\psi_2\lambda_T A_H \end{bmatrix} \tag{3.25}$$

In equation (3.25), $\widehat{G}_5(X,Z) < 0$, $\widehat{G}_6(X,Z) < 0$ and $\widehat{G}_8(X,Z) < 0$ hence $\widehat{G}(X,Z) < 0$.The second requirement (L2) in (3.23) is not satisfied, so $U^0 = (X^0, 0)$ is not globally asymptotically stable when $R_0 < 1$.

□

3.2.7 Endemic Equilibrium Point

We set the right side of the equation system (3.2)equal to zero to obtain this equilibrium point (E^*).We substitute for $S = S^*$, $L_T = L_T^*$, $I_T = I_T^*$, $R = R^*$, $I_H = I_H^*$, $A_H = A_H^*$, $L_{HT} = L_{HT}^*$, $I_{HT} = I_{HT}^*$, $T_{HT} = T_{HT}^*$,$A_{HT} = A_{HT}^*$, $\lambda_T = \lambda_T^* = (1-\xi_1)\varpi_1(I_T^* + I_{HT}^* + A_{HT}^*)$

and $\lambda_H = \lambda_H^* = (1-\xi_2)\varpi_2(I_H^* + L_{HT}^* + I_{HT}^* + A_H^* + T_{HT}^* + A_{HT}^*)$. Thus

$$\begin{aligned}
0 &= \Lambda - j_1 S^* \\
0 &= \lambda_T^* S^* + \eta\lambda_T^* R^* - j_2 L_T^* \\
0 &= \alpha\kappa_1 L_T^* - j_3 I_T \\
0 &= \tau_1 L_T^* + \tau_2 I_T^* - j_4 R^* \\
0 &= \lambda_H^* S^* + \lambda_H^* R^* - j_5 I_H^* \\
0 &= \beta I_H^* + \pi T_{HT}^* + \tau_4 A_{HT}^* - j_6 A_H^* \\
0 &= \lambda_H^* L_T^* + \psi_1 \lambda_T^* I_H^* - j_7 L_{HT}^* \\
0 &= \gamma\kappa_2 L_{HT}^* - j_8 I_{HT}^* + \phi\lambda_H I_T^* \\
0 &= \tau_3 I_{HT}^* - j_9 T_{HT}^* \\
0 &= \omega I_{HT}^* + \psi_2 \lambda_T^* A_H^* - j_{10} A_{HT}^*
\end{aligned} \tag{3.26}$$

where

$j_1 = \lambda_H^* + \lambda_T^* + \mu$ $j_2 = \mu + \alpha\kappa_1 + \tau_1 + \lambda_H^*$ $j_3 = \mu + \delta_T + \tau_2 + \phi\lambda_H^*$ $j_4 = \mu + \lambda_H^* + \eta\lambda_T^*$ $j_5 = \mu + \beta + \psi_1\lambda_T^*$ $j_6 = \mu + \delta_A + \psi_2\lambda_T^*$ $j_7 = \mu + \gamma\kappa_2$ $j_8 = \omega + \tau_3 + \mu + \delta_T$ $j_9 = \mu + \pi$ $j_{10} = \tau_4 + \mu + \delta_{TA}$

From system (3.26), by solving for S^*, L_T^*, I_T^*, R^*, I_H^*, A_H^*, L_{HT}^*, I_{HT}^*, T_{HT}^* and A_{HT}^*, we get

$$
\begin{aligned}
S^* &= \frac{\Lambda}{j_1} \\
L_T^* &= \frac{\lambda_T^*(\Lambda + j_1\eta R^*)}{j_1 j_2} \\
I_T^* &= \frac{\alpha\kappa_1\lambda_T^*(\Lambda + j_1\eta R^*)}{j_1 j_2 j_3} \\
R^* &= \frac{(\tau_1\lambda_T^* j_3 + \tau_2\alpha\kappa_1\lambda_T^*)\Lambda}{(j_2 j_3 j_4 - (\tau_1\lambda_T^* j_3 + \tau_2\alpha\kappa_1\lambda_T^*)\eta)j_1} \\
I_H^* &= \frac{\lambda_H^*(\Lambda + j_1 R^*)}{j_1 j_5} \\
A_H^* &= \frac{\begin{array}{c}\tau_3\lambda_H^*\lambda_T^* j_6(\pi j_{10} + \omega\tau_4)(\gamma\kappa_2 j_3(j_5(\Lambda + j_1\eta R^*) + \psi_1 j_2(\Lambda + j_1 R^*)) \\ +\phi\alpha\kappa_1 j_5 j_7(\Lambda + j_1\eta R^*)) + \beta\lambda_H^* j_2 j_3 j_6 j_7 j_8 j_9 j_{10}(\Lambda + j_1 R^*)\end{array}}{j_1 j_2 j_3 j_5 j_6 j_7 j_8 j_9(j_6 j_{10} - \psi_2\lambda_T^*\tau_4)} \\
L_{HT}^* &= \frac{\lambda_H^*\lambda_T^*(j_5(\Lambda + j_1\eta R^*) + \psi_1 j_2(\Lambda + j_1 R^*))}{j_1 j_2 j_5 j_7} \\
I_{HT}^* &= \frac{\lambda_H^*\lambda_T^*(\gamma\kappa_2 j_3(j_5(\Lambda + j_1\eta R^*) + \psi_1 j_2(\Lambda + j_1 R^*)) + \phi\alpha\kappa_1 j_5 j_7(\Lambda + j_1\eta R^*))}{j_1 j_2 j_3 j_5 j_7 j_8} \\
T_{HT}^* &= \frac{\tau_3\lambda_H^*\lambda_T^*(\gamma\kappa_2 j_3(j_5(\Lambda + j_1\eta R^*) + \psi_1 j_2(\Lambda + j_1 R^*)) + \phi\alpha\kappa_1 j_5 j_7(\Lambda + j_1\eta R^*))}{j_1 j_2 j_3 j_5 j_7 j_8 j_9} \\
A_{HT}^* &= \frac{\begin{array}{c}\tau_3\lambda_H^*\lambda_T^*(\omega j_6 + \psi_2\pi\lambda_T^*)(\gamma\kappa_2 j_3(j_5(\Lambda + j_1\eta R^*) + \psi_1 j_2(\Lambda + j_1 R^*)) \\ +\phi\alpha\kappa_1 j_5 j_7(\Lambda + j_1\eta R^*)) + \psi_2\lambda_T^*\beta\lambda_H^* j_2 j_3 j_7 j_8 j_9(\Lambda + j_1 R^*)\end{array}}{j_1 j_2 j_3 j_5 j_7 j_8 j_9(j_6 j_{10} - \psi_2\lambda_T^*\tau_4)}
\end{aligned}
$$

3.2.8 Bifurcation Analysis

Theorem 3. *Theorem 4.1 of Castillo-Chavez and Song (2004) Consider the following general system of ODEs with a parameter ϕ.*

$$\frac{dx}{dt} = h(x,\phi), \quad h : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R} \quad \text{and} \quad h \in C^2(\mathbb{R}^n \times \mathbb{R}) \tag{3.27}$$

where 0 is an equilibrium point of the system (that is, $h(0,\phi) \equiv 0 \quad \forall\ \phi$) and assume

1. *$A = D_x h(0,0) = \frac{dh_i}{dx_j}(0,0)$ is the linearization matrix of the system given by (3.27) around the equilibrium 0 with ϕ evaluated at 0. Zero is a simple eigenvalue of A.The other eigenvalues of A have real parts which are negative.*

2. *Matrix A has a nonnegative right and left eigenvector u and v respectively that corresponds to the zero eigenvalue.*

Let h_k be the k^{th} component of h and

$$a = \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 h_k}{\partial x_i \partial x_j}(0,0)$$

$$b = \sum_{k,i=1}^{n} v_k u_i \frac{\partial^2 h_k}{\partial x_i \partial \phi}(0,0)$$

The sign of a and b has a complete bearing on the local dynamics of (3.27) around 0.

i. *$a > 0$, $b > 0$ when $\phi < 0$ with $|\phi| << 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \phi << 1$, 0 is unstable and there exists a negative, locally asymptotically stable equilibrium;*

ii. *$a < 0$, $b < 0$ when $\phi < 0$ with $|\phi| << 1$, 0 is unstable; when $0 < \phi << 1$, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium;*

iii. *$a > 0$, $b < 0$ when $\phi < 0$ with $|\phi| << 1$, 0 is unstable; and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi << 1$, 0 is stable, and a positive unstable equilibrium appears;*

iv. *$a < 0$, $b > 0$ when $\phi < 0$ changes to positive, 0 becomes unstable. Corresponding to a negative unstable equilibrium becomes positive and locally asymptotically stable. Particularly, if $a > 0$ and $b > 0$, then a backward bifurcation occurs at $\phi = 0$.*

Applying the theorem (3), we take into consideration, ϖ_1 and ϖ_2,the rates of transmissions as bifurcation parameters so that $R_{0T} = 1$ and $R_{0H} = 1$ if and only if

$\varpi_1 = \varpi_1^* = \frac{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}{(1-\xi_1)\Lambda(\alpha\kappa_1)}$ and

$\varpi_2 = \varpi_2^* = \frac{(1-\xi_1)\varpi_1(\alpha\kappa_1)(\mu+\beta)(\mu+\delta_A)}{(1-\xi_2)(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)(\mu+\delta_A+\beta)R_{0T}}$

Then we let $S = x_1$, $L_T = x_2$, $I_T = x_3$, $R = x_4$, $I_H = x_5$, $A_H = x_6$, $L_{HT} = x_7$, $I_{HT} = x_8$,

$T_{HT} = x_9,\ A_{HT} = x_{10}$

The system (3.2) becomes

$$
\begin{aligned}
\frac{dx_1}{dt} &= \Lambda - (\lambda_{Hx} + \lambda_{Tx} + \mu)x_1 \\
\frac{dx_2}{dt} &= \lambda_{Tx}x_1 + \eta\lambda_{Tx}x_4 - (\mu + \alpha\kappa_1 + \tau_1 + \lambda_{Hx})x_2 \\
\frac{dx_3}{dt} &= \alpha\kappa_1 x_2 - (\mu + \delta_T + \tau_2 + \phi\lambda_{Hx})x_3 \\
\frac{dx_4}{dt} &= \tau_1 x_2 + \tau_2 x_3 - (\mu + \lambda_{Hx} + \eta\lambda_{Tx})x_4 \\
\frac{dx_5}{dt} &= \lambda_{Hx}x_1 + \lambda_{Hx}x_4 - (\mu + \beta + \psi_1\lambda_{Tx})x_5 \\
\frac{dx_6}{dt} &= \beta x_5 + \pi x_9 + \tau_4 x_{10} - (\mu + \delta_A + \psi_2\lambda_{Tx})x_6 \\
\frac{dx_7}{dt} &= \lambda_{Hx}x_2 + \psi_1\lambda_{Tx}x_5 - (\mu + \gamma\kappa_2)x_7 \\
\frac{dx_8}{dt} &= \gamma\kappa_2 x_7 - (\omega + \tau_3 + \mu + \delta_T)x_8 + \phi\lambda_{Hx}x_3 \\
\frac{dx_9}{dt} &= \tau_3 x_8 - (\mu + \pi)x_9 \\
\frac{dx_{10}}{dt} &= \omega x_8 + \psi_2\lambda_{Tx}x_6 - (\tau_4 + \mu + \delta_{TA})x_{10}
\end{aligned}
\tag{3.28}
$$

where $\lambda_{Tx} = (1-\xi_1)\varpi_1(x_3 + x_8 + x_{10})$ and

$\lambda_{Hx} = (1-\xi_2)\varpi_2(x_5 + x_7 + x_8 + x_6 + x_9 + x_{10})$

The Jacobian of system (3.28) at the disease free equilibrium E^0 is;

$$
J(E^0) = \begin{bmatrix}
-\mu & 0 & -f_1 & 0 & -f_2 & -f_2 & -f_2 & f_3 & -f_2 & f_3 \\
0 & -g_1 & f_1 & 0 & 0 & 0 & 0 & f_1 & 0 & f_1 \\
0 & \alpha\kappa_1 & -g_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & \tau_1 & \tau_2 & -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & g_3 & f_2 & f_2 & f_2 & f_2 & f_2 \\
0 & 0 & 0 & 0 & \beta & -g_4 & 0 & 0 & \pi & \tau_4 \\
0 & 0 & 0 & 0 & 0 & 0 & -g_5 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & \gamma\kappa_2 & -g_6 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_3 & -g_7 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & \omega & 0 & -g_8
\end{bmatrix}
\tag{3.29}
$$

where

$f_1 = \frac{(1-\xi_1)\varpi_1\Lambda}{\mu}$ $\quad f_2 = \frac{(1-\xi_2)\varpi_2^*\Lambda}{\mu}$ $\quad f_3 = \frac{-((1-\xi_1)\varpi_1 + (1-\xi_2)\varpi_2^*)\Lambda}{\mu}$ $\quad g_1 = \mu + \alpha\kappa_1 + \tau_1$

$g_2 = \mu + \delta_T + \tau_2$ $\quad g_3 = \frac{(1-\xi_2)\varpi_2^*\Lambda}{\mu} - (\mu + \beta)$ $\quad g_4 = \mu + \delta_A$ $\quad g_5 = \mu + \gamma\kappa_2$ $\quad g_6 = \omega + \tau_3 + \mu + \delta_T$

$g_7 = \mu + \pi \quad g_8 = \tau_4 + \mu + \delta_{TA}$

Using the centre Manifold theory, we let the right and the left eigenvectors of the Jacobian matrix $J(E^0)$ when $R_0 = 1$ be given by $\mathbf{u} = (u_1, u_2, u_3, u_4, u_5, u_6, u_7, u_8, u_9, u_{10})$ and $\mathbf{v} = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9, v_{10})$ respectively. The right eigenvector is computed by multiplying $\mathbf{u}$ by the Jacobian Matrix (3.29) and equating the result to zero. Thus

$$\begin{bmatrix} -\mu & 0 & -f_1 & 0 & -f_2 & -f_2 & -f_2 & f_3 & -f_2 & f_3 \\ 0 & -g_1 & f_1 & 0 & 0 & 0 & 0 & f_1 & 0 & f_1 \\ 0 & \alpha\kappa_1 & -g_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau_1 & \tau_2 & -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & g_3 & f_2 & f_2 & f_2 & f_2 & f_2 \\ 0 & 0 & 0 & 0 & \beta & -g_4 & 0 & 0 & \pi & \tau_4 \\ 0 & 0 & 0 & 0 & 0 & 0 & -g_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \gamma\kappa_2 & -g_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_3 & -g_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \omega & 0 & -g_8 \end{bmatrix} \begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \\ u_7 \\ u_8 \\ u_9 \\ u_{10} \end{pmatrix} = \mathbf{0}$$

$$\Rightarrow \begin{cases} -\mu u_1 - f_1 u_3 - f_2 u_5 - f_2 u_6 - f_2 u_7 + f_3 u_8 - f_2 u_9 + f_3 u_{10} = 0 \\ -g_1 u_2 + f_1 u_3 + f_1 u_8 + f_1 u_{10} = 0 \\ \alpha\kappa_1 u_2 - g_2 u_3 = 0 \\ \tau_1 u_2 + \tau_2 u_3 - \mu u_4 = 0 \\ g_3 u_5 + f_2 u_6 + f_2 u_7 + f_2 u_8 + f_2 u_9 + f_2 u_{10} = 0 \\ \beta u_5 - g_4 u_6 + \pi u_9 + \tau_4 u_{10} = 0 \\ -g_5 u_7 = 0 \\ \gamma\kappa_2 u_7 - g_6 u_8 = 0 \\ \tau_3 u_8 - g_7 u_9 = 0 \\ \omega u_8 - g_8 u_{10} = 0 \end{cases}$$

Upon simplification we get

$$\begin{cases} -\mu u_1 - f_1 u_3 - f_2 u_5 - f_2 u_6 = 0 \\ -g_1 u_2 + f_1 u_3 = 0 \\ \alpha\kappa_1 u_2 - g_2 u_3 = 0 \\ \tau_1 u_2 + \tau_2 u_3 - \mu u_4 = 0 \\ g_3 u_5 + f_2 u_6 = 0 \\ \beta u_5 - g_4 u_6 = 0 \\ u_7 = 0 \\ u_8 = 0 \\ u_9 = 0 \\ u_{10} = 0 \end{cases} \Rightarrow \begin{cases} \mu u_1 = -f_1 u_3 - \frac{f_2^2 + g_3 f_2}{g_3} u_6 \\ u_2 = \frac{f_1}{g_1} u_3 \\ u_3 = u_3 \\ u_4 = (\frac{f_1\tau_1 + g_1\tau_2}{g_1\mu}) u_3 \\ u_5 = -\frac{f_2}{g_3} u_6 \\ u_6 = u_6 \\ u_7 = 0 \\ u_8 = 0 \\ u_9 = 0 \\ u_{10} = 0 \end{cases}$$

Also we compute the left eigenvector by multiplying $\mathbf{v}$ with the transpose of the Jacobian Matrix (3.29) and equating to zero. Thus

$$
\begin{bmatrix}
-\mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & -g_1 & \alpha\kappa_1 & \tau_1 & 0 & 0 & 0 & 0 & 0 & 0 \\
-f_1 & f_1 & -g_2 & \tau_2 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\
-f_2 & 0 & 0 & 0 & g_3 & \beta & 0 & 0 & 0 & 0 \\
-f_2 & 0 & 0 & 0 & f_2 & -g_4 & 0 & 0 & 0 & 0 \\
-f_2 & 0 & 0 & 0 & f_2 & 0 & -g_5 & \gamma\kappa_2 & 0 & 0 \\
f_3 & f_1 & 0 & 0 & f_2 & 0 & 0 & -g_6 & \tau_3 & \omega \\
-f_2 & 0 & 0 & 0 & f_2 & \pi & 0 & 0 & -g_7 & 0 \\
f_3 & f_1 & 0 & 0 & f_2 & \tau_4 & 0 & 0 & 0 & -g_8
\end{bmatrix}
\begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \\ v_8 \\ v_9 \\ v_{10} \end{pmatrix} = \mathbf{0}
$$

$$
\begin{cases}
-\mu v_1 = 0 \\
-g_1 v_2 + \alpha\kappa_1 v_3 + \tau_1 v_4 = 0 \\
-f_1 v_1 + f_1 v_2 - g_2 v_3 + \tau_2 v_4 = 0 \\
-\mu v_4 = 0 \\
-f_2 v_1 + g_3 v_5 + \beta v_6 = 0 \\
-f_2 v_1 + f_2 v_5 - g_4 v_6 = 0 \\
-f_2 v_1 + f_2 v_5 - g_5 v_7 + \gamma\kappa_2 v_8 = 0 \\
f_3 v_1 + f_1 v_2 + f_2 v_5 - g_6 v_8 + \tau_3 v_9 + \omega v_{10} = 0 \\
-f_2 v_1 + f_2 v_5 + \pi v_6 - g_7 v_9 = 0 \\
f_3 v_1 + f_1 v_2 + f_2 v_5 + \tau_4 v_6 - g_8 v_{10} = 0
\end{cases}
$$

$$
\begin{cases}
v_1 = 0 \\
-g_1 v_2 + \alpha\kappa_1 v_3 = 0 \\
f_1 v_2 - g_2 v_3 = 0 \\
v_4 = 0 \\
g_3 v_5 + \beta v_6 = 0 \\
f_2 v_5 - g_4 v_6 = 0 \\
f_2 v_5 - g_5 v_7 + \gamma\kappa_2 v_8 = 0 \\
f_1 v_2 + f_2 v_5 - g_6 v_8 + \tau_3 v_9 + \omega v_{10} = 0 \\
f_2 v_5 + \pi v_6 - g_7 v_9 = 0 \\
f_1 v_2 + f_2 v_5 + \tau_4 v_6 - g_8 v_{10} = 0
\end{cases}
$$

$$
\begin{cases}
v_1 = 0 \\
v_2 = \frac{g_2}{f_1} v_3 \\
v_3 = v_3 \\
v_4 = 0 \\
v_5 = \frac{g_4}{f_2} v_6 \\
v_6 = v_6 \\
v_7 = \frac{f_2 v_5 + \gamma\kappa_2 v_8}{g_5} = \frac{\gamma\kappa_2 (g_2 g_7 g_8 + \omega g_2 g_7) v_3 + (\gamma\kappa_2 (g_4 g_7 g_8 + \tau_3 g_8 (g_4 + \pi) + \omega g_7 (g_4 + \tau_4)) + g_4 g_6 g_7 g_8) v_6}{g_5 g_6 g_7 g_8} \\
v_8 = \frac{f_1 v_2 + f_2 v_5 + \tau_3 v_9 + \omega v_{10}}{g_6} = \frac{(g_2 g_7 g_8 + \omega g_2 g_7) v_3 + (g_4 g_7 g_8 + \tau_3 g_8 (g_4 + \pi) + \omega g_7 (g_4 + \tau_4)) v_6}{g_6 g_7 g_8} \\
v_9 = \frac{g_4 + \pi}{g_7} v_6 \\
v_{10} = \frac{f_1 v_2 + (g_4 + \tau_4) v_6}{g_8} = \frac{g_2 v_3 + (g_4 + \tau_4) v_6}{g_8}
\end{cases}
$$

where u_3, u_6, v_3 and v_6 are computed to make sure the eigenvectors meet the requirements

$\mathbf{u} \cdot \mathbf{v} = 1.$

Computations of a and b

The non-vanishing partial derivatives of the system (3.28) at the DFE are;

$\frac{\partial^2 h_1}{\partial x_1 \partial x_3} = -(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_5} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_6} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_7} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_8} = -(1-\xi_1)\varpi_1 - (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_9} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_1}{\partial x_1 \partial x_{10}} = -(1-\xi_1)\varpi_1 - (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_1 \partial x_3} = (1-\xi_1)\varpi_1$
$\frac{\partial^2 h_2}{\partial x_1 \partial x_8} = (1-\xi_1)\varpi_1$
$\frac{\partial^2 h_2}{\partial x_1 \partial x_{10}} = (1-\xi_1)\varpi_1$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_5} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_6} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_7} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_8} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_9} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_2 \partial x_{10}} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_2}{\partial x_4 \partial x_3} = \eta(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_2}{\partial x_4 \partial x_8} = \eta(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_2}{\partial x_4 \partial x_{10}} = \eta(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_5} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_6} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_7} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_8} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_9} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_3}{\partial x_3 \partial x_{10}} = -\phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_3} = -\eta(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_5} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_6} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_7} = -(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_8} = -\eta(1-\xi_1)\varpi_1 - (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_9} = -(1-\xi_2)\varpi_2$
$\frac{\partial^2 h_4}{\partial x_4 \partial x_{10}} = -\eta(1-\xi_1)\varpi_1 - (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_5} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_6} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_7} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_8} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_9} = (1-\xi_2)\varpi_2$
$\frac{\partial^2 h_5}{\partial x_1 \partial x_{10}} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_5} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_6} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_7} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_8} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_9} = (1-\xi_2)\varpi_2$
$\frac{\partial^2 h_5}{\partial x_4 \partial x_{10}} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_5}{\partial x_5 \partial x_3} = -\psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_5}{\partial x_5 \partial x_8} = -\psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_5}{\partial x_5 \partial x_{10}} = -\psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_6}{\partial x_6 \partial x_3} = -\psi_2(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_6}{\partial x_6 \partial x_8} = -\psi_2(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_6}{\partial x_6 \partial x_{10}} = -\psi_2(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_5} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_6} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_7} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_8} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_9} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_2 \partial x_{10}} = (1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_7}{\partial x_5 \partial x_3} = \psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_7}{\partial x_5 \partial x_8} = \psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_7}{\partial x_5 \partial x_{10}} = \psi_1(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_5} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_6} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_7} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_8} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_9} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_8}{\partial x_3 \partial x_{10}} = \phi(1-\xi_2)\varpi_2^*$
$\frac{\partial^2 h_{10}}{\partial x_6 \partial x_3} = \psi_2(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_{10}}{\partial x_6 \partial x_8} = \psi_2(1-\xi_1)\varpi_1$
$\frac{\partial^2 h_{10}}{\partial x_6 \partial x_{10}} = \psi_2(1-\xi_1)\varpi_1$

a is given by

$$a = \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 h_k}{\partial x_i \partial x_j}(E^0)$$

$$
\begin{aligned}
a = & -v_1(u_1u_3(1-\xi_1)\varpi_1 + u_1u_5(1-\xi_2)\varpi_2 + u_1u_6(1-\xi_2)\varpi_2 + u_1u_7(1-\xi_2)\varpi_2 \\
& + u_1u_8[(1-\xi_1)\varpi_1 + (1-\xi_2)\varpi_2] + u_1u_9(1-\xi_2)\varpi_2 + u_1u_{10}[(1-\xi_1)\varpi_1 + (1-\xi_2)\varpi_2]) \\
& + v_2(u_1u_3(1-\xi_1)\varpi_1 + u_1u_8(1-\xi_1)\varpi_1 + u_1u_{10}(1-\xi_1)\varpi_1) \\
& - v_2(u_2u_5(1-\xi_2)\varpi_2 + u_2u_6(1-\xi_2)\varpi_2 + u_2u_7(1-\xi_2)\varpi_2 + u_2u_8(1-\xi_2)\varpi_2 \\
& \qquad + u_2u_9(1-\xi_2)\varpi_2 + u_2u_{10}(1-\xi_2)\varpi_2) \\
v_2&(u_4u_3\eta(1-\xi_1)\varpi_1 + u_4u_8\eta(1-\xi_1)\varpi_1 + u_4u_{10}\eta(1-\xi_1)\varpi_1) \\
& - v_3(u_3u_5\phi(1-\xi_2)\varpi_2^* + u_3u_6\phi(1-\xi_2)\varpi_2^* + u_3u_7\phi(1-\xi_2)\varpi_2^* + u_3u_8\phi(1-\xi_2)\varpi_2^* \\
& \qquad + u_3u_9\phi(1-\xi_2)\varpi_2^* + u_3u_{10}\phi(1-\xi_2)\varpi_2^*) \\
& - v_4(u_4u_3\eta(1-\xi_1)\varpi_1 + u_4u_5(1-\xi_2)\varpi_2 + u_4u_6(1-\xi_2)\varpi_2 + u_4u_7(1-\xi_2)\varpi_2 \\
& + u_4u_8[(1-\xi_1)\eta\varpi_1 + (1-\xi_2)\varpi_2] + u_4u_9(1-\xi_2)\varpi_2 + u_4u_{10}[(1-\xi_1)\eta\varpi_1 + (1-\xi_2)\varpi_2]) \\
& + v_5(u_1u_5(1-\xi_2)\varpi_2^* + u_1u_6(1-\xi_2)\varpi_2^* + u_1u_7(1-\xi_2)\varpi_2^* + u_1u_8(1-\xi_2)\varpi_2^* \\
& \qquad + v_1v_9(1-\xi_2)\varpi_2^* + u_1u_{10}(1-\xi_2)\varpi_2^*) \\
& + v_5(u_4u_5(1-\xi_2)\varpi_2 + u_4u_6(1-\xi_2)\varpi_2 + u_4u_7(1-\xi_2)\varpi_2 + u_4u_8(1-\xi_2)\varpi_2 \\
& \qquad + u_4u_9(1-\xi_2)\varpi_2 + u_4u_{10}(1-\xi_2)\varpi_2) \\
& - v_5(u_5u_3\psi_1(1-\xi_1)\varpi_1 + u_5u_8\psi_1(1-\xi_1)\varpi_1 + u_5u_{10}\psi_1(1-\xi_1)\varpi_1) \\
& - v_6(u_6u_3\psi_2(1-\xi_1)\varpi_1 + u_6u_8\psi_2(1-\xi_1)\varpi_1 + u_6u_{10}\psi_2(1-\xi_1)\varpi_1) \\
& + v_7(u_2u_5(1-\xi_2)\varpi_2^* + u_2u_6(1-\xi_2)\varpi_2^* + u_2u_7(1-\xi_2)\varpi_2^* + u_1u_8(1-\xi_2)\varpi_2^* \\
& \qquad + v_2v_9(1-\xi_2)\varpi_2^* + u_2u_{10}(1-\xi_2)\varpi_2^*) \\
& + v_7(u_5u_3\psi_1(1-\xi_1)\varpi_1 + u_5u_8\psi_1(1-\xi_1)\varpi_1 + u_5u_{10}\psi_1(1-\xi_1)\varpi_1) \\
& + v_8(u_3u_5\phi(1-\xi_2)\varpi_2^* + u_3u_6\phi(1-\xi_2)\varpi_2^* + u_3u_7\phi(1-\xi_2)\varpi_2^* + u_3u_8\phi(1-\xi_2)\varpi_2^* \\
& \qquad + u_3u_9\phi(1-\xi_2)\varpi_2^* + u_3u_{10}\phi(1-\xi_2)\varpi_2^*) \\
& + v_{10}(u_6u_3\psi_2(1-\xi_1)\varpi_1 + u_6u_8\psi_2(1-\xi_1)\varpi_1 + u_6u_{10}\psi_2(1-\xi_1)\varpi_1)
\end{aligned}
$$

For $v_1 = v_4 = 0 \;\; u_7 = u_8 = u_9 = u_{10} = 0$

$$\begin{aligned}
a = {} & v_2 u_1 u_3 (1-\xi_1)\varpi_1 \\
& - v_2(u_2 u_5 (1-\xi_2)\varpi_2^* + u_2 u_6 (1-\xi_2)\varpi_2^*) \\
& + v_2(u_4 u_3 \eta (1-\xi_1)\varpi_1) \\
& - v_3(u_3 u_5 \phi (1-\xi_2)\varpi_2^* + u_3 u_6 \phi (1-\xi_2)\varpi_2^*) \\
& + v_5(u_1 u_5 (1-\xi_2)\varpi_2^* + u_1 u_6 (1-\xi_2)\varpi_2^*) \\
& + v_5(u_4 u_5 (1-\xi_2)\varpi_2^* + u_4 u_6 (1-\xi_2)\varpi_2^*) \\
& - v_5 u_5 u_3 \psi_1 (1-\xi_1)\varpi_1 \\
& - v_6 u_6 u_3 \psi_2 (1-\xi_1)\varpi_1 \\
& + v_7(u_2 u_5 (1-\xi_2)\varpi_2^* + u_2 u_6 (1-\xi_2)\varpi_2^*) \\
& + v_7 u_5 u_3 \psi_1 (1-\xi_1)\varpi_1 \\
& + v_8(u_3 u_5 \phi (1-\xi_2)\varpi_2^* + u_3 u_6 \phi (1-\xi_2)\varpi_2^*) \\
& + v_{10} u_6 u_3 \psi_2 (1-\xi_1)\varpi_1
\end{aligned}$$

Given that $u_3, u_6, v_3, v_6, v_7, v_8, v_9, v_{10} > 0$, $a > 0$ for

$$\begin{aligned}
& \Big(v_3 u_3^2 \frac{g_2(f_1\tau_1 + g_1\tau_2)}{f_1 g_1 \mu}\eta(1-\xi_1)\varpi_1 \\
& \quad + v_6 u_3 u_6 \frac{g_4(f_1\tau_1 + g_1\tau_2)}{f_2 g_1 \mu}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \quad + v_7 u_3 u_6 \frac{f_1}{g_1}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \quad\quad + v_7 u_3 u_6 \frac{g_4}{\beta}\psi_1(1-\xi_1)\varpi_1 \\
& \quad\quad + v_8 u_3 u_6 \phi(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \quad\quad + v_{10} u_3 u_6 \psi_2 (1-\xi_1)\varpi_1\Big) > \Big(v_6 u_6 \frac{g_4(\beta f_1 u_3 + (g_4 f_2 + \beta f_2) u_6)}{f_2 \mu \beta}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \qquad + v_3 u_3 \frac{g_2(\beta f_1 u_3 + (g_4 f_2 + \beta f_2) u_6)}{f_1 \mu \beta}(1-\xi_1)\varpi_1 \\
& \qquad + v_3 u_3 u_6 \frac{g_2}{g_1}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \qquad + v_3 u_3 u_6 \phi (1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
& \qquad + v_6 u_3 u_6 \frac{g_4^2}{f_2\beta}\psi_1(1-\xi_1)\varpi_1 \\
& \qquad + v_6 u_3 u_6 \psi_2 (1-\xi_1)\varpi_1\Big)
\end{aligned}$$

and $a < 0$ for

$$
\begin{aligned}
&(v_3 u_3^2 \frac{g_2(f_1\tau_1 + g_1\tau_2)}{f_1 g_1 \mu} \eta(1-\xi_1)\varpi_1 \\
&+ v_6 u_3 u_6 \frac{g_4(f_1\tau_1 + g_1\tau_2)}{f_2 g_1 \mu}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_7 u_3 u_6 \frac{f_1}{g_1}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_7 u_3 u_6 \frac{g_4}{\beta}\psi_1(1-\xi_1)\varpi_1 \\
&+ v_8 u_3 u_6 \phi(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_{10} u_3 u_6 \psi_2(1-\xi_1)\varpi_1) < (v_6 u_6 \frac{g_4(\beta f_1 u_3 + (g_4 f_2 + \beta f_2)u_6)}{f_2 \mu \beta}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_3 u_3 \frac{g_2(\beta f_1 u_3 + (g_4 f_2 + \beta f_2)u_6)}{f_1 \mu \beta}(1-\xi_1)\varpi_1 \\
&+ v_3 u_3 u_6 \frac{g_2}{g_1}(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_3 u_3 u_6 \phi(1-\xi_2)\varpi_2^*(\frac{g_4}{\beta}+1) \\
&+ v_6 u_3 u_6 \frac{g_4^2}{f_2\beta}\psi_1(1-\xi_1)\varpi_1 \\
&+ v_6 u_3 u_6 \psi_2(1-\xi_1)\varpi_1)
\end{aligned}
$$

For, the non-vanishing partial derivatives of the system (3.28) at the DFE are;

$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_5} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_6} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_7} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_8} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_9} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_1}{\partial \varpi_2^* \partial x_{10}} = -\frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_5} = \frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_6} = \frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_7} = \frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_8} = \frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_9} = \frac{(1-\xi_2)\Lambda}{\mu}$
$\frac{\partial^2 h_5}{\partial \varpi_2^* \partial x_{10}} = \frac{(1-\xi_2)\Lambda}{\mu}$

b is given by

$$b = \sum_{k,i=1}^{n} v_k u_i \frac{\partial^2 h_k}{\partial x_i \partial \varpi_2^*}(E^0)$$

$b = -\frac{(1-\xi_2)\Lambda}{\mu}v_1(u_5+u_6+u_7+u_8+u_9+u_{10}) + \frac{(1-\xi_2)\Lambda}{\mu}v_5(u_5+u_6+u_7+u_8+u_9+u_{10})$

$b = \frac{(1-\xi_2)\Lambda}{\mu}v_5(u_5+u_6)$

Clearly $b > 0$ for $v_5 > 0$ and $u_5 + u_6 > 0$

Theorem 4. *The model (3.2) exhibits a backward bifurcation at $R_0 = 1$ if $a > 0$ and $b > 0$.A positive unstable and stable endemic equilibrium points exist when $\varpi_2^* < 0$ and $\varpi_2^* > 0$ respectively. Therefore, the endemic equilibrium point E^* is locally asymptotically stable for $R_0 > 1$ but close to 1 when $a < 0$ and $b > 0$.*

3.2.9 Sensitivity analysis

Sensitivity analysis of the model (3.2) is is performed in the sense of Mushayabasa and Bhunu (2011) to ascertain how variations in parameters impact the spread of the disease.

Definition 1. *The following defination applies to the normalized forward-sensitivity index of a variable, v, that differentiably depends on a parameter, p:*

$$\Upsilon_p^v = \frac{\partial p}{\partial v} \times \frac{v}{p} \tag{3.30}$$

We look at the basic reproduction number's, $R_0 = \max[R_{0T}, R_{0H}]$, sensitivity indices with regard to the parameters of the model. From (3.30), we obtain sensitivity of R_{0T} and R_{0H} separately:

$\frac{\partial R_{0T}}{\partial \Lambda}\frac{\Lambda}{R_{0T}} = \left(\frac{(1-\xi_1)\varpi_1(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}\right)\left(\frac{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\Lambda}{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}\right) = 1 > 0$

$\frac{\partial R_{0T}}{\partial \varpi_1}\frac{\varpi_1}{R_{0T}} = \left(\frac{(1-\xi_1)\Lambda(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}\right)\left(\frac{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)\varpi_1}{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}\right) = 1 > 0$

$\frac{\partial R_{0T}}{\partial \kappa_1}\frac{\kappa_1}{R_{0T}} = \frac{\mu+\tau_1}{(\mu+\alpha\kappa_1+\tau_1)} > 0$

$\frac{\partial R_{0T}}{\partial \mu}\frac{\mu}{R_{0T}} = -\frac{[(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)+\mu(\mu+\delta_T+\tau_2)+\mu(\mu+\alpha\kappa_1+\tau_1)]}{(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)} < 0$

$\frac{\partial R_{0T}}{\partial \tau_1}\frac{\tau_1}{R_{0T}} = -\frac{\tau_1}{(\mu+\alpha\kappa_1+\tau_1)} < 0$

$\frac{\partial R_{0T}}{\partial \tau_2}\frac{\tau_2}{R_{0T}} = -\frac{\tau_2}{(\mu+\delta_T+\tau_2)} < 0$

$\frac{\partial R_{0T}}{\partial \delta_T}\frac{\delta_T}{R_{0T}} = -\frac{\delta_T}{(\mu+\delta_T+\tau_2)} < 0$

$\frac{\partial R_{0T}}{\partial \xi_1}\frac{\xi_1}{R_{0T}} = -\frac{\xi_1}{(1-\xi_1)} < 0$

$\frac{\partial R_{0H}}{\partial \Lambda}\frac{\Lambda}{R_{0H}} = \left(\frac{(1-\xi_2)\varpi_2(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)}\right)\left(\frac{\mu(\mu+\beta)(\mu+\delta_A)\Lambda}{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}\right) = 1 > 0$

$\frac{\partial R_{0H}}{\partial \varpi_2}\frac{\varpi_2}{R_{0H}} = \left(\frac{(1-\xi_2)\Lambda(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)}\right)\left(\frac{\mu(\mu+\beta)(\mu+\delta_A)\varpi_2}{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}\right) = 1 > 0$

$\frac{\partial R_{0H}}{\partial \mu}\frac{\mu}{R_{0H}} = \frac{-\mu[\mu(\mu+\delta_A)+\mu(\mu+\beta)]-(\delta_A+\beta)[(\mu+\beta)(\mu+\delta_A)+\mu(\mu+\delta_A)+\mu(\mu+\beta)]}{(\mu+\beta)(\mu+\delta_A)(\mu+\delta_A+\beta)} < 0$

$\frac{\partial R_{0H}}{\partial \beta}\frac{\beta}{R_{0H}} = -\frac{\delta_A\beta}{(\mu+\beta)(\mu+\delta_A)(\mu+\delta_A+\beta)} < 0$

$\frac{\partial R_{0H}}{\partial \delta_A}\frac{\delta_A}{R_{0H}} = -\frac{\beta\delta_A}{(\mu+\delta_A)(\mu+\delta_A+\beta)} < 0$

$\frac{\partial R_{0H}}{\partial \xi_2}\frac{\xi_2}{R_{0H}} = -\frac{\xi_2}{(1-\xi_2)} < 0$

$R_{0T} = \frac{(1-\xi_1)\varpi_1\Lambda(\alpha\kappa_1)}{\mu(\mu+\alpha\kappa_1+\tau_1)(\mu+\delta_T+\tau_2)}$

$R_{0H} = \frac{(1-\xi_2)\varpi_2\Lambda(\mu+\delta_A+\beta)}{\mu(\mu+\beta)(\mu+\delta_A)}$

It can be seen that, R_{0T} responds to changes in Λ, ϖ_1 and κ_1 the most. When Λincreases or decreases, R_{0T} also rises or reduces in the same proportion. But physically, lowering the natural birth, Λ, rate is neither morally right nor practicable.If ϖ_1 and κ_1 are increased(or decreased), R_{0T} will also rise(or reduce) in proportion. The other parameters, τ_1, τ_2, δ_T, μ and $\xi_1$on the other hand have an inversely proportionate connection with R_{0T}. R_{0T} will reduce to a smaller proportion as τ_1, τ_2, δ_T, μ and ξ_1 are increased. Recall that δ_T and μ are TB-related mortality rate and natural death rates respectively. It is obvious that raising δ_T and μ is neither moral nor useful.

Additionally, it is evident that R_{0H} is most sensitive to the changes in Λ and ϖ_2. An increase or decrease in Λ will result in an equivalent rise or reduction in R_{0H}. Again,lowering the natural birth rate ,Λ,is neither morally right nor practicable. R_{0H} increases (or decreases) in direct proportion to variations in ϖ_2. The remaining parameters β, δ_A, μ and ξ_2, on the other hand,have an inversely proportionate relationship with R_{0H}. R_{0H} will drop as β, δ_A, μ and ξ_2 are increased. Recall that β, δ_A and μ are rates of progression from I_H to A_H, HIV-related mortality rate and rate of natural death respectively. It is clear that increase in β, δ_A and μ is neither ethical nor practical. From this sensitivity analysis, it is clear that control intervent ions should focus on prevention since it is ethical and practical to decrease ϖ_1 and ϖ_2. ϖ_1 can be reduced by increasing ξ_1. This is done through early ART to reduce occurence of active TB in individuals with HIV.

4. NUMERICAL SIMULATION,RESULTS AND DISCUSSION

In this chapter, we simulate the model using MATLAB to examine the role of intervention measures. To achieve this, we use parameter values as indicated in the Table 4.3.

Table 4.3: Parameter values of the model

Parameter symbol	**Value**	**Source**
Λ	0.029 yr^{-1}	Bhunu et al. (2009)
μ	0.02 yr^{-1}	Bhunu et al. (2009)
ϖ_1	0.00035 yr^{-1}	Estimate
ϖ_2	0.000075 yr^{-1}	Estimate
τ_1, τ_2, τ_3 & τ_4	$0 < \tau_{1-4} < 1$	Variable
κ_1	0.1 yr^{-1}	KLTBI (2020)
κ_2	0.2 yr^{-1}	Assumed
β	0.1 yr^{-1}	Estimate
π	0.5 yr^{-1}	Estimate
ω	0.3 yr^{-1}	Estimate
δ_A	0.04 yr^{-1}	Muthuri and Malonza (2018)
δ_T	0.05 yr^{-1}	Muthuri and Malonza (2018)
δ_{TA}	0.4 yr^{-1}	Assumed
ψ_1	0.71 yr^{-1}	Estimate
ψ_2	1.07 yr^{-1}	Estimate
ϕ	0.1 yr^{-1}	Estimate
η	0.1 yr^{-1}	Estimate
α	0.1 yr^{-1}	Estimate
γ	1.0 yr^{-1}	Estimate

Figures 2-9 presents graphs of variation of interventions rate on infected human population in various compartments against time. In Figure 2, their is a sharp decrease in latent TB in the population with increase in treatment. Treatment of latent TB reduces cases of the disease in a population. In Figure 3, it can be seen that as we increase ξ_1 (the measure of interventions that reduce progression of dormant TB disease to active TB), TB infectives decrease. This means that apart from treatment of latent and active TB, HIV interventions such as early ART and prevention from HIV infection reduces the cases of latent TB progressing to active TB.Figure 4 shows that t HIV positive cases first increased even though there are interventions. This means that ART only lowers the viral load in

HIV infected persons but does not stop the transmission. A combination of ART and intensification of campaigns on prevention from infection reduces cases of new infections. In Figure 5, the number of symptomatic AIDS cases decreases with increase in detection and consequently treatment with ART. The AIDS cases become asymptomatic with HIV. In figure 6, the population of persons with both latent TB and HIV decrease. Treatment of latent TB eliminates the disease amongst individuals with HIV. On the other hand, protection from HIV infection reduces new cases of HIV infection amongst individuals with latent TB. The overall result is that the number of co-infected individuals will decrease. In Figure 7, we observe that increasing ξ_1(prevention of latent TB cases progressing to active TB through early ART) and intensification of treatment of active TB decreases TB cases among persons with HIV hence reduces the co-infection. Protection from HIV infection also reduces cases of new HIV infections among the active TB cases. The decline in the population of co-infected persons indicates the effectiveness of a combination of treatment and prevention from infection. Without the interventions, the number of co-infections will increase and eventually decrease due to massive deaths. However, this is unethical. In Figure 8, the number of HIV cases who had recovered from TB decreases. There are no new cases of HIV infection due to intensification of protection from HIV infection.

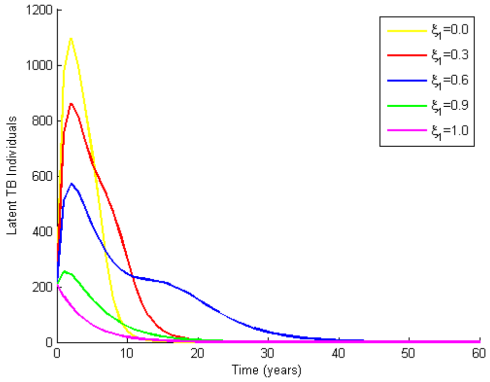

Fig. 2. Variation of Latent TB individuals with changes in ξ_1

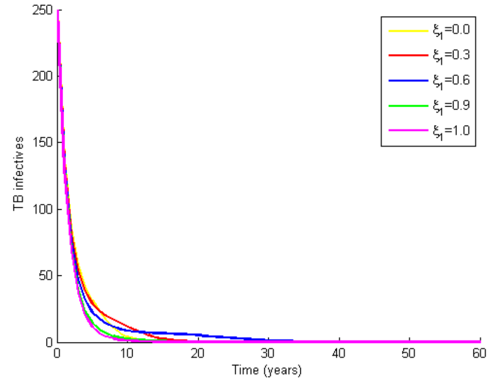

Fig. 3. Variation of TB infectives with changes in ξ_1

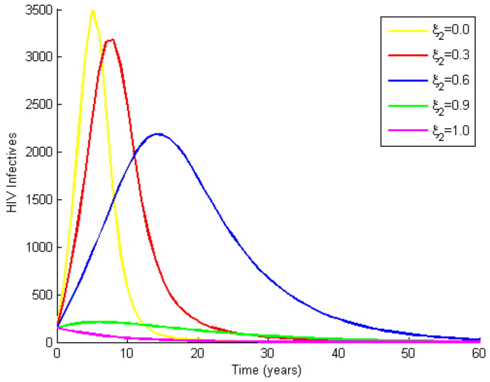

Fig. 4. Variation of HIV infectives with changes in ξ_2

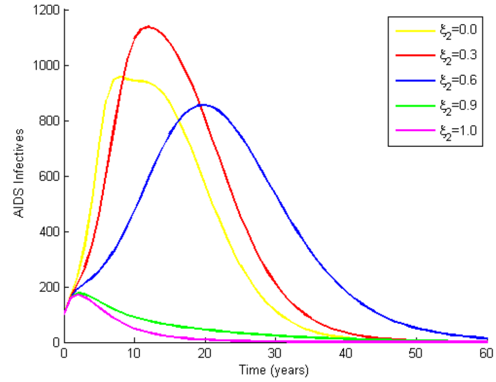

Fig. 5. Variation of AIDS infectives with changes in ξ_2

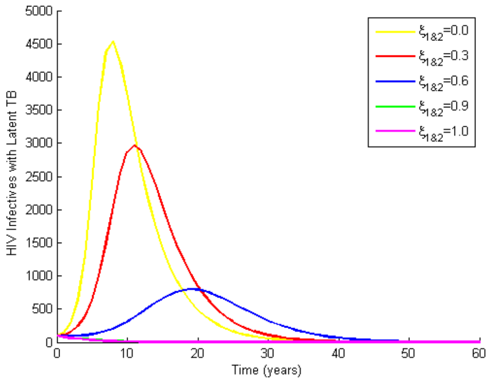

Fig. 6. Variation of HIV infectives with Latent TB with changes in ξ_1 and ξ_2

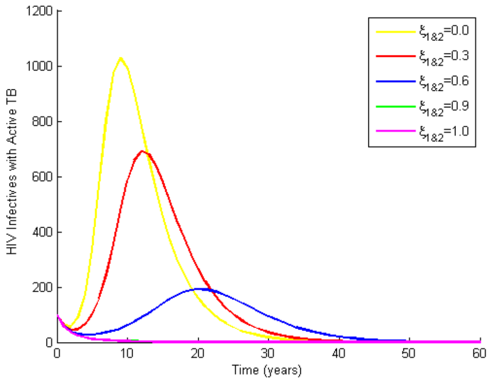

Fig. 7. Variation of HIV infectives with active TB with changes in ξ_1 and ξ_2

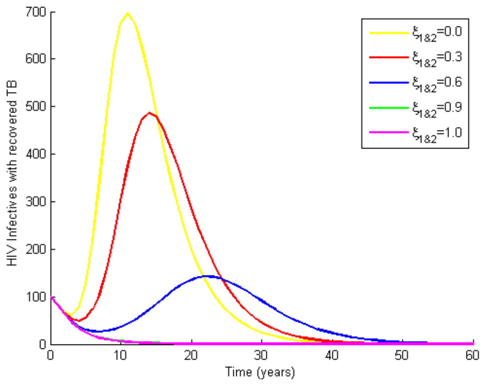

Fig. 8. Variation of HIV infectives with Recovered TB with changes in ξ_1 and ξ_2

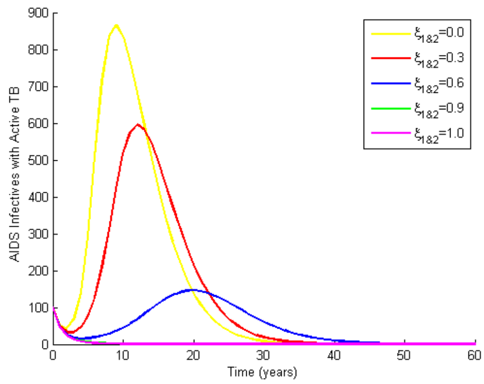

Fig. 9. Variation of HIV infectives with Recovered TB for different values of ξ_1 and ξ_2

5.CONCLUSION

We have developed a TB and HIV co-infection model, derived the fundamental reproduction number, the disease-free and endemic equilibria and the stability criteria. When the model's reproduction number is less than one,it has an equilibrium that is locally asymptotically stable and disease free. Sensitivity analysis of R_{0T} and R_{0H} shows that the important parameters to target for lowering of R_{0T} and R_{0H} are ϖ_1 and ϖ_2, the contact rates for TB and HIV transmission respectively , in order to eliminate the two diseases. Numerical simulation indicates the impact of varrying HIV interventions on TB. As we increase HIV interventions, cases of latent TB progressing to active TB is minimised. This reduces the contact rate for TB transmission and therefore the disease is eventually eliminated in the County. This research provides an additional control strategy in the fight against TB in Siaya county. Treatment of active TB alone may not be enough in eliminating the disease in a community where HIV is prevalent. Measures that will decrease the progression from dormant to active tuberculosis are crucial in the fight against the disease. We recommend that HIV testing be scaled upwards in the County and the HIV positive cases be put under a monitored ART. We also advise that latent TB testing and treatment be done at the health facilities.

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