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RESEARCH PAPER

Dynamical analysis of HIV-TB co-infection transmission model in the presence of treatment for TB

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Abstract

The immense disease burden of tuberculosis (TB) infection is well-documented, particularly among those co-infected with HIV and TB. To better understand the transmission dynamics of HIV-TB co-infection in the absence of readily available HIV treatment, we develop a deterministic compartmental co-infection model. Our model helps to identify the effects of TB infection on the co-infection dynamics of the two diseases, especially when treatment for TB is readily available. We find that susceptibility to TB reinfection after a previous infection leads to backward bifurcation in the TB-only model when the associated reproduction number (R_0) is less than unity. However, when we make the susceptibility to TB re-infection insignificant in the model, the disease-free equilibrium of the TB-only model is locally asymptotically stable when the associated R_0 is less than unity. We conduct sensitivity and uncertainty analyses to identify the key parameters driving TB infection dynamics, using the R_0 as the response function. We discover that the transmission rate for TB, the modification parameters accounting for the infectiousness of infected individuals with TB-only, and the treatment rates for singly infected individuals with latently infected TB are the top drivers of TB infection in the given population. Our numerical simulations suggest that concentrating treatment on TB-infected individuals in the diagnosed latently infected stage (singly or dually infected with HIV) could effectively reduce the co-infection disease burden and HIV incidence in the population under study.

Keywords: Tuberculosis; HIV; co-infection; symptoms; stability; simulations

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1 Introduction

HIV, the Human Immunodeficiency Syndrome, is a virus that attacks cells aiding human resistance to infections, thus increasing vulnerability to numerous other infections and diseases [1–3]. When a person is infected with the virus, it targets and destroys CD4 cells of the immune system. As the HIV infection progresses within the human system, the viral load increases, weakening the immune system. Without antiretroviral treatment, the infection advances to Acquired Immune Deficiency Syndrome (AIDS), the advanced stage of HIV infection, where the immune system becomes severely compromised. The virus was initially identified among homosexuals in the United States of America in 1983, though other reports claim its discovery among apes in 1982 in Kenya [4]. Causes of HIV include vaginal intercourse with an HIV-positive individual without using a condom or pre-exposure prophylaxis (PrEP), as well as sharing equipment for injectable illicit drugs, hormones, and steroids with someone infected with HIV [5]. The virus can be transmitted through blood, semen, pre-seminal fluid, vaginal fluids, rectal fluids, and breast milk [4]. HIV can be prevented by avoiding risky behaviors, using condoms during sex, and receiving regular vaccinations for potential opportunistic infections. An individual with an undetectable level of HIV cannot transmit the virus to another individual [5].

Tuberculosis, also known as TB, is a bacterial infection caused by Mycobacterium tuberculosis bacteria [6]. It primarily affects the lungs but can also affect other parts of the body. Transmission occurs through the air when a person inhales droplet nuclei containing the bacteria. Active TB manifests with symptoms such as coughing up mucus or blood, chest pain, fever, night sweats, loss of appetite, fatigue, and persistent coughing for three or more weeks [3, 7]. The disease can be prevented and treated with medication. TB/HIV co-infection presents special diagnostic and therapeutic challenges and places a significant burden on healthcare systems in many countries [8–10]. TB remains one of the leading causes of death worldwide in the era of HIV, with both diseases collectively responsible for the deaths of 4 million people annually [8]. Studies indicate that while not all HIV patients develop TB disease, those co-infected with both HIV and TB have a higher risk of progressing from TB infection to TB disease due to weakened immune systems. Unlike HIV, TB is entirely preventable, treatable, and curable. While treatment is a fraction of the cost of medications used for HIV, TB co-infection accelerates HIV progression to AIDS [11]. Infected HIV patients are at a heightened risk of contracting tuberculosis [8]. Therefore, adequate attention to the prevention and control of TB/HIV co-infections in a population is crucial.

Several studies have investigated the co-infection of HIV and TB, developing models to understand their epidemics' dynamics. These studies emphasize the importance of incorporating each disease's effects and formulating models for their transmission mechanisms. Wang et al. [12] proposed a dynamic epidemiological model of HIV-TB co-infection incorporating latent age, emphasizing the significance of assessing each disease's effects on co-infection dynamics. Kaur et al. [13] formulated a simple compartmental deterministic model for HIV-TB co-infection, highlighting the existence of an unstable co-infection equilibrium point under certain parameter restrictions. Azeez et al. [1] developed a deterministic compartmental epidemiological model to study the transmission mechanism of HIV-TB co-interaction, revealing that individuals with HIV infection are at greater risk of TB co-infection compared to those without HIV infection. Fatmawati et al. [14] formulated an optimal control co-infection model of HIV-TB, demonstrating that combining anti-TB and antiretroviral treatment is optimal for reducing the burden of co-infection. Omale et al. [15] developed a deterministic co-infection model incorporating control measures to study the scenario where both HIV and tuberculosis infect the same individual, finding that the infectiousness of one disease increases the risk of infectiousness of the other and that the implemented control measures significantly reduce tuberculosis infection, ultimately reducing co-infection rates.

In general, epidemiological models, such as those in [16–25], are valuable tools for studying the transmission dynamics of infectious diseases. Therefore, this research study aims to develop and analyze a mathematical model for HIV/TB co-infection in the presence of treatment. The study has six specific objectives, including:

- Demonstrating the stability of the disease-free equilibrium.
- Analyzing the reproduction number to identify parameters that can reduce the spread of the disease.
- Conducting sensitivity analysis to identify key parameters that drive infectiousness.
- Validating theoretical results with numerical simulations.
- Creating contour plots involving key parameters and the reproduction numbers for the diseases with the aim of determining the threshold for control measures that can help eradicate the diseases from the human population.
- Providing qualitative and empirically-based recommendations to policymakers in the health sector to assist them in controlling the spread of the two diseases and obtaining necessary and sufficient conditions for their eradication in the human population.

In general, from this study, it is anticipated that its findings will significantly contribute to the body of knowledge that informs health policymakers, planners, project implementers, and future researchers by providing strategies for the prevention and control of HIV/TB co-infections through the dynamic analysis of our model.
The manuscript is organized into six sections, including a description of the model formulation, theoretical analysis, sensitivity analysis, numerical simulations, discussion of the plots, and conclusion.

2 Model formulation

The total human population $N(t)$, at any time t is divided into 13 compartments, as listed in Table 1, to obtain:

$$\begin{aligned} N(t) = S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t) + I_H(t) + E_{TH}(t) + I_{HU}(t) \\ + I_{HUA}(t) + I_{HDA}(t) + T_{HT}(t). \end{aligned}$$

It is assumed that individuals who are dually infected can only transmit one of the diseases at a time. The equations for the new co-infection model are formulated as follows.

Transmissions by singly infected individuals

Individuals acquire HIV infection $I_H(t)$, from effective contact with those infected with HIV only, at a rate given by:

$$\dot{\lambda}_H = \beta_H \frac{I_H(t)}{N}, \tag{1}$$

where β_H represents the transmission rate for HIV.
Likewise, the acquisition of TB infection by individuals from those in I_{UA}, and T, compartments, at a rate λ_T, is given as:

$$\lambda_T = \beta_T \frac{(I_{UA} + \eta_1 T)}{N}. \tag{2}$$

Here, the rate of TB transmission is β_T, where the modification parameter $\eta_1 \geq 1$, accounts for the

relative infectiousness of individuals with diagnosed actively infected TB compared to those with undiagnosed actively infected TB infection. The assumption is that those individuals diagnosed as actively infected with TB are more infectious than those undiagnosed [9].

Transmissions by dually infected individuals

TB is transmitted by dually infected individuals at a rate given by:

$$\lambda_{TH} = \frac{\beta_T(\eta_2 I_{HUA} + \eta_3 I_{HDA})}{N}. \tag{3}$$

The transmission rate for TB is modified by the parameters η_2, while η_3, accounts for the increased infectiousness of dually infected individuals with HIV and undiagnosed active TB infection compared to those with dually infected HIV diagnosed TB only. It is assumed that $\eta_3 \geq \eta_2 > 1$. HIV transmission by those infected with both diseases occurs at the following rate:

$$\lambda_{HT} = \frac{\beta_H(E_{HT} + \phi_1 I_{HU} + \phi_2 I_{HUA} + \phi_3 I_{HDA} + \phi_4 I_{HT})}{N}. \tag{4}$$

Here, the relative infectiousness of HIV-infected individuals with primary, secondary, early latent, and late latent TB, respectively, compared to HIV-only infected individuals is accounted for by parameters ϕ_1, ϕ_2, ϕ_3, and ϕ_4.

Description of model equation formation

The rate of recruitment for susceptible individuals to the two diseases occurs at the rate π. Those that acquire HIV and TB infection do so at the rates λ_H, and λ_T, respectively. Likewise, HIV and TB are transmitted by dually infected individuals at rates given by λ_{TH}, and λ_{HT} (where λ_H, λ_T, λ_{TH}, and λ_{HT}, are as initially defined in Section 2. The natural death rate for individuals in all compartments occurs at the uniform rate μ. The contact rates for HIV and tuberculosis are given by β_H, and β_T, respectively. Singly infected individuals with latently infected TB, undiagnosed latently infected TB, undiagnosed actively infected, and diagnosed actively infected individuals with TB on prompt treatment are treated at rates σ_1, σ_2, σ_3, and σ_4, respectively.
On the other hand, treatment rates for dually infected individuals with HIV and latently infected TB, HIV and undiagnosed latently infected TB, HIV and undiagnosed actively infected TB, and HIV and diagnosed actively infected individuals with TB are σ_{T1}, σ_{T2}, σ_{T3}, and σ_{T4} respectively, while the modification parameters that account for the infectiousness of dually infected individuals are ϕ_1, ϕ_2, ϕ_3, and ϕ_4. Individuals who are singly infected progress from exposed class, diagnosed latently infected class, undiagnosed latently infected class, undiagnosed actively infected class, diagnosed actively infected with TB on prompt treatment class to classes E_L, E_{UL}, I_{UA}, T, and R, at the rates ψ_1, ψ_2, ψ_3, and ψ_4, respectively. Likewise, individuals that are infected with the two diseases in the classes E_{HT}, I_{HU}, I_{HUA}, I_{HDA}, and T_{HT}, progress to classes I_{HU}, I_{HUA}, I_{HDA}, and T_{HT}, at the rates ψ_{HU}, ψ_{HUA}, ψ_{HDA}, and ψ_{HT}, respectively.
The modification parameters accounting for variability in the susceptibility of recovered individuals to TB infection are given by ε_1, and ε_2, while those accounting for the susceptibility of recovered individuals to TB infection are represented by γ_1, and γ_2. Similarly, the modification parameters accounting for the susceptibility of TB-infected individuals to HIV infection are given as θ_1, θ_2, θ_3, θ_4, θ_5, θ_6, θ_7, and θ_8, respectively, while those accounting for the infectiousness of infected individuals with TB only, HIV and undiagnosed actively infected TB, HIV and diagnosed actively infected TB are η_1, η_2, and η_3, respectively. It should be noted that the disease-induced

death rate in each of the disease-infected compartments occurs at uniform rates δ_1, δ_2, δ_3, δ_4, δ_5, and δ_6, respectively.

Table 1. Description of the model variables and parameters

Variable	**Description**
S_h	Group of individuals that are susceptible to the two infections
E	Group of exposed individuals to TB
E_L	Group of diagnosed latently infected individuals to TB
E_{UL}	Group of undiagnosed latently infected individuals to TB
I_{UA}	Group of undiagnosed actively infected individuals to TB
T	Group of diagnosed actively infected individuals to TB on prompt treatment
R	Group of recovered individuals
I_H	Group of HIV infected individuals
E_{HT}	Group of dually infected individuals with diagnosed latent HIV and TB
I_{HU}	Group of dually infected individuals with HIV and undiagnosed latently infected TB
I_{HUA}	Group of dually infected individuals with HIV and undiagnosed active TB
I_{HDA}	Group of dually infected individuals with HIV and diagnosed active TB
T_{HT}	Group of dually infected individuals with HIV and TB on prompt treatment for both diseases
Parameter	**Description**
π	Recruitment rate into the susceptible class
μ	Rate at which individuals die naturally
$\beta_T\,(\beta_H)$	Contact rates for tuberculosis (HIV)
$\sigma_1, \sigma_2, \sigma_3, \sigma_4$	Treatment rates for singly infected individuals with latently-infected TB, undiagnosed latently-infected TB, undiagnosed actively-infected and diagnosed actively-infected individuals with TB on prompt treatment
$\sigma_{T1}, \sigma_{T2}, \sigma_{T3}, \sigma_{T4}$	Treatment rates for dually infected individuals with HIV and latently-infected TB, HIV and undiagnosed latently-infected with TB, HIV and undiagnosed actively-infected with TB, HIV and diagnosed actively-infected individuals with TB
$\psi_1, \psi_2, \psi_3, \psi_4$	Rate of progression for singly infected individuals from exposed, diagnosed latently-infected, undiagnosed latently-infected, undiagnosed actively infected, diagnosed actively infected with TB on prompt treatment to classes E_L, E_{UL}, I_{UA}, T, and R, respectively
$\varepsilon_1, \varepsilon_2$	Modification parameters accounting for variability in susceptibility of recovered individuals to TB infection
ψ_{HU}, ψ_{HUA}, ψ_{HDA}, ψ_{HT}	Rate of progression for dually infected individuals from classes E_{HT}, I_{HU}, I_{HUA}, I_{HDA}, and T_{HT}, to classes I_{HU}, I_{HUA}, I_{HDA}, and T_{HT}, respectively
γ_1, γ_2	Modification parameters accounting for the susceptibility of recovered individuals to TB infection
θ_1, θ_2, θ_3, θ_4, θ_5, θ_6, θ_7, θ_8	Modification parameters accounting for the susceptibility of TB-infected individuals to HIV infection
η_1, η_2, η_3	Modification parameters accounting for the infectiousness of infected individuals with TB only, HIV, and undiagnosed actively infected TB, HIV, and diagnosed actively-infected TB respectively
$\phi_1, \phi_2, \phi_3, \phi_4$	Modification parameters accounting for the infectiousness of dually infected individuals
$\delta_1, \delta_2, \delta_3, \delta_4, \delta_5, \delta_6$	Disease-induced death rates due to HIV with TB co-infection

Based on the description above, the model assumptions, and the schematic diagram below, we formulate the following system of non-linear differential equations as that which captures the transmission dynamics of HIV-TB co-infection in a given population:

$$
\begin{aligned}
\frac{dS}{dt} &= \pi - \lambda_T S - \lambda_H S - \lambda_{TH} S - \lambda_{HT} S - \mu S,\\
\frac{dE}{dt} &= \lambda_T S + \lambda_{TH} S + \varepsilon_1 \lambda_T R + \varepsilon_2 \lambda_{TH} R - \lambda_H E - \lambda_{HT} E - (\psi_1 + \mu) E,\\
\frac{dE_L}{dt} &= \psi_1 E - \theta_1 \lambda_H E_L - \theta_2 \lambda_{HT} E_L - (\psi_2 + \sigma_1 + \mu) E_L,\\
\frac{dE_{UL}}{dt} &= \psi_2 E_L - \theta_3 \lambda_H E_{UL} - \theta_4 \lambda_H E_{UL} - (\psi_3 + \sigma_2 + \mu) E_{UL},\\
\frac{dI_{UA}}{dt} &= \psi_3 E_{UL} - \theta_5 \lambda_H I_{UA} - \theta_6 \lambda_{HT} I_{UA} - (\psi_4 + \sigma_3 + \mu) I_{UA},\\
\frac{dT}{dt} &= \psi_4 I_{UA} - \theta_7 \lambda_H T - \theta_8 \lambda_{HT} T - (\psi_5 + \sigma_4 + \mu) T,\\
\frac{dR}{dt} &= \sigma_1 E_L + \sigma_2 E_{UL} + \sigma_3 I_{UA} + \sigma_4 T - \varepsilon_1 \lambda_T R - \lambda_H R - \varepsilon_2 \lambda_{TH} R - \lambda_{HT} R - \mu R,\\
\frac{dI_H}{dt} &= \lambda_H S + \lambda_{HT} S + \lambda_H R + \lambda_{HT} R - \gamma_1 \lambda_T I_H - \gamma_2 \lambda_{TH} I_H + \sigma_{T1} E_{HT} + \sigma_{T2} I_{HU}\\
&\quad + \sigma_{T3} I_{HUA} + \sigma_{T4} I_{HDA} + \sigma_{T5} T_{HT} - (\mu + \delta_1) I_H,\\
\frac{dE_{HT}}{dt} &= \sigma_1 \lambda_T I_H + \sigma_2 \lambda_{TH} I_H + \lambda_{HT} E - (\psi_{HU} + \sigma_{T1} + \delta_2 + \mu) E_{HT},\\
\frac{dI_{HU}}{dt} &= \psi_{HU} E_{HT} + \theta_1 \lambda_H E_L + \theta_2 \lambda_{HT} E_L - (\psi_{HUA} + \delta_3 + \sigma_{T2} + \mu) I_{HU},\\
\frac{dI_{HUA}}{dt} &= \psi_{HUA} I_{HU} + \theta_3 \lambda_H E_{UL} + \theta_4 \lambda_{HT} E_{UL} - (\psi_{HDA} + \sigma_{T3} + \delta_4 + \mu) I_{HUA},\\
\frac{dI_{HDA}}{dt} &= \psi_{HDA} I_{HUA} + \theta_5 \lambda_H I_{UA} + \theta_6 \lambda_{HT} I_{UA} - (\psi_{HT} + \sigma_{T4} + \delta_5 + \mu) I_{HDA},\\
\frac{dT_{HT}}{dt} &= \psi_{HU} I_{HDA} + \theta_7 \lambda_H T + \theta_8 \lambda_{HT} T - (\sigma_{T5} + \delta_6 + \mu) T_{HT},
\end{aligned}
\tag{5}
$$

where

$$
\lambda_H = \frac{\beta_H I_H}{N}, \quad \lambda_T = \frac{\beta_T (I_{UA} + \eta_1 T)}{N}, \quad \lambda_{TH} = \frac{\beta_T (\eta_2 I_{HUA} + \eta_3 I_{HDA})}{N},
$$

and

$$
\lambda_{HT} = \frac{\beta_H (E_{HT} + \phi_1 I_{HU} + \phi_2 I_{HUA} + \phi_3 I_{HDA} + \phi_4 I_{HT})}{N}.
$$

It is pertinent to note that due to the fact that model (5) is monitoring the human population, consequently, we assumed that all variables and parameters in the model are non-negative. Therefore, we shall carry out the analysis of model (5) in the invariant region given as follows:

$$
\begin{aligned}
\Omega_1 \;=\; & \Big\{ (S(t), E(t), E_L(t), E_{UL}(t), I_{UA}(t), T(t), R(t), I_H(t), E_{TH}(t), I_{HU}(t), I_{HUA}(t),\\
& I_{HDA}(t), T_{HT}(t)) \in \mathfrak{R}_+^{13} : N \leq \frac{\pi}{\mu} \Big\}.
\end{aligned}
$$

Model assumptions

In formulating our model, some assumptions have been considered which are listed as follows:

- Individuals infected with tuberculosis can recover through treatment, but there is no treatment-induced recovery for those infected with HIV [14, 19].
- Natural death occurs uniformly for all individuals in each class of the model at a constant rate μ.
- The disease-induced death rate in all the infected compartments is uniform.
- We have not included in the model those individuals who progress from being infected with HIV to being infected with AIDS after some time.
- In cognizance of the fact that findings show that 80% of individuals afflicted with HIV infection are practically bound to suffer from TB infection [19], we assume that only those suffering from TB affliction are infected with HIV infection.

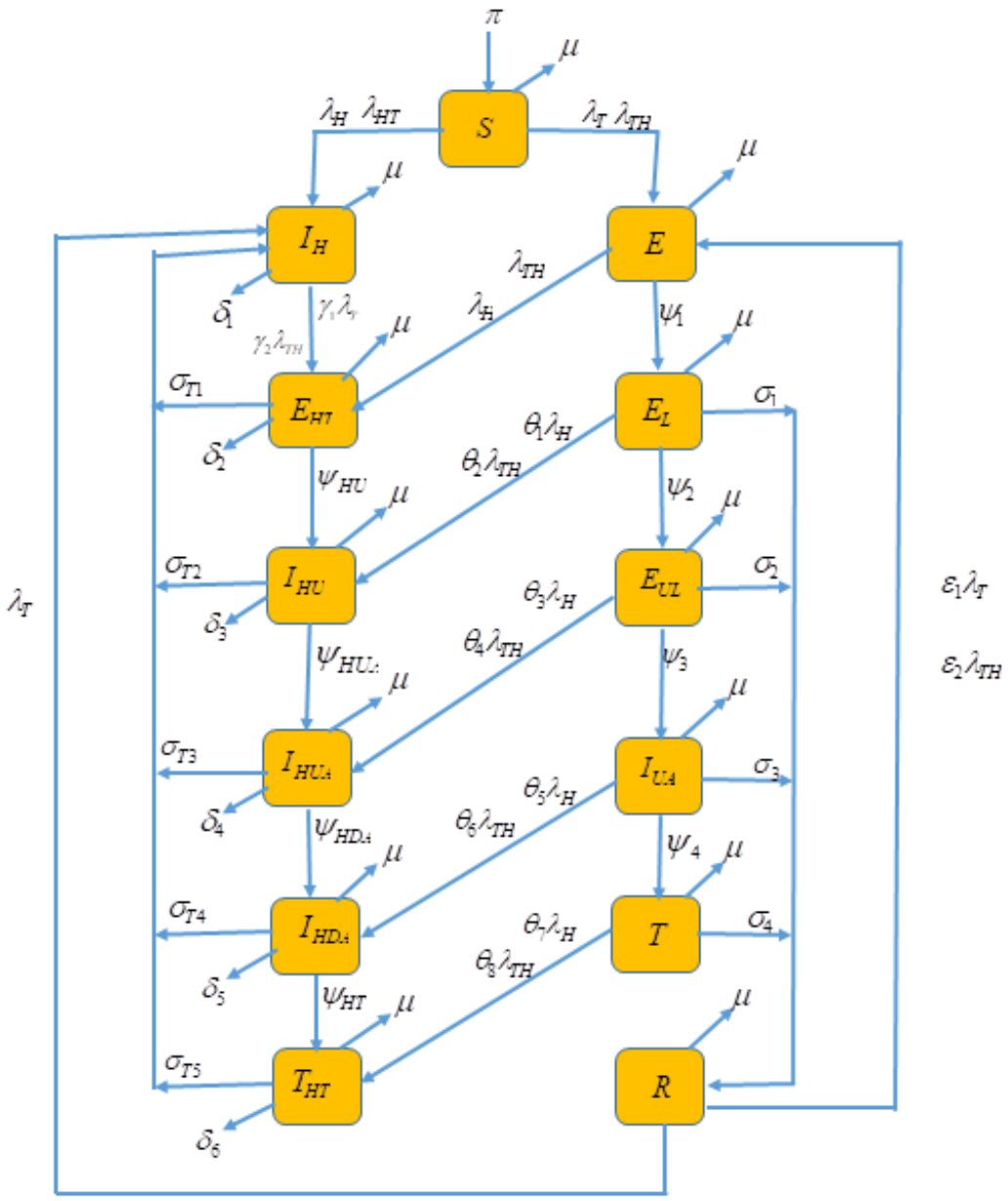


Figure 1. Flow chart of co-infection model (5) where λ_H, λ_T, λ_{HT}, and λ_{TH}, are as defined in Eqs. (2) and (3), respectively

Invariance region

Lemma 1 *The solution of the model equations is feasible for all $t > 0$, if they are contained in the invariant region:*

$$\begin{aligned}\Omega_1 = \{&S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t) + I_H(t) + E_{TH}(t) + I_{HU}(t) \\ &+ I_{HUA}(t) + I_{HDA}(t) + T_{HT}(t)\} \in \mathfrak{R}_+^{13}\}.\end{aligned} \tag{6}$$

Proof Suppose

$$\begin{aligned}\Omega_1 = \{&S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t) + I_H(t) + E_{TH}(t) + I_{HU}(t) \\ &+ I_{HUA}(t) + I_{HDA}(t) + T_{HT}(t)\} \in \mathfrak{R}_+^{13}\},\end{aligned}$$

be any solution of model Eq. (5) with non-negative initial conditions.

In the absence of disease-induced death rate, $\frac{dN}{dt}$ becomes:

$$\frac{dN}{dt} \leq \pi - \mu N,$$

we have

$$\frac{dN}{dt} + \mu N \leq \pi.$$

Solving the equation above by multiplying both sides by $e^{\mu t}$, the integrating factor

$$\frac{dN}{dt}(e^{\mu t}) + \mu N(e^{\mu t}) \leq \pi(e^{\mu t}).$$

From the above equation, we obtain

$$d(Ne^{\mu t}) \leq \pi e^{\mu t} dt,$$

by integrating both sides of the above equation, we have that

$$Ne^{\mu t} \leq \frac{\pi e^{\mu t}}{\mu} + k_0.$$

Dividing all through by $e^{\mu t}$, we have

$$N(t) \leq \frac{\pi}{\mu} + k_0 e^{-\mu t}. \tag{7}$$

Applying the initial conditions $t(0) = N(0)$, we have

$$N(0) \leq \frac{\pi}{\mu} + k_0,$$

$$N(0) - \frac{\pi}{\mu} \leq k_0.$$

Eq. (7) becomes

$$N(t) \leq \frac{\pi}{\mu} + \left(N(0) - \frac{\pi}{\mu}\right) e^{-\mu t}. \tag{8}$$

Therefore, the human population approaches the carrying capacity $\frac{\pi}{\mu}$, as $t \to \infty$. Obviously, the feasible solution set of the model Eq. (5) enters the invariant region:

$$\begin{aligned}\Omega_1 = \{&(S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t) + I_H(t) + E_{TH}(t) + I_{HU}(t) \\ &+ I_{HUA}(t) + I_{HDA}(t) + T_{HT}(t)) \in \mathfrak{R}_+^{13} : N < \frac{\pi}{\mu}\},\end{aligned}$$

where $S(0) > 0,\ E(0) > 0,\ E_L(0) > 0,\ E_{UL}(0) > 0,\ I_{UA}(0) > 0,\ T(0) > 0,\ R(0) > 0,\ I_H(0) > 0,\ E_{TH}(0) > 0,\ I_{HU}(0) > 0,\ I_{HUA}(0) > 0,\ I_{HDA}(0) > 0,\ T_{HT}(0) > 0$. Therefore, model (5) is biologically and mathematically feasible. Hence whenever $N > \frac{\pi}{\mu}$, then $N < 0$, which means that the population reduces asymptotically to the carrying capacity. Whenever $N \leq \frac{\pi}{\mu}$, every solution with an initial condition in Ω_1, remains positive for all $t > 0$, and the model is said to be mathematically well-posed and biologically meaningful.

Lemma 2 *Let the initial condition be:*

$$\begin{aligned}&\{S(0) > 0, E(0) > 0, E_L(0) > 0, E_{UL}(0) > 0, I_{UA}(0) > 0, T(0) > 0, R(0) > 0, I_H(0) > 0, \\ &E_{TH}(0) > 0, I_{HU}(0) > 0, I_{HUA}(0) > 0, I_{HDA}(0) > 0, T_{HT}(0) > 0\}.\end{aligned} \tag{9}$$

Consequently, the solution set:

$$\{S(t), E(t), E_L(t), E_{UL}(t), I_{UA}(t), T(t), R(t), I_H(t), E_{TH}(t), I_{HU}(t), I_{HUA}(t), I_{HDA}(t), T_{HT}(t)\},$$

of the system of model Eq. (5) is positive for all $t > 0$.

Proof From the first equation of the model system (5), we have

$$\frac{dS}{dt} = \pi - (\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu)\, S,$$

$$\frac{dS}{dt} = \pi - (\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu)\, S \geq -(\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu)\, S.$$

Which can be re-written as

$$\frac{dS}{S} \geq -(\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu)\, dt.$$

Integrating the equation above, we have

$$\ln S \geq -(\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu)\, t + k_1,$$

$$S(t) \geq e^{-(\lambda_T+\lambda_H+\lambda_{TH}+\lambda_{HT}+\mu)t+k_1},$$

$$S(t) \geq k_1 e^{-(\lambda_T+\lambda_H+\lambda_{TH}+\lambda_{HT}+\mu)t}.$$

Applying the initial conditions $t = 0, S(0) = k_1$ gives

$$S(t) \geq S(0)e^{-(\lambda_T+\lambda_H+\lambda_{TH}+\lambda_{HT}+\mu)t}, \quad \text{and} \quad (\lambda_T + \lambda_H + \lambda_{TH} + \lambda_{HT} + \mu) > 0.$$

Similarly, the above integration can be shown for other state variables, for $E(t) > 0$, $E_L(t) > 0$, $E_{UL}(t) > 0$, $I_{UA}(t) > 0$, $T(t) > 0$, $R(0) > 0$, $I_H(t) > 0$, $E_{TH}(t) > 0$, $I_{HU}(t) > 0$, $I_{HUA}(t) > 0$, $I_{HDA}(t) > 0$, and $T_{HT}(t) > 0$.

3 Theoretical analysis of the model

To conduct the analysis of the model, we first analyze the singly infected system before proceeding to analyze the dually infected system.

HIV-only model

To obtain the HIV-only model, we set all the TB components to zero as follows:

$$E = 0, E_L = 0, E_{UL} = 0, I_{HU} = 0, T = 0, E_{HT} = 0, I_H = 0, I_{HUA} = 0, I_{HDA} = 0, I_{HT} = 0.$$

Therefore, the HIV-only model is given by:

$$\begin{aligned} \frac{dS}{dt} &= \pi - (\lambda_H + \mu)S, \\ \frac{dI_H}{dt} &= \lambda_H S - (\mu + \delta_1)I_H, \end{aligned} \tag{10}$$

where

$$\lambda_H = \frac{\beta_H I_H}{N}, \quad \text{and} \quad N(t) = S(t) + I_H(t).$$

HIV-only disease-free equilibrium (DFE)

The DFE of the HIV-only model (10) is:

$$(S^+, I_H^+) = (\frac{\pi}{\mu}, 0). \tag{11}$$

Existence of endemic equilibrium point (EEP) of HIV-only model

The endemic equilibrium (S^{++}, I_H^{++}), of the model Eq. (10) is given by:

$$(S^{++}, I_H^{++}) = (\frac{\pi}{\lambda_H^{++} + \mu}, \frac{\pi\lambda_H^{++}}{(\lambda_H^{++} + \mu)(\mu + \delta_1)}).$$

The basic reproduction number

The threat posed by any infectious disease on humans depends on the rate at which it invades a population. The measure of the potential for disease to spread in a population is the basic

reproduction number ($\mathcal{R}_0$). It represents the average number of secondary cases of infection that will be generated by the influx of just one infected person into a healthy population [18]. If the reproduction number of the disease is less than unity ($\mathcal{R}_0 < 1$), when there is an influx of at least one infected individual into a healthy population, then it means that, on average, each infected individual produces less than one newly infected individual throughout an infection period. In this case, the disease might gradually die out over time. On the other hand, if $\mathcal{R}_0 > 1$, each infected individual produces, on average, more than one new infection, and the infection will continue to spread rapidly in the given population. The basic reproduction number of the HIV-only model (10) follows from [20] and is given by:

$$\mathcal{R}_{0H} = \rho\left(\frac{\beta_H}{\mu + \delta_1}\right).$$

Local stability of disease-free equilibrium of HIV-only model

Theorem 1 *If $\omega_1, \omega_2, \ldots, \omega_n$ are the eigenvalues of the Jacobian matrix of the HIV-only model (10), its disease-free equilibrium is locally asymptotically stable (LAS) whenever $\omega_1, \omega_2, ..., \omega_n < 0$.*

Proof Let $A = \pi - (\lambda_H + \mu)S$, and $B = \lambda_H S - (\mu + \delta_1)I_H$, we have that

$$\frac{\partial A}{\partial S} = (\lambda_H + \mu), \quad \frac{\partial A}{\partial I_H} = 0,$$

$$\frac{\partial B}{\partial S} = \lambda_H, \quad \frac{\partial B}{\partial I_H} = -(\mu + \delta_1).$$

The Jacobian matrix is given as:

$$J(\varepsilon f) = \begin{vmatrix} \frac{\partial A}{\partial S} & \frac{\partial A}{\partial I_H} \\ \\ \frac{\partial B}{\partial S} & \frac{\partial B}{\partial I_H} \end{vmatrix}.$$

So that

$$J(\varepsilon f) = \begin{vmatrix} -(\lambda_H + \mu) & 0 \\ \lambda_H & -(\mu + \delta_1) \end{vmatrix},$$

$$J(\varepsilon f - \lambda I) = \begin{vmatrix} -(\lambda_H + \mu) - \lambda & 0 \\ \lambda_H & -(\mu + \delta_1) - \lambda \end{vmatrix}.$$

The characteristic equation of the matrix $J(\varepsilon f - \lambda I)$ is given by:

$$P(\lambda) = (-(\lambda_H + \mu) - \lambda)(-(\mu + \delta_1) - \lambda) = 0.$$

The eigenvalues of the characteristic equation $P(\lambda)$, are

$$\omega_1 = \lambda_1 = -(\lambda_H + \mu), \quad \text{and} \quad \omega_2 = \lambda_2 = -(\mu + \delta_1).$$

Observe that the eigenvalues $\omega_1 < 0$, and $\omega_2 < 0$. Hence, arising from Theorem 1, the disease-free equilibrium of the model is locally asymptotically stable.

Local stability of endemic equilibrium point (EEP) of HIV-only model

The endemic equilibrium of the HIV-only model (10) is obtained by solving for the force of infection (λ_H^{++}), at steady-state, giving:

$$(S^{++}, I_H^{++}) = \left(\frac{\pi}{\lambda_H^{++} + \mu}, \frac{\pi \lambda_H^{++}}{(\lambda_H^{++} + \mu)(\mu + \delta_1)} \right). \tag{12}$$

In terms of the total subpopulation, we have:

$$N^{++} = \frac{\pi(\mu + \delta_1 + \lambda_H^{++})}{(\lambda_H^{++} + \mu)(\mu + \delta_1)}.$$

Substituting N^{++}, and I_H^{++}, into:

$$\lambda_H^{++} = \beta_H \frac{I_H^{++}}{N^{++}},$$

we have:

$$\lambda_H^{++} + (\mu + \delta_1)(1 - \mathcal{R}_{0H}) = 0.$$

It implies that $\lambda_H^{++} = (\mu + \delta_1)(\mathcal{R}_{0H} - 1)$. Hence, if $\mathcal{R}_{0H} > 1$, then $\lambda_H^{++} > 0$. Therefore, the HIV-only model (10) has a unique endemic equilibrium if $\mathcal{R}_{0H} > 1$. Next is to investigate the local asymptotic stability (LAS) of the HIV-only model (10). We evaluate the Jacobian matrix of model (10) at the EEP as follows:

$$J_{/EEP} = \begin{vmatrix} -\beta_H \frac{I_H^{++2}}{N^{++2}} & -\beta_H \frac{S^{++2}}{N^{++2}} \\ \beta_H \frac{I_H^{++2}}{N^{++2}} & \beta_H \frac{S^{++2}}{N^{++2}} - \mu - \sigma_1 \end{vmatrix}.$$

Evaluating the determinant, we have:

$$Det(J_{/EEP}) = \beta_H \frac{I_H^{++2}}{N^{++2}}(\mu + \sigma_1) + \frac{\mu \beta_H S^{++2}}{\mathcal{R}_{0H}}(1 - \frac{1}{\mathcal{R}_{0H}}).$$

The trace of the Jacobian matrix is given as:

$$Tr(J_{/EEP}) = -\mu - \frac{\beta_H}{\mathcal{R}_{0H}}(\mathcal{R}_{0H} - 1).$$

It is clear that $Det(J_{/EEP}) > 0$, and $Tr(J_{/EEP}) > 0$, if $\mathcal{R}_{0H} > 1$. Using the Routh-Hurwitz criterion, the conditions derived in the previous section indicate that the endemic equilibrium of the HIV-only model (10) is locally and asymptotically stable if $\mathcal{R}_{0H} > 1$, provided that all the model parameters remain positive. This means that HIV infection will invade the subpopulation.

Global asymptotic stability of DFE of HIV-only model

To demonstrate that the model Eq. (10) do not undergo a backward bifurcation at $\mathcal{R}_{0H} = 1$, we need to prove the global asymptotic stability (GAS) of the disease-free equilibrium (DFE) of the model (10).

Theorem 2 *The disease-free equilibrium (DFE) of model (10) is globally asymptotically stable (GAS) if* $\mathcal{R}_{0H} \leq 1$, *and it is unstable if* $\mathcal{R}_{0H} \geq 1$.

Proof We construct a linear Lyapunov function as follows:

$$\mathcal{L}_1 = I_H. \tag{13}$$

Differentiating (13) with respect to time (t) (where the dot represents derivative with respect to time) we have:

$$\dot{\mathcal{L}}_1 = \dot{I}_H = I_H \left(\beta_H \frac{S}{N} - (\mu - \delta_1) \right). \tag{14}$$

Recall that $S \leq N$, and $N \leq \frac{\pi}{\mu}$, for all $t > 0$, Eq. (14) becomes

$$\dot{\mathcal{L}}_1 \leq I_H \left(\mu - \delta_1 \right) \left(\mathcal{R}_{0H} - 1 \right). \tag{15}$$

Therefore $\dot{\mathcal{L}}_1 = 0$, if $\mathcal{R}_{0H} \leq 1$, with $\dot{\mathcal{L}}_1 = 0$, if and only if $I_H = 0$. Hence, it follows from Driessche and Watmough in [20] that every solution to the HIV-only model (10) with non-negative initial conditions converges to DFE as $t \to 0$. At point $I_H = 0$, in the first Eq. (10) yields $S(t) \to \frac{\pi}{\mu}$, as $t \to \infty$. Thus $(S, I_H) \to \left(\frac{\pi}{\mu}, 0 \right)$. As $t \to \infty$ for $R_H \leq 1$. Therefore, the disease-free equilibrium of HIV-only model (10) is globally asymptotically stable in the region $\mathcal{R}_{0H} \leq 1$.

Implication of Theorem 1 and Theorem 2:

Theorem 1 and Theorem 2, which center on the local stability of the disease-free equilibrium, form the basis by which we obtained the threshold for disease control and are able to confirm that the conditions for disease control have been met. As shown in the two theorems, the threshold for disease control is that the reproduction number of the disease must be less than one. This means that the introduction of a single infected individual into the susceptible human population, considered to be free from HIV and TB infection, will fail to generate an average of a single infected individual, resulting in the disease ultimately dying out in no time.

Global asymptotic stability of the EEP of HIV-only model

In this section, we consider the asymptotic stability of the endemic equilibrium point of HIV-only model (10).

Theorem 3 *The unique EEP of model (10) is globally asymptotically stable (GAS) in* Ω_1/Ω_2, *whenever* $\bar{\mathcal{R}}_{0H} > 1$, *and unstable whenever* $\bar{\mathcal{R}}_{0H} < 1$, *and* $\mathcal{L}_2 = 0$.

Proof Consider HIV-only model (10), with the conditions: $\bar{\mathcal{R}}_{0H} = \bar{\mathcal{R}}_{0H} > 1$, when $\mathcal{L}_2 = 0$, for existence of unique equilibrium, therefore we construct the non-linear Lyapunov function of the Goh-Volterra type as follows:

$$\mathcal{L}_2 = S - S^{++} - S^{++} \ln \left(\frac{S}{S^{++}} \right) + I_H - I_H^{++} \ln \left(\frac{I_H}{I_H^{++}} \right). \tag{16}$$

Differentiating (16) with respect to time, yields

$$\dot{\mathcal{L}}_2 = \dot{S} - \frac{S^{++}}{S}\dot{S} + \left(\dot{I}_H - \frac{I_H^{++}}{I_H}\dot{I}_H\right). \tag{17}$$

From Eqs. (10) and (17), we have:

$$\dot{\mathcal{L}}_2 = \pi - \bar{\beta}_H I_H S - \mu S - \frac{S^{++}}{S}\left(\pi - \bar{\beta}_H I_H S - \mu S\right) + \bar{\beta}_H I_H S - \mu I_H - \frac{I_H^{++}}{I_H}\left(\bar{\beta}_H I_H S - \mu I_H\right), \tag{18}$$

$$\pi = \bar{\beta}_H I_H^{++} S^{++} + \mu S^{++}, \tag{19}$$

where

$$\mu = \bar{\beta}_H S^{++}. \tag{20}$$

Putting (19) and (20) into (18) we have:

$$\dot{\mathcal{L}}_2 = \mu S^{++}\left(2 - \frac{S^{++}}{S} - \frac{S}{S^{++}}\right) + \bar{\beta}_H I_H^{++} S^{++}\left(2 - \frac{S^{++}}{S} - \frac{S}{S^{++}}\right). \tag{21}$$

Observe that $\dot{\mathcal{L}}_2$, is a Lyapunov function in Ω_1/Ω_2, and the endemic equilibrium of HIV-only model (10) is unique under these conditions.

TB - only model

The TB-only model is obtained by setting all HIV components to zero in the co-infection model (5), that is, setting: $I_H = 0, I_{HT} = 0, I_{HU} = 0, I_{HDA} = 0, I_{TH} = 0$, to give TB-only model:

$$\begin{aligned}
\frac{dS}{dt} &= \pi - \lambda_T S - \mu S,\\
\frac{dE}{dt} &= \lambda_T S + \varepsilon_1 \lambda_T R - (\psi_1 + \mu) E,\\
\frac{dE_L}{dt} &= \psi_1 E - (\psi_2 + \sigma_1 + \mu) E_L,\\
\frac{dE_{UL}}{dt} &= \psi_2 E_L - (\psi_3 + \sigma_2 + \mu) E_{UL},\\
\frac{dI_{UA}}{dt} &= \psi_3 E_{UL} - (\psi_4 + \sigma_3 + \mu) I_{UA},\\
\frac{dT}{dt} &= \psi_4 I_{UA} - (\psi_5 + \sigma_4 + \mu) T,\\
\frac{dR}{dt} &= \sigma_1 E_L + \sigma_2 E_{UL} + \sigma_3 I_{UA} + \sigma_4 T - \varepsilon_1 \lambda_T R - \mu R,
\end{aligned}$$

with

$$\lambda_T = \beta_T \frac{(I_{UA} + \eta_1 T)}{N},$$

where

$$N(t) = S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t). \tag{22}$$

It can equally be shown that the solution set of TB-only model (22) are all positive when they enter the invariant region Ω_3, defined as:

$$\Omega_3 = \left\{ S(t) + E(t) + E_L(t) + E_{UL}(t) + I_{UA}(t) + T(t) + R(t) \in \Re_+^7 : N \leq \frac{\pi}{\mu} \right\}.$$

Therefore, we can conclude that it is appropriate to analyze the transmission dynamics of the TB-only model (22) within the domain Ω_3. This allows us to consider the model as biologically and mathematically well-posed, as indicated by previous studies [18].

Disease–free equilibrium (DFE) of TB-only model

To find the disease-free equilibrium of the TB-only model, we set all the disease components to zero at a steady-state. Thus, we have:

$$\Omega_3 = \left(S^+, E^+, E_L^+, E_{UL}^+, I_{UA}^+, T^+, R^+\right) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0\right).$$

Local stability of disease-free equilibrium of TB-only model

To determine the local asymptotic stability (LAS) of the disease-free equilibrium (DFE) in the TB-only model (22), we can use the next-generation matrix method. This approach is based on the method proposed by Van den Driessche and Wartmough [20], which involves defining a next-generation matrix where the new infection terms and the remaining transfer terms are represented by, respectively.

$$\mathcal{F}_2 = \begin{pmatrix} 0 & 0 & 0 & \beta_T & \eta_1\beta_T \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad \mathcal{V}_2 = \begin{pmatrix} c_1 & 0 & 0 & 0 & 0 \\ -\psi_1 & c_2 & 0 & 0 & 0 \\ 0 & -\psi_2 & c_3 & 0 & 0 \\ 0 & 0 & -\psi_3 & c_4 & 0 \\ 0 & 0 & 0 & -\psi_4 & c_5 \end{pmatrix},$$

where
$c_1 = (\psi_1 + \mu), c_2 = (\psi_2 + \sigma_1 + \mu), c_3 = (\psi_3 + \sigma_2 + \mu), c_4 = (\psi_4 + \sigma_3 + \mu)$, and $c_5 = (\psi_5 + \sigma_4 + \mu)$.
ρ is the spectral radius of $(\mathcal{F}_2\mathcal{V}_2^{-1})$. It follows from [26] that, the effective reproduction number of TB-only model (22) is given as

$$\mathcal{R}_T = \rho\left(\mathcal{F}_2\mathcal{V}_2^{-1}\right),$$

$$\Rightarrow \mathcal{R}_T = \frac{\beta_T\psi_1\psi_2\psi_3\left(c_5 + \eta_1\psi_4\right)}{\left(\psi_1 + \mu\right)\left(\psi_2 + \sigma_1 + \mu\right)(\psi_3 + \sigma_2 + \mu)(\psi_4 + \sigma_3 + \mu)(\psi_5 + \sigma_4 + \mu)}. \tag{23}$$

Lemma 3 *The disease-free equilibrium (DFE) of the TB-only model (22) is locally asymptotically stable whenever $\mathcal{R}_T < 1$, and unstable whenever $\mathcal{R}_T > 1$.*

The threshold parameter, denoted by $\mathcal{R}_T$, is the basic reproduction number for the TB-only model (22), representing the average number of secondary TB infections caused by an infected individual introduced to a population completely free of TB infections [26].
Based on Lemma 3, TB can be eradicated from the population if the initial sizes of the subpopulation of the submodel are in the region of attraction of the DFE.

Analysis of the reproduction number for the TB-only model

It is important to analyze the basic reproduction number with respect to the treatment parameters, in order to determine the sufficient and necessary conditions required to control and eradicate the disease in the population. By taking the following limits, we can obtain:

$$\lim_{\sigma_1\to\infty} \mathcal{R}_T = 0, \tag{24}$$

$$\lim_{\sigma_2\to\infty} \mathcal{R}_T = 0, \tag{25}$$

$$\lim_{\sigma_3\to\infty} \mathcal{R}_T = 0, \tag{26}$$

and

$$\lim_{\sigma_4\to\infty} \mathcal{R}_T = \frac{\beta_T\psi_1\psi_2\psi_3}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\mu+\sigma_2+\psi_3)(\psi_4+\sigma_3+\mu)} > 0. \tag{27}$$

It can be inferred from the Eqs. (24)-(27) that implementing a control strategy that emphasizes high treatment rates for undiagnosed and diagnosed latent TB infections, as well as undiagnosed and diagnosed active TB infections, can lead to effective control of the disease in the population, provided that the right-hand sides of these equations are reduced to less than one.
However, it should be noted that near-total eradication of TB can only be achieved if high treatment rates are applied to all stages of the disease, rather than just focusing on the treatment of diagnosed active cases, as the limit in Eq. (27) does not approach zero. Furthermore, the effect of the treatment parameters and on the control of TB in the population can be determined by computing the partial derivatives of the reproduction number with respect to these parameters. This analysis will shed light on how changes in and impact the control of TB. Specifically, we obtain:

$$\frac{\partial\mathcal{R}_T}{\partial\sigma_1} = -\frac{\beta_T\psi_1\psi_2\psi_3\,(\mu+\sigma_4+\psi_5+\eta_1\psi_3\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)^2(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)} < 0, \tag{28}$$

$$\frac{\partial\mathcal{R}_T}{\partial\sigma_2} = -\frac{\beta_T\psi_1\psi_2\psi_3\,(\mu+\sigma_4+\psi_5+\eta_1\psi_3\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\psi_3+\sigma_2+\mu)^2(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)} < 0, \tag{29}$$

$$\frac{\partial\mathcal{R}_T}{\partial\sigma_3} = -\frac{\beta_T\psi_1\psi_2\psi_3\,(\mu+\sigma_4+\psi_5+\eta_1\psi_3\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)^2(\psi_5+\sigma_4+\mu)} < 0, \tag{30}$$

and

$$\frac{\partial\mathcal{R}_T}{\partial\sigma_4} = -\frac{\beta_T\psi_1\psi_2\psi_3\,(\mu+\sigma_4+\psi_5+\eta_1\psi_3\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)^2(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)} < 0. \tag{31}$$

The results of the previous analysis indicate that effective treatment of undiagnosed and diagnosed latently infected individuals, as well as undiagnosed and diagnosed actively infected individuals, can have a positive impact on reducing the spread of TB in the population. This is supported by the fact that the partial derivatives of the reproduction number with respect to the treatment parameters were found to be negative. However, the analysis also revealed that a treatment strategy that places a higher emphasis on the treatment of diagnosed actively-infected individuals is more effective for controlling the disease than focusing on other stages of the disease.

Theorem 4 *The treatment of individuals infected with TB, regardless of the stage of infection, will have a positive impact on the dynamics of TB in the population.*

Further analysis of the relationship between the reproduction number and treatment rates for singly infected individuals with latent TB, as well as undiagnosed cases of latent TB, reveals that increasing the values of the treatment parameters would lead to a corresponding decrease in the value of the reproduction number. It was also found that a high treatment rate for individuals with latent TB can compensate for a lower treatment rate for undiagnosed cases of latent TB by reducing the value of the reproduction number to below unity. However, it is important to note that this conclusion was based on the specific parameter values used in the analysis.

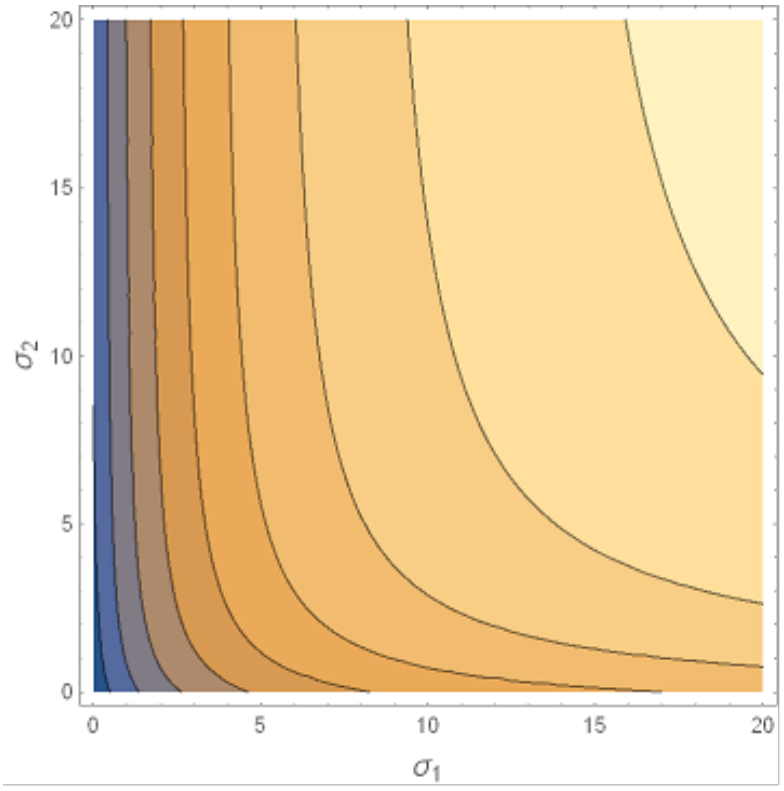


Figure 2. A contour plot of $\mathcal{R}_T$, as a function of σ_1, and σ_2, where parameter values are as given in Table 3

Existence of endemic equilibrium for the TB-only model

To find the endemic equilibrium point (EEP) of TB-only model (22) in the TB-only model (20) context, we can set each equation of model (22) to zero and solve for the force of infection. This

gives us:

$$\begin{aligned}
S^{++} &= \left(\frac{\pi}{\lambda_T^{++}+\mu}\right), \ E^{++} = \left(\frac{\pi c_2c_3c_4c_5\lambda_T^{++}(\mu+\eta_1\lambda_T^{++})}{P}\right),\\
E_L^{++} &= \left(\frac{\pi\psi_1 c_1c_3c_4c_5\lambda_T^{++}(\mu+\eta_1\lambda_T^{++})}{P}\right), E_{UL}^{++} = \left(\frac{\pi\psi_1 c_3c_4c_5\lambda_T^{++}(\mu+\eta_1\lambda_T^{++})}{P}\right),\\
I_{UA}^{++} &= \left(\frac{\pi c_1c_2c_3c_5\lambda_T^{++}(\mu+\eta_1\lambda_T^{++})}{P}\right), \ T^{++} = \left(\frac{\pi c_1c_2c_3c_4\lambda_T^{++}(\mu+\eta_1\lambda_T^{++})}{P}\right),\\
R^{++} &= \frac{Q}{P}, \quad \text{and} \quad N^{++} = \frac{R}{P},
\end{aligned} \tag{32}$$

where

$$\begin{aligned}
P &= (\mu+\lambda_T^{++})(c_1c_2c_3c_4c_5(\mu+\eta_1\lambda_T^{++})\\
&\quad -\eta_1\lambda_T^{++}\psi_1(\sigma_1c_3c_4c_5+\sigma_2\psi_2c_4c_5+\sigma_3\psi_2\psi_3c_5+\sigma_4\psi_2\psi_3\psi_4c_5+\sigma_4\psi_2\psi_3\psi_4)),\\
Q &= \pi\psi_1\lambda_T^{++}(\sigma_1c_3c_4c_5+\sigma_2\psi_2c_4c_5+\sigma_3\psi_2\psi_3c_4+\sigma_4\psi_2\psi_3\psi_4c_5+\sigma_4\psi_2\psi_3),\\
R &= c_1c_2c_3c_4c_5\left(\mu+\eta_1\lambda_T^{++}\right)\pi c_2c_3c_4c_5\lambda_T^{++}\left(\mu+\eta_1\lambda_T^{++}\right)+\pi c_1c_2c_4c_5\lambda_T^{++}\left(\mu+\eta_1\lambda_T^{++}\right)\\
&\quad +\pi c_1c_2c_3c_5\lambda_T^{++}\left(\mu+\eta_1\lambda_T^{++}\right)-\pi\psi_1\eta_1\lambda_T^{++}(\sigma_1c_3c_4c_5+\sigma_2\psi_2c_4c_5+\sigma_3\psi_2\psi_3c_5+\sigma_4\psi_2\psi_3\psi_4c_5+\sigma_4\psi_2\psi_3)\\
&\quad +\pi c_1c_2c_3c_4c_5\lambda_T^{++}\left(\mu+\eta_1\lambda_T^{++}\right)+\pi c_1c_2c_3c_4c_5\lambda_T^{++}\left(\mu+\eta_1\lambda_T^{++}\right)\\
&\quad +\pi c_1\lambda_T^{++}(\sigma_1c_3c_4c_5+\sigma_2\psi_2c_4c_5+\sigma_3\psi_2\psi_3c_4+\sigma_4\psi_2\psi_3\psi_4c_5+\sigma_4\psi_2\psi_3\psi_4).
\end{aligned}$$

It is important to note that on expansion, it can be shown that $P>0$, and $R>0$, likewise. By letting the TB force of infection at a steady state by:

$$\lambda_T^{++} = \beta_T^{++}\frac{\left(I_{UA}^{++}+\eta_1T^{++}\right)}{N^{++}}. \tag{33}$$

By substituting the values I_{UA}^{++}, T^{++}, and N^{++}, above into the force of infection in (33), we obtain:

$$P_0\lambda_T^{++2}+P_1\lambda_T^{++}+P_2=0, \tag{34}$$

where

$$\begin{aligned}
P_0 &= \eta_1(c_2c_3c_4c_5+\psi_1c_3c_4c_5+\psi_1\psi_2c_4c_5+\psi_1\psi_2\psi_3c_3c_5+\psi_1\psi_2\psi_3\psi_4c_5+\psi_1\psi_2\psi_3\psi_4),\\
P_1 &= \eta_1c_1c_2c_3c_4c_5(1-R_T)-\eta_1\sigma_1\psi_1c_3c_4c_5-\eta_1\sigma_2\psi_1c_3c_4c_5-\eta_1\sigma_3\psi_1\psi_2\psi_3c_4c_5-\eta_1\sigma_4\psi_1\psi_2\psi_3\psi_4c_5\\
&\quad -\eta_1\sigma_4\psi_1\psi_2\psi_3\psi_4+\mu c_2c_3c_4c_5+\mu\psi_1c_3c_4c_5+\mu\psi_1\psi_2c_4c_5+\mu\psi_1\psi_2\psi_3c_5+\mu\psi_1\psi_2\psi_3\psi_4c_5\\
&\quad +\mu\psi_1\psi_2\psi_3\psi_4+\sigma_1\psi_1c_3c_4c_5+\sigma_2\psi_1\psi_2c_4c_5+\sigma_3\psi_1\psi_2\psi_3c_5+\sigma_4\psi_1\psi_2\psi_3\psi_4+\sigma_4\psi_1\psi_2-3\psi_3\psi_4,\\
P_2 &= \mu c_1c_2c_3c_4c_5\left(1-\mathcal{R}_T\right).
\end{aligned}$$

A careful look at the quadratic equation in (34) shows that P_0, has a positive coefficient while P_1 has a positive (negative) coefficient which depends on whether the basic reproduction number $\mathcal{R}_T$ is less (greater) than unity. From this, we establish the following results:

Lemma 4 *The TB-only model (22) has:*

- *A unique endemic equilibrium if $A_2<0 \leftrightarrow \mathcal{R}_T>1$;*
- *A unique endemic equilibrium if $A_2<0$, and $A_0=0$, or $A_1^2-4A_2A_0=0$;*
- *Two endemic equilibria if $A_0>0$, $A_1<0$, and $A_{21}-4A_2A_0>0$, and $\mathcal{R}_T<1$;*

- *No endemic equilibrium otherwise.*

From the above, the occurrence of item (22) gives rise to the suggestion of the possibility of the existence of backward bifurcation in the TB-only model (22), where there is coexistence of locally asymptotically stable DFE and locally asymptotically stable endemic equilibrium whenever the basic reproduction number $\mathcal{R}_T < 1$. The causes of this kind of phenomenon in epidemiological models were extensively discussed in the works of [9, 16, 27–29]. Biologically, the existence of backward bifurcation in a model implies that the classical epidemiological requirement, that for the effective control of a disease in a population, the basic reproduction number of the disease must be less than unity, though necessary, in this circumstance, it is not sufficient for the effective control of such a disease. Consequently, we now explore the existence of backward bifurcation in the TB-only model (22).

Analysis of bifurcation

Consequently, it becomes highly imperative to explore the possibility of backward bifurcation in the TB-only model (22) as follows:

Theorem 5 *For the TB-only model (22) there is the exhibition of the phenomenon of backward bifurcation at $\mathcal{R}_T = 1$, whenever the inequality $\varepsilon_1 > \frac{(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)(\omega_3+\eta_1\omega_4)}{\omega_8(\omega_3+\eta_1\omega_4)}$ holds.*
It should be noted that ε_1, stands for the modification parameter accounting for reduced susceptibility to tuberculosis reinfection after an individual has been successfully treated for a previous tuberculosis infection.

Proof Let

$$\Delta_3 = \left(S^{++}, E^{++}, E_L^{++}, E_{UL}^{++}, I_{UA}^{++}, T^{++}, R^{++}\right), \tag{35}$$

denote an arbitrary endemic equilibrium point of the TB-only model (22). We then investigate whether a backward bifurcation exists in the model by using the 'center manifold theory' [30]. For convenience, we carry out the following change of variables before applying the theory: Let $S = x_1$, $E = x_2$, $E_L = x_3$, $E_{UL} = x_4$, $I_{UA} = x_5$, $T = x_6$, and $R = x_7$. Consequently, we rewrite model (22) as follows:

$$\begin{aligned}
\dot{x_1} &\equiv f_1 = \pi - \frac{\beta_T(x_5+\eta_1 x_6)x_1}{\sum_{i=1} x_i} - \mu x_1,\\
\dot{x_2} &\equiv f_2 = \frac{\xi_1\beta_T(x_5+\eta_1 x_6)x_7}{\sum_{i=1}^{7} x_i} - c_1 x_2,\\
\dot{x_3} &\equiv f_3 = \phi_1 x_2 - c_2 x_3,\\
\dot{x_4} &\equiv f_4 = \phi_2 x_3 - c_3 x_4,\\
\dot{x_5} &\equiv f_5 = \phi_3 x_4 - c_4 x_5,\\
\dot{x_6} &\equiv f_6 = \phi_4 x_5 - c_5 x_6,\\
\dot{x_7} &\equiv f_7 = \sigma_1 x_3 + \sigma_2 x_5 + \sigma_3 x_5 + \sigma_5 x_6 - \frac{\beta_T(x_5+\eta_1 x_6)x_2}{\sum_{i=1} x_i} - \mu x_7.
\end{aligned} \tag{36}$$

Considering a bifurcation parameter $\beta_T = \beta_T^*$. By solving for $\beta_T = \beta_T^*$, from R_T, yields

$$\beta_T^* = \frac{c_1c_2c_3c_4c_5}{\phi_1\phi_2\phi_3(1+\sigma_1)(c_5+\mu\eta\phi_4+\eta\phi_3\phi_4)},$$

where

$c_1 = (\phi_1 + \mu)$, $c_2 = (\phi_2 + \sigma_1 + \mu)$, $c_3 = (\phi_3 + \sigma_2 + \mu)$, $c_4 = (\phi_4 + \sigma_3 + \mu)$, and $c_5 = (\varphi_5 + \sigma_4 + \mu)$. We then evaluate the Jacobian of the transformed system (36) evaluated at DFE (Δ_3) with $\beta_T = \beta_T^*$, to obtain

$$J(\Delta_3) = \begin{bmatrix} -\mu & 0 & 0 & 0 & -\beta_T^* & -\eta_1\beta_T^* & 0 \\ 0 & -c_1 & 0 & 0 & \beta_T^* & \eta_1\beta_T^* & 0 \\ 0 & \phi_1 & -c_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & \phi_2 & -c_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & \phi_3 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & \phi_4 & 0 & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & \sigma_3 & \sigma_4 & -\mu \end{bmatrix}.$$

The matrix J^* has a simple zero eigenvalue and the remaining eigenvalues have real parts indicating that "center manifold theory" is applicable. It is noted that matrix J^* has a right eigenvector given by $\omega = (\omega_1, \omega_2, ..., \omega_7)^T$, where $\omega_1 = \frac{-(\beta_T^*\omega_5 - \eta_1\beta_T^*\omega_5)}{\mu}$, $\omega_2 > 0$, $\omega_3 = \frac{\phi_1\phi_2}{c_2}$, $\omega_5 = \frac{\phi_1\phi_2\phi_3\omega_3}{c_2c_3c_4}$, $\omega_6 = \frac{\phi_1\phi_2\phi_3\phi_4\omega_2}{c_2c_3c_4c_5}$, and $\omega_7 = \frac{\sigma_1\omega_3 + \sigma_2\omega_4 + \sigma_3\omega_5 + \sigma_4\omega_6}{\mu}$. Similarly, J^* has left eigenvectors $V = (v_1, v_2, ..., v_7)$, satisfying $v.\omega = 1$, with $v_1 = 0$, $v_2 = \frac{\phi_1 v_3}{c_1}$, $v_3 > 0$, $v_4 = \frac{c_2 v_3}{\phi_2}$, $v_5 = \frac{c_2c_3\omega_2}{\phi_3}$, $v_6 = \frac{\eta_1\beta_T^*\phi_3\phi_1}{c_1c_5}$, and $v_7 = 0$.

Arising from Theorem 4.1 in [30] computation of the associated non-zero partial derivatives of $f(x)$, evaluated at DFE (Δ_3), the associated bifurcation coefficients a, and b defined as

$$a = \sum v_k\omega_i\omega_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \quad \text{and} \quad b = \sum v_k\omega_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_T^*}(0,0),$$

are: $a = 2v_2\eta_1\beta_T\frac{\mu}{\pi}(\omega_3\omega_7 + \omega_4\omega_7) - 2v_2\eta_1\beta_T\frac{\mu}{\pi}(\omega_2\omega_3 + \omega_3\omega_5 + \omega_3\omega_6 + \omega_3^2 + \omega_3\omega_7 + \omega_3\omega_4) - 2v_2\eta_1\beta_T * \frac{\mu}{\pi}(\omega_2\omega_4 + \omega_4\omega_5 + \omega_3\omega_4 + \omega_4\omega_7 + \omega_4^2 + \omega_4\omega_5 + \omega_4\omega_6)$, and $b = v_2\omega_3 + \eta_1 v_2\omega_4 > 0$, with $v_2, \omega_2, \omega_3, \omega_4, \omega_5, \omega_6$, and ω_7, being positive. Consequently, due to the fact that the bifurcation coefficient $b > 0$, it can be deduced from Theorem 4.1 in [30] that the TB-only model (22) undergoes the phenomena of a backward bifurcation whenever the backward bifurcation coefficient $a > 0$. This is so if

$$\epsilon_1 > \frac{(\omega_2 + \omega_3 + \omega_4 + \omega_5 + \omega_6 + \omega_7)(\omega_3 + \eta_1\omega_4)}{\omega_8(\omega_3 + \eta_1\omega_4)} = \epsilon^* \tag{37}$$

holds. It should be recalled that ϵ_1, stands for the modification parameter accounting for the reduction in susceptibility to tuberculosis reinfection after an infected individual has been successfully treated for a previous tuberculosis infection. It should be noted that all parameters of model (22) are non-zero, and $\beta_T^* > 0$. Setting $\epsilon_1 = 0$, the bifurcation coefficient a, is reduced to

$$\begin{aligned} a = -[&2v_2\beta_T^*\frac{\mu}{\pi}(\omega_2\omega_3 + \omega_3\omega_5 + \omega_3\omega_6 + \omega_3^2 + \omega_3\omega_6 + \omega_3\omega_4) \\ &+ 2v_2\eta_1\beta_T^*\frac{\mu}{\pi}(\omega_2\omega_4 + \omega_4\omega_5 + \omega_3\omega_4 + \omega_4\omega_7\omega_4^2 + \omega_4\omega_6 + \omega_4\omega_6)], \end{aligned} \tag{38}$$

with $v_2 > 0$, $\omega_2 > 0$, $\omega_3 > 0$, $\omega_4 > 0$, $\omega_5 > 0$, $\omega_6 > 0$, and $\omega_7 > 0$, where each of them are as defined earlier. Consequently, since $b > 0$, it can be deduced from Theorem 4.1 in [30] that the TB-only model (22) does not undergo a backward bifurcation if $\epsilon = 0$, since the backward bifurcation coefficient $a < 0$. The revelation from here is that the cause of backward bifurcation in

the model (22) is the susceptibility to tuberculosis reinfection after a successful treatment from a previous infection. Obviously, for the TB-only model (22) to undergo backward bifurcation at $R_T = 1$, requires that the bifurcation coefficient $a > 0$, for ϵ_1, is of greater value than the quantity on the right-hand side of (37), that is $\epsilon_1 > \epsilon^*$. On the other hand, if $\epsilon_1 < \epsilon^*$, model (22) will not undergo backward bifurcation at $R_T = 1$. As a matter of fact, if $\epsilon_1 = 0$, for the TB-model (22), there will be the existence of the phenomenon of backward bifurcation. See Figure 3 for the schematic diagram of the phenomenon of backward bifurcation that the TB-only model (22) undergoes.

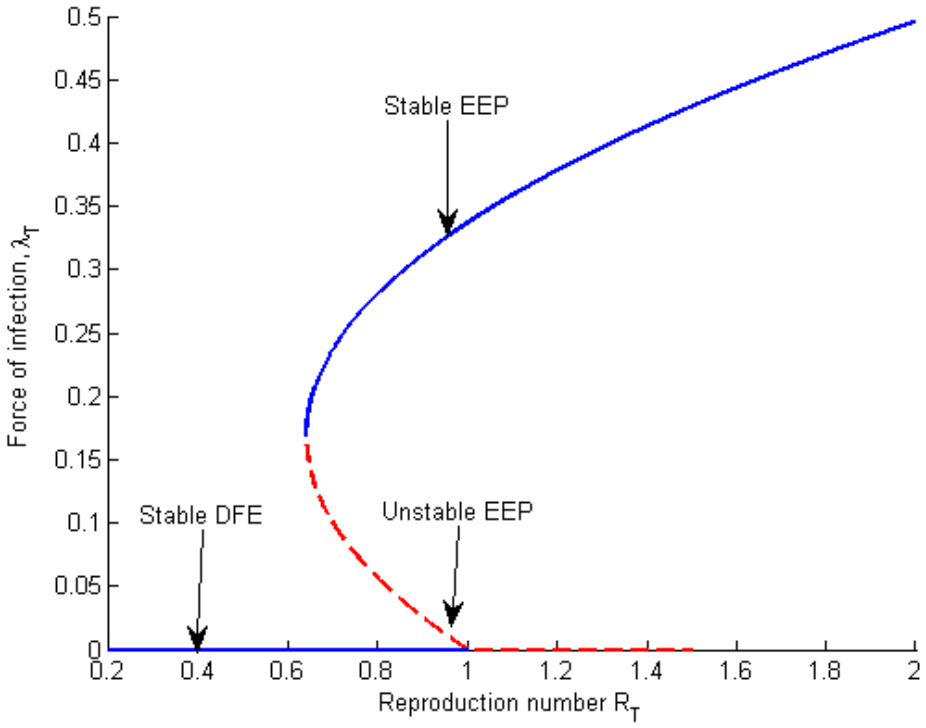


Figure 3. Bifurcation diagram of the TB-only model

Global asymptotic stability of DFE of TB-only model

In this section, we remove the cause of backward bifurcation, by setting $\varepsilon_1 = 0$, and then show that the given model (22) is globally asymptotically stable.

By considering model (22) with $\varepsilon_1 = 0$, the following is claimed:

Theorem 6 *The DFE of TB-only model (22) is globally asymptotically stable in Ω_3, whenever the reproduction number $\mathcal{R}_T < 1$.*

See the proof of this theorem in ''Appendix A''. The implication of Theorem 6 epidemiologically is that a previous infection of the disease covers a lifelong immunity to reinfection of susceptible individuals to tuberculosis. Thus, tuberculosis can ultimately be eradicated from the given human population when the reproduction number $\mathcal{R}_T < 1$.
Furthermore, since with $\varepsilon_1 = 0$, the global stability of the DFE of the TB-only model (22) follows if $\mathcal{R}_T < 1$, from here, we carry out the estimates of the range of values of the treatment parameters σ_1, σ_2, σ_3, and σ_4, for which the objectives of tuberculosis eradication is possible. When we set $\mathcal{R}_T < 1$, and make the treatment parameters σ_1, σ_2, σ_3, and σ_4, the subject of the expression in the

reproduction number of the model (22), we obtain the following:

$$\begin{aligned}
\sigma_1 &> \beta_T\psi_1\psi_2\psi_3\frac{(c_5+\eta_1\psi_4)}{(\psi_1+\mu)\,(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)}-(\psi_2+\mu),\\
\sigma_2 &> \beta_T\psi_1\psi_2\psi_3\frac{(c_5+\eta_1\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)}-(\psi_3+\mu),\\
\sigma_3 &> \beta_T\psi_1\psi_2\psi_3\frac{(c_5+\eta_1\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\psi_3+\sigma_2+\mu)(\psi_5+\sigma_4+\mu)}-(\psi_4+\mu),\\
\sigma_4 &> \beta_T\psi_1\psi_2\psi_3\frac{(c_5+\eta_1\psi_4)}{(\psi_1+\mu)\,(\psi_2+\sigma_1+\mu)(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)}-(\psi_5+\mu).
\end{aligned} \tag{39}$$

If the inequalities in (39) above are satisfied, then the reproduction number $\mathcal{R}_T < 1$, and tuberculosis can be completely eradicated in the human population.
However, from the first inequalities in (39), if

$$\beta_T\psi_1\psi_2\psi_3\frac{(c_5+\eta_1\psi_4)}{(\psi_1+\mu)\,(\psi_3+\sigma_2+\mu)(\psi_4+\sigma_3+\mu)(\psi_5+\sigma_4+\mu)} < (\psi_2+\mu),$$

then treating individuals that are latently-infected with TB is not necessary as $\sigma_1 = 0$, will result in $\mathcal{R}_T < 1$. Likewise, the same results are obtained from other inequalities in (39).

4 Analysis of the co-infection model of TB-HIV

We carry out the analysis of the HIV-TB Co-infection model (5) for its basic properties as follows:

Local asymptotic stability of the DFE of the TB-HIV co-infection model

The disease free equilibrium of the TB-HIV co-infection model (5) is as given below:

$$\begin{aligned}
D_4 &= \left(S^+, E^+, E_L^+, E_{UL}^+, I_{UA}^+, T^+, R^+, I_H^+, E_{HT}^+, I_{HU}^+, I_{HUA}^+, I_{HDA}^+, T_{HT}^+\right)\\
&= \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \right).
\end{aligned} \tag{40}$$

By using the next-generation matrix method, we obtain the Local Asymptotic Stability (LAS) of the DFE of co-infection model (5). It follows from Driessche and Watmough in [20] which is defined by FV^{-1}. Where F, and V, are the terms for new infection and the terms for the remainder respectively, given as:

$$F = \begin{bmatrix}
0 & 0 & 0 & \beta_T & \eta_1\beta_T & 0 & 0 & 0 & \eta_2\beta_T & \eta_3\beta_T & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & \beta_H & \beta_H & \phi_1\beta_H & \phi_2\beta_H & \phi_3\beta_H & \phi_4\beta_H\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix},$$

and

$$V = \begin{bmatrix} c_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\psi_1 & c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\psi_2 & c_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\psi_3 & c_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\psi_4 & c_5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & c_6 & -\sigma_{T1} & -\sigma_{T2} & -\sigma_{T3} & -\sigma_{T4} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & c_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & c_8 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\psi_{HUA} & c_9 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\psi_{HDA} & c_{10} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\psi_{HU} & c_{11} \end{bmatrix},$$

where
$c_1 = (\psi_1 + \mu), c_2 = (\psi_2 + \sigma_1 + \mu), c_3 = (\psi_3 + \sigma_2 + \mu), c_4 = (\psi_4 + \sigma_3 + \mu), c_5 = (\psi_5 + \sigma_4 + \mu), c_6 = (\delta_1 + \mu)$, $c_7 = (\psi_{HU} + \sigma_{T1} + \delta_2 + \mu)$, $c_8 = (\psi_{HUA} + \delta_3 + \sigma_{T2} + \mu)$, $c_9 = (\psi_{HDA} + \sigma_{T3} + \delta_4 + \mu)$, $c_{10} = (\psi_{HT} + \sigma_{T4} + \delta_5 + \mu)$, and $c_{11} = (\sigma_{T5} + \delta_6 + \mu)$.
Consequently, arising from [26], the basic reproduction number for the disease is obtained as:

$$\mathcal{R}_C = \rho\left(FV^{-1}\right) = \max\{\mathcal{R}_H, \mathcal{R}_T\},$$

where

$$\mathcal{R}_H = \frac{\beta_H}{(\mu + \sigma_1)}, \quad \text{and} \quad \mathcal{R}_T = \frac{\beta_T \psi_1 \psi_2 \psi_3 \left(c_5 + \eta_1 \psi_4\right)}{(\psi_1 + \mu)\left(\psi_2 + \sigma_1 + \mu\right)(\psi_3 + \sigma_2 + \mu)(\psi_4 + \sigma_3 + \mu)(\psi_5 + \sigma_4 + \mu)}.$$

That is,

$$\mathcal{R}_C = \frac{\beta_T \psi_1 \psi_2 \psi_3 \left(c_5 + \eta_1 \psi_4\right)}{(\psi_1 + \mu)\left(\psi_2 + \sigma_1 + \mu\right)(\psi_3 + \sigma_2 + \mu)(\psi_4 + \sigma_3 + \mu)(\psi_5 + \sigma_4 + \mu)}. \tag{41}$$

It should be noted that Theorem 2 in [20] gives rise to the result below.

Lemma 5 *The disease-free equilibrium, (DFE), D_4 of the co-infection model (5), is locally asymptotically stable (LAS) whenever the reproduction number of the model is less than unity ($\mathcal{R}_C < 1$), and unstable when $\mathcal{R}_C > 1$.*

It is pertinent to note that the quantity $\mathcal{R}_C = max\{\mathcal{R}_H, \mathcal{R}_T\}$, is the effective reproduction number of the co-infection model (5), in which case is previously defined. By adopting the same approach as we did in Section 3, it can be shown that there is an exhibition of the phenomenon of backward bifurcation at $\mathcal{R}_C = 1$, for co-infection model (5). It is pertinent to note that the same conclusion is arrived at for TB-only model (22) in the previous section, that susceptibility to tuberculosis reinfection after a successful treatment of the disease is the cause of this backward bifurcation in the co-infection model (5).

Theorem 7 *There is an exhibition of backward bifurcation at $\mathcal{R}_C = 1$, for co-infection model (5) whenever*

$$\varepsilon_1 > \frac{\left(\omega_2 + \omega_3 + \omega_4 + \omega_5 + \omega_6 + \omega_7 + \omega_8\right)\left(\omega_3 + \eta_1 \omega_4\right)}{\omega_8\left(\omega_3 + \eta_1 \omega_4\right)}$$

holds.

For the proof of this theorem, see ''Appendix B''.

5 Sensitivity analysis and uncertainty analysis of TB-only model

In the TB-only model, many parameters are involved in its formulation. Therefore, expectedly, uncertainties do arise in the estimation of the values of these parameters adopted for the numerical simulations of the model. By adopting the approach in [16, 26, 31], using Latin hypercube sampling (LHS), we carried out in this section, uncertainty analysis with a view to accounting for the effect that such uncertainties have on the numerical simulation results obtained in this work. Additionally, by using partial rank correlation coefficients (PRCC), we equally carried out a global sensitivity analysis to quantify the impact of the variations or sensitivity of each parameter on the associated numerical simulations.

The Latin hypercube sampling (LHS) method is adopted here by defining baseline values and ranges for each of the parameters of the TB-only model (22), as stated in Table 3, where multiple runs for $NR = 1000$, are done for the sample data for the response output [26, 31]. In this case, it is the control reproduction number $\mathcal{R}_T$. It is worth mentioning that each parameter is assumed to obey a uniform distribution [32].

On the other hand, we computed the sensitivity of the parameters in the Tuberculosis-only model (22) by finding PRCC between each parameter and the control reproduction number $\mathcal{R}_T$. The values of these PRCC values making up the effective reproduction number of the model (22) are as given in Table 2, while Figure 4 gives the distribution of PRCC values. From the PRCC distribution in Figure 4, it could be seen that the transmission rate for tuberculosis β_T, the modification parameters that account for the infectiousness of infected individuals with TB-only η_1, and the treatment rates for singly infected individuals with latently-infected TB, σ_1, are the parameters that play a dominant role in driving the dynamics of tuberculosis with respect to the response function $\mathcal{R}_T$. It is worth mentioning that while β_T, and η_1, are positively correlated with the response function $\mathcal{R}_T$, on the other hand, σ_1, is negatively correlated with the response function $\mathcal{R}_T$. The epidemiological implication of this is that tuberculosis can be effectively controlled and eradicated by procuring all strategies that can help minimize the transmission rate of the disease, such as measures like public awareness and educational enlightenment campaigns for susceptible individuals always to cover their mouth when coughing or sneezing, and the need for infants to be vaccinated against tuberculosis.

Likewise, the infectiousness of individuals with latent tuberculosis can be minimized by testing and adequate treatment of latently infected individuals.

Table 2. PRCC values of the parameters of TB-only model (22), with $\mathcal{R}_T$, as the output (response function). Parameter values and ranges used are as given in Table 3

S/N	**Parameters**	**PRCC (R_T)**
1.	β_T	0.9013
2.	σ_1	0.0412
3.	u_2	-0.03712
4.	σ_2	-0.3124
5.	ψ_3	-0.4021
6.	ψ_2	-0.4202
7.	η_1	0.5633
8.	σ_3	-0.6234

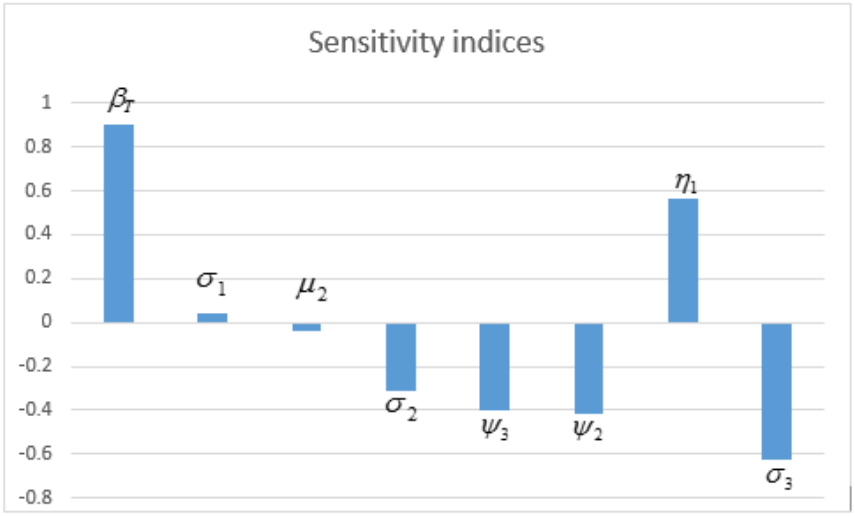


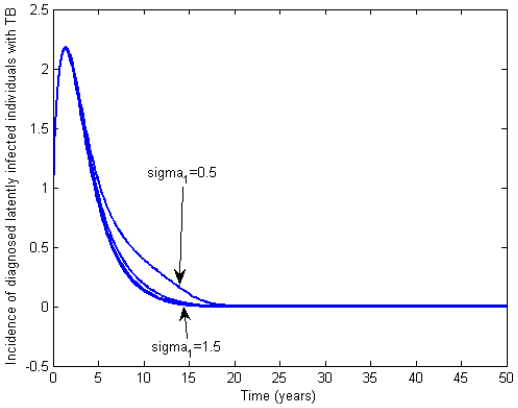
Figure 4. Schematic diagram of the sensitivity indices for the TB-only model (22). Values and ranges of parameters used are as given in Table 3

6 Numerical simulation

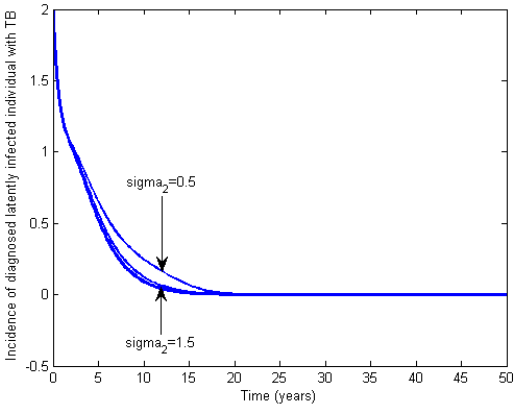
For the illustration of some of the theoretical results obtained earlier in this study, it is necessary to conduct numerical simulations of the co-infection model. We performed numerical simulations of the model using the parameter values presented in the table below. The numerical simulation of the model was carried out using MATLAB's ODE45 solver, which is well-known for its high convergence, consistency, and stability. The embedded numerical scheme in MATLAB, like other computing software such as Maple, Mathematica, and Scientific Workplace, is known for its reliability and efficiency in numerical simulations of epidemiological models.

Table 3. Values of parameters of the co-infection model (5) with the total population of Nigeria as of January 1st, 2023 estimated at 200,000,000 (real-life data as obtained from National Population Commission (NPC) of Nigeria)

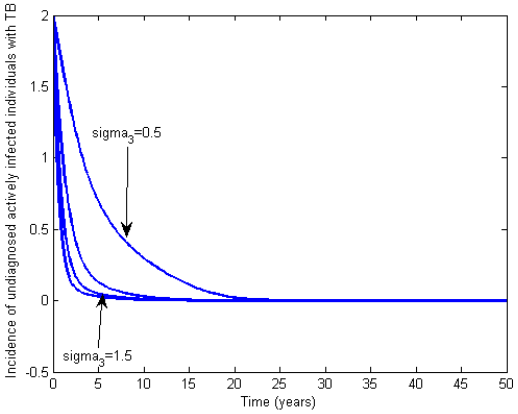
Parameter	Baseline (Range)	Sources
π	5,000 [3,500 - 6500] year^{-1}	[1]
μ	0.02043 [0.02034 - 0.02052] year^{-1}	[16]
$\beta_T(\beta_H)$	0.1 year^{-1}	[1]
$\sigma_1, \sigma_2, \sigma_3, \sigma_4$	0.7, 0.7, 0.7, 0.7 year^{-1}	[15]
$\sigma_{T1}, \sigma_{T2}, \sigma_{T3}, \sigma_{T4}$	0.7, 0.7, 0.7, 0.7 year^{-1}	[15]
$\psi_1, \psi_2, \psi_3, \psi_4$	6, 4.18, 2.5, 3 year^{-1}	[16]
$\psi_{HU}, \psi_{HUA}, \psi_{HDA}, \psi_{HT}$	6, 4.5, 3, 3 year^{-1}	[16]
$\varepsilon_1, \varepsilon_2$	1, 1.2 [0.8-1.2, 1-1.5]	Assumed
γ_1, γ_2	0.6, 0.8 [0-1, 0-1]	Assumed
$\theta_1, \theta_2, \theta_3, \theta_4, \theta_5, \theta_6, \theta_7, \theta_8$	3.2, 3, 3.2, 2, 2, 2, 2, 2 [2.8-3.6, 2.5-3.5, 1.7 -2.3]	[16]
η_1, η_2, η_3	1.2, 1.3, 1.5 [1-2, 0.9-1.7, 1-2.3]	[16]
$\phi_1, \phi_2, \phi_3, \phi_4$	1.3, 1.7, 1.2, 1.1 [1-1.6, 1-2.4, 0.8-1.6, 0.7-1.5, 0.75-1.25]	[16]
$\delta_1, \delta_2, \delta_3, \delta_4, \delta_5, \delta_6$	0.08, 0.05, 0.8, 0.1, 0.1, 0.01 year^{-1}	[15]



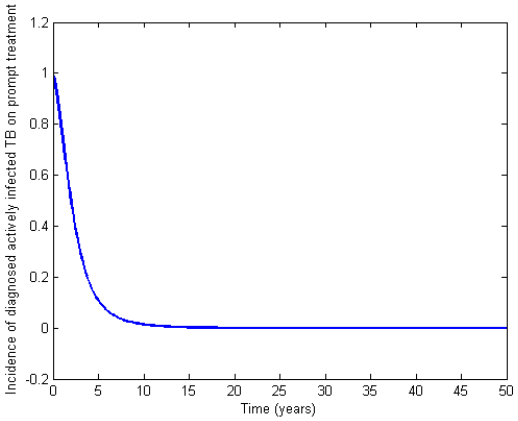
(a) Incidence of diagnosed latently infected individuals with TB with the effect of σ_1



(b) Incidence of diagnosed latently infected individuals with TB with the effect of σ_2

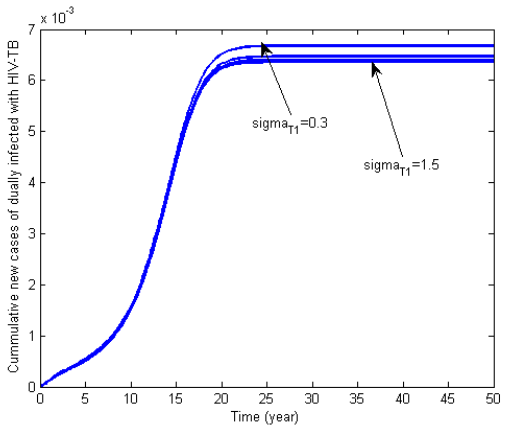


(c) Incidence of diagnosed latently infected individuals with TB with the effect of σ_3

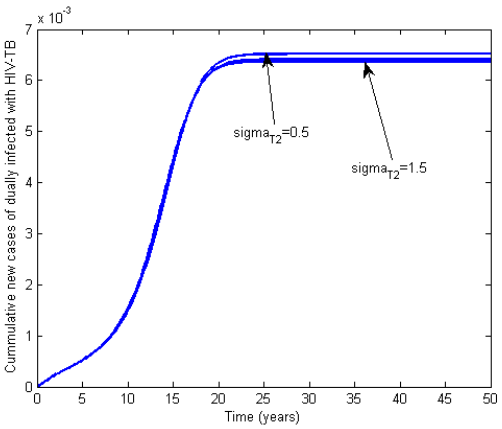


(d) Incidence of diagnosed latently infected individuals with TB with the effect of σ_4

Figure 5. Incidence of diagnosed latently infected individuals with TB with the effect of σ

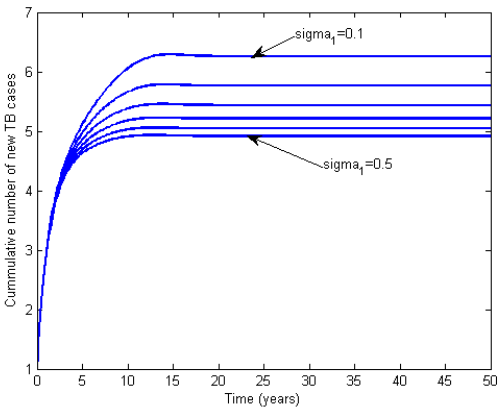


(a) Cumulative number of new cases of dually infected HIV-TB with the effect of σ_{T3}

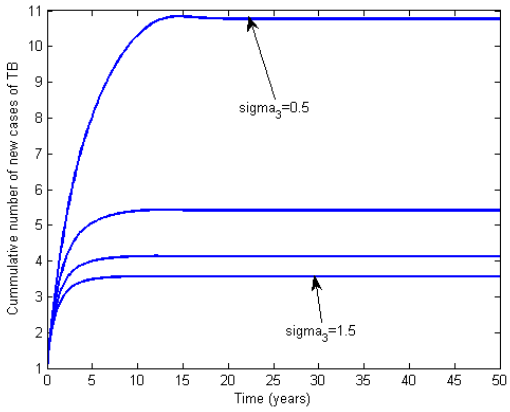


(b) Cumulative number of new cases of dually infected HIV-TB with the effect of σ_{T4}

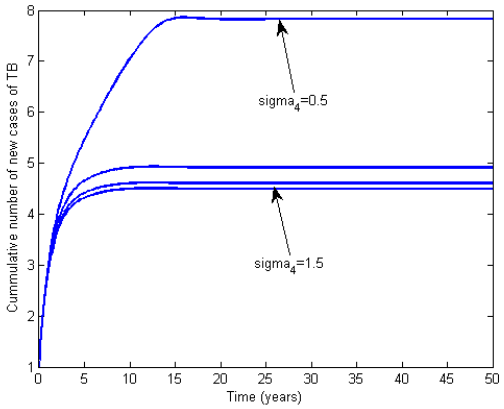
Figure 6. Cumulative number of new cases of dually infected HIV-TB with the effect of σ



(a) Cumulative number of new cases of TB with the effect of σ_1



(b) Cumulative number of new cases of Tuberculosis with the effect of σ_3



(c) Cumulative number of new cases of TB with the effect of σ_4

Figure 7. Cumulative number of new cases of TB with the effect of σ

Discussion of numerical simulation of the model

For the simulation of the co-infection model for dually infected individuals with the two diseases TB and HIV, from Figure 5a, it is observed that there is a steady rise in the number of cumulative cases for dual infection until day eighteen when it flattens out with a slight drop in its values as the treatment rate σ_{T1} increases. Likewise, from Figure 5b, it is observed that there is a steady rise in the number of cumulative cases of dually infected individuals with the two diseases until about day twenty, for an increase in treatment rate σ_{T2}, accompanied by a slight drop in the values of the cumulative number of new cases of dually infected individuals. However, as observed from Figure 5c, there is a significant effect of the treatment rate σ_{T3} on the cumulative number of new cases of dually infected individuals of HIV-TB. As the treatment rate increases, it is accompanied by a drop in the values of the cumulative number of new cases of infections of individuals infected with both diseases. The same effect is observed for the treatment rate σ_{T4} on the cumulative number of new cases of individuals infected with both diseases, as seen in Figure 5d.
From Figure 6a, it can be seen that the cumulative number of new cases of TB rises steadily until day three when it flattens out with an increase in the values of the treatment rates σ_1. In Figure 6b, we observe that the cumulative number of new cases of TB rises generally and starts flattening out almost immediately with a drop in the values of the cumulative number of new cases of TB as the

treatment rate σ_2 increases. Similarly, there is a significant effect of treatment rate σ_4 on the value of the cumulative number of new cases of TB, which drops as the treatment rate is increased. The reproduction number $\mathcal{R}_C$ for the TB-HIV co-infection model (5) is 0.0715997. As shown in Figure 7a, where we plotted the incidence of diagnosed latently infected individuals with TB with the effect of treatment rate σ_1, there was a general steady rise in the first two days followed by a decline until day ten, when it flattens out as the treatment rate increases. From Figure 7b, it can be observed that the incidence of diagnosed latently infected individuals decreases steadily until day seven when it flattens out as the treatment rate σ_2 decreases in value. Similarly, in Figure 7c, the incidence of diagnosed latently infected individuals decreases from day one and flattens out immediately as the treatment rate σ_3 increases. The implication of this is that as the values of the treatment rates σ_1, σ_2, and σ_3 increase, there is a decrease in the incidence of the disease, ultimately bringing the disease under control.

7 Findings from the research work

The major findings from this work are:

- The HIV-only model possesses a locally asymptotically stable disease-free equilibrium whenever the associated reproduction number $\mathcal{R}_H$ is less than unity.
- The co-infection model (5) and the TB-only model (22) undergo the phenomenon of backward bifurcation due to susceptibility to TB re-infection after recovery from previous tuberculosis infection. The implication of this is that the classical requirement that the reproduction number of the disease be less than unity, though still necessary for disease control, is no longer sufficient for its control, meaning that more strategies are needed to be procured for effective control of the disease in the given population.
- When the cause of backward bifurcation is removed from the TB-only model and the co-infection model, the disease-free equilibrium of the TB-only model and co-infection model is shown to be locally asymptotically stable when the associated reproduction number $\mathcal{R}_T$ is less than unity.
- The disease-free equilibrium of the TB-only model and that of the co-infection model are each shown to be locally asymptotically stable when the associated reproduction number $\mathcal{R}_T$ and $\mathcal{R}_C$ respectively are not up to unity.
- From the sensitivity and uncertainty analysis of the TB model, it could be seen that the transmission rate for tuberculosis β_T, the modification parameters accounting for the infectiousness of infected individuals with TB-only η_1, and the treatment rates for singly infected individuals with latently-infected TB, σ_1 are the three top drivers of tuberculosis infection in the given population.
- From the numerical simulation of the model, it could be seen that different treatment rates have a significant effect on the reduction of the incidence of tuberculosis infection and on the cumulative number of new cases of TB-HIV co-infection.

Of importance is the revelation that through this work, it has been shown that with adequate treatment of tuberculosis, even though there is currently no treatment available for HIV, the burden of the co-infection of the two diseases will be significantly reduced in the population. It is pertinent to note that this work has made a modest contribution to the control of the spread of tuberculosis and HIV in a population where both diseases are co-circulating.

8 Recommendations

The primary purpose of research in mathematical epidemiology is to provide healthcare policy-makers with evidence-based recommendations that can guide the formulation of effective policies for controlling the spread of contagious diseases and reducing the burden of disease in both

human and animal populations. With this objective in mind, it is essential to present actionable recommendations that can be readily utilized by healthcare policymakers. Below are some crucial recommendations:

- Every effort must be made to launch a comprehensive educational campaign aimed at individuals who are susceptible to TB. The campaign should emphasize the importance of consistently covering their mouths when coughing or sneezing in public spaces. Additionally, ensuring that infants receive vaccination against the disease should be a priority.
- It is essential to implement a highly visible awareness program targeting all members of communities. This program should stress the significance of practicing safe sexual activities by consistently using condom protection during sexual encounters.
- A comprehensive educational awareness campaign is crucial for educating all individuals about the importance of being cautious to avoid contact with bodily secretions and droplets from infected patients. Additionally, it is essential to implement appropriate measures to prevent the vertical transmission of these diseases.
- A campaign should be initiated to encourage regular screening for both diseases among individuals. It is imperative that infected individuals seek prompt medical attention as soon as they are aware of their status.

9 Conclusion

In this research work, we developed a co-infection model to gain insights into the transmission of HIV-Tuberculosis in a human population where HIV treatment is not readily available but tuberculosis treatment is accessible. We rigorously analyzed both the HIV-only and TB-only models to understand their fundamental properties. Subsequently, we extended our analysis to the co-infection model.
The key contributions in this work are:

- We show that the disease-free equilibrium of the sub-models and the full co-infection model were locally asymptotically stable.
- We conducted a rigorous analysis of the reproduction number to identify parameters that can reduce the spread of the disease.
- We conducted the sensitivity analysis to identify key parameters that drive the infectiousness of each of the diseases and that which is of great influence on the co-infection of both diseases.
- The theoretical results were validated appropriately with numerical simulations, and the plots from the simulations were extensively interpreted.
- We plotted contour plots involving key parameters and the reproduction numbers for the diseases with a view to determining the threshold for control and measures that can help eradicate the disease from the human population.

Specifically, by using parameter values sourced from existing literature and employing the MATLAB programming language, we conducted numerical simulations of the model, allowing us to validate the theoretical results obtained from the model analysis. Our findings revealed that a specific subgroup of individuals, those with varying treatments for tuberculosis, plays a pivotal role in significantly reducing the disease burden caused by co-infection. Notably, our simulations highlighted that targeting treatment towards individuals with tuberculosis in the diagnosed latent infection stage (whether singly or dually infected with HIV) is an effective strategy for reducing both the co-infection disease burden and HIV incidence within the studied population. This work's merit lies in demonstrating the promising potential for controlling co-infection when HIV treatment is not readily accessible.
Furthermore, the outcomes of this study can be valuable for healthcare policymakers, especially

in regions with limited healthcare resources. In societies where tuberculosis treatment, albeit occasionally scarce, is available while HIV treatment is not, our results suggest that careful application of these findings can aid in formulating robust public awareness campaigns and disease control strategies. Ultimately, this approach has the potential to reduce the incidence and prevalence of both HIV and tuberculosis in populations where these diseases co-circulate.
The formulation of our model has a notable limitation: it does not account for the simultaneous transmission of both diseases from the same source. We acknowledge that this is a potential scenario, as suggested by the findings of Ciesielski et al. [33], where they demonstrated the possibility of an individual acquiring both HIV and Hepatitis C virus (HCV) from a single source. As an area for further contribution to knowledge by other researchers, this work can be extended by incorporating time-dependent control functions into the proposed model. This extension would yield a model with optimal control, facilitating the development of optimal strategies for preventing the spread of the disease within the given population and implementing other strategies to mitigate the disease burden. Furthermore, the model proposed herein can be reformulated as a fractional-order model, incorporating fractional-order derivatives. The resulting system of nonlinear fractional-order derivatives can be solved using appropriate methods, such as Laplace Adomian decomposition or other techniques commonly employed for solving fractional-order models.

Declarations

Ethical approval

The authors hereby state that the project is in compliance with ethical standards. This research does not involve human or animal participants.

Consent for publication

Not applicable

Conflict of Interest

The authors hereby declare that there are no known competing interests.

Data availability statement

Data availability is not applicable to this research work, as no new data was created or analyzed in the work.

Authors' contributions

B.B.: Conceptualization, Project administration, supervision, Model analysis. T.O.: Compliment in model formulation, Joined in model analysis. AC: Coding for numerical simulation, Script writing, O.U. and O.B.: Model validation, Interpretation of plots. The authors have read and agreed to the published version of the manuscript.

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Appendix A: Proof of Theorem 6

Proof Consider the following linear Lyapunov function

$$g_2 = \psi_1 \left(c_3 + \psi_2\eta_1\right) E + c_1 \left(c_3 + \psi_2\eta_1\right) I_{UA} + c_3c_3c_3T.$$

With Lyapunov derivatives

$$\dot{g}_2 = \left(I_{UA} + \eta_1 T\right) \left[\frac{\beta_T S}{N} \left(\psi_1 \left(c_3 + \psi_2\eta_1\right) - c_1c_2c_3\right)\right],$$

$$\dot{g}_2 = c_1c_2c_3 \left(I_{UA} + \eta_1 T\right) \left[{}^{S}/_{N} R_T - 1\right].$$

By taking note that $S(t) \leq N(t)$, and $N(t) \leq {}^{\pi}/_{\mu}$, in Ω_2, for all $t > 0$, it follow from the above that $\dot{g}_2 = c_1c_2c_3 \left(I_{UA} + \eta_1 T\right) \left(R_T - 1\right)$.

Hence, $\dot{g}_2 \leq 0$, if $R_T \leq 1$, with $\dot{g}_2 = 0$, if and only if $E = E_L = E_{UL} = I_{UA} = T = R = 0$. Therefore, $\dot{g}_2$, is a Lyapunov function in Ω_2, and it follows from Lasalle's invariance principle [34] that every solution to the equations in TB-only model (22) with initial conditions in Ω_2, converges to ξ, as $t \to \infty$. That is, $(E(t), E_L(t), E_{UL}(t), I_{UA}(t), T(t), R(t)) \to (0, 0, 0, 0, 0, 0)$, as $t \to \infty$. By substituting $E = E_L = E_{UL} = I_{UA} = T = R = 0$, into the first equation in model (22) with $S(t) \to {}^{\pi}/_{\mu}$, as $t \to \infty$. Therefore $(S(t), E(t), E_L(t), E_{UL}(t), I_{UA}(t), T(t), R(t)) \to \left({}^{\pi}/_{\mu}, 0, 0, 0, 0, 0, 0\right)$, as $t \to \infty$, for $R_T \leq 1$, so that the DFE, ξ, of TB-only model (22) is locally asymptotically stable in Ω_2, when $R_T \leq 1$.

Appendix B: Proof of Theorem 7

Proof For convenience, let $S = x_1$, $E = x_2$, $E_L = x_3$, $E_{UL} = x_4$, $I_{UA} = x_5$, $T = x_6$, $R = x_7$, $I_H = x_8$, $E_{HT} = x_9$, $I_{HU} = x_{10}$, $I_{HUA} = x_{11}$, $I_{HDA} = x_{12}$, and $T_{HT} = x_{13}$. It then follows that the model (22) can be rewritten as:

$$\begin{aligned}
\dot{x}_1 \equiv f_1 &= \pi - \frac{\beta_T \left(x_5 + \eta_1 x_6\right) x_1}{N} - \frac{\beta_H x_8 x_1}{N} - \frac{\beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_1}{N} \\
&\quad - \frac{\beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_1}{N} - \mu x_1, \\
\dot{x}_2 \equiv f_2 &= \frac{\beta_T \left(x_5 + \eta_1 x_6\right) x_1}{N} - \frac{\beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_1}{N} + \frac{\varepsilon_1 \beta_T \left(x_5 + \eta_1 x_6\right) x_7}{N} + \frac{\beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_7}{N} \\
&\quad - \frac{\beta_H x_8 x_2}{N} - \frac{\varepsilon_2 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_2}{N} - c_1 x_2, \\
\dot{x}_3 \equiv f_3 &= \psi_1 x_2 - \frac{\phi_1 \beta_H x_8 x_3}{N} - \frac{\phi_2 \beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_3}{N} - c_2 x_3, \\
\dot{x}_4 \equiv f_4 &= \psi_2 x_3 - \frac{\phi_3 \beta_H x_8 x_4}{N} - \frac{\phi_4 \beta_H x_8 x_4}{N} - c_3 x_4, \\
\dot{x}_5 \equiv f_5 &= \psi_3 x_4 - \frac{\phi_5 \beta_H x_8 x_5}{N} - \frac{\phi_6 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_5}{N} - c_4 x_5, \\
\dot{x}_6 \equiv f_6 &= \psi_4 x_5 - \frac{\theta_7 \beta_H x_8 x_6}{N} - \frac{\phi_8 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_6}{N} - c_5 x_6,
\end{aligned} \tag{42}$$

$$
\begin{aligned}
\dot{x}_7 \equiv f_7 &= \sigma_1 x_3 + \sigma_2 x_4 + \sigma_3 x_5 + \sigma_4 x_6 - \frac{\varepsilon_1 \beta_T \left(x_5 + \eta_1 x_6\right) x_7}{N} - \frac{\varepsilon_2 \beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_7}{N} \\
&\quad - \frac{\beta_H x_8 x_7}{N} - \frac{\varepsilon_2 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_6}{N} - \mu x_7, \\
\dot{x}_8 \equiv f_8 &= \frac{\beta_H x_8 x_1}{N} + \frac{\beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_1}{N} - \frac{\psi_1 \beta_T \left(x_5 + \eta_1 x_6\right) x_7}{N} \\
&\quad + \frac{\beta_H x_8 x_1}{N} + \frac{\beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_6}{N} - \frac{\psi_2 \beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_8}{N} \\
&\quad + \sigma_{T1} x_9 + \sigma_{T2} x_{10} + \sigma_{T3} x_{11} + \sigma_{T4} x_{12} + \sigma_{T5} x_{13} - c_6 x_8, \\
\dot{x}_9 \equiv f_9 &= \frac{\sigma_1 \beta_T \left(x_5 + \eta_1 x_6\right) x_8}{N} + \frac{\sigma_2 \beta_T \left(\eta_2 x_{11} + \eta_3 x_{12}\right) x_8}{N} \\
&\quad + \frac{\beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_6}{N} - c_7 x_9, \\
\dot{x}_{10} \equiv f_{10} &= \psi_{HU} x_9 + \frac{\theta_1 \beta_H x_8 x_3}{N} + \frac{\theta_2 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_3}{N} - c_8 x_{10}, \\
\dot{x}_{11} \equiv f_{11} &= \psi_{HUA} x_{10} + \frac{\theta_3 \beta_H x_8 x_4}{N} + \frac{\theta_4 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_4}{N} - c_9 x_{11}, \\
\dot{x}_{12} \equiv f_{12} &= \psi_{HDA} x_{11} + \frac{\theta_5 \beta_H x_8 x_5}{N} + \frac{\theta_6 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_5}{N} - c_{10} x_{12}, \\
\dot{x}_{13} \equiv f_{13} &= \psi_{HU} x_{12} + \frac{\theta_7 \beta_H x_8 x_6}{N} + \frac{\theta_8 \beta_H \left(x_9 + \phi_1 x_{10} + \phi_2 x_{11} + \phi_3 x_{12} + \phi_4 x_{13}\right) x_6}{N} - c_{11} x_{13},
\end{aligned}
\tag{43}
$$

where $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7$. The Jacobian of the transformed system evaluated at DFE is given by:

$$
J^*\left(\xi_0\right) = \begin{pmatrix} J1_{(7\times 7)} J2_{(7\times 6)} \\ J3_{(6\times 7)} J4_{(6\times 6)} \end{pmatrix},
$$

where

$$
J1 = \begin{bmatrix}
-\mu & 0 & 0 & 0 & -\beta_T^* & -\eta_1 \beta_T^* & 0 \\
0 & -c_1 & 0 & 0 & \beta_T^* & \eta_1 \beta_T^* & 0 \\
0 & \psi_1 & -c_2 & 0 & 0 & 0 & 0 \\
0 & 0 & \psi_2 & -c_3 & 0 & 0 & 0 \\
0 & 0 & 0 & \psi_3 & -c_4 & 0 & 0 \\
0 & 0 & 0 & 0 & \psi_4 & -c_5 & 0 \\
0 & 0 & \sigma_1 & \sigma_2 & \sigma_3 & \sigma_4 & -\mu
\end{bmatrix},
$$

$$
J2 = \begin{bmatrix}
\beta_H^* & \beta_H^* & -\left(\eta_2 \beta_T^* + \phi_2 \beta_H^*\right) & -\left(\eta_3 \beta_T^* + \phi_3 \beta_H^*\right) & -\eta_2 \beta_T^* & -\eta_3 \beta_T^* \\
0 & 0 & \eta_2 \beta_T^* & \eta_2 \beta_T^* & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix},
$$

$$J3 = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

$$J4 = \begin{bmatrix} \beta_H^* - c_6 & \beta_H^* & \phi_1\beta_H^* + \sigma_{T1} & \phi_2\beta_H^* + \sigma_{T2} & \phi_3\beta_H^* + \sigma_{T3} & \phi_4\beta_H^* + \sigma_{T4} \\ 0 & -c_7 & 0 & 0 & 0 & 0 \\ 0 & \psi_{HU} & -c_8 & 0 & 0 & 0 \\ 0 & 0 & \psi_{HUA} & -c_9 & 0 & 0 \\ 0 & 0 & 0 & \psi_{HDA} & -c_{10} & 0 \\ 0 & 0 & 0 & 0 & \psi_{HT} & -c_{11} \end{bmatrix}.$$

We consider the case with $\beta_T = \beta_T^*$, a bifurcation parameter. By solving for $\beta_T = \beta_T^*$, from R_T, yields:

$$\beta_T^* = \frac{c_1c_2c_3c_4c_5}{\psi_1\psi_2\psi_3\left(1+\sigma_1\right)\left(c_5+\mu\eta\psi_4+\eta\sigma_2\psi_4+\eta\psi_3\psi_4\right)},$$

where $c_1 = (\psi_1 + \mu)$, $c_2 = (\psi_2 + \sigma_1 + \mu)$, $c_3 = (\psi_3 + \sigma_2 + \mu)$, $c_4 = (\psi_4 + \sigma_3 + \mu)$, and $c_5 = (\psi_5 + \sigma_4 + \mu)$.
It is noted that matrix $J^*(\xi_0)$, has a right eigenvector given by: $w = (w_1, w_2, ...w_{13})^T$, where
$w_1 = \frac{-\left(\beta_T^* w_5 - \eta_1\beta_T^* w_5\right)}{\mu}$, $w_2 > 0$, $w_3 = \frac{\psi_1 w_2}{c_2}$, $w_4 = \frac{\psi_1\psi_2 w_2}{c_2c_3}$, $w_5 = \frac{\psi_1\psi_2\psi_3 w_2}{c_2c_3c_4}$, $w_6 = \frac{\psi_1\psi_2\psi_3\psi_4 w_2}{c_2c_3c_4c_5}$, $w_7 = \frac{\sigma_1 w_3 + \sigma_2 w_4 + \sigma_3 w_5 + \sigma_4 w_6}{\mu}$, $w_8 = w_9 = w_{10} = w_{11} = w_{12} = w_{13} = 0$.
Similarly, the component of the left eigenvectors of $J^*(\xi_0)|_{\beta_T = \beta_T^*}$, $v = (v_1, v_2, ...v_{13})$, satisfying $v.w = 1$, are
$v_1 = 0$, $v_2 = \frac{\psi_1 v_3}{c_1}$, $v_3 > 0$, $v_4 = \frac{c_2 v_3}{\psi_2}$, $v_5 = \frac{c_2c_3w_2}{\psi_3}$, $v_6 = \frac{\eta_1\beta_T^*\psi_3\psi_1}{c_1c_5}$, $v_7 = v_8 = v_9 = 0$, $v_{10} = \frac{\psi_{UA} v_{11}}{c_8}$, $v_{11} = \frac{\psi_{HUA} v_{12} + \phi_2\beta_T^* v_2}{c_9}$, $v_{12} = v_{13} = 0$. It then follows from Theorem 4.1 in [30] that by computing the associated nonzero partial derivatives of $f(x)$, evaluated at the DFE (D_3), the associated bifurcation coefficients a, and b, are defined as: $a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$, and $b = \sum_{k,i,j=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_T^*}(0,0)$, are computed to be:

$$a = 2v_2\varepsilon_1\beta_T^*\frac{\mu}{\pi}\left(w_3w_7 + \phi_1w_4w_7\right)$$

$$-2v_2\beta_T^*\frac{\mu}{\pi}\left(w_2w_3 + w_3w_5 + w_3w_6 + w_3w_7 + w_3^2 + w_3w_7 + w_3w_4\right)$$

$$-2v_2\eta_1\beta_T^*\frac{\mu}{\pi}\left(w_2w_4 + w_4w_5 + w_3w_4 + w_3w_7 + w_4^2 + w_4w_5 + w_3w_6\right),$$

and

$$b = v_2w_3 + \eta_1v_2w_4 > 0,$$

with $v_2, w_2, w_3, w_4, w_5, w_6$, and w_7, being positive. Consequently, since the bifurcation coefficient $b > 0$, it can be deduced from Theorem 4.1 in [30] that TB-only model (22) undergoes a backward bifurcation if the backward bifurcation coefficient $a > 0$. This is so if,

$$\varepsilon_1 > \frac{(\omega_2 + \omega_3 + \omega_4 + \omega_5 + \omega_6 + \omega_7)(\omega_3 + \eta_1\omega_4)}{\omega_8(\omega_3 + \eta_1\omega_4)}.$$

Obviously, if $\varepsilon_1 = 0$, then $a < 0$, and HIV and TB co-infection model (5) will not undergo backward bifurcation at $\mathcal{R}_C = 1$.

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