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Analysis of the impact of treatments on HIV/AIDS and Tuberculosis co-infected population under random perturbations

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A R T I C L E I N F O

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A B S T R A C T

In this work, we study the impact of treatments at different stages of Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) co-infection in a population under the influence of random perturbations. This is achieved by constructing a stochastic epidemic model describing the transmission and treatment of the diseases. The model is created with the assumption that transmission rates fluctuate rapidly compared to the evolution of the untreated diseases. The basic reproduction numbers corresponding to the population with HIV infection only (with n stages of infections and treatments), the population with tuberculosis infection only, and the overall population with co-infection (with n stages of infection/treatments) are derived in the presence and absence of noise perturbations. These are used to discuss the long term behavior of the population around a disease-free equilibrium and an endemic equilibrium, and to analyze the effect of noise and treatments on the system. We also showed conditions under which TB infected population dynamic undergoes backward bifurcation and give conditions for disease eradication in the entire population. Analysis shows that small perturbations to the disease-free equilibrium can initially grow under certain conditions, and the introduction of TB treatment is effective in eliminating the co-infection. Numerical simulations are presented for validation of our results using published parameters.

1. Introduction

Several authors (Birrell, Presanis, & De Angelis, 2012; Granich, Gilks, Dye, De Cock, & Williams, 2009; Hollingsworth, Anderson, & Fraser, 2008; Kretzschmar, Schim van der Loeff, Birrell, Angelis, & Coutinho, 2013; Otunuga, 2018) have studied mathematical models governing the transfer of HIV infections in humans and various stages of the disease. In their work, Birrell et al. (Birrell et al., 2012) studied different states of HIV progression in homosexual men while a collaborative analysis of the time from HIV-1 seroconversion stage to AIDS and to death is studied extensively by the group on AIDS Incubation and HIV Survival in Europe (Collaborative Group on AIDS, 2000). HIV and AIDS continue to remain a serious health issue for most countries in the world (Center for Disease Control and Prevention, 2017a). Without treatment of HIV/AIDS with Antiretrovial

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medicine (United States Department of Health and Human Services, 2017), HIV infection advances into several stages and individuals with AIDS typically survive about 3 years (Center for Disease Control and Prevention, 2017b; Otunuga, 2018).

Tuberculosis (TB) disease, which could be inactive (called latent TB) or active (called TB disease), is another health issue for the part of the world. According to UNAIDS (UNAIDS. Tuberculosis and HIV), Tuberculosis (TB) is the top infectious killer worldwide, claiming around 4400 lives a day. According to the World Health Organization (WHO) (Tuberculosis and HIV: World Health Organization, 2018), TB risk is higher in people living with HIV (about 16–27 times higher) than those without the infection. Several works have been done to study HIV/AIDS and TB co-infection (Barnes et al., 1991; Bekker and Wood, 2010; Sonnenberg et al., 2005). The risk of death in co-infected individuals is twice that of HIV infected individuals without TB because Tuberculosis accelerates the progress of HIV infection. Reducing TB deaths among people living with HIV by 75% by 2020 is one of the major priority of the United Nations Member States (UNAIDS. Tuberculosis and HIV). This is in an effort to stop people living with HIV from getting sick and dying as a result of the TB infection.

There is no cure for HIV infection. The antiretroviral therapy (ART) treatment can help prevent HIV infected individuals from advancing to the next stage of the infection by reducing the risk of transmission. According to WHO (World Health Organization, 2018), the antiretroviral therapy helps to reduce the number of people dying from HIV-related causes. This number reduces significantly in 2015 to 45% fewer than in 2005. The Centers for Disease Control and Prevention (CDC) (Center for Disease Control and Prevention, 2017c) recommends a treatment for latent TB infection which includes a new combination regimen of isoniazid and rifapentine taken weekly for 12 weeks.

Existing mathematical epidemiological models (Granich et al., 2009; Kretzschmar et al., 2013; Mallela, Lenhart, & Vaidya, 2016; Naresh, Tripathi, & Sharma, 2009; Otunuga, 2018; Sharomi, Podder, & Gumel, 2008) on HIV and TB co-infection has shed light on the diseases' transmission dynamics. In this paper, we discuss transmission and treatment of the HIV/AIDS and TB diseases. We are particularly interested in how the diseases are transmitted at various stages of infection and phases of treatment. Dynamic model is developed to explore the transmission and treatment of HIV and TB infections at different stages of the disease and phases of treatment. Also, co-infection of the HIV and TB diseases is analyzed by constructing a deterministic and stochastic models describing progression of susceptible populations through n stages of HIV-TB infections and treatments. We assume that HIV infected individuals can go through any of the n stages of HIV infection and that infected individual in stage k of the infection can receive the ART treatment. Also, we assume that the HIV-TB co-infected individual can go through any n phases of treatment.

In their work, Grassly et al. (Grassly & Fraser, 2006) explains different causes of seasonality in infectious diseases of humans and give different representations of the transmission rate based on the causes of seasonality. The effects of fluctuations in transmission rate of diseases have also been widely explored by several authors (Hattaf, Mahrouf, Adnani, & Yousfi, 2018; Horsthemke & Lefever, 1984; Keeling & Ross, 2008; Mendez, Campos, & Horsthemke, 2012; Otunuga, 2017, 2018, 2019). According to the work of Mendez et al. (Mendez et al., 2012), demographic noise or internal fluctuations are due to the discrete nature of the constituents of the population and external fluctuations in transmission rate could be caused by varying susceptibilities between individuals, variability in the number of contacts between infected and susceptible individuals, etc. We assume in this work that external fluctuations in the transmission rates of HIV/AIDS and Tuberculosis can be caused by variability in the number of contacts between untreated infected (HIV-only, TB-only and HIV & TB co-infected individuals) and susceptible individuals and such random variations can be modeled by a Gaussian white noise process. This is because such random variations occur on a short time scale compared to that of the epidemic dynamics. We confirm the claim that external noise can affect the stability of the disease-free equilibrium and also show that transient epidemic advances can occur due to the presence of external noise.

The paper is organized as follows. In Section 2, we present a stochastic and deterministic HIV & TB co-infection epidemic models describing the transmission and spread of the diseases in different stages of infections and treatments. The models are presented in the presence and absence of noise. The basic reproduction numbers for the populations with HIV disease only, TB disease only, and HIV & TB co-infections in the presence of noise are calculated. These numbers are also calculated in the absence of noise in Appendix A.1. In Section 3, the stability of the equilibrium points of the models describing populations with HIV disease only, TB disease only, and HIV & TB co-infection are analyzed. The condition for the occurrence of backward bifurcation is analyzed. The effect of treatments on the expected number of secondary infections is discussed. Thresholds for disease eradication and transient epidemic advances in the presence of noise are discussed. Numerical simulations are presented using published parameters to support our claims. Summary and conclusion of this work is given in Section 4.

2. Methods

In order to study the transmission, spread, treatments of HIV/AIDS, Tuberculosis, and co-infection of both diseases, we formulate a stochastic model by first subdivididing the total population $N(t)$ at time t into population $(\mathcal{S})$ susceptible to both HIV and TB, HIV infected (untreated) population $(\mathcal{H}_k)$ in stage/phase k of the infection and susceptible to TB, HIV infected population $(\mathcal{I}_k)$ in stage/phase k of infection under the Antiretroviral treatment, individuals infected with TB in latent stage $(\mathcal{L})$,

TB infected (untreated) population ($\mathcal{T}$) in active stage and susceptible to HIV, TB infected population ($\mathcal{A}$) under TB treatment, population ($\mathcal{R}$) who recovered from TB with temporal immunity, population ($\mathcal{C}_L$) of untreated dual-infected individuals (with both diseases) having latent TB and HIV infection, population ($\mathcal{C}_T$) of untreated dual-infected individuals with active TB and HIV infection, population ($\mathcal{C}_k$) with dual infection having HIV infection and in stage k of TB treatments, population ($\overline{\mathcal{C}}_k$) with dual infection having active TB and in stage k of HIV treatments, population ($\mathcal{U}_k$) with dual infection treated of TB and in stage k of HIV treatment, for $k = 1, 2, \ldots, n$. All recruitment is into the susceptible class, and occurs at a constant rate ΛN. We assume that treated individuals are also infectious and that individuals in stage k of HIV infection (that is, those in class ($\mathcal{H}_k$)) are more infectious than those in stage $k-1$. Likewise, we assume individuals in stage k of HIV treatment (that is, those in class ($\mathcal{I}_k$)) are less infectious than those in stage $k-1$ of treatment and that individuals in the latent TB class do not transmit infection. Infected (treated or untreated) HIV and TB individuals are capable of transmitting HIV or TB (but not the mixed infection). Treated individuals (with single or dual infection) transmit disease at a lower rate than those that are untreated. According to Kwan (Kwan & Ernst, 2011), TB accelerates the progression of HIV infection and treatment with ART decreases incidence of TB. They also state in their work that HIV infection increases the progression to reactivation of TB. For these reasons, we assume that dually-infected individuals with active TB transmit HIV at a higher rate than dual infected individuals with latent TB. Also, we assume dually-infected individuals under HIV ART treatment (with active TB) transmits TB at a lower rate than dually-infected individuals receiving no ART treatment.

We note here that the deterministic model described in this work is an extension of the work of Sharomi et al. (Sharomi et al., 2008) from a 2-stage HIV infection class (asymptotic and symptomatic stage) to an n-stage HIV infection class, with n-phase of HIV treatments, n-stages of dual infections, and an additional compartment for the recovered class $\mathcal{R}$. We also study the effects of noise on the transmission rates and infectivities of HIV and TB. We assume that variability in the number of contacts between infected individuals (receiving some sort of treatments) and susceptible individuals is insignificant due to their awareness of the disease and the treatment they are receiving. We also assume that there is fluctuation in the infectivity parameters of untreated individuals in stage k of the HIV, untreated TB, and of co-infected HIV & TB, infections. In addition, we assume.

1. Susceptible individuals get exposed to HIV when in contact with HIV only infected individuals with force of infection $\tilde{\beta}_H$ which is directly proportional to $\mathcal{H}_k$ and I_k and described by $\tilde{\beta}_H = \beta \sum_{j=1}^{n} \left(\frac{\tilde{h}_j \mathcal{H}_j + \epsilon_j \mathcal{I}_j}{N} \right)$, where β is the rate of transmission between susceptible and infected HIV individuals, $\tilde{h}_k$ is the noise-induced infectivity of untreated HIV individuals in stage k of infection, ϵ_k quantifies the reduced HIV infectiousness due to ART treatment in stage k of infection. The parameter $\tilde{h}_j$ is assumed to fluctuate rapidly (compared to the evolution of the disease) around an average value h_k so that $\tilde{h}_k = h_k + \sigma_{h,k}\, \mathcal{E}_{h,k}(t), \quad k = 1, 2, \ldots, n$ and the rate $\tilde{\beta}_H$ reduces to

$$\tilde{\beta}_H = \beta_H + \beta \sum_{j=1}^{n} \left(\frac{\sigma_{h,j} \mathcal{E}_{h,j}(t) \mathcal{H}_j}{N} \right),$$

where $\beta_H = \beta \sum_{j=1}^{n} \left(\frac{h_j \mathcal{H}_j + \epsilon_j \mathcal{I}_j}{N} \right)$, $\mathcal{E}_{h,j}(t), j = 1, 2, \ldots, n$ are standard Gaussian white noise and $\sigma_{h,j} \geq 0, j = 1, 2, \ldots, n$, are noise intensities due to fluctuations in infectivities of HIV/AIDS untreated individuals in stage j of infection.

2. Susceptible individuals get exposed to TB when in contact with TB only individuals at a rate $\tilde{\beta}_T = \tau_* \left(\frac{\tilde{\tau}_1 \mathcal{T} + \overline{\tau}_2 \mathcal{A}}{N} \right)$, where τ_* is the rate of transmission between susceptible and infected TB individuals, $\tilde{\tau}_1$ is the noise-induced infectivity of untreated TB individuals, $\overline{\tau}_2$ quantifies the reduced TB infectiousness due to TB treatment. The parameter $\tilde{\tau}_1$ is assumed to fluctuate around an average value $\overline{\tau}_1$ so that $\tilde{\tau}_1 = \overline{\tau}_{\tau,1} + \sigma_{\tau,n+3} \mathcal{E}_{\tau,n+3}(t)$ and $\tilde{\beta}_T$ reduces to

$$\tilde{\beta}_T = \beta_T + \tau_* \left(\frac{\sigma_{\tau,n+3} \mathcal{E}_{\tau,n+3}(t) \mathcal{T}}{N} \right),$$

where $\beta_T = \tau_* \left(\frac{\overline{\tau}_1 \mathcal{T} + \overline{\tau}_2 \mathcal{A}}{N} \right)$, $\mathcal{E}_{\tau,n+3}(t)$ is a standard Gaussian white noise, $\sigma_{\tau,n+3} \geq 0$ is the noise intensity for the untreated TB.

3. Untreated HIV and TB infected individuals (i.e those in class C_L and C_T) transmit HIV at a rate $\tilde{\beta}_{LT} = \beta \left(\frac{\tilde{\nu}_1 \mathcal{C}_L + \tilde{\nu}_2 \mathcal{C}_T}{N} \right)$, where $\tilde{\nu}_1$ is the infectivity of HIV and latent TB co-infectiousness, $\tilde{\nu}_2$ is the infectivity of HIV and active

TB co-infectiousness. The parameters are assumed to fluctuate around average values ν_1 and ν_2, respectively, so that $\tilde{\nu}_k = \nu_k + \sigma_{\nu,n+k}\mathcal{E}_{\nu,n+k}(t), \ \ k = 1,2$, and $\tilde{\beta}_{LT}$ reduces to

$$\tilde{\beta}_{LT} = \beta_{LT} + \beta\left(\frac{\sigma_{\nu,n+1}\mathcal{E}_{\nu,n+1}\mathcal{C}_L + \sigma_{\nu,n+2}\mathcal{E}_{\nu,n+2}\mathcal{C}_T}{N}\right),$$

where $\beta_{LT} = \beta\left(\frac{\nu_1\mathcal{C}_L+\nu_2\mathcal{C}_T}{N}\right)$, $\mathcal{E}_{\nu,n+j}(t), j = 1, 2$ are standard Gaussian white noise and $\sigma_{\nu,n+1} \geq 0$, $\sigma_{\nu,n+2} \geq 0$ are the noise intensities of the white noise due to fluctuations in infectivities of coinfected HIV & TB in class C_L and class C_T, respectively.

4. Untreated HIV and TB infected individuals with active TB in class $(\mathcal{C}_T)$ transmit TB at a rate $\tilde{\beta}_{TT} = \tau_*\tilde{\overline{\tau}}_3\frac{\mathcal{C}_T}{N}$, where τ_* is the rate of transmission between susceptible and infected TB individuals, $\tilde{\overline{\tau}}_3$ is the infectivity of co-infected HIV & TB individuals, assumed to fluctuate around average value $\overline{\tau}_3$ so that $\tilde{\overline{\tau}}_3 = \overline{\tau}_3 + \sigma_{\tau,3}\mathcal{E}_{\tau,n+4}(t)$, and $\tilde{\beta}_{TT}$ reduces to

$$\tilde{\beta}_{TT} = \beta_{TT} + \tau_*\left(\frac{\sigma_{\tau,n+4}\mathcal{E}_{\tau,n+4}(t)\mathcal{C}_T}{N}\right),$$

where $\beta_{TT} = \tau_*\overline{\tau}_3\frac{\mathcal{C}_T}{N}$, $\mathcal{E}_{\tau,n+4}(t)$ is standard Gaussian white noise and $\sigma_{\tau,n+4} \geq 0$ is the noise intensity for the HIV & TB co-infectiousness.

5. Treated individuals with mixed infections transmit HIV at a rate $\beta_{MH} = \beta\sum_{j=1}^{n}\left(\frac{\phi_j\mathcal{C}_j+\overline{\phi}_j\overline{\mathcal{C}}_j+\sigma\mathcal{U}_j}{N}\right)$, where ϕ_k is the reduced HIV and TB co-infectiousness due to TB treatment in phase k of TB treatment, $\overline{\phi}_k$ is the reduced HIV and TB co-infectiousness due to HIV treatment in phase k of HIV treatment, and σ is the reduced HIV and TB co-infectiousness due to ART and TB treatments.
6. Treated individuals with mixed infections transmit TB at a rate $\beta_{MT} = \tau_*\phi\sum_{j=1}^{n}\left(\frac{\phi_j\mathcal{C}_j+\overline{\phi}_j\overline{\mathcal{C}}_j+\sigma\mathcal{U}_j}{N}\right)$.
7. Individuals with latent TB only are reinfected (exogeneously) after effective contact with individuals in active TB class at a rate $\beta_R = \tau_*\tau_r\frac{\mathcal{T}}{N}$, where τ_r is the reinfection parameter.
8. Individuals with latent TB only are reinfected (exogeneous) after effective contact with individuals having mixed infection at a rate
$\beta_{R1} = \tau_*\tau_r\phi\sum_{j=1}^{n}\left(\frac{(\phi_j\mathcal{C}_j+\overline{\phi}_j\overline{\mathcal{C}}_j+\sigma\mathcal{U}_j)+\mathcal{C}_T}{N}\right)$, with $\tau_r > 0$.
9. Individuals in $\mathcal{C}_L$ are reinfected (exogeneous) at a rate $\beta_{R2} = \tau_*\tau_r\phi\sum_{j=1}^{n}\left(\frac{(\phi_j\mathcal{C}_j+\overline{\phi}_j\overline{\mathcal{C}}_j+\sigma\mathcal{U}_j)+\mathcal{C}_T+\mathcal{T}}{N}\right)$.

Also, we define τ_k and ϕ_k as the rates per year of moving from HIV untreated to HIV treated population (rates per year of receiving HIV treatment), and from HIV treated to HIV untreated population (rates per year of stopping HIV treatment) in stage k of infection, respectively. The natural death rate is μ and ρ_k and γ_k are transition rates from stage k to stage $k+1$ for HIV untreated $\mathcal{H}_k$ and treated $\mathcal{I}_k$ individuals, respectively, for $k = 1, 2, \ldots, n-1$. Furthermore, δ is the rate at which individuals infected with active TB-only are being treated, p is the rate at which infected active TB individuals naturally recover, ψ is the rate at which individual co-infected with HIV and TB is receiving phase 1 of TB treatment, η is the rate at which individual co-infected with HIV and TB and undergoing TB treatment starts receiving HIV treatment, r_k is the rate at which co-infected individuals with HIV and TB undergoing phase k of TB treatment move to phase $k+1$ of the treatment, with r_n being the completion phase, ϱ_k is the rate at which co-infected individual with HIV and TB undergoing HIV treatment and in phase k of TB treatment move to phase $k+1$ of the treatment, q is the rate at which recovered TB individual become reinfected with TB, f is the rate at which latent TB individuals become active, w is the rate at which individuals under TB treatment recovered, x is the rate at which infected TB individuals receiving TB treatment stopped receiving the treatment, s is the rate at which infected individual with HIV and TB undergoing HIV and TB treatment stops receiving HIV treatment, ψ_k and $\overline{\psi}_k$ are the rates at which HIV-untreated and HIV-treated infected individuals in stage k get infected with TB, respectively, ν_k $(\overline{\nu}_k)$ is the rate at which co-infected individuals receiving some form of treatment infects individuals in class $\mathcal{H}_k$ (individuals in class $\mathcal{I}_k$). The stochastic model governing $\mathcal{X}(t) = (\mathcal{S}, \mathcal{H}_1\cdots\mathcal{H}_n, \mathcal{I}_1\cdots\mathcal{I}_n, L, \mathcal{T}, \mathcal{C}_L, \mathcal{C}_\mathcal{T}, \mathcal{C}_1\cdots\mathcal{C}_n, \overline{\mathcal{C}}_1\cdots\overline{\mathcal{C}}_n, \mathcal{U}_1\cdots\mathcal{U}_n, \mathcal{A}, \mathcal{R})^\top$ is

$$
\begin{aligned}
d\mathcal{S}&=(\Lambda N-\mathcal{S}(\beta_H+\beta_{MH}+\beta_{LT})-\mathcal{S}(\beta_T+\beta_{TT}+\beta_{MT})-\mu\mathcal{S})dt-\beta\mathcal{S}\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t)-\beta\sigma_{\nu,n+1}\mathcal{S}\mathcal{C}_L\circ dW_{\nu,n+1}(t)\\
&\quad-\beta\sigma_{\nu,n+2}\mathcal{S}\mathcal{C}_T\circ dW_{\nu,n+2}(t)-\tau_*\sigma_{\tau,n+3}\mathcal{S}\mathcal{T}\circ dW_{\tau,n+3}(t)-\tau_*\sigma_{\tau,n+4}\mathcal{S}\mathcal{C}_T\circ dW_{\tau,n+4}(t),\\
d\mathcal{H}_1&=(\mathcal{S}(\beta_H+\beta_{MH}+\beta_{LT})-a_1H_1+\phi_1\mathcal{I}_1-(\beta_T+\beta_{TT}+\beta_{MT})\psi_1\mathcal{H}_1-\beta_{MT}\nu_1\mathcal{H}_1)dt+\beta\mathcal{S}\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t)\\
&\quad+\beta\sigma_{\nu,n+1}\mathcal{S}\mathcal{C}_L\circ dW_{\nu,n+1}(t)+\beta\sigma_{\nu,n+2}\mathcal{S}\mathcal{C}_T\circ dW_{\nu,n+2}(t)-\tau_*\psi_1\mathcal{H}_1\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big),\\
d\mathcal{H}_k&=(\rho_{k-1}\mathcal{H}_{k-1}-a_k\mathcal{H}_k+\phi_k\mathcal{I}_k-(\beta_T+\beta_{TT}+\beta_{MT})\psi_k\mathcal{H}_k-\beta_{MT}\nu_k\mathcal{H}_k)dt\\
&\quad-\tau_*\psi_k\mathcal{H}_k\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big),\text{for}k=2,\ldots,n,\\
d\mathcal{I}_1&=(\tau_1\mathcal{H}_1-b_1\mathcal{I}_1-(\beta_T+\beta_{TT}+\beta_{MT})\overline{\psi}_1\mathcal{I}_1-\beta_{MT}\overline{\nu}_1\mathcal{I}_1)dt-\tau_*\overline{\psi}_1\mathcal{I}_1\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big),\\
d\mathcal{I}_k&=(\tau_k\mathcal{H}_k+\gamma_{k-1}\mathcal{I}_{k-1}-b_k\mathcal{I}_k-(\beta_T+\beta_{TT}+\beta_{MT})\overline{\psi}_k\mathcal{I}_k-\beta_{MT}\overline{\nu}_k\mathcal{I}_k)dt\\
&\quad-\tau_*\overline{\psi}_k\mathcal{I}_k\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big),\text{for}k=2,\\
d\mathcal{L}&=(l\mathcal{S}(\beta_T+\beta_{TT}+\beta_{MT})-z_1\mathcal{L}-\mathcal{L}(\beta_H+\beta_{MH}+\beta_{LT}+\beta_R+\beta_{R1})+q\mathcal{R}+x\mathcal{A})dt+l\tau_*\mathcal{S}\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}(t)\\
&\quad+l\tau_*\mathcal{S}\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}(t)-\beta\mathcal{L}\left(\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t)+\sigma_{\nu,n+1}\mathcal{C}_L\circ dW_{\nu,n+1}(t)+\sigma_{\nu,n+2}\mathcal{C}_T\circ dW_{\nu,n+2}(t)\right)\\
d\mathcal{T}&=((1-l)\mathcal{S}(\beta_T+\beta_{TT}+\beta_{MT})+f\mathcal{L}+\mathcal{L}(\beta_R+\overline{\phi}\beta_{R1})-\mathcal{T}(\beta_H+\beta_{MH}+\beta_{LT})-z_2\mathcal{T})dt+(1-l)\tau_*\mathcal{S}\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}(t)\\
&\quad+(1-l)\tau_*\mathcal{S}\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}(t)-\beta\mathcal{T}\left(\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t)+\sigma_{\nu,n+1}\mathcal{C}_L\circ dW_{\nu,n+1}(t)+\sigma_{\nu,n+2}\mathcal{C}_T\circ dW_{\nu,n+2}(t)\right)\\
d\mathcal{C}_L&=\left((\mathcal{L}+\mathcal{A})(\beta_H+\beta_{MH}+\beta_{LT})+l(\beta_T+\beta_{TT}+\beta_{MT})\sum_{j=1}^{n}[\psi_j\mathcal{H}_j+\overline{\psi}_j\mathcal{I}_j]-\beta_{R2}\mathcal{C}_L-d_L\mathcal{C}_L\right)dt\\
&\quad+\beta(\mathcal{L}+\mathcal{A})\left(\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}+\sigma_{\nu,n+1}\mathcal{C}_L\circ dW_{\nu,n+1}+\sigma_{\nu,n+2}\mathcal{C}_T\circ dW_{\nu,n+2}\right)\\
&\quad+l\tau_*\sum_{i=1}^{n}[\psi_i\mathcal{H}_i+\overline{\psi}_i\mathcal{I}_i]\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big)\\
d\mathcal{C}_T&=\left(\mathcal{T}(\beta_H+\beta_{MH}+\beta_{LT})+(1-l)(\beta_T+\beta_{TT}+\beta_{MT})\sum_{j=1}^{n}[\psi_j\mathcal{H}_j+\overline{\psi}_j\mathcal{I}_j]+\beta_{R2}\mathcal{C}_L+(1-\overline{\phi})\beta_{R1}\mathcal{L}-d_T\mathcal{C}_T\right)dt\\
&\quad+\beta\mathcal{T}\left(\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}+\sigma_{\nu,n+1}\mathcal{C}_L\circ dW_{\nu,n+1}+\sigma_{\nu,n+2}\mathcal{C}_T\circ dW_{\nu,n+2}\right)\\
&+(1-l)l\tau_*\sum_{i=1}^{n}[\psi_i\mathcal{H}_i+\overline{\psi}_i\mathcal{I}_i]\big(\mathcal{T}\sigma_{\tau,n+3}\circ dW_{\tau,n+3}+\mathcal{C}_T\sigma_{\tau,n+4}\circ dW_{\tau,n+4}\big),d\mathcal{C}_1=\left(\psi\mathcal{C}_T-(\mu+r_1+\eta)\mathcal{C}_1+s\mathcal{U}_1+m_1\beta_{MT}\sum_{j=1}^{n}\nu_j\mathcal{H}_j\right)dt,\\
d\mathcal{C}_k&=\left(r_{k-1}\mathcal{C}_{k-1}-(\mu+r_k+\eta)\mathcal{C}_k+s\mathcal{U}_k+m_k\beta_{MT}\sum_{j=1}^{n}\nu_j\mathcal{H}_j\right)dt,\text{for}k=2,\ldots,n,\\
d\overline{\mathcal{C}}_1&=\left(e_L\mathcal{C}_L+e_T\mathcal{C}_T-(\mu+\overline{r}_1+\overline{\eta})\overline{\mathcal{C}}_1+\overline{s}\mathcal{U}_1+\overline{m}_1\beta_{MT}\sum_{j=1}^{n}\nu_j\mathcal{I}_j\right)dt,\\
d\overline{\mathcal{C}}_k&=\left(\overline{r}_{k-1}\overline{\mathcal{C}}_{k-1}-(\mu+\overline{r}_k+\overline{\eta})\overline{\mathcal{C}}_k+\overline{s}\mathcal{U}_k+\overline{m}_k\beta_{MT}\sum_{j=1}^{n}\nu_j\mathcal{I}_j\right)dt,d\mathcal{U}_1=(\eta\mathcal{C}_1+\overline{\eta}\overline{\mathcal{C}}_1-(\mu+\varrho_1+s+\overline{s})\mathcal{U}_1)dt,\\
d\mathcal{U}_k&=(\eta\mathcal{C}_k+\overline{\eta}\overline{\mathcal{C}}_k+\varrho_{k-1}\mathcal{U}_{k-1}-(\mu+\varrho_k+s+\overline{s})\mathcal{U}_k)dt,\text{for}k=2,\ldots,n,\\
d\mathcal{A}&=(\delta\mathcal{T}-\theta\mathcal{A}-\mathcal{A}(\beta_H+\beta_{MH}+\beta_{LT}))dt-\beta\mathcal{A}\left(\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t)+\sigma_{\nu,n+1}\mathcal{C}_L\circ dW_{\nu,n+1}(t)+\sigma_{\nu,n+2}\mathcal{C}_T\circ dW_{\nu,n+2}(t)\right),\\
d\mathcal{R}&=(p\mathcal{T}-(\mu+q)\mathcal{R}+w\mathcal{A})dt,
\end{aligned}
\tag{2.1}
$$

Table 1
Parameter description for the epidemic model.

Parameter Description	Parameter Description	Parameter Description
$a_k = \mu + \rho_k + \tau_k$	$\overline{a}_k = \mu + \rho_k$	$z_1 = \mu + f$
$b_k = \mu + \gamma_k + \phi_k$	$\overline{b}_k = \mu + \gamma_k$	$z_2 = \mu + \delta + p$
$d_L = \mu + e_L$	$d_k = \mu + r_k + \eta$	$\overline{z}_1 = \mu$
$d_T = \mu + \psi + e_T$	$\overline{d}_k = \mu + \overline{r}_k + \overline{\eta}$	$\overline{z}_2 = \mu + p,$
$\overline{\kappa} = \Lambda/\mu$	$\theta = \mu + w + x$	$\theta = \mu + w + x,$
$\sum_{j=1}^{n} m_j = \sum_{j=1}^{n} \overline{m}_j = 1$	$e_k = \mu + \varrho_k + s + \overline{s}$	$g = \mu + q$

where $dW_{h,i}(t) = \mathcal{E}_{h,i}dt$, $i = 1, 2, \ldots, n$, $dW_{\nu,n+i}(t) = \mathcal{E}_{\nu,n+i}dt$, $i = 1, 2$, $dW_{\tau,n+j}(t) = \mathcal{E}_{\tau,n+j}dt$, $j = 3, 4$, are independent standard Wiener processes on a filtered probability space $(\Omega, \mathbb{A}, (\mathcal{F}_t)_{t\geq 0}, \mathbb{P})$, the filtration function $(\mathcal{F}_t)_{t\geq 0}$ is right-continuous and each $\mathcal{F}_t$ with $t \geq 0$ contains all $\mathbb{P}$-null sets in $\mathcal{F}_t$; $\circ$ denotes the Stratonovich integral (Arnold, 1974), the initial process $X(t_0)$ is $\mathcal{F}_{t_0}$ measurable and independent of $W_{\cdot,i}(t) - W_{\cdot,i}(t_0)$. Table 1 describes some composite parameters used in this work for $k = 1, 2, \ldots, n$, $\rho_n = \gamma_n = r_n = \overline{r}_n = \varrho_n = 0$.

The next theorem shows that model (2.1) is well-posed. Definition 1. We define the differential operator $\mathbb{L}$ on a function $\mathbf{V}(t, \mathbf{u}) \in C^{1,2}$ corresponding to a stochastic differential equation with drift and diffusion coefficients $A(t, \mathbf{u})$ and $B(t, \mathbf{u})$, respectively, by

$$L\mathbf{V}(t,\mathbf{u}) = \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial t} + \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}} A + \frac{1}{2}\text{trace}\left[B^T \frac{\partial^2 \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}^2} B\right] \tag{2.2}$$

where $\frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}} = \left(\frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial u_1}, \ldots, \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial u_n}\right)$ and $\frac{\partial^2 \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}^2} = \left(\frac{\partial^2 \mathbf{V}(t,\mathbf{u})}{\partial u_i \partial u_j}\right)_{n\times n}$.

Theorem 1. *There exists a solution* $\mathcal{X}(t) = (\mathcal{S}, \mathcal{H}_1 \cdots \mathcal{H}_n, \mathcal{I}_1 \cdots \mathcal{I}_n, L, \mathcal{T}, \mathcal{C}_L, \mathcal{C}_\mathcal{T}, \mathcal{C}_1 \cdots \mathcal{C}_n, \overline{\mathcal{C}}_1 \cdots \overline{\mathcal{C}}_n, \mathcal{U}_1 \cdots \mathcal{U}_n, \mathcal{A}, \mathcal{R})^\top$ *of* (2.1) *which is an almost surely continuous stochastic process and is unique up to equivalence if* $\mathcal{X}(t_0)$ *is independent of the processes* $W_{\cdot,i}(t) - W_{\cdot,i}(t_0)$, $i = 1, 2, \ldots, n + 4$.

Proof. *It is easy to show that the drift and diffusion coefficients of* (2.1) *satisfy the Lipschitz and linear growth, locally, in* $[a, b] \times D_r$, *with* $D_r = \{|\mathcal{X}| < r\}$. *Let* $\mathcal{X}$ *satisfies* (2.1), *and define* $\mathbf{V} : [0, \mathcal{T}] \times \mathbb{R}_+^{5n+7} \to \mathbb{R}_+$ *by*

$$\mathbf{V}(t,\mathcal{X}) = \ln\left(\mathcal{S} + \sum_{j=1}^{n}\left(\mathcal{H}_j + \mathcal{I}_j + \mathcal{C}_j + \overline{\mathcal{C}}_j + \mathcal{U}_j\right) + \mathcal{L} + \mathcal{T} + \mathcal{C}_L + \mathcal{C}_\mathcal{T} + \mathcal{A} + \mathcal{R} + e^{\Lambda}\right),$$

where $\mathbb{R}_+$ denotes non-negative real numbers. It follows directly that $\mathbf{V} > 0$. Using (2.2), we have

$$\mathbb{L}\mathbf{V} \leq \frac{\Lambda N - \mu\left(\mathcal{S} + \sum_{j=1}^{n}\left(\mathcal{H}_j + \mathcal{I}_j + \mathcal{C}_j + \overline{\mathcal{C}}_j + \mathcal{U}_j\right) + \mathcal{L} + \mathcal{T} + \mathcal{C}_L + \mathcal{C}_\mathcal{T} + \mathcal{A} + \mathcal{R} + e^{\Lambda}\right)}{\mathcal{S} + \sum_{j=1}^{n}\left(\mathcal{H}_j + \mathcal{I}_j + \mathcal{C}_j + \overline{\mathcal{C}}_j + \mathcal{U}_j\right) + \mathcal{L} + \mathcal{T} + \mathcal{C}_L + \mathcal{C}_\mathcal{T} + A + \mathcal{R} + e^{\Lambda}} < \mathbf{V}.$$

Define $\mathbf{V}_r = \inf_{|\mathcal{X}|>r} \mathbf{V}(t,\mathcal{X})$. Since $\mathbf{V}(t,\mathcal{X}) \geq \ln(|\mathcal{X}| + e^{\Lambda})$, it follows that $\mathbf{V}_r \to \infty$ as $r \to \infty$. The existence and uniqueness of solution $\mathcal{X}(t)$ with initial condition $\mathcal{X}(t_0)$ independent of $W_{\cdot,i}(t) - W_{\cdot,i}(t_0)$, $i = 1, 2, \ldots, n + 3$, n+4, follow directly from Theorem 3.5 of the work of Khasminskii (Rafail, 2012, p. 66). ■

In the absence of noise, the model (2.1) reduces to the deterministic model (2.3) given by

$$
\begin{aligned}
d\mathcal{S} &= (\Lambda N - \mathcal{S}(\beta_H + \beta_{MH} + \beta_{LT}) - \mu\mathcal{S} - \mathcal{S}(\beta_T + \beta_{TT} + \beta_{MT})\,)dt,\\
d\mathcal{H}_1 &= (\mathcal{S}(\beta_H + \beta_{MH} + \beta_{LT}) - a_1\mathcal{H}_1 + \phi_1\mathcal{I}_1 - (\beta_T + \beta_{TT} + \beta_{MT})\psi_1\mathcal{H}_1 - \beta_{MT}v_1\mathcal{H}_1\,)\ dt,\\
d\mathcal{H}_k &= (\rho_{k-1}\mathcal{H}_{k-1} - a_k\mathcal{H}_k + \phi_k\mathcal{I}_k - (\beta_T + \beta_{TT} + \beta_{MT})\psi_k\mathcal{H}_k - \beta_{MT}v_k\mathcal{H}_k\,)\ dt,\quad \text{for}\quad k = 2, \ldots, n,\\
d\mathcal{I}_1 &= (\tau_1\mathcal{H}_1 - b_1\mathcal{I}_1 - (\beta_T + \beta_{TT} + \beta_{MT})\overline{\psi}_1\mathcal{I}_1 - \beta_{MT}\overline{v}_1\mathcal{I}_1\,)dt,\\
d\mathcal{I}_k &= (\tau_k\mathcal{H}_k + \gamma_{k-1}\mathcal{I}_{k-1} - b_k\mathcal{I}_k - (\beta_T + \beta_{TT} + \beta_{MT})\overline{\psi}_k\mathcal{I}_k - \beta_{MT}\overline{v}_k\mathcal{I}_k\,)\ dt,\quad \text{for}\quad k = 2, \ldots, n,\\
d\mathcal{L} &= (l\mathcal{S}(\beta_T + \beta_{TT} + \beta_{MT}) - (\mu + f)\mathcal{L} - \mathcal{L}(\beta_H + \beta_{MH} + \beta_{LT} + \beta_R + \beta_{R1}) + q\mathcal{R} + x\mathcal{A}\,)\ dt,\\
d\mathcal{T} &= ((1-l)\mathcal{S}(\beta_T + \beta_{TT} + \beta_{MT}) + f\mathcal{L} + \mathcal{L}(\beta_R + \overline{\phi}\beta_{R1}) - \mathcal{T}(\beta_H + \beta_{MH} + \beta_{LT}) - (\mu + \delta + p)\mathcal{T}\,)\ dt,\\
d\mathcal{C}_L &= \left(\mathcal{L}(\beta_H + \beta_{MH} + \beta_{LT}) + l(\beta_T + \beta_{TT} + \beta_{MT})\sum_{j=1}^{n}[\psi_j\mathcal{H}_j + \overline{\psi}_j\mathcal{I}_j] + \mathcal{A}(\beta_H + \beta_{MH} + \beta_{LT}) - \beta_{R2}\mathcal{C}_L - d_L\mathcal{C}_L\right)\ dt,\\
d\mathcal{C}_T &= \left(\mathcal{T}(\beta_H + \beta_{MH} + \beta_{LT}) + (1-l)(\beta_T + \beta_{TT} + \beta_{MT})\sum_{j=1}^{n}[\psi_j\mathcal{H}_j + \overline{\psi}_j\mathcal{I}_j] + \beta_{R2}\mathcal{C}_L + (1-\overline{\phi})\beta_{R1}\mathcal{L} - d_T\mathcal{C}_T\right)\ dt,\\
d\mathcal{C}_1 &= \left(\psi\mathcal{C}_T - (\mu + r_1 + \eta)\mathcal{C}_1 + s\mathcal{U}_1 + m_1\beta_{MT}\sum_{j=1}^{n}v_j\mathcal{H}_j\right)\ dt,\\
d\mathcal{C}_k &= \left(r_{k-1}\mathcal{C}_{k-1} - (\mu + r_k + \eta)\mathcal{C}_k + s\mathcal{U}_k + m_k\beta_{MT}\sum_{j=1}^{n}v_j\mathcal{H}_j\right)\ dt,\quad \text{for}\quad k = 2, \ldots, n,\\
d\overline{\mathcal{C}}_1 &= \left(e_L\mathcal{C}_L + e_T\mathcal{C}_T - (\mu + \overline{r}_1 + \overline{\eta})\overline{\mathcal{C}}_1 + \overline{s}\mathcal{U}_1 + \overline{m}_1\beta_{MT}\sum_{j=1}^{n}v_j\mathcal{I}_j\right)\ dt,\\
d\overline{\mathcal{C}}_k &= \left(\overline{r}_{k-1}\overline{\mathcal{C}}_{k-1} - (\mu + \overline{r}_k + \overline{\eta})\overline{\mathcal{C}}_k + \overline{s}\mathcal{U}_k + \overline{m}_k\beta_{MT}\sum_{j=1}^{n}v_j\mathcal{I}_j\right)\ dt,\\
d\mathcal{U}_1 &= (\eta\mathcal{C}_1 + \overline{\eta}\overline{\mathcal{C}}_1 - (\mu + \varrho_1 + s + \overline{s})\mathcal{U}_1\,)\ dt,\\
d\mathcal{U}_k &= (\eta\mathcal{C}_k + \overline{\eta}\overline{\mathcal{C}}_k + \varrho_{k-1}\mathcal{U}_{k-1} - (\mu + \varrho_k + s + \overline{s})\mathcal{U}_k\,)\ dt,\quad \text{for}\quad k = 2, \ldots, n,\\
d\mathcal{A} &= (\delta\mathcal{T} - (\mu + w + x)\mathcal{A} - \mathcal{A}(\beta_H + \beta_{MH} + \beta_{LT})\,)\ dt,\\
d\mathcal{R} &= (p\mathcal{T} - (\mu + q)\mathcal{R} + w\mathcal{A})\ dt.
\end{aligned}
\tag{2.3}
$$

We note here that in the absence of noise, model (2.3) reduced to the HIV-only model described in the work of Kretzschmar et al. (Kretzschmar et al., 2013) and Otunuga (2018) (Otunuga, 2018) for the case where $\mathcal{T} = \mathcal{C}_L = \mathcal{C}_T = \mathcal{C}_j = \overline{\mathcal{C}}_j = \mathcal{U}_j = \mathcal{A} = \mathcal{R} = 0$ for $j = 1, 2, \ldots, n$. The Mallela model (Mallela et al., 2016) and the model described in Sharomi et al. (Sharomi et al., 2008) are special cases of (2.3). It follows that the population size $N = \mathcal{S} + \mathcal{L} + \mathcal{T} + \mathcal{A} + \mathcal{R} + \mathcal{C}_L + \mathcal{C}_T + \sum_{j=1}^{n}(\mathcal{H}_j + \mathcal{I}_j + \mathcal{C}_j + \overline{\mathcal{C}}_k + \mathcal{U}_j)$ satisfies the equation if $\Lambda = \mu$. For the rest of this work, we set $\Lambda = \mu$.

By denoting $X = (S, H_1 \cdots H_n, I_1 \cdots I_n, L, T, C_L, C_T, C_1 \cdots C_n, \overline{C}_1 \cdots \overline{C}_n, U_1 \cdots U_n, A, R)^\top$ as the fraction $\mathcal{X}/N = (\mathcal{S}/N, \mathcal{H}_1/N \cdots \mathcal{H}_n/N, \mathcal{I}_1/N \cdots \mathcal{I}_n/N, \mathcal{L}/N, \mathcal{T}/N, \mathcal{C}_L/N, \mathcal{C}_T/N, \mathcal{C}_1/N \cdots \mathcal{C}_n/N, \overline{\mathcal{C}}_1/N \cdots \overline{\mathcal{C}}_n/N, \mathcal{U}_1/N \cdots \mathcal{U}_n/N, \mathcal{A}/N, \mathcal{R}/N)^\top$, we consider model (2.1) in the feasible region

$$
\mathcal{Y} := \left\{(S, H_1 \cdots H_n, I_1 \cdots I_n, L, T, C_L, C_T, C_1 \cdots C_n, \overline{C}_1 \cdots \overline{C}_n, U_1 \cdots U_n, A, R)^\top \in \mathbb{R}_+^{5n+7} \ :\ 0 \le N \le \frac{\Lambda}{\mu}\right\},
\tag{2.4}
$$

where $^\top$ denotes transpose operator. It can be shown that $\mathcal{Y}$ is positively invariant and attracting with respect to (2.3).

In order to study the epidemic dynamic (2.1), we first study the threshold over which the population satisfying model (2.1) evolves into an endemic almost surely. The stability of the equilibrium states of (2.1) can be explained by first studying the stability of the linearized associated system about its equilibrium points (Tornatore et al.). For this reason, we shall first study the conditions under which the linear associated system to (2.1) evolves into an endemic or transient epidemic advance state. We find condition under which expected infected population (with respect to linear associated system to (2.1)) becomes extinct.

In the following, we obtain, in the presence of noise, the expected number $\mathbf{R}_{0,n}$ of secondary (HIV and TB) cases produced by an infected individual when introduced into a completely susceptible population. Define $\overline{\kappa} = \Lambda/\mu$ as in Table 1. It can be shown that the point

$$P_0 := \left\{S^0, H_1^0, \ldots, H_n^0, I_1^0, \ldots, I_n^0, C_1^0, \ldots, C_n^0, \overline{C}_1^0, \ldots, \overline{C}_n^0, U_1^0, \ldots, U_n^0, L^0, T^0, C_L^0, C_T^0, A^0, R^0\right\} = \{\overline{\kappa}, 0_{1\times 5n+6}\} \tag{2.5}$$

is a disease-free equilibrium point for system (2.1).

Define

$$\Phi = (S-\overline{\kappa},\quad H_1,\ldots H_n,\quad I_1,\ldots,I_n,C_1,\ldots,C_n,\quad \overline{C}_1,\ldots,\overline{C}_n,\quad U_1,\ldots,U_n,L,T,C_L,C_T,A,R)^\top.$$

For any vectors $\mathbf{x},\mathbf{y}\in\mathbb{R}^n$ and scalar $c\in\mathbb{R}$, define the matrices

$$M^{\mathbf{x},\mathbf{y}} = \begin{pmatrix} -y_1 & 0 & 0 & \ldots & 0 & 0 \\ x_1 & -y_2 & 0 & \ldots & 0 & 0 \\ 0 & x_2 & -y_3 & \ldots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \ldots & x_{n-2} & -y_{n-1} & 0 \\ 0 & 0 & 0 & 0 & x_{n-1} & -y_n \end{pmatrix}, \tag{2.6}$$

$$\mathcal{I}_{\mathbf{x}} = \operatorname{diag}(x_1,x_2,\ldots,x_n), \quad \text{with} \quad \mathcal{I}_c = \operatorname{diag}(c,c,\ldots,c).$$

The linearization of (2.1) along the infection-free equilibrium P_0 is given by

$$d\,\Phi = \mathbf{A}\,\Phi\,dt + \sum_{i=1}^{n+3}\mathcal{M}_i\,\Phi\,dW_i(t), \quad \Phi(t_0)=\Phi_0, \tag{2.7}$$

where $\mathbf{A} = \begin{pmatrix} \Delta_{1,1} & \Delta_{1,2} \\ 0_{3n+6\times 2n+1} & \Delta_{2,2}\end{pmatrix}$, with $\Delta_{1,1}\equiv\Delta_{1,1}(\sigma_{h,1}) = \begin{pmatrix} A_{11}(\sigma_{h,1}) & A_{12} \\ A_{21} & A_{22}\end{pmatrix}$ depending on noise intensity $\sigma_{h,1}$,

$$A_{1,1}(\sigma_{h,1}) = \begin{pmatrix} -\mu & -\left(\beta h_1 + \sigma_{h,1}^2\overline{\kappa}/2\right)\overline{\kappa} & -\beta\overline{\kappa}h_2 & -\beta\overline{\kappa}h_3 & \ldots & -\beta\overline{\kappa}h_n \\ 0 & -\left(a_1 - \beta h_1\overline{\kappa} - \sigma_{h,1}^2\beta^2\overline{\kappa}^2/2\right) & \beta\overline{\kappa}h_2 & \beta\overline{\kappa}h_3 & \ldots & \beta\overline{\kappa}h_n \\ 0 & \rho_1 & -a_2 & 0 & \ldots & 0 \\ 0 & 0 & \rho_2 & -a_3 & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \ldots & \rho_{n-1} & -a_n \end{pmatrix}_{n+1\times n+1},$$

$$A_{1,2} = \begin{pmatrix} -\beta\overline{\kappa}\epsilon_1 & -\beta\overline{\kappa}\epsilon_2 & -\beta\overline{\kappa}\epsilon_3 & \ldots & -\beta\overline{\kappa}\epsilon_n \\ \phi_1+\beta\overline{\kappa}\epsilon_1 & \beta\overline{\kappa}\epsilon_2 & \beta\overline{\kappa}\epsilon_3 & \ldots & \beta\overline{\kappa}\epsilon_n \\ 0 & \phi_2 & 0 & 0 & \ldots \\ 0 & 0 & \phi_3 & 0 & \ldots \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \ldots & \ldots & \phi_n \end{pmatrix}_{n+1\times n}, A_{2,1} = \begin{pmatrix} 0 & \tau_1 & 0 & \ldots & 0 & 0 \\ 0 & 0 & \tau_2 & \ldots & 0 & 0 \\ 0 & 0 & 0 & \tau_3 & \ldots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \ldots & \ldots & 0 & \tau_n \end{pmatrix}_{n\times n+1}, A_{2,2} = M^{\boldsymbol{\gamma},\mathbf{b}},$$

$$\Delta_{2,2} = \begin{pmatrix} \mathcal{G}_{11} & \mathcal{G}_{12} \\ \mathcal{G}_{21} & \mathcal{G}_{22}\end{pmatrix}, \text{with } \mathcal{G}_{11} = \begin{pmatrix} M^{\mathbf{r},\mathbf{d}} & 0_{n\times n} & \mathcal{I}_s \\ 0_{n\times n} & M^{\overline{\mathbf{e}},\overline{\mathbf{d}}} & \mathcal{I}_{\overline{s}} \\ \mathcal{I}_\eta & \mathcal{I}_{\overline{\eta}} & M^{\boldsymbol{\varrho},\mathbf{e}} \end{pmatrix}, \mathcal{G}_{12} = \begin{pmatrix} 0 & 0 & 0 & \psi & 0 & 0 \\ & & 0_{n-1\times 6} & & & \\ 0 & 0 & e_L & e_T & 0 & 0 \\ & & 0_{2n-1\times 6} & & & \end{pmatrix},$$

$$\mathcal{G}_{21} = \tau_*\overline{\kappa}\phi\begin{pmatrix} \phi_1 l & \ldots & \phi_n l & \overline{\phi}_1 l & \ldots & \overline{\phi}_n l & \sigma l & \ldots & \sigma l \\ \phi_1(1-l) & \ldots & \phi_1(1-l) & \overline{\phi}_1(1-l) & \ldots & \overline{\phi}_n(1-l) & \sigma(1-l) & \ldots & \sigma(1-l) \\ & & & & 0_{4\times 3n} & & & & \end{pmatrix},$$

$\mathcal{G}_{2,2}\equiv\mathcal{G}_{2,2}(\sigma_{\tau,n+3})$ depends on noise intensity $\sigma_{\tau,n+3}$ and defined by.

$$\mathcal{G}_{22}=\begin{pmatrix} -z_1 & \tau_*\overline{\tau}_1 l\overline{\kappa}+(1-l)l\tau_*^2\overline{\kappa}^2\sigma^2_{\tau,n+3}/2 & 0 & \tau_*\overline{\tau}_3\overline{\kappa}l & (x+\tau_*\overline{\tau}_2 l\overline{\kappa}) & q\\ f & -\left(z_2-\tau_*\overline{\tau}_1(1-l)\overline{\kappa}-(1-l)^2\tau_*^2\overline{\kappa}^2\sigma^2_{\tau,n+3}/2\right) & 0 & \tau_*\overline{\tau}_3\overline{\kappa}(1-l) & \tau_*\overline{\tau}_2(1-l)\overline{\kappa} & 0\\ 0 & 0 & -d_L & 0 & 0 & 0\\ 0 & 0 & 0 & -d_T & 0 & 0\\ 0 & \delta & 0 & 0 & -\theta & 0\\ 0 & p & 0 & 0 & w & -g \end{pmatrix},$$

$\Delta_{1,2}\equiv\Delta_{1,2}(\sigma_{\tau,n+3})=\begin{pmatrix} c_{1,1} & c_{1,2}\end{pmatrix}$ depends on noise intensity $\sigma_{\tau,n+3}$, where.

$$c_{1,1}=\overline{\kappa}\begin{pmatrix} -(\beta+\tau_*\phi)\phi_1 & \dots & -(\beta+\tau_*\phi)\phi_n & -(\beta+\tau_*\phi)\overline{\phi}_1 & \dots & -(\beta+\tau_*\phi)\overline{\phi}_n & -(\beta+\tau_*\phi)\sigma & \dots & -(\beta+\tau_*\phi)\sigma\\ \beta\phi_1 & \dots & \beta\phi_n & \beta\overline{\phi}_1 & \dots & \beta\overline{\phi}_n & \beta\sigma & \dots & \beta\sigma\\ & & & & 0_{2n-1\times 3n} & & & & \end{pmatrix},$$

$$c_{1,2}\equiv c_{1,2}(\sigma_{\tau,n+3})=\begin{pmatrix} 0 & -\tau_*\overline{\tau}_1\overline{\kappa}-(1-l)\tau_*^2\overline{\kappa}^2\sigma^2_{\tau,n+3}/2 & -\overline{\kappa}\beta\nu_1 & -\overline{\kappa}(\beta\nu_2+\tau_*\overline{\tau}_3) & -\overline{\kappa}\tau_*\overline{\tau}_2 & 0\\ 0 & 0 & \overline{\kappa}\beta\nu_1 & \overline{\kappa}\beta\nu_2 & 0 & 0\\ & & & 0_{2n-1\times 6} & & \end{pmatrix},$$

and $\mathcal{M}_j=\begin{pmatrix} O_j & \Gamma_{0,j} & O_{5n-j+6}\end{pmatrix}, 1\le j\le n$, $\mathcal{M}_{n+j}=\begin{pmatrix} O_{5n+j+2} & \Gamma_1 & O_{4-j}\end{pmatrix}\sigma_{\nu,n+j}, j=1,2$, $\mathcal{M}_{n+3}=\begin{pmatrix} O_{5n+2} & \Gamma_2 & O_4\end{pmatrix}\sigma_{\tau,n+3}$, where O_m is a $(5n+7)\times m$ zero matrix and $\Gamma_{0,j}=\sigma_j\overline{\kappa}\begin{pmatrix} -1 & 1 & 0\dots 0\end{pmatrix}^\top_{5n+7\times 1}$, $\Gamma_1=\overline{\kappa}\beta\begin{pmatrix} -1 & 1 & 0\dots 0\end{pmatrix}^\top_{5n+7\times 1}$, $\Gamma_2=\tau_*\overline{\kappa}\begin{pmatrix} -1 & 0 & 0\dots 0 & l & 1-l & 0 & 0\end{pmatrix}^\top_{5n+7\times 1}$.

The block matrix representation of **A** suggests that under certain conditions, the long term behavior of the dynamic (2.1) can be studied by first studying the stability of the disease-free equilibrium with respect to population satisfying a HIV-only stochastic dynamic

$$\begin{aligned} dS &= \left(\Lambda-\beta S\sum_{j=1}^{n}(h_jH_j+\epsilon_jI_j)-\mu S\right)dt-\beta\mathcal{S}\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t),\quad S(t_0)=S_0,\\ dH_1 &= \left(\beta S\sum_{j=1}^{n}(h_jH_j+\epsilon_jI_j)-a_1H_1+\phi_1I_1\right)dt+\beta\mathcal{S}\sum_{j=1}^{n}\sigma_{h,j}\mathcal{H}_j\circ dW_{h,j}(t),\quad H_1(t_0)=H_{01},\\ dH_k &= (\rho_{k-1}H_{k-1}-a_kH_k+\phi_kI_k)\,dt,\quad H_k(t_0)=H_{0k},\\ dI_1 &= (\tau_1H_1-b_1I_1)dt,\quad I_1(t_0)=I_{01},\\ dI_k &= (\tau_kH_k+\gamma_{k-1}I_{k-1}-b_kI_k)\,dt,\quad I_k(t_0)=I_{0k},\ \text{for } k=2,3,\dots,n. \end{aligned}\tag{2.8}$$

and TB-only stochastic dynamic

$$\begin{aligned} dS &= (\Lambda-\mu S-\tau_*(\overline{\tau}_1T+\overline{\tau}_2A)S)dt-\tau_*\sigma_{\tau,n+3}S\mathcal{T}\circ dW_{\tau,n+3}(t),\\ dL &= (\tau_*l(\overline{\tau}_1T+\overline{\tau}_2A)S-\tau_*\tau_rTL-z_1L+qR+xA)dt+l\tau_*\sigma_{\tau,n+3}S\mathcal{T}\circ dW_{\tau,n+3}(t),\\ dT &= (\tau_*(1-l)(\overline{\tau}_1T+\overline{\tau}_2A)S+\tau_*\tau_rTL+fL-z_2T)\,dt+(1-l)\tau_*\sigma_{\tau,n+3}S\mathcal{T}\circ dW_{\tau,n+3}(t),\\ dA &= (\delta T-\theta A)\,dt,\\ dR &= (pT-gR+wA)\,dt. \end{aligned}\tag{2.9}$$

In the absence of noise, the schematics of the HIV-only and TB-only transmissions are given in Figs. 1 and 2, respectively, with dynamics (2.8) and (2.9) reducing to models (2.10) and (2.11), respectively, given by

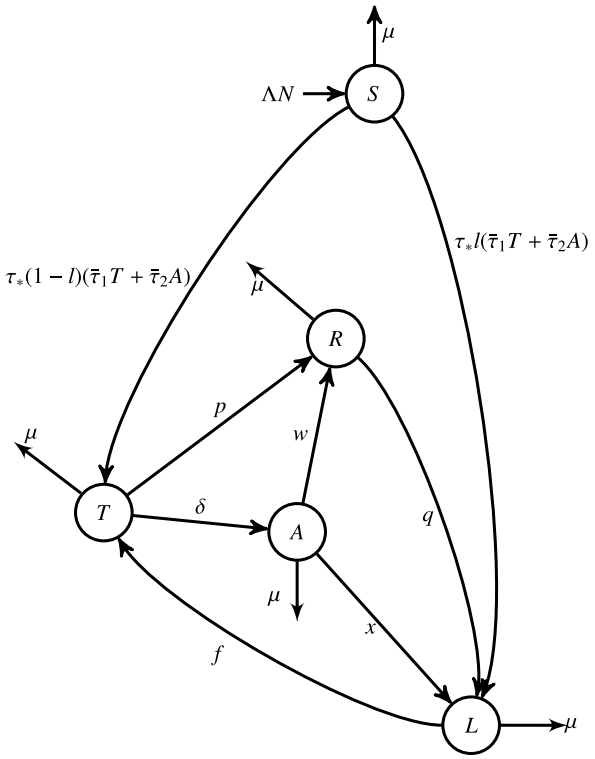

Fig. 1. Schematic diagram for TB-only model.

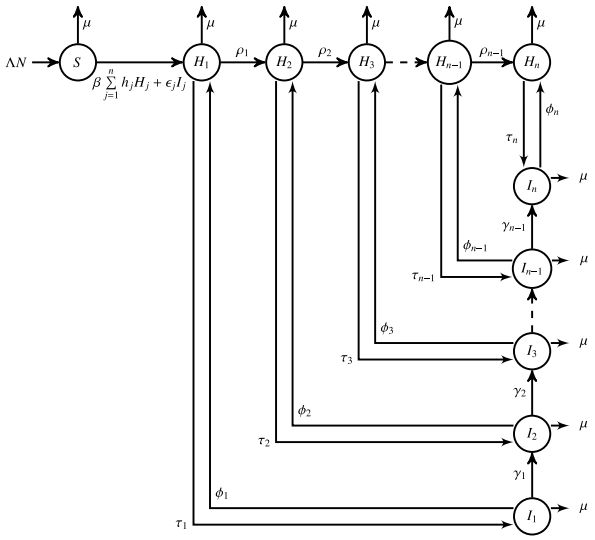

Fig. 2. Schematic diagram for HIV-only model.

$$\begin{aligned}
dS &= \left(\Lambda - \beta S\sum_{j=1}^{n}(h_jH_j + \epsilon_jI_j) - \mu S\right)dt, \quad S(t_0) = S_0,\\
dH_1 &= \left(\beta S\sum_{j=1}^{n}(h_jH_j + \epsilon_jI_j) - a_1H_1 + \phi_1I_1\right)dt, \quad H_1(t_0) = H_{01},\\
dH_k &= (\rho_{k-1}H_{k-1} - a_kH_k + \phi_kI_k)\,dt, \quad H_k(t_0) = H_{0k},\\
dI_1 &= (\tau_1H_1 - b_1I_1)dt, \quad I_1(t_0) = I_{01},\\
dI_k &= (\tau_kH_k + \gamma_{k-1}I_{k-1} - b_kI_k)\,dt, \quad I_k(t_0) = I_{0k}, \text{ for } k = 2,3,\ldots,n.
\end{aligned} \tag{2.10}$$

$$\begin{aligned}
dS &= (\Lambda - \mu S - \tau_*(\overline{\tau}_1T + \overline{\tau}_2A)S)dt,\\
dL &= (\tau_*l(\overline{\tau}_1T + \overline{\tau}_2A)S - \tau_*\tau_rTL - z_1L + qR + xA)dt,\\
dT &= (\tau_*(1-l)(\overline{\tau}_1T + \overline{\tau}_2A)S + \tau_*\tau_rTL + fL - z_2T)\,dt,\\
dA &= (\delta T - \theta A)\,dt,\\
dR &= (pT - gR + wA)\,dt.
\end{aligned} \tag{2.11}$$

The expected numbers of infections, denoted $\mathcal{R}_{n,H}$ and $\mathcal{R}_T$, produced by individuals infected with HIV-only and TB-only in a population (satisfying (2.10) and (2.11)) susceptible to HIV-only and TB-only infections are obtained in Appendix A as

$$\mathcal{R}_{n,H} = \overline{\kappa}\beta\sum_{k=1}^{n}\left[\frac{u_kh_k + \epsilon_kv_k}{\prod_{j=1}^{k}\left(a_jb_j - \tau_j\phi_j\right)}\right], \tag{2.12}$$

where u_k and v_k satisfy

$$\begin{cases} u_k &= b_k\rho_{k-1}u_{k-1} + \phi_k\gamma_{k-1}v_{k-1},\\ v_k &= \tau_k\rho_{k-1}u_{k-1} + a_k\gamma_{k-1}v_{k-1}, \quad \text{for } k = 1,2,\ldots,n, \end{cases} \tag{2.13}$$

$\rho_0 = 1$; $u_0 = 1$; $\gamma_0 = 1$ and $v_0 = 0$, and

$$\mathcal{R}_T = \frac{\overline{\kappa}g\tau_*(\overline{\tau}_1\theta + \overline{\tau}_2\delta)(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta}, \tag{2.14}$$

respectively, and $(gz_1z_2 - fpq)\theta - (qw + gx)f\delta > 0$. See parameter description in Table 1. Likewise, we also note here that $a_jb_j - \tau_j\phi_j > 0$ for $j = 1, 2, \ldots, n$. It is further shown in Appendix A that in a population co-infected with HIV and Tuberculosis, the number $\mathcal{R}_{0,n}$ of expected number of HIV and Tuberculosis infections produced by an infected individual in a population satisfying (2.3) where a certain fraction of infected individuals are receiving treatment is

$$\mathcal{R}_{0,n} = \max\{\mathcal{R}_{n,H}, \mathcal{R}_T\}, \quad n \geq 1. \tag{2.15}$$

Define $\mathbf{m}(t) = \mathbb{E}[\Phi(t)]$. Then $\mathbf{m}(t)$ satisfies the deterministic differential equation

$$d\mathbf{m} = \mathbf{A}\,\mathbf{m}\,dt. \tag{2.16}$$

Let $\tilde{t}$ be an eigenvalue of $\mathbf{A}$. It can be shown that the characteristic polynomial of $\mathbf{A}$ is given by

$$det(\mathbf{A} - \tilde{t}\mathcal{I}_{5n+7\times 5n+7}) = -(\tilde{t} + \mu)\;\; det(\overline{\mathbf{A}} - \tilde{t}\mathcal{I}_{5n+6\times 5n+6}), \tag{2.17}$$

where $\overline{\mathbf{A}}$ is the submatrix of $\mathbf{A}$ in (2.7) formed by deleting the first row and column of $\mathbf{A}$. Using the idea presented in Appendix A.1.3, we calculate the reproduction number $\mathbf{R}_{0,n}$ with respect to (2.16) as

$$\mathbf{R}_{0,n} = \max\{\mathbf{R}_{n,H}, \mathbf{R}_T\}, \tag{2.18}$$

where

$$\begin{aligned}\mathbf{R}_{n,H} &= \overline{\kappa}\beta \sum_{k=1}^{n}\left[\frac{u_k h_k + \epsilon_k \nu_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau_j \phi_j\right)}\right] + \frac{1}{2}\left(\frac{b_1\beta^2\sigma_{h,1}^2\overline{\kappa}^2}{a_1 b_1 - \tau_1\phi_1}\right), \\ &= \mathcal{R}_{n,H} + \frac{1}{2}\left(\frac{b_1\beta^2\sigma_{h,1}^2\overline{\kappa}^2}{a_1 b_1 - \tau_1\phi_1}\right),\end{aligned} \tag{2.19}$$

is the expected the number of HIV infections produced by an infected individual in a HIV-only infected random population where a certain fraction of infected individuals are receiving treatment,

$$\begin{aligned}\mathbf{R}_T &= \frac{\overline{\kappa} g\tau_*(\overline{\tau}_1\theta + \overline{\tau}_2\delta)(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta} + \frac{1}{2}\frac{g\overline{\kappa}^2\tau_*^2\theta(1-l)\sigma_{\tau,n+3}^2(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta} \\ &= \mathcal{R}_T + \frac{1}{2}\frac{g\overline{\kappa}^2\tau_*^2\theta(1-l)\sigma_{\tau,n+3}^2(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta},\end{aligned} \tag{2.20}$$

is the expected number of Tuberculosis infections produced by an infected individual in a Tuberculosis-only infected random population where a certain fraction of infected individuals are receiving treatment.

3. Results: analysis of stochastic model (2.1)

In this section, we discuss the long term behavior of the HIV and TB infected population satisfying model (2.1). In addition, we also study the impacts of HIV/AIDS and TB treatments at different stages of infections in a population under the influence of random perturbations.

Following (2.18), we see that the number of infections produced by an infected individual in a HIV-Tuberculosis co-infected population is only determined by $\mathbf{R}_{n,H}$ and $\mathbf{R}_T$. It follows directly from (2.7) that $a_1 - \beta h_1\overline{\kappa} - \sigma_{h,1}^2\beta^2\overline{\kappa}^2/2 = a_1\left(1 - \beta\overline{\kappa}h_1/a_1 - \sigma_{h,1}^2\beta^2\overline{\kappa}^2/(2a_1)\right) > a_1(1 - \mathbf{R}_{1,H}) > 0$ if $\mathbf{R}_{n,H} < 1$ for $n \geq 1$. Also, $z_2 - \tau_*\tau_1(1-l)\overline{\kappa} - (1-l)^2\tau_*^2\overline{\kappa}^2\sigma_{\tau,n+3}^2/2 > 0$ if $\mathbf{R}_T < 1$. It also follows from (2.19) and (2.20) that $\mathcal{R}_{n,H} < \mathbf{R}_{n,H}$, $\mathcal{R}_T < \mathbf{R}_T$ and $\mathcal{R}_{0,n} < \mathbf{R}_{0,n}$. This implies that the number of secondary infections produced by an infective individual in a susceptible population is higher in the presence of noise in the transmission rate of diseases than when there is no noise in the transmission rate. This signifies that random fluctuations in the HIV and Tuberculosis transmission rates offset the transmission dynamics of an infectious individual positively by increasing the number of expected secondary infection cases for the HIV and Tuberculosis infections. As the noise intensities reduce to zero, the number of secondary infections, $\mathbf{R}_{0,n}$ reduces to $\mathcal{R}_{0,n}$. Further impacts of noise on the population dynamic (2.1) are studied by analyzing the stability analysis of the disease free equilibrium under certain threshold.

In this section, we study the stability of the infection-free equilibrium P_0 with respect to the stochastic system (2.1). According to KHasminski (Rafail, 2012, p. 66) and Tornatore et al. (Tornatore et al.), many problems concerning the stability of the equilibrium states of a non-linear stochastic system can be reduced to problems concerning stability of solutions of the linear associated system. Here, we study the stability of (2.7) and later use Theorem 7.1 in (Rafail, 2012, p. 66) to extend the result to that of the nonlinear system (2.1). Since (2.18), (2.19), and (2.20) suggest that the dynamic of the population satisfying (2.1) depends on the dynamics (2.8) and (2.9) with the HIV-only and Tuberculosis-only stochastic models, respectively, we first discuss the stability analysis for the case where the population is noise-free and infected by only one disease.

3.1. Analysis of the HIV-only deterministic model (2.10)

In this section, we discuss the stability analysis of the infection-free and endemic equilibrium of the HIV-only sub-model (2.10). We aim to study the condition under which the population converges to either the infection-free or endemic equilibrium on the long run.

3.1.1. Stability analysis of the disease-free equilibrium of (2.10)

We first analyze the asymptotic stability of the disease-free equilibrium

$$P_0^H := \{S^0, H_1^0, \ldots, H_n^0, I_1^0, \ldots, I_n^0\} = \{\overline{\kappa}, 0, \ldots, 0, 0, \ldots, 0\} \tag{3.1}$$

of (2.10) and later discuss its global stability. By defining

$$\Phi = (\, S - \overline{\kappa} \quad H_1 \quad \ldots \quad H_n \quad I_1 \quad \ldots \quad I_n \,)^{\top}, \tag{3.2}$$

the linearization of (2.10) about P_0^H is equivalent to

$$d\,\Phi = \mathcal{A}\,\Phi\,dt \tag{3.3}$$

where $\mathcal{A} = \begin{pmatrix} A_{1,1}(0) & A_{1,2} \\ A_{2,1} & A_{2,2} \end{pmatrix}$ is as defined in (2.7). We note here that $a_1 - \beta h_1 \overline{\kappa} > 0$ if $\mathcal{R}_{n,H} < 1$ since the inequality $\mathcal{R}_{1,H} < \mathcal{R}_{n,H} < 1$ is equivalent to $0 < (1 - \mathcal{R}_{1,H})(a_1 b_1 - \tau_1 \phi_1) = b_1(a_1 - \beta h_1 \overline{\kappa}) - \tau_1(\phi_1 + \overline{\kappa}\beta\epsilon_1)$. Let $\bar{t}$ be an eigenvalue of $\mathcal{A}$. The characteristic polynomial of $\mathcal{A}$ can be written as

$$det(\mathcal{A} - \bar{t}\; I_{2n+1,2n+1}) = -(\bar{t} + \mu)\;\; det(M_{1,1} - \bar{t}\; \mathcal{I}_{2n\times 2n}), \tag{3.4}$$

where $I_{2n+1,2n+1}$ is a $2n+1 \times 2n+1$ identity matrix and $M_{1,1}$ is formed by deleting the first row and column of $\mathcal{A}$. The proof of the local (and global) stability of the disease-free equilibrium P_0^H is given in the work of Otunuga (Otunuga, 2018, 2020). The statement of the local (and global) stability theorem is given below without proof in the feasible region

$$\mathcal{Y}^H := \left\{ (S, H_1, \ldots, H_n, I_1, \ldots, I_n)^{\top} \in \mathbb{R}_+^{2n+1} \;:\; 0 \le N_H \le \frac{\Lambda}{\mu} \right\}, \tag{3.5}$$

with $N_H = S + \sum_{j=1}^{n} (H_j + I_j)$.

Theorem 2. *The disease-free equilibrium P_0^H of the model* (2.10) *is locally asymptotically stable if $\mathcal{R}_{n,H} < 1$ and unstable if $\mathcal{R}_{n,H} > 1$.*

proof. *The proof follows from Theorem* 6 *of* (Otunuga, 2018).

Theorem 3. *The disease-free equilibrium P_0^H of* (2.10) *is globally stable in the feasible region $\mathcal{Y}^H$ if $\mathcal{R}_{n,H} \le 1$.*

proof. *The proof is similar to Theorem* 7 *of* (Otunuga, 2018).

3.1.2. Stability analysis of the endemic equilibrium of model (2.10)

The endemic equilibrium $\overline{P}^H = (\, \overline{S}^* \quad \overline{H}_1^* \quad \ldots \quad \overline{H}_n^* \quad \overline{I}_1^* \quad \ldots \quad \overline{I}_n^* \,)^{\top}$ of system (2.10) is given by

$$\begin{cases} \overline{S}^* & = \dfrac{\overline{\kappa}}{\mathcal{R}_{n,H}}, \\ \overline{H}_k^* & = \dfrac{\Lambda u_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau_j \phi_j\right)}\left(1 - \dfrac{1}{\mathcal{R}_{n,H}}\right), \\ \overline{I}_k^* & = \dfrac{\Lambda v_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau_j \phi_j\right)}\left(1 - \dfrac{1}{\mathcal{R}_{n,H}}\right), \quad k = 1, 2, \ldots, n, \end{cases} \tag{3.6}$$

where u_k and v_k are defined in (2.12). It is clear that the endemic equilibrium $\overline{P}^H$ of (2.10) exists if and only if $\mathcal{R}_{n,H} > 1$. The endemic equilibrium becomes disease-free (that is, $\overline{P}^H = P_0^H$) if $\mathcal{R}_{n,H} = 1$.

We follow the same procedure used in (Otunuga, 2018) to show the global stability of the endemic equilibrium $\overline{P}^H$.

Theorem 4. *The endemic equilibrium $\overline{P}^H$ of the system* (2.10) *is globally stable if $\mathcal{R}_{n,H} > 1, f_k > 0, k = 1, 2, \ldots, n$, and $f_k > 0, m_k > 0$, $k = 2, 3, \ldots, n$, where f_k and m_k satisfy*

$$\begin{aligned} m_k &= \overline{\theta}_k^* \gamma_{k-1} \overline{T}_{k-1}^* - \overline{\theta}_{k+1}^* \gamma_k \overline{T}_k^*, \quad \text{for } k = 2, 3, \ldots, n-1, \\ m_n &= \overline{\theta}_n^* \gamma_{n-1} \overline{T}_{n-1}^*, \\ f_1 &= \beta \overline{S}^* \epsilon_1 \overline{T}_1^*, \\ f_k &= \overline{\theta}_k^* \tau_k \overline{I}_k^* - \overline{\phi}_k^* \phi_k \overline{T}_k^*, \quad \text{for } k = 2, 3, \ldots, n, \end{aligned} \tag{3.7}$$

and $\overline{\phi}_k^*$, $\overline{\theta}_k^*$ satisfy

$$\begin{pmatrix} \overline{\phi}_n^* \\ \overline{\theta}_n^* \end{pmatrix} = \frac{\beta \overline{S}^*}{a_n b_n - \tau_n \phi_n} \begin{pmatrix} h_n b_n + \tau_n \epsilon_n \\ h_n \phi_n + a_n \epsilon_n \end{pmatrix},$$

$$\begin{pmatrix} \overline{\phi}_{n-k}^* \\ \overline{\theta}_{n-k}^* \end{pmatrix} = \frac{1}{a_{n-k} b_{n-k} - \tau_{n-k} \phi_{n-k}} \left[\begin{pmatrix} b_{n-k} \rho_{n-k} & \gamma_{n-k} \tau_{n-k} \\ \phi_{n-k} \rho_{n-k} & \gamma_{n-k} a_{n-k} \end{pmatrix} \begin{pmatrix} \overline{\phi}_{n-k+1}^* \\ \overline{\theta}_{n-k+1}^* \end{pmatrix} + \beta \overline{S}^* \begin{pmatrix} h_{n-k} b_{n-k} + \tau_{n-k} \epsilon_{n-k} \\ h_{n-k} \phi_{n-k} + a_{n-k} \epsilon_{n-k} \end{pmatrix} \right], \text{for } k = 1, 2, 3, \ldots, n-1, \tag{3.8}$$

proof. See Otunuga (Otunuga, 2020) for the proof.

3.2. Effect of treatment on a population infected with HIV only: model (2.10)

Write $\mathcal{R}_{j,H}(\tau_i) \equiv \mathcal{R}_{j,H}$ as a function of the treatment rate τ_i in stage j of infection, for $1 \le i <= j \le n$. In a population where treatment is administered at a very high rate during stage i of infection (so that we say $\tau_i \to \infty$), the expected number of secondary infection produced by a typical infected individual in stage j of infection (with $i \le j$) is denoted and defined by $\mathcal{R}_{j,H}(\tau_i \to \infty) \equiv \lim_{\tau_i \to \infty} R_{j,H}(\tau_i)$. Likewise, if no treatment is given in stage i of infection, we denote the expected number of secondary infection produced by a typical infected individual in stage j of infection (with $i \le j$) by $R_j(\tau_i = 0) \equiv \mathcal{R}_{j,H}(\tau_i)|_{\tau_i = 0}$. Following similar approach in Otunuga (Otunuga, 2020), we obtain these numbers as

$$\begin{cases} \mathcal{R}_{j,H}(\tau_1 \to \infty) = \dfrac{\overline{\kappa}\beta}{\overline{b}_1} \displaystyle\sum_{k=1}^{j} \frac{\widehat{u}_k h_k + \widehat{v}_k \epsilon_k}{\displaystyle\prod_{\substack{r=1 \\ r \ne 1}}^{k} (\overline{a}_r b_r + \overline{b}_r \tau_r)}, \\ \mathcal{R}_{j,H}(\tau_i \to \infty) = \mathcal{R}_{i-1,H} + \dfrac{\overline{\kappa}\beta}{\overline{b}_i} (u_{i-1}\rho_{i-1} + v_{i-1}\gamma_{i-1}) \displaystyle\sum_{k=i}^{j} \frac{\widehat{u}_k h_k + \widehat{v}_k \epsilon_k}{\displaystyle\prod_{\substack{r=1 \\ r \ne 1}}^{k} (\overline{a}_r b_r + \overline{b}_r \tau_r)}, \quad \text{for } 2 \le i \le j \le n, \\ \widehat{u}_i = 0, \ \ \widehat{v}_i = 1, \ i = 1, \ldots, n, \text{ and } \widehat{u}_k, \widehat{v}_k, k \ne i \text{ are defined in (3.11), and } \overline{a}_k, \ \overline{b}_k \text{ are given in Table 1.} \end{cases} \tag{3.9}$$

$$\begin{cases} \mathcal{R}_{j,H}(\tau_1=0) &= \dfrac{\overline{\kappa}\beta}{\overline{a}_1}\displaystyle\sum_{k=1}^{j}\frac{\breve{u}_k h_k+\breve{v}_k\epsilon_k}{\displaystyle\prod_{\substack{r=1\\ r\neq 1}}^{k}(\overline{a}_r b_r+\overline{b}_r\tau_r)}, \\ \breve{u}_1 &= 1, \quad \breve{v}_1=0, \quad \text{and} \quad \breve{u}_k,\breve{v}_k, k\neq 1 \text{ are defined in (3.11)} \\ \mathcal{R}_{j,H}(\tau_i=0) &= \mathcal{R}_{i-1,H}+\dfrac{\overline{\kappa}\beta}{\overline{a}_i b_i}\displaystyle\sum_{k=i}^{j}\frac{\breve{u}_k h_k+\breve{v}_k\epsilon_k}{\displaystyle\prod_{\substack{r=1\\ r\neq i}}^{k}(\overline{a}_r b_r+\overline{b}_r\tau_r)}, \quad \text{for } \ 2\le i\le j\le n, \\ \breve{u}_i &= b_i\rho_{i-1}\breve{u}_{i-1}+\phi_i\gamma_{i-1}\breve{v}_{i-1}, \quad \breve{v}_i=\overline{a}_i\gamma_{i-1}\breve{v}_{i-1}, \quad \text{and} \quad \breve{u}_k,\breve{v}_k, k\neq i \text{ are defined in (3.11)}, \end{cases} \tag{3.10}$$

and $\mathcal{R}_{j,H}(\tau_i\to\infty)=\mathcal{R}_{j,H}(\tau_i=0)=\mathcal{R}_{j,H}$ if $i>j$, where u_i, v_i are defined in (2.13) for $i=1,2,\ldots,n$, $\breve{u}_0=1$, $\breve{v}_0=0$, and

$$\begin{cases} \begin{cases} \widehat{u}_k &= b_k\rho_{k-1}\widehat{u}_{k-1}+\phi_k\gamma_{k-1}\widehat{v}_{k-1}, \\ \widehat{v}_k &= \tau_k\rho_{k-1}\widehat{u}_{k-1}+a_k\gamma_{k-1}\widehat{v}_{k-1}, \quad \text{for } k=i+1,\ldots,n, \quad 1\le i\le n \end{cases} \\ \begin{cases} \breve{u}_k &= b_k\rho_{k-1}\breve{u}_{k-1}+\phi_k\gamma_{k-1}\breve{v}_{k-1}, \\ \breve{v}_k &= \tau_k\rho_{k-1}\breve{u}_{k-1}+a_k\gamma_{k-1}\breve{v}_{k-1}, \quad \text{for } k\neq i. \end{cases} \end{cases} \tag{3.11}$$

Furthermore,

$$\begin{cases} \dfrac{d\mathcal{R}_{j,H}}{d\tau_i} &= \dfrac{\overline{a}_i\overline{b}_i b_i}{(\overline{a}_i b_i+\overline{b}_i\tau_i)^2}\left(\mathcal{R}_{j,H}(\tau_i\to\infty)-\mathcal{R}_{j,H}(\tau_i=0)\right), \\ \dfrac{d^2\mathcal{R}_{j,H}}{d\tau_i^2} &= -\dfrac{2\overline{a}_i\overline{b}_i^2 b_i}{(\overline{a}_i b_i+\overline{b}_i\tau_i)^3}\left(\mathcal{R}_{j,H}(\tau_i\to\infty)-\mathcal{R}_{j,H}(\tau_i=0)\right), \quad \text{for } \ 1\le i,j\le n. \end{cases} \tag{3.12}$$

It follows from (3.12) that the rate at which the expected number of secondary HIV infection in stage j of infection is changing with respect to treatment administered at stage i depends on how high the treatment rate is. We see that $\frac{d\mathcal{R}_{j,H}(\tau_i)}{d\tau_i}<0$ and the graph of $\mathcal{R}_{j,H}(\tau_i)$ concaves up for all $\tau_i\ge 0$ if and only if $\mathcal{R}_{j,H}(\tau_i\to\infty)<\mathcal{R}_{j,H}(\tau_i=0)$, for $1\le i\le j\le n$. That is, showing that the expected number of secondary HIV infection in stage j of infection decreases and slows down as the treatment rate in stage i of infection increases ($i\le j\le n$) is equivalent to showing that the number is smaller when treatment is administered at a very high rate in stage i than when no treatment is administered.

3.2.1. Numerical simulation for the HIV-only model (2.10)

In this section, we give simulation results for the trajectory of the susceptible, HIV infected population satisfying (2.10) using demographical data published in (Birrell et al., 2012; Granich et al., 2009; Hollingsworth et al., 2008; Kretzschmar et al.,

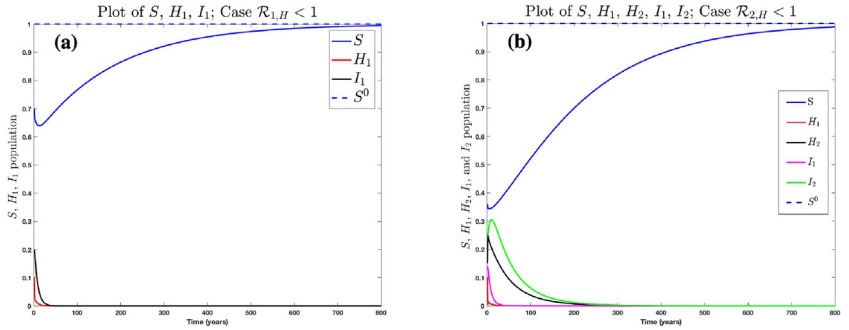

Fig. 3. Graph of the trajectories of S, H_k, I_k, $k=1,2,\ldots,n$, for the cases where $n=1$ and 2, respectively, and $\mathcal{R}_{n,H}<1$.

Table 2
Parameter values for the epidemic model: Case study HIV/AIDS.

Parameter	Description	Default Value	References
Λ	Recruitment rate into the population	0.018year^{-1}	(Granich et al., 2009; Kretzschmar et al., 2013)
β	Transmission rate of infection	Estimated	Kretzschmar et al. (2013)
h_k	Infectivity of untreated individuals in stage k of infection	$h_1 = 2.76$, $h_2 = 0.106$, $h_2 = 0.106$	Hollingsworth et al. (2008)
ϵ_k	Reduced infectiousness due to treatment in stage k of infection	$\epsilon_1 = 0.01$	Granich et al. (2009)
μ	Natural death rate	Λ	[15, 24]
τ_k	Treatment rate of individuals in stage k of infection	Range 0–100%	Kretzschmar et al. (2013)
ϕ_k	Rate of dropping out of treatment in stage k	Range 0–100%	Kretzschmar et al. (2013)
ρ_k	Average duration of untreated infection	$\rho_1 = \frac{1}{0.271}$, $\rho_2 = \frac{1}{8.31}$, $\rho_3 = \frac{1}{1.184}$	[5, 20, 24]
γ_k	Average duration of treated infection	$\gamma_1 = \frac{1}{8.21}$, $\gamma_2 = \frac{1}{54}$, $\gamma_3 = \frac{1}{2.463}$	Kretzschmar et al. (2013)

2013; The CASCADE Collaboration; Collaborative Group on AIDS, 2000). We verify the global stability criteria discussed in Section 3.1. All simulations are carried out using MATLAB R2018a.

Fig. 3 **(a)** and **(b)** show the trajectory of $S, H_k, I_k, k = 1, 2, \ldots, n$ for the cases where $n = 1$ and 2, respectively, and $\mathcal{R}_{n,H} < 1$. For Fig. 3 **(a)**, we use the initial condition $S_0 = 0.7, H_{10} = 0.1, I_{10} = 0.2$. Parameters' unit are in year^{-1}, with parameter values given in Table 2, where $\mathcal{R}_{1,H} = 0.4295$ and disease-free equilibrium $P_0^H = \left(S^0 = 1, H_1^0 = 0, I_1^0 = 0\right)^\top$. For Fig. 3 **(b)**, we use the initial condition (in percentages) $S_0 = 0.36$, $H_{10} = 0.1$, $H_{20} = 0.15$, $I_{10} = 0.14$, $H_{20} = 0.25$, where $\mathcal{R}_{2,H} = 0.7880$ and disease-free equilibrium $P_0^H = \left(S^0 = 1, H_1^0 = 0, H_2^0 = 0, I_1^0 = 0, I_2^0 = 0,\right)^\top$. Fig. 3 **(a)** and **(b)** confirms that if $\mathcal{R}_{n,H} < 1$, then $S(t) \to \overline{\kappa} = 1$, $H_k(t) \to 0$, $I_k(t) \to 0$ as $t \to \infty$.

Fig. 4 **(a)** and **(b)** show the trajectory of $S, H_k, I_k, k = 1, 2, \ldots, n$ for the cases where $n = 1$ and 2, respectively, and $\mathcal{R}_{n,H} > 1$. For Fig. 4 **(a)**, we use the initial condition $S_0 = 0.7, H_{10} = 0.1, I_{10} = 0.2$ and parameters given in Table 2, where $\mathcal{R}_{1,H} = 1.8847$ and endemic equilibrium $\overline{P}^H = \left(\overline{S}^* = 0.5284, \overline{H}_1^* = 0.0018, \overline{I}_1^* = 0.0120\right)^\top$. For Fig. 4 **(b)**, we use the initial condition $S_0 = 0.36$, $H_{10} = 0.1$, $H_{20} = 0.15$, $I_{10} = 0.14$, $I_{20} = 0.25$, where $\mathcal{R}_{2,H} = 3.0828$ and endemic equilibrium $\overline{P}^H = \left(\overline{S}^* = 0.3173, \overline{H}_1^* = 0.0027, \overline{H}_2^* = 0.0259, \overline{I}_1^* = 0.0173, \overline{I}_2^* = 0.2242\right)^\top$. Fig. 4 **(a)** and **(b)** confirm that if $\mathcal{R}_{n,H} > 1$, then $S(t) \to \frac{\overline{\kappa}}{\mathcal{R}_{n,H}}$, $H_k(t) \to \frac{\beta u_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau_j \phi_j\right)}\left(1 - \frac{1}{\mathcal{R}_{n,H}}\right)$, $I_k(t) \to \frac{\beta v_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau_j \phi_j\right)}\left(1 - \frac{1}{\mathcal{R}_{n,H}}\right)$ as $t \to \infty$, for $n = 1$ and $n = 2$, respectively.

The graph on the far left in Fig. 5 shows how the expected number of secondary HIV infections in stage 1 of infection changes as a result of changes in the transmission rate β and the treatment rate in stage i using parameters in Table 2 with $\epsilon_2 = 0.05$, $\tau_1 = 0.08$, $\tau_2 = 0.12$, $\phi_1 = 1/3$, $\phi_2 = 1/4$. The middle graph and the graph to the right show how the expected number of secondary HIV infections in stages 1 and 2 of infections change as a result of changes in the treatment rate in stages 1 and 2 and the rate of dropping out of treatment. It is evident here that these numbers decrease as the treatment rates in stages 1 and 2 increase, and increase as the rates at which individuals drop out of treatment increases in stages 1 and 2. This confirms Theorem 3.9 in the sense that $\mathcal{R}_{1,H}(\tau_1 \to \infty) = 0.2985$ is less than $\mathcal{R}_{1,H}(\tau_1 = 0) = 0.5933$, and $\mathcal{R}_{2,H}(\tau_2 \to \infty) = 0.6197$ is less than $\mathcal{R}_{2,H}(\tau_2 = 0) = 1.5953$.Although the population is in an endemic state in stage 2 of infection with $\mathcal{R}_{2,H} = 1.001$, we see

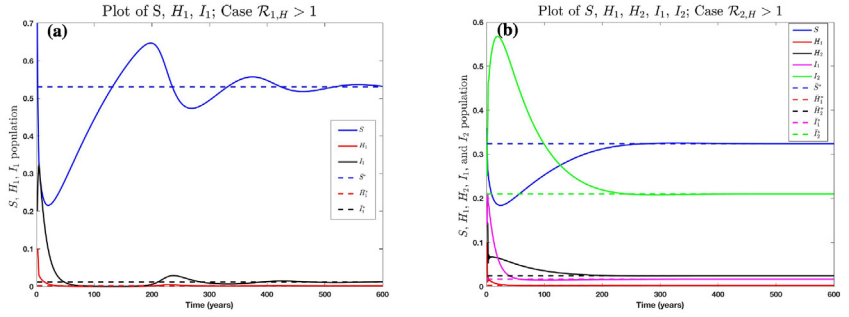

Fig. 4. Graph of the trajectories of $S, H_k, I_k, k = 1, 2, \ldots, n$, for the cases where $n = 1$ and 2, respectively, and $\mathcal{R}_{n,H} > 1$.

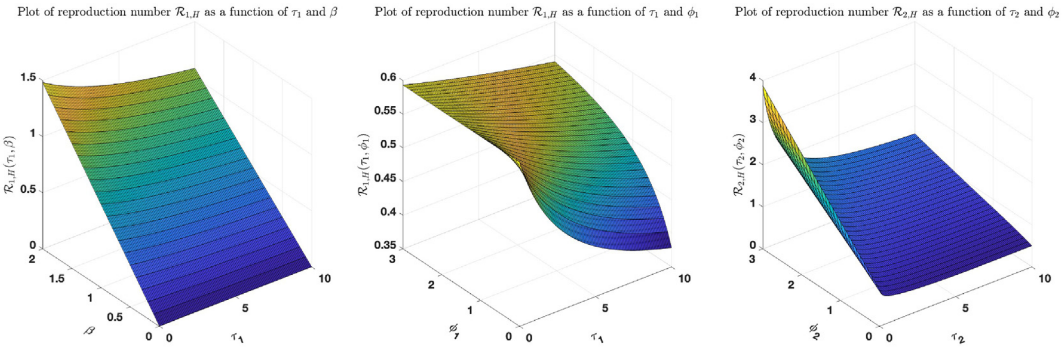

Fig. 5. Graphs showing the impact of infections and treatments on the expected number of secondary infections $\mathcal{R}_{1,H}$ and $\mathcal{R}_{2,H}$.

here that treatment administered at a very high rate changes the dynamics of the population by reducing the number of infection tremendously to $\mathcal{R}_{2,H}(\tau_2 \to \infty) = 0.6197$ so that the population now becomes disease-free on the long run.

3.3. Analysis of the TB-only model (2.11)

In this section, we discuss the stability analysis of the disease-free and endemic equilibrium of the TB-only model (2.11). The disease-free equilibrium, denoted P_0^T of the TB-only model (2.11) is given by

$$P_0^T = \{S^0, L^0, T^0, A^0, R^0\} = \{\overline{\kappa}, 0, 0, 0, 0\}, \tag{3.13}$$

where

$$\begin{aligned}
\overline{S} &= \frac{\overline{\kappa}}{\mathcal{R}_T}, \\
\overline{T} &= \frac{\mu\theta}{\tau_*(\overline{\tau}_1\theta + \overline{\tau}_2\delta)}(\mathcal{R}_T - 1), \\
\overline{A} &= \frac{\mu\delta}{\tau_*(\overline{\tau}_1\theta + \overline{\tau}_2\delta)}(\mathcal{R}_T - 1), \\
\overline{R} &= \frac{\mu(p\theta + w\delta)}{\tau_*(\overline{\tau}_1\theta + \overline{\tau}_2\delta)g}(\mathcal{R}_T - 1).
\end{aligned}$$

3.3.1. Stability analysis of the disease-free equilibrium P_0^T

The Jacobian of the population rates in (2.11) about P_0^T is given by

$$\overline{\mathcal{A}} = \begin{pmatrix}
-\mu & 0 & -\tau_*\overline{\tau}_1\overline{\kappa} & \tau_*\overline{\tau}_2\overline{\kappa} & 0 \\
0 & -z_1 & \tau_*\overline{\tau}_1 l\overline{\kappa} & (x + \tau_*\overline{\tau}_2 l\overline{\kappa}) & q \\
0 & f & -(z_2 - \tau_*\overline{\tau}_1(1-l)\overline{\kappa}) & \tau_*\overline{\tau}_2(1-l)\overline{\kappa} & 0 \\
0 & 0 & \delta & -\theta & 0 \\
0 & 0 & p & w & -g
\end{pmatrix}.$$

We note here that $z_2 - \tau_*\overline{\tau}_1(1-l)\overline{\kappa} > 0$ if $\mathcal{R}_T < 1$. We use Theorem 4.1 in Castillo-Chavez et al. (Castillo-Chavez & Song, 2004) to show the local stability of the disease-free equilibrium P_0^T. To do this, we first show that the real part of all eigenvalues of $\overline{\mathcal{A}}$ is negative if $\mathcal{R}_T < 1$. Let $\overline{t}$ be an eigenvalue of $\overline{\mathcal{A}}$. The characteristic polynomial of $\overline{\mathcal{A}}$ can be written as

$$det(\overline{\mathcal{A}} - \overline{t}\ I_{5\times 5}) = -(\overline{t} + \mu)\ \ det(\overline{M}_{1,1} - \overline{t}\ \mathcal{I}_{4\times 4}), \tag{3.14}$$

where $I_{4\times 4}$ is a 4×4 identity matrix and $\overline{M}_{1,1}$ is the square matrix derived by deleting the first row and column of $\overline{\mathcal{A}}$.

Remark 1. The determinant $\det(\overline{\mathcal{A}})$ can be computed as $\det(\overline{\mathcal{A}}) = \mu[(gz_1z_2 - fpq)\theta - (qw + gx)f\delta](1 - \mathcal{R}_T)$. It follows directly that $\det(\overline{\mathcal{A}}) < 0$ if $\mathcal{R}_T > 1$. Since $\det(\overline{\mathcal{A}})$ is the product of all the five eigenvalues of $\overline{\mathcal{A}}$, then it follows that one of the five

eigenvalues of $\overline{\mathcal{A}}$ is real and positive if $\mathcal{R}_T > 1$. On the other hand, if $\mathcal{R}_T = 1$, then $\det(\overline{\mathcal{A}}) = 0$ and one of the eigenvalues of $\overline{\mathcal{A}}$ is zero.

Theorem 5. *The maximum real part of all eigenvalues of the matrix $\overline{\mathcal{A}}$ is negative if $\mathcal{R}_T < 1$. At least one of the real eigenvalues of $\overline{\mathcal{A}}$ is positive if $\mathcal{R}_T > 1$. There exist a zero eigenvalue if $\mathcal{R}_T = 1$*

Proof.

Using (3.14), it suffices to show that the real part of all eigenvalues of $\overline{M}_{1,1}$ is negative if $\mathcal{R}_T < 1$. Define $\overline{\mathcal{B}} = -\overline{M}_{1,1}$. We can write $\overline{\mathcal{B}}$ in the form

$$\overline{\mathcal{B}} = \overline{\mathcal{L}}\ \overline{\mathcal{U}}, \tag{3.15}$$

where $\overline{\mathcal{L}}$ and $\overline{\mathcal{U}}$ are lower and upper diagonal matrices, respectively, with positive diagonal entries. The entries of $\overline{\mathcal{L}}$ and $\overline{\mathcal{U}}$ are defined by

$$\begin{aligned}
\overline{\mathcal{L}}_{i,j} &= 0, \text{ for } j > i, \overline{\mathcal{L}}_{i,i} = 1, \text{ for } i = 1,2,3,4,\\
\overline{\mathcal{L}}_{2,1} &= -f\Big/ z_1, \overline{\mathcal{L}}_{3,1} = 0, \overline{\mathcal{L}}_{3,2} = \frac{\delta z_1}{(fl + (1-l)z_1)\tau_* \overline{\tau}_1 \overline{\kappa} - z_1 z_2},\\
\overline{\mathcal{L}}_{4,1} &= 0, \ \overline{\mathcal{L}}_{4,2} = \frac{pz_1}{(fl + (1-l)z_1)\tau_* \overline{\tau}_1 \overline{\kappa} - z_1 z_2}, \overline{\mathcal{L}}_{4,3} = \frac{\tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_2 p - \overline{\tau}_1 w) + fxp + wz_1 z_2}{\tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_1 \theta + \overline{\tau}_2 \delta) + fx\delta - \theta z_1 z_2}\\
\overline{\mathcal{U}}_{i,j} &= 0, \text{ for } j < i, \overline{\mathcal{U}}_{1,1} = z_1, \overline{\mathcal{U}}_{1,2} = -l\tau_* \overline{\tau}_1 \overline{\kappa},\\
\overline{\mathcal{U}}_{1,3} &= -(x + l\tau_* \overline{\tau}_2 \overline{\kappa}), \ \overline{\mathcal{U}}_{1,4} = -q, \overline{\mathcal{U}}_{2,2} = \frac{z_1 z_2 - \tau_* \overline{\tau}_1 \overline{\kappa}(fl + (1-l)z_1)}{z_1},\\
\overline{\mathcal{U}}_{2,3} &= -\frac{fx + \tau_* \overline{\tau}_2 \overline{\kappa}(fl + (1-l)z_1)}{z_1}, \overline{\mathcal{U}}_{3,3} = \frac{\tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_1 \theta + \overline{\tau}_2 \delta) + fx\delta - \theta z_1 z_2}{(fl + (1-l)z_1)\tau_* \overline{\tau}_1 \overline{\kappa} - z_1 z_2}, \overline{\mathcal{U}}_{4,4}\\
&= \frac{(gz_1 z_2 - fpq)\theta - (qw + gx)f\delta}{\theta z_1 z_2 - fx\delta - \tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_1 \theta + \overline{\tau}_2 \delta)}(1 - \mathcal{R}_T).
\end{aligned}$$

If $\mathcal{R}_T < 1$, we have $(fl + (1-l)z_1)\tau_* \overline{\tau}_1 \overline{\kappa} - z_1 z_2 < 0$, $\tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_1 \theta + \overline{\tau}_2 \delta) + fx\delta - \theta z_1 z_2 < 0, (gz_1 z_2 - fpq)\theta - (qw + gx) f\delta > 0, \theta z_1 z_2 - fx\delta - \tau_* \overline{\kappa}(fl + (1-l)z_1)(\overline{\tau}_1 \theta + \overline{\tau}_2 \delta) > 0$. Hence, $\overline{\mathcal{L}}_{j,j} > 0$ and $\overline{\mathcal{U}}_{j,j} > 0$ for all $j = 1, 2, 3, 4$. Since $\overline{\mathcal{B}}$ is a Z-matrix, it follows from relations D_{12} and J_{29} of (Plemmons, 1977) that the real part of each eigenvalues of matrix $\overline{\mathcal{B}}$ is positive, which is in turn equivalent to the maximum real part, $s(\overline{M}_{1,1})$, of $\overline{M}_{1,1}$ being negative. On the other hand, it follows from Remark 1 that one of the real eigenvalues of $\overline{\mathcal{A}}$ is positive if $\mathcal{R}_T > 1$, and one of the eigenvalues is zero if $\mathcal{R}_T = 1$. ■

Theorem 6. The disease-free equilibrium P_0^T of (2.11) is locally asymptotically stable if $\mathcal{R}_T < 1$ and unstable if $\mathcal{R}_T > 1$.

proof. The proof follows from Theorem 5. ■

We give the proof of the global stability of the disease-free equilibrium P_0^T in the feasible region

$$\mathcal{Y}^T := \left\{ (S, L, T, A, R)^\top \in \mathbb{R}_+^5 \ : \ 0 \le N_T \le \frac{\Lambda}{\mu} \right\}, \tag{3.16}$$

where $N_T = S + L + T + A + R$, provided $\mathcal{R}_T \le 1$.

Theorem 7. *The disease-free equilibrium P_0^T of (2.11) is globally stable in the feasible region $\mathcal{Y}^T$ if $\mathcal{R}_T \le 1$.*

Proof. *Consider the Lyapunov function $V : \mathbb{R}_5^+ \to \mathbb{R}^+$ defined by*

$$V(S, L, T, A, R) = \left(S - S^0 - S^0 \ln \frac{S}{S^0} \right) + \alpha_L L + \alpha_T T + \alpha_A A + \alpha_R R,$$

where

$$\begin{aligned}
\alpha_L &= \frac{f}{fl+(1-l)z_1},\\
\alpha_T &= \frac{z_1}{fl+(1-l)z_1},\\
\alpha_A &= \frac{f(qw+gx)\overline{\tau}_1+(gz_1z_2-fpq)\overline{\tau}_2}{g(fl+(1-l)z_1)(\theta\overline{\tau}_1+\delta\overline{\tau}_2)} > 0 \text{ using Table 1},\\
\alpha_R &= \frac{fq}{g(fl+(1-l)z_1)}.
\end{aligned} \tag{3.17}$$

The derivative of V computed along solution of (2.11) is

$$\begin{aligned}
\frac{dV}{dt} &= \Lambda+\mu S^0-\Lambda S^0\Big/S-\mu S+(\alpha_L l+\alpha_T(1-l)-1)\tau_*(\overline{\tau}_1T+\overline{\tau}_2A)S-T(\alpha_Tz_2-\tau_*\overline{\tau}_1\overline{\kappa}-\alpha_A\delta-\alpha_Rp)\\
&\quad -A(\alpha_A\theta-\tau_*\overline{\tau}_2\overline{\kappa}-\alpha_Lx-\alpha_Rw)-R(\alpha_Rg-\alpha_Lq)-\tau_*\tau_rTL(\alpha_L-\alpha_T)-L(z_1\alpha_L-f\alpha_T).
\end{aligned}$$

If $\mathcal{R}_T \le 1$, then

$$\begin{aligned}
\alpha_Tz_2-\tau_*\overline{\tau}_1\overline{\kappa}-\alpha_A\delta-\alpha_Rp &= \tau_*\overline{\tau}_1\overline{\kappa}\frac{(1-\mathcal{R}_T)}{\mathcal{R}_T}\ge 0,\\
\alpha_A\theta-\tau_*\overline{\tau}_2\overline{\kappa}-\alpha_Lx-\alpha_Rw &= \tau_*\overline{\tau}_2\overline{\kappa}\frac{(1-\mathcal{R}_T)}{\mathcal{R}_T}\ge 0,\\
\alpha_Rg-\alpha_Lq &= z_1\alpha_L-f\alpha_T=\alpha_Ll+\alpha_T(1-l)-1=0,
\end{aligned}$$

and

$$\frac{dV}{dt}\le -\Lambda\left(\frac{S^0}{S}+\frac{S}{S^0}-2\right)\le 0,$$

using the fact that $S^0=\overline{\kappa}=\Lambda/\mu$ and $1=\left(\frac{S^0}{S}\frac{S}{S^0}\right)^{1/2}\le\frac{1}{2}\left(\frac{S^0}{S}+\frac{S}{S^0}\right)$. If $\mathcal{R}_T\le 1$, then $dV/dt=0$ if and only if $S=S^0$, $L=0$, $T=0$, $A=0$. If $\mathcal{R}_T=1$, then $dV/dt=0$ if and only if $S=S^0$. It follows that the largest invariant set of (2.11) contained in $\{(S,L,T,A,R)^\top\in\mathcal{T}^T : dV/dt=0\}$ is the set $\{P_0^T\}$. The global stability of P_0^T follows from the LaSalle invariant principle (LaSalle, 1976). ■

3.3.2. Effect of treatment on population infected with TB-only: model (2.11)

Here, we wish to study how the number of secondary infection produced by a TB-infected individual changes as treatment is introduced into the system. In this case, we write $\mathcal{R}_T\equiv\mathcal{R}_T(\delta)$ as a function of δ. We note here that if there are no individual receiving treatment with respect to the model (2.11), (that is, if $\delta=0$), then (2.14) reduces to

$$\tilde{\mathcal{R}}_T=\frac{\overline{\kappa}g\tau_*\overline{\tau}_1(fl+(1-l)z_1)}{(gz_1\overline{z}_2-fpq)}, \tag{3.18}$$

where $\overline{z}_2$ is defined in Table 1. This is the expected number of secondary TB infection produced by a typical infected individual in a population not receiving any form of treatment ($\delta=0$), when introduced into a population consisting of susceptible individuals only (with respect to model (2.11)).

As $\delta\to\infty$, it follows that $\mathcal{R}_T(\delta)\to f_T$, where

$$f_T=\frac{\tau_*\overline{\tau}_2g\overline{\kappa}(fl+(1-l)z_1)}{g(\theta z_1-fx)-fqw}. \tag{3.19}$$

As the rate at which TB-infected individuals receiving treatment goes to infinity (meaning as every infected TB individuals receive treatment), the reproduction number $\mathcal{R}_T$ tends to f_T. The derivative of $\mathcal{R}_T(\delta)$ with respect to δ is $\frac{d\mathcal{R}_T}{d\delta}=\frac{m_1m_4-m_2m_3}{(m_3\delta+m_4)^2}$, where $m_1=\tau_*\overline{\tau}_2g\overline{\kappa}(fl+(1-l)z_1)$, $m_2=\tau_*\overline{\tau}_1g\overline{\kappa}\theta(fl+(1-l)z_1)$, $m_3=gz_1\theta-(qw+gx)f$, and $m_4=gz_1\theta\overline{z}_2-fpq\theta$. Using the fact that $\frac{d\mathcal{R}_T}{d\delta}>0(<0)$ if and only if $f_T>\tilde{\mathcal{R}}_T\quad\left(f_T<\tilde{\mathcal{R}}_T\right)$, it follows that $\mathcal{R}_T<\tilde{\mathcal{R}}_T$ if $f_T<\tilde{\mathcal{R}}_T$ and $\mathcal{R}_T>\tilde{\mathcal{R}}_T$ if $f_T>\tilde{\mathcal{R}}_T$. This analysis

shows that if the transmission potential of TB at the beginning of TB treatment ($\delta = 0$) is greater than the transmission potential when maximum treatment is administered ($\delta \to \infty$), then the expected number of secondary TB infection produced in a population containing TB treated and untreated individuals is lower than that produced in an untreated population. The impact of not administering any form of treatment ($\delta = 0$) on the expected number of infection is greater than the impact resulting from everyone dropping out of treatment ($x \to \infty$) in the sense that $\tilde{\mathcal{R}}_T > \frac{\overline{\kappa} g \tau_* \overline{\tau}_1 (fl+(1-l)z_1)}{(gz_1\overline{z}_2 - fpq)+g\delta\mu}$, where $\frac{\overline{\kappa} g \tau_* \overline{\tau}_1 (fl+(1-l)z_1)}{(gz_1\overline{z}_2 - fpq)+g\delta\mu}$ is the number obtained as $\lim_{x\to\infty} \mathcal{R}_T$.

3.3.3. Bifurcation analysis for TB-only model (2.11)

Center manifold theory has been widely used to completely determine the local dynamics of TB-models with exogeneous re-infection, and it is well known that TB-models with exogeneous re-infection exhibit backward bifurcation (Castillo-Chavez & Song, 2004; Sharomi et al., 2008). We analyze model (2.11) to see if the introduction of the parameter l (fraction of newly-infected individuals with latent TB) and the reinfection parameter τ_r have effect on the expected reinfection-induced backward bifurcation property. Write system (2.11) in the form

$$\frac{dx}{dt} = f(x, \tau_*), \quad f: \mathbb{R}^5 \times \mathbb{R}. \tag{3.20}$$

Choose τ^* to be a bifurcation parameter. Solving the equation $\mathcal{R}_T = 1$ for τ^* gives the solution

$$\tau^* = \frac{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta}{\overline{\kappa} g(\overline{\tau}_1\theta + \overline{\tau}_2\delta)(fl + (1-l)z_1)}.$$

According to Remark 1, the matrix $\overline{\mathcal{A}}$ has a zero eigenvalue if $\mathcal{R}_T = 1$. Let $\mathbf{w}$ and $\mathbf{v}$ be the right and left eigenvectors of $\overline{\mathcal{A}}$ corresponding to the zero eigenvalue. Using Theorem 4.1 of Castillo (Castillo-Chavez & Song, 2004), we wish to show that the numbers

$$\begin{cases} \mathbf{a} &= \sum_{k,i,j=1}^{n} \mathbf{v}_k \mathbf{w}_i \mathbf{w}_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0^T, \tau^*), \\ \mathbf{b} &= \sum_{k,i=1}^{n} \mathbf{v}_k \mathbf{w}_i \frac{\partial^2 f_k}{\partial x_i \partial \tau^*}(P_0^T, \tau^*), \end{cases} \tag{3.21}$$

are positive when evaluated at the disease-free equilibrium.

Computation of $\mathbf{w}$, $\mathbf{v}$, $\mathbf{a}$ *and* $\mathbf{b}$.

It can be shown that the right and left eigenvectors of $\overline{\mathcal{A}}$ corresponding to the zero eigenvalue are

$$\mathbf{w} = \left(\frac{-\tau^* \overline{\kappa} g(\overline{\tau}_1\theta + \overline{\tau}_2\delta)}{\mu(w\delta + p\theta)}, \quad \frac{(1-l)[(qw+gx)\delta + pq\theta] + gl\theta z_2}{(w\delta + p\theta)(fl + (1-l)z_1)}, \quad \frac{g\theta}{w\delta + p\theta}, \quad \frac{g\delta}{w\delta + p\theta}, \quad 1 \right)$$

$$\mathbf{v} = \left(0, \quad \frac{g}{q}, \quad \frac{g}{q}\frac{z_1}{f}, \quad \frac{(gz_1z_2 - fpq)\overline{\tau}_2 + (qw+gx)f\overline{\tau}_1}{fq(\overline{\tau}_1\theta + \overline{\tau}_2\delta)}, \quad 1 \right).$$

Likewise, the numbers $\mathbf{a}$ and $\mathbf{b}$ are obtained as

$$\begin{cases} \mathbf{a} &= 2\mathbf{w}_1\tau^*(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_2 l + \mathbf{v}_3(1-l)) + 2\mathbf{w}_2\mathbf{w}_3\tau^*\tau_r g\overline{z}_1/(qf), \\ \mathbf{b} &= \overline{\kappa}(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_2 l + \mathbf{v}_3(1-l)). \end{cases} \tag{3.22}$$

It follows from Table 1 that $\mathbf{v}_2 l + \mathbf{v}_3(1-l) > 0$ and hence $\mathbf{b} > 0$. We state and prove the following theorems using (3.22).

Theorem 8. *If* $\mathcal{R}_T < 1$ *with* $|\mathcal{R}_T - 1| \ll 1$ *and* $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$, *then the disease-free equilibrium* P_0^T *of* (2.11) *is locally asymptotically stable, and there exists a positive endemic unstable equilibrium.*

proof. *The condition* $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$ *is equivalent to* $\mathbf{a} > 0$. *The proof follows from Theorem* 4.1, *case* 1 *of Castillo* (Castillo-Chavez & Song, 2004). ■

Theorem 9. *Assume* $\tau_r < \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$. *When* $\mathcal{R}_T - 1$ *changes from negative to positive, the disease-free equilibrium point* P_0^T *changes its stability from stable to unstable.*

Proof. *The result follows from Theorem* 4.1, *case iv of Castillo* (Castillo-Chavez & Song, 2004).

The following theorem shows the condition for existence of bifurcation.

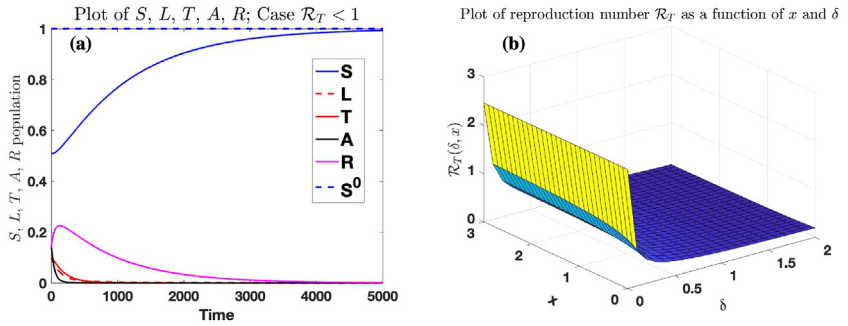

Fig. 6. Graph of (a) the trajectories of S, L, T, A and R for the case where $\mathcal{R}_T < 1$ and (b) effect of TB treatment on the expected number of TB infections.

Table 3
Parameter values for the epidemic model: Case study TB.

Parameter	Description	Default Value	References
Λ	Recruitment rate into the population	0.018year^{-1}	[15, 24]
μ	Natural death rate	Λ	[15, 24]
p	Natural recovery rate of active TB individuals	0.02	
x	Rate of dropping out of TB treatment	0.001	
w	Recovery rate due to TB treatments	0.3	
q	Reinfection rate for recovered TB individuals	0.004	
f	Rate at which latent TB individuals become active	0.03	
δ	Treatment rate for active TB individuals	0.02	
$\overline{\tau}_1$	Infectivity of untreated TB individuals	0.7	
$\overline{\tau}_2$	Reduced TB infectiousness due to TB treatments	0.4	
τ_*	Transmission rate between susceptible and TB infected individuals	0.12	
τ_r	Reinfection rate for latent TB individuals	0.1	

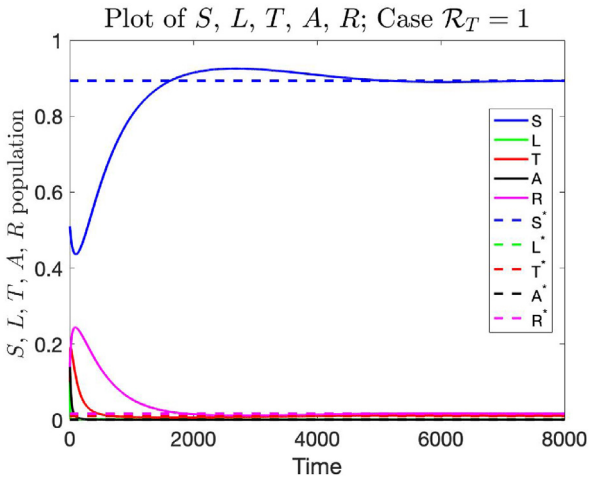

Fig. 7. Graph of the trajectories of S, L, T, A and R for the case where $\mathcal{R}_T = 1$ and $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$.

Theorem 10. *If* $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$, *then backward bifurcation occurs for the TB-only model* (2.11) *if* $\mathcal{R}_T = 1$.

proof. *Clearly,* $\mathbf{b} > 0$. *As discussed earlier, the condition* $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$ *is equivalent to* $\mathbf{a} > 0$. *The proof follows from Theorem* 4.1 *of* (Castillo-Chavez & Song, 2004). ■

3.3.4. Numerical simulation for the TB-only model (2.11)

In this section, we give simulation result for the susceptible, TB infected population satisfying (2.11). The following graphs verify the global stability criteria discussed in Section 3.3. All simulations are carried out using MATLAB R2018a.

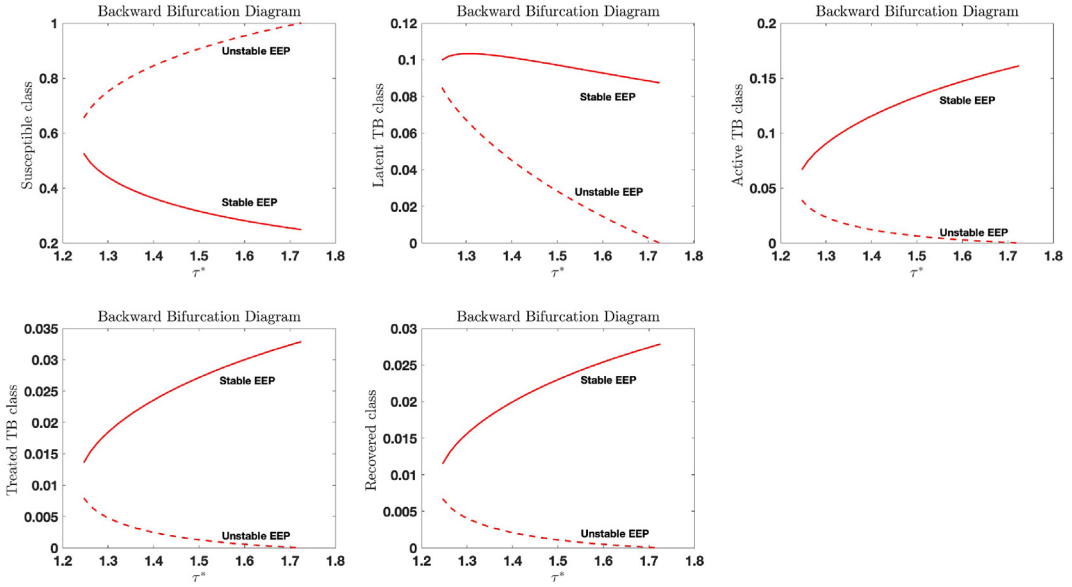

Fig. 8. Bifurcation diagram. Trajectory of the Endemic Equilibrium Points(EEP) of (2.11) as a function of τ^*.

Fig. 6 (a) shows the trajectory of S, L, T, A and R with initial conditions (in percentages) $S_0 = 0.51, L_0 = 0.1, T_0 = 0.1, A_0 = 0.15$, and $R_0 = 0.15$. Parameters' unit are in year^{-1} and the values are given in Table 3. Here, $\mathcal{R}_T = 0.4416$ and disease-free equilibrium $P_0^T = \left(\overline{S}^0 = 1, L^0 = 0, T^0 = 0, A^0 = 0, R^0 = 0\right)^\top$. It confirms that if $\mathcal{R}_T < 1$, then $S(t) \to \overline{\kappa} = 1$, $L(t) \to 0$, $T(t) \to 0$, $A(t) \to 0$, and $R(t) \to 0$ as $t \to \infty$.Fig. 6 (b) shows how the expected number of secondary TB infection changes as a result of changes in the TB treatment rate δ and the treatment drop-out rate x using parameters in Table 3. The result shows that the expected number $\mathcal{R}_T$ of secondary TB infections decreases as the treatment rate increases. Also, dropping out of TB treatment cause the reproduction number $\mathcal{R}_T$ to rise.

Remark 2. **Endemic Equilibrium for the case** $\mathcal{R}_T = 1$.

For the case where $\tau_r > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1}$ and $\mathcal{R}_T = 1$, the unique endemic equilibrium $P_1^T = \{S^*, L^*, T^*, A^*, R^*\}$ of system (2.11) is obtained as

$$
\begin{aligned}
S^* &= \frac{\theta\Lambda(fl + (1-l)z_1)\tau_r((pq - gz_2)\theta + (qw + gx)\delta)}{[(gz_1z_2 - fpq)\theta - (qw + gx)f\delta][(fl + (1-l)z_1)(\theta\tau_1 + \delta\tau_2) - \theta\mu\tau_r]},\\
L^* &= \frac{(fl + (1-l)z_1)(\theta\tau_1 + \delta\tau_2)((pq - gz_2)\theta + (qw + gx)\delta)}{(w\delta + p\theta)(z_1 - f)[(fl + (1-l)z_1)(\theta\tau_1 + \delta\tau_2) - \theta\mu\tau_r]}R^*,\\
T^* &= \mathbf{w}_3 R^*,\\
A^* &= \mathbf{w}_4 R^*,\\
R^* &= \frac{(w\delta + p\theta)\Lambda[(fl + (1-l)z_1)(\theta\tau_1 + \delta\tau_2)((gz_1z_2 - fpq)\theta - (qw + gx)f\delta) + \tau_r\theta\mu(z_1 - f)\{(l-1)(qw\delta + gx\delta + pq\theta) - gl\theta z_2\}]}{\tau_r\theta\mu[(gz_1z_2 - fpq)\theta - (qw + gx)f\delta][qw\delta + gx\delta + pq\theta - g\theta z_2]}.
\end{aligned}
$$

Fig. 7 shows the trajectory of S, L, T, A and R with initial conditions (in percentages) $S_0 = 0.51, L_0 = 0.1, T_0 = 0.1, A_0 = 0.15$, and $R_0 = 0.14$. Parameters' unit are in year^{-1}. We use parameters in Table 3 with $\mu = 0.128$, $\tau_* = 0.2717$, $l = 0.2$, $\tau_r = 60$, $\frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1} = 28.7622$, where $\mathcal{R}_T = 1$ and endemic equilibrium $P_1^T = \left(S^* = 0.8928, L^* = 0.0013, T^* = 0.0106, A^* = 4.9487 \times 10^{-4}, R^* = 0.0164\right)^\top$. In this case, $S(t) \to S^*$, $L(t) \to L^*$, $T(t) \to T^*$, $A(t) \to A^*$, and $R(t) \to R^*$ as $t \to \infty$ if $\mathcal{R}_T = 1$.Fig. 8 shows the trajectory of the Endemic Equilibrium Points (EEP) of (2.11) as a function of τ^* using the parameters $\mu = 0.07; p = 0.02; x = 0.5; w = 0.3; \delta = 0.2; \overline{\tau}_1 = 0.7; \overline{\tau}_2 = 0.3; q = 0.4; l = 0.7; f = 0.001; \tau_r = 2$. In this case, $\tau_r = 2 > \frac{\mathbf{w}_1 qf(\mathbf{w}_3\overline{\tau}_1 + \mathbf{w}_4\overline{\tau}_2)(\mathbf{v}_3(l-1) - \mathbf{v}_2 l)}{\mathbf{w}_2\mathbf{w}_3 g\overline{z}_1} = 0.724316$. We note here that $\tau^* = 1.725$ is equivalent to $R_T = 1$.

From the graph, we note that system (2.11) has two positive endemic equilibrium if $\tau^* < 1.72518$ (or equivalently if $\mathcal{R}_T < 1$) and one positive endemic equilibrium if $\tau^* > 1.72518$ (or equivalently if $\mathcal{R}_T > 1$).

3.4. Analysis of the overall model (2.3)

In this section, we discuss the stability analysis of the disease-free equilibrium P_0 (defined in (A.5)) corresponding to the overall model (2.3).

3.4.1. Stability analysis of the disease-free equilibrium P_0 of model (2.3)

In this subsection, we first analyze the asymptotic stability of the disease-free quilibrium P_0 by linearizing (2.3) about P_0 and later discuss its global stability. By defining

$$\Psi = (S-\overline{\kappa} \quad H_1 \quad \cdots \quad H_n \quad I_1 \quad \cdots \quad I_n \quad C_1 \quad \cdots \quad C_n \quad \overline{C}_1 \quad \cdots \quad \overline{C}_n \quad U_1 \quad \cdots \quad U_n \; L \; T \; C_L \; C_T \; A \; R)^\top, \tag{3.23}$$

the linearization of (2.3) about P_0 is equivalent to

$$d\,\Psi = \Delta\,\Psi\,dt, \tag{3.24}$$

where $\Delta = \mathbf{A}$ as defined in (2.7), with the block matrices $\Delta_{1,1} \equiv \Delta_{1,1}(0)$, $\Delta_{1,2} \equiv \Delta_{1,2}(0,0)$, $\Delta_{2,2} \equiv \Delta_{2,2}(0,0)$ independent of noise intensities. We note here that if $\mathcal{R}_{0,n} < 1$, then $a_1 - \beta h_1 \overline{\kappa} > 0$ and $z_2 - \tau_* \overline{\tau}_1 \overline{\kappa} > 0$. We prove the local asymptotic stability of the disease-free equilibrium P_0 using the idea presented in (Otunuga, 2018) and relations D_{12} and J_{29} in the work of Plemmons (Plemmons, 1977). We shall show that $s(\Delta) < 0$ if $\mathcal{R}_{0,n} < 1$.

Theorem 11. *The disease-free equilibrium P_0 of the model (2.3) is asymptotically stable if $\mathcal{R}_{0,n} < 1$.*

Proof. *Assume $\mathcal{R}_{0,n} < 1$. From the block structure of the matrix Δ, the eigenvalues of Δ are the collections of the eigenvalues of the block matrices $\mathcal{A}$ (defined in (3.3)), $\mathcal{G}_{11}$ and $\mathcal{G}_{22}$. As shown in Theorem 2, all the eigenvalues of $\mathcal{A}$ are negative if $\mathcal{R}_{n,H} < 1$. Likewise, following the same idea in Theorem 6 and the fact that the matrix -$\mathcal{G}_{22} \in Z^4$ is a Z- matrix, it can be shown that the real part of all eigenvalues of $\mathcal{G}_{22}$ is negative if $\mathcal{R}_T < 1$. Lastly, the determinant $\det(\mathcal{G}_{11}) = (-1)^n \prod_{j=1}^{n} (d_j \overline{d}_j e_j - s\eta \overline{d}_j - \overline{s\eta} d_j)$, where $d_j \overline{d}_j e_j - s\eta \overline{d}_j - \overline{s\eta} d_j > 0$ for all $j = 1, 2, \ldots, n$. This shows that $\det(\mathcal{G}_{11})$ is negative (or positive) if the value of n is odd (or even), respectively. Following similar approach in Theorem 2, it follows that the real part of all eigenvalues of $\mathcal{G}_{11}$ is negative. Thus, since $\mathcal{R}_{n,H} \le \mathcal{R}_{0,n}$ and $\mathcal{R}_T \le \mathcal{R}_{0,n}$, it follows that the real part of all eigenvalues of Δ is negative.*

■

3.4.2. Numerical verification of asymptotic stability of equilibrium point for the overall model (2.3)

In this section, we give simulation result for the trajectory of the susceptible, HIV and TB co-infected population satisfying (2.3) using demographical data published in (Birrell et al., 2012; Granich et al., 2009; Hollingsworth et al., 2008; Kretzschmar et al., 2013; The CASCADE Collaboration; Collaborative Group on AIDS, 2000) and estimated parameters. The following graphs verify the global stability criteria discussed in Section 3.4.

Fig. 9 shows the trajectory of H_1, I_1, L, T, C_L, C_T, C_1, $\overline{C}_1$, U_1, A for the case where $\mathcal{R}_{0,1} < 1$. We use the initial conditions (in percentages) $S_0 = 0.36$, $H_{10} = 0.15$, $I_{10} = 0.1$, $T_0 = 0.15$, $C_0 = 0.05$, $C_{10} = 0.03$, $U_{10} = 0.02$, $A_0 = 0.06$, $R_0 = 0.08$. Parameters' unit are in year^{-1} and parameters $\beta = 0.6$, $h_1 = 2.76$, $\mu = 0.026$, $\rho_1 = 1/0.271$, $\epsilon_1 = 0.01$, $\tau_1 = 0.5$, $\phi_1 = 0.7$, $\gamma_1 = 1/8.21$, $\sigma = 0.08$, $\nu_1 = 0.09$, $p = 0.02$, $x = 0.001$, $w = 0.3$, $q = 0.004$, $\delta = 0.1$, $\overline{\tau}_1 = 0.7$, $\overline{\tau}_2 = 0.7$, $\overline{\tau}_3 = 0.7$, $\tau_* = 0.1$, $r_1 = 1/0.4$, $\eta = 0.3$, $s = 0.202$, $\varrho_1 = 1/9.5$, $\varrho_2 = 1/70$, $\psi = 0.07$, $\phi_1 = 2$, $\phi_2 = 0.09$, $e_L = e_T = 0.22$, where $\mathcal{R}_{0,1} = 0.4403$ and disease-free equilibrium $P_0^H = \left(S^0 = 1, H_1^0 = 0, I_1^0 = 0, T^0 = 0, C_L^0 = 0, C_T^0 = 0, C_1^0 = 0, \overline{C}_1^0 = 0, U_1^0 = 0, A^0 = 0, R^0 = 0\right)^\top$. Fig. 9 confirms that if $\mathcal{R}_{0,1} < 1$, then $S(t) \to \overline{\kappa} = 1$, $H_1(t) \to 0$, $I_1(t) \to 0$, $T(t) \to 0$, $C_L^0 \to 0, C_T^0 \to 0$, $C_1(t) \to 0$, $\overline{C}_1(t)$ 0, $U_1(t) \to 0$, $A(t) \to 0$, and $R(t) \to 0$ as $t \to \infty$.

3.5. Stability of disease-free equilibrium P_0 of (2.1)

In this section, we analyze the noise influenced population (2.1) based on the results derived in Sections (3.1), (3.3), and (3.4).

Theorem 12. *The real part of all eigenvalues of $\mathbf{A}$ is negative if $\mathbf{R}_{0,n} < 1$.*

Proof. *The result follows from Theorem 11 by replacing $\overline{\kappa}\beta h_1$ with $\overline{\kappa}\beta h_1 + \sigma_{h,1}^2 \overline{\kappa}^2 \beta^2/2$ and $\tau_* \tau_1 \overline{\kappa}$ with $\tau_* \tau_1 \overline{\kappa} + (1-l)\tau_*^2 \overline{\kappa}^2 \sigma_{\tau,n+3}^2/2$.*

Theorem 13. *The trivial solution $\Phi = 0$ of (2.7) is asymptotically stable in probability in the feasible region $\mathcal{Y}$ if $\mathbf{R}_{0,n} < 1$.*

proof. *A similar proof is given in Otunuga* (Otunuga, 2018, 2020).■

Theorem 14. *The disease-free equilibrium P_0 of the system* (2.1) *is asymptotically stable in probability in the feasible region $\mathcal{Y}$ if* $\mathbf{R}_{0,n} < 1$.

To prove this, we show that Theorem 7.1 of Khasminskii (Rafail, 2012, p. 66) is satisfied. Let f and g be the drift and diffusion coefficients, respectively, of (2.7), and F and G be the drift and diffusion coefficients, respectively, of the system derived by substituting Φ into (2.1).

Proof. Assume $\mathbf{R}_{0,n} < 1$. It follows from Theorem 14 that the trivial solution $\Phi = 0$ of (2.7) is asymptotically stable in probability. Following Theorem 6.2 of Otunuga (Otunuga, 2020), it can be shown that in a sufficiently small neighborhood of $\Phi = 0$, there exists a sufficiently small constant $\varepsilon > 0$ such that

$$\|F(t,\Phi) - f(t,\Phi)\| + \|G(t,\Phi) - g(t,\Phi)\| < \epsilon\|\Phi\|.$$

The proof follows from Theorem 7.1 of Khasminskii (Rafail, 2012, p. 66). ■.

3.5.1. Conditions for short-time disease outbreak

In this section, we seek conditions under which small perturbations to the disease-free equilibrium P_0 can initially grow. Assume

$$\begin{cases} 1 \le \mathbf{R}_{n,H} < 1 + \dfrac{1}{2}\left(\dfrac{b_1\sigma_1^2\beta^2\bar{\kappa}^2}{a_1b_1 - \tau_1\phi_1}\right), \quad \text{and} \\ \\ 1 \le \mathbf{R}_T < 1 + \dfrac{1}{2}\dfrac{g\bar{\kappa}^2\tau_*^2\theta(1-l)\sigma_{\tau,n+3}^2(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta} \end{cases} \tag{3.25}$$

or equivalently,

$$\begin{cases} 1 - \dfrac{1}{2}\left(\dfrac{b_1\sigma_{h,1}^2\beta^2\bar{\kappa}^2}{a_1b_1 - \tau_1\phi_1}\right) \le \mathcal{R}_{n,H} < 1, \quad \text{and} \\ \\ 1 - \dfrac{1}{2}\dfrac{g\bar{\kappa}^2\tau_*^2\theta(1-l)\sigma_{\tau,n+3}^2(fl + (1-l)z_1)}{(gz_1z_2 - fpq)\theta - (qw + gx)f\delta} \le \mathcal{R}_T < 1 \end{cases} \tag{3.26}$$

Equation (3.25) shows a condition for epidemic growth as a result of noise, while equation (3.26) shows that the epidemic growth occurs initially, with the growth caused by perturbations in the transmission rates of HIV-only and TB-only infected untreated individuals with noise intensities $\sigma_{h,1}$ and $\sigma_{\tau,n+3}$, respectively.

3.5.2. Numerical verification of stability of disease-free equilibrium point for model (2.1)

In this section, we give simulation results for the susceptible, HIV/AIDS & TB infected population satisfying the stochastic model (2.1) using demographical data presented in Section 3.4.2. Numerical simulations are carried out using the composite

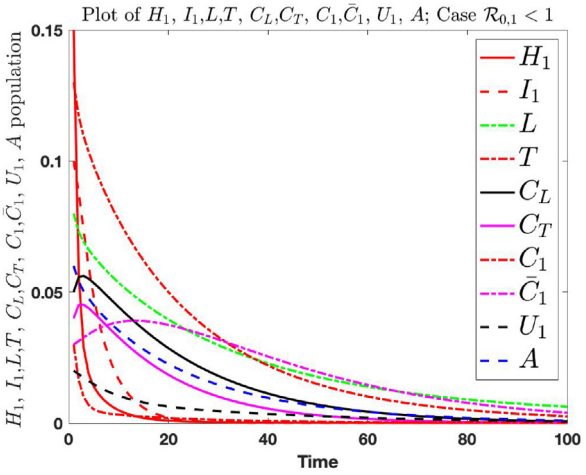

Fig. 9. Graph of the trajectories of H_1, I_1, L, T, C, C_L, C_T, C_1, $\overline{C}_1$, U_1, A for case $\mathcal{R}_{0,1} < 1$.

Euler method (a combination of the semi-implicit Euler and the Implicit Euler method). The following graphs verify the stochastic asymptotic stability criteria discussed in Section 3.5.

We use the initial conditions and parameters presented in Subsection 3.4.2 with noise intensities $\sigma_{h,1} = 0.3$, $\sigma_{h,2} = 0.21$, $\sigma_{h,3} = 0.23$, where $\mathbf{R}_{0,2} = 0.9611$. Fig. 10 ((**a**)- (**b**)) and 11 ((**a**)- (**b**)) confirm that if $\mathbf{R}_{0,n} < 1$, $n = 1$ and $n = 2$, respectively, then $S(t) \to \overline{\kappa} = 1$ and $H_k(t) \to 0$, $I_k(t) \to 0$, $T(t) \to 0$, $C(t) \to 0$, $C_k(t) \to 0$, $U_k(t) \to 0$, $A(t) \to 0$, $R(t) \to 0$ as $t \to \infty$, for $k = 1, 2$. We use the initial conditions and parameters presented in Fig. 11 with noise intensities $\sigma_{h,1} = 0.5$, $\sigma_{h,2} = 0.3$, $\sigma_{h,3} = 0.23$, where $\mathcal{R}_{1,H} = 0.4403$, $\mathcal{R}_{2,H} = 0.8540$, $\mathcal{R}_T = 0.7160$, $\mathcal{R}_{0,1} = 0.7160$, $\mathcal{R}_{0,2} = 0.8540$, $\mathbf{R}_{1,H} = 0.4735$, $\mathbf{R}_{2,H} = 0.9204$, $\mathbf{R}_T = 1.3436$, $\mathbf{R}_{0,1} = \mathbf{R}_{0,2} = 1.3436$. These results suggest that there is epidemic advances caused by noise intensity in the transmission rate of TB disease. These advances can be seen in the trajectories of the functions T, C, A, U_1, U_2, H_2.

Fig. 12 ((**a**)- (**b**)) confirm that if $\mathcal{R}_{0,2} < 1$ and $\mathbf{R}_{0,2} > 1$, there will be transient epidemic advances, even if $S(t) \to \overline{\kappa} = 1$ and $H_k(t) \to 0$, $I_k(t) \to 0$, $T(t) \to 0$, $C(t) \to 0$, $C_k(t) \to 0$, $U_k(t) \to 0$, $A(t) \to 0$, $R(t) \to 0$ as $t \to \infty$, for $k = 1, 2$.

4. Discussion

In this paper, we present a deterministic and stochastic HIV/AIDS & Tuberculosis epidemic model describing the co-infection of HIV/AIDS and Tuberculosis diseases between individuals susceptible to both HIV and TB, infected with HIV but not receiving any kind of treatment (and in stage/phase $k = 1, \ldots, n$ of infection), HIV infected individuals under the Anti-retroviral treatment (and in stage/phase $k = 1, \ldots, n$ of infection), TB infected untreated individuals susceptible to HIV, TB infected individuals under TB treatment, individuals who recovered from TB with temporal immunity, individuals co-infected with HIV and TB, individuals co-infected with HIV and TB and undergoing different phases of TB treatment, and individuals infected with HIV and TB undergoing HIV treatment and different phases of TB treatment. We also considered the effect of noise/perturbations in the transmission rate of the diseases. We are particularly interested in how the diseases are transmitted at various stages of the disease and phases of treatment and the effect of noise and treatments on the long-term behavior of the population. We obtain the basic deterministic reproduction numbers for the models containing HIV-only, TB-only, and HIV-TB co-infection population in (2.10), (2.11) and (2.3), respectively. By studying the reproduction number of the general model containing the entire population, our analysis shows that there are no impact of treating co-infected populations on $\mathcal{R}_{0,n}$. In order to study the effect of the ART (and TB) treatments, we derive the basic reproduction numbers, $\tilde{\mathcal{R}}_{n,H}$ (and $\tilde{\mathcal{R}}_T$), derived from the HIV-only (and TB-only) model in the absence of treatments. Our result confirms that the transmission potential of HIV (and TB) in a population under treatment is lower than the transmission potential in an untreated population if the number of secondary infection produced by a typical infected individual under the treatment is lower than the number of secondary infection produced by a typical infected individual receiving no treatment in the

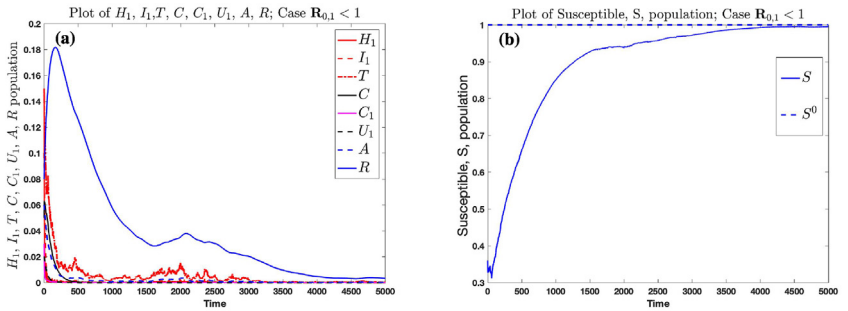

Fig. 10. Graph of the stochastic trajectories of S, H_1, I_1, T, C, C_1, U_1, A and R for the cases where $\mathbf{R}_{0,1} < 1$.

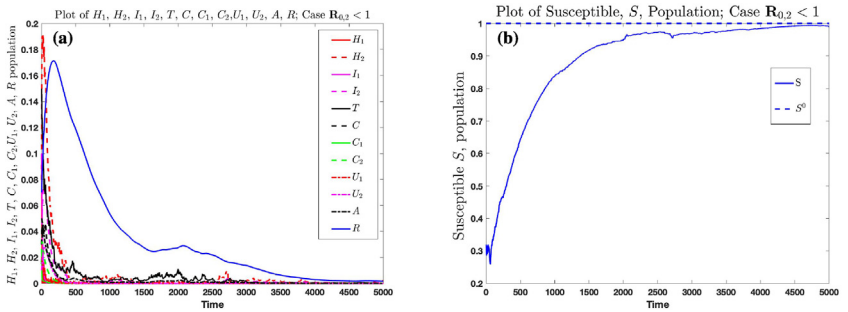

Fig. 11. Graph of the stochastic trajectories of S, H_j, I_j, T, C, C_j, U_j, A and R for $j = 1, 2$, for the case where $\mathbf{R}_{0,2} < 1$.

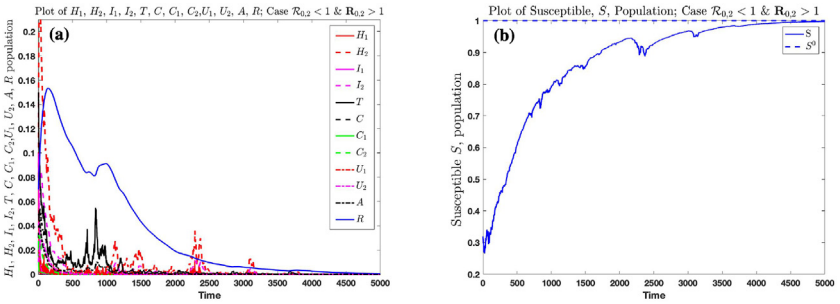

Fig. 12. Graph of the stochastic trajectories of S, H_j, I_j, T, C, C_j, U_j, A and R for $j = 1, 2$, for the case where $\mathcal{R}_{0,2} < 1$ and $\mathbf{R}_{0,2} > 1$.

population. We discuss the stability of the disease-free and endemic equilibrium by showing that if the reproduction number $\mathcal{R}_{n,H} \leq 1$ ($\mathcal{R}_T \leq 1$), the disease-free equilibrium derived from the HIV-only (TB-only) model is globally asymptotically stable in the feasible region. Likewise, we show that extinction occurs if the disease-free equilibrium corresponding to (2.3) is globally stable, given the threshold $\mathcal{R}_{0,n} \leq 1$. Also, we further show that if $\mathcal{R}_{n,H} > 1$ ($\mathcal{R}_T > 1$), the endemic equilibrium derived from HIV-only (TB-only) model is globally asymptotically stable. Similar result is shown for the case where noise is present in the transmission rates of the HIV/AIDS and TB diseases. We show that even if $\mathcal{R}_{0,n} < 1$ and $\mathbf{R}_{0,n} > 1$, there will be transient epidemic advances in the population. Numerical results are carried out to verify our claim using demographical data published in (Birrell et al., 2012; Granich et al., 2009; Hollingsworth et al., 2008; Kretzschmar et al., 2013; The CASCADE Collaboration; Collaborative Group on AIDS, 2000).

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CRediT authorship contribution statement

Olusegun Michael Otunuga: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors have no competing interests to declare that are relevant to the content of this article.

Appendix A. Reproduction numbers for HIV-only and TB-only infected populations for model (2.3)

Appendix A.1. Basic reproduction number, $\mathcal{R}_{0,n}$, for model (2.3)

In this section, we derive an expression for the basic reproduction number, $\mathcal{R}_{0,n}$, corresponding to (2.3) using the next-generation matrix method. We define $\mathcal{R}_{0,n}$ as the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual (Diekmann, Heesterbeek, & Metz, 1990; Driessche & Watmough, 2002). Since individuals can be infected with either HIV or TB, then, in order to derive the expression for $\mathcal{R}_{0,n}$, we first find the expression for the basic reproduction numbers $\mathcal{R}_{n,H}$, and $\mathcal{R}_T$ corresponding to the sub-models of (2.3) involving population infected with HIV only and TB only, respectively.

Appendix A.1.1. Basic reproduction number $\mathcal{R}_{n,H}$

The sub-model of (2.3) involving the presence of HIV disease only is given by (2.10).

We note here that system (2.10) is an extension of model (2.3) discussed in the work of Otunuga (2018) (Otunuga, 2018) since the reduced infectivities $\epsilon_k, j = 1, 2, \ldots, n$, the treatment rates $\tau_k, j = 1, 2, \ldots, n$ and treatment dropout rates $\phi_k, j = 1, 2, \ldots, n$ may vary. Here, we define the basic reproduction number $\mathcal{R}_{n,H}$ corresponding to model (2.10) as the expected number of secondary cases produced, in a completely susceptible population receiving treatment, by a typical HIV infective individual only (Diekmann et al., 1990). We consider model (2.10) in the feasible region $\mathcal{Y}^H$ in (3.5) with $N_H = S + \sum_{j=1}^{n} (H_j + I_j)$. The model (2.10) has disease-free equilibrium P_0^H given in (3.1). In the presence of Antiretroviral Therapy (ART) treatments, we derive the reproduction number $\mathcal{R}_{n,H}$ with respect to (2.10) using the next-generation matrix (Driessche & Watmough, 2002). Following

the work of Otunuga (2018) (Otunuga, 2018) and Otunuga (2020) (Otunuga, 2020), the reproduction number $\mathcal{R}_{n,H}$ is obtained as

$$\mathcal{R}_{n,H} = \overline{\kappa}\beta \sum_{k=1}^{n} \left[\frac{u_k h_k + \epsilon_k v_k}{\prod_{j=1}^{k} \left(a_j b_j - \tau_j \phi_j \right)} \right],$$

where u_k and v_k satisfy

$$\begin{cases} u_k = b_k \rho_{k-1} u_{k-1} + \phi_k \gamma_{k-1} v_{k-1}, \\ v_k = \tau_k \rho_{k-1} u_{k-1} + a_k \gamma_{k-1} v_{k-1}, \quad \text{for } k = 1, 2, \ldots, n, \end{cases}$$

and $\rho_0 = 1$; $u_0 = 1$; $\gamma_0 = 1$ and $v_0 = 0$. We note here that $a_j b_j - \tau_j \phi_j = (\mu + \rho_j) b_j + \tau_j (\mu + \gamma_j) > 0$ for $j = 1, 2, \ldots, n$.

Remark 3. Reproduction number in the absence of treatment

We also note here that if there are no HIV infected individual receiving treatment with respect to model (2.10), that is, if $\tau_k = 0 \ \forall \ k = 1, \ldots, n$, then model (2.10) reduces to

$$\begin{aligned} dS &= \left(\Lambda - \beta S \sum_{j=1}^{n} h_j H_j - \mu S \right) dt, \quad S(t_0) = S_0, \\ dH_1 &= \left(\beta S \sum_{j=1}^{n} h_j H_j - (\mu + \rho_1) H_1 \right) dt, \quad H_1(t_0) = H_{01}, \\ dH_k &= \left(\rho_{k-1} H_{k-1} - (\mu + \rho_k) H_k \right) dt, \quad H_k(t_0) = H_{0k}. \end{aligned} \tag{A.1}$$

and $u_k = \prod_{j=1}^{k} (b_j \rho_{j-1})$ for $k = 1, 2, \ldots, n$. In this case, the basic reproduction number $\mathcal{R}_{n,H}$ reduces to

$$\tilde{\mathcal{R}}_{n,H} = \overline{\kappa}\beta \sum_{r=1}^{n} \left[h_r \prod_{j=1}^{r} \left(\frac{\rho_{j-1}}{\mu + \rho_j} \right) \right]. \tag{A.2}$$

This is the expected number of secondary infection produced by a typical untreated infected individual when introduced into a population consisting of susceptible individuals only.

Appendix A.1.2. Basic reproduction number $\mathcal{R}_T$ for the TB-only model

The sub-model of (2.3) involving the presence of TB disease only is given by (2.11). Here, we define the basic reproduction number $\mathcal{R}_T$ corresponding to model (2.11) as the number of TB infections produced by an active TB case. We consider model (2.11) in the feasible region $\mathcal{Y}^T$ described in (3.16). The model (2.11) has disease-free equilibrium

$$P_0^T := \{S^0, L^0, T^0, A^0, R^0\} = \{\overline{\kappa}, 0, 0, 0, 0\}. \tag{A.3}$$

For the next-generation matrix, we consider equations corresponding to the infected compartments T, and A. The nonnegative matrix, $\mathcal{F}$, and nonsingular matrix, $\mathcal{V}$, corresponding to the new infections in the population (evaluated at the disease-free equilibrium P_0^T with respect to (2.11)) and the transfer of individuals in and our of compartment, respectively, are given by

$$\mathcal{F} = \tau_* \overline{\kappa} \begin{pmatrix} 0 & \overline{\tau}_1 l & \overline{\tau}_2 l & 0 \\ 0 & \overline{\tau}_1 (1-l) & \overline{\tau}_2 (1-l) & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad \mathcal{V} = \begin{pmatrix} z_1 & 0 & -x & -q \\ -f & z_2 & 0 & 0 \\ 0 & -\delta & \theta & 0 \\ 0 & -p & -w & g \end{pmatrix}, \tag{A.4}$$

It follows that the spectral radius, $\mathcal{R}_T$, of the next generation matrix $\mathcal{F}\mathcal{V}^{-1}$ is given by

$$\mathcal{R}_T = \frac{\overline{\kappa} g \tau_* (\overline{\tau}_1 \theta + \overline{\tau}_2 \delta)(fl + (1-l) z_1)}{(g z_1 z_2 - fpq)\theta - (qw + gx) f \delta}.$$

It is easy to show that $(g z_1 z_2 - fpq)\theta - (qw + gx) f\delta > 0$ using Table 1.

Appendix A.1.3. The overall basic reproduction number $\mathcal{R}_{0,n}$ corresponding to (2.3)

Here, we derive the expression for the basic reproduction number, $\mathcal{R}_{0,n}$, corresponding to (2.3). The model (2.3) has disease-free equilibrium

$$P_0 := \left\{S^0, H_1^0, \ldots, H_n^0, I_1^0, \ldots, I_n^0, C_1^0, \ldots, C_n^0, \overline{C}_1^0, \ldots, \overline{C}_n^0, U_1^0, \ldots, U_n^0, L^0, T^0, C_L^0, C_T^0, A^0, R^0\right\} = \{\overline{\kappa}, 0_{1\times 5n+6}\}. \tag{A.5}$$

Define $d_j, \overline{d}_j, \theta$, and $e_j, j = 1, 2, \ldots, n$ as in Table 1. For any vectors $\mathbf{x}, \mathbf{y} \in \mathbb{R}^n$ and scalar $c \in \mathbb{R}$, define the matrices $M^{\mathbf{x},\mathbf{y}}$, $\mathcal{I}_{\mathbf{x}}$, and $\mathcal{I}_x$ as in (2.6). Let $\mathbf{h}$ and $\boldsymbol{\epsilon}$ be the vectors $\mathbf{h} = (\,h_1 \quad h_2 \quad \cdots \quad h_n\,)$ and $\boldsymbol{\epsilon} = (\,\epsilon_1 \quad \epsilon_2 \quad \cdots \quad \epsilon_n\,)$, respectively. The non negative matrix, F, and nonsingular matrix, V, corresponding to the new infections in the population (evaluated at the disease-free equilibrium P_0) and the transfer of individuals in and our of compartment, respectively, are given by

$$F = \begin{pmatrix} F_{11} & F_{12} & F_{13} \\ 0_{3n\times 2n} & 0_{3n\times 3n} & 0_{3n\times 6} \\ 0_{6\times 2n} & F_{3,2} & F_{33} \end{pmatrix}, \quad V = \begin{pmatrix} V_{11} & 0_{2n\times 3n} & 0_{2n\times 6} \\ 0_{3n\times 2n} & V_{22} & V_{23} \\ 0_{6\times 2n} & 0_{6\times 3n} & V_{33} \end{pmatrix}, \tag{A.6}$$

where $F_{11} = \beta\overline{\kappa}\begin{pmatrix} \mathbf{h} & \boldsymbol{\epsilon} \\ 0_{2n-1\times 2n} & 0_{2n-1\times 2n} \end{pmatrix}$, $F_{12} = \beta\overline{\kappa}\begin{pmatrix} \phi_1 & \cdots & \phi_n & \overline{\phi}_1 & \cdots & \overline{\phi}_n & \sigma & \cdots & \sigma \\ 0 & \ldots & 0 & 0 & \ldots & 0 & 0 & \ldots & 0 \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ 0 & \ldots & 0 & 0 & \ldots & 0 & 0 & \ldots & 0 \end{pmatrix}_{2n\times 3n}$,

$$F_{13} = \beta\overline{\kappa}\begin{pmatrix} 0 & 0 & v_1 & v_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \vdots & \ddots & \ddots & \vdots & & \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}_{2n\times 6},$$

$$F_{32} = \tau_*\overline{\kappa}\phi\begin{pmatrix} \phi_1 l & \cdots & \phi_n l & \overline{\phi}_1 l & \cdots & \overline{\phi}_n l & \sigma l & \cdots & \sigma l \\ \phi_1(1-l) & \cdots & \phi_n(1-l) & \overline{\phi}_1(1-l) & \cdots & \overline{\phi}_n(1-l) & \sigma(1-l) & \cdots & \sigma(1-l) \\ 0 & \cdots & 0 & 0 & \cdots & 0 & 0 & \cdots & 0 \\ \vdots & \cdots & \vdots & \vdots & \cdots & \vdots & \vdots & \cdots & \vdots \\ 0 & \cdots & 0 & 0 & \cdots & 0 & 0 & \cdots & 0 \end{pmatrix}_{6\times 3n},$$

$$F_{33} = \tau_*\overline{\kappa}\begin{pmatrix} 0 & \overline{\tau}_1 l & 0 & \overline{\tau}_3 l & \overline{\tau}_2 l & 0 \\ 0 & \overline{\tau}_1(1-l) & 0 & \overline{\tau}_3(1-l) & \overline{\tau}_2(1-l) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}_{6\times 6}, \quad V_{11} = -\begin{pmatrix} M^{\boldsymbol{\rho},\mathbf{a}} & \mathcal{I}_{\boldsymbol{\phi}} \\ \mathcal{I}_{\boldsymbol{\tau}} & M^{\boldsymbol{\gamma},\mathbf{b}} \end{pmatrix}, \quad V_{22} = -\begin{pmatrix} M^{\mathbf{r},\mathbf{d}} & 0_{n\times n} & \mathcal{I}_s \\ 0_{n\times n} & M^{\overline{\mathbf{e}},\overline{\mathbf{d}}} & \mathcal{I}_{\overline{s}} \\ \mathcal{I}_\eta & \mathcal{I}_{\overline{\eta}} & M^{\mathbf{e},\mathbf{e}} \end{pmatrix}$$

defined in (2.6), $V_{23} = \mathcal{G}_{12}$ defined in (2.7), $V_{33} = \begin{pmatrix} z_1 & 0 & 0 & 0 & -x & -q \\ -f & z_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & d_L & 0 & 0 & 0 \\ 0 & 0 & 0 & d_T & 0 & 0 \\ 0 & -\delta & 0 & 0 & \theta & 0 \\ 0 & -p & 0 & 0 & -w & g \end{pmatrix}$. The next generation matrix FV^{-1} is of the form

$$FV^{-1} = \begin{pmatrix} G^H & G^{HT} & G^{TH} \\ 0_{3n\times 2n} & 0_{3n\times 3n} & 0_{3n\times 6} \\ 0_{6\times 2n} & F_{32}V_{22}^{-1} & G^T \end{pmatrix} \tag{A.7}$$

where $G^H = F_{11}V_{11}^{-1}$, $G^{HT} = F_{12}V_{22}^{-1}$, $G^{TH} = (F_{13} - F_{12}V_{22}^{-1}V_{23})V_{33}^{-1}$, and $G^T = (F_{33} - F_{32}V_{22}^{-1}V_{23})V_{33}^{-1}$ are $2n\times 2n$, $2n\times 3n$, $2n\times 6$, and 6×6 matrices, respectively. Since the next generation matrix FV^{-1} has G^H (generation matrix for HIV-only matrix), a zero matrix and G^T (generation matrix for TB-only matrix) in its block diagonal entries, it follows directly that the spectral radius, $\mathcal{R}_{0,n}$, of the next generation matrix FV^{-1} in (A.7) is given by

$$\mathcal{R}_{0,n} = \max\{\mathcal{R}_{n,H}, \mathcal{R}_T\}. \tag{A.8}$$

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