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Global stability for a $2n + 1$ dimensional HIV/AIDS epidemic model with treatments[+]

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Abstract

In this work, we derive and analyze a $2n+1$-dimensional deterministic differential equation modeling the transmission and treatment of HIV (Human Immunodeficiency Virus) disease. The model is extended to a stochastic differential equation by introducing noise in the transmission rate of the disease. A theoretical treatment strategy of regular HIV testing and immediate treatment with Antiretroviral Therapy (ART) is investigated in the presence and absence of noise. By defining $R_{0,n}$, $R_{t,n}$ and $\mathcal{R}_{t,n}$ as the deterministic basic reproduction number in the absence of ART treatments, deterministic basic reproduction number in the presence of ART treatments and stochastic reproduction number in the presence of ART treatment, respectively, we discuss the stability of the infection-free and endemic equilibrium in the presence and absence of treatments by first deriving the closed form expression for $R_{0,n}$, $R_{t,n}$ and $\mathcal{R}_{t,n}$. We show that there is enough treatment to avoid persistence of infection in the endemic equilibrium state if $R_{t,n} = 1$. We further show by studying the effect of noise in the transmission rate of the disease that transient epidemic invasion can still occur even if $R_{t,n} < 1$. This happens due to the presence of noise (with high intensity) in the transmission rate, causing $\mathcal{R}_{t,n} > 1$. A threshold criterion for epidemic invasion in the presence and absence of noise is derived. Numerical simulation is presented for validation.

Keywords: Susceptible; Infection; Treatment; HIV; Stochastic model; Stability; Reproduction number

1. Introduction

HIV and AIDS remain a persistent problem for the United States and countries around the world. According to a report by the Center for Disease Control and Prevention, (CDC), [3] " HIV disease continues to be a serious health

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issue for parts of the world. Worldwide, there were about 1.8 million new cases of HIV in 2016. About 36.7 million people were living with HIV around the world in 2016, and 19.5 million of them were receiving medicines to treat HIV, called antiretroviral therapy (ART). An estimated 1 million people died from AIDS-related illnesses in 2016. Sub-Saharan Africa, which bears the heaviest burden of HIV and AIDS worldwide, accounts for about 64% of all new HIV infections. Other regions significantly affected by HIV and AIDS include Asia and the Pacific, Latin America and the Caribbean, and Eastern Europe and Central Asia." Without treatment of HIV/AIDS with Antiretrovial medicine, HIV infection advances into several stages and individuals with AIDS typically survive about 3 years [3]. The stages and phases of HIV/AIDS starts with the primary infection stage (the stage where an individual first become infected with HIV virus), the Seroconversion illness stage (the stage where individual develop symptoms before the appearance of antibodies to HIV in the blood), the Seroconversion stage (the stage where HIV replicates rapidly and build up HIV anti-bodies), the window period (the time it takes for a person who has been infected with HIV to produce antibodies to the virus), the asymptomatic infection stage (the period after testing positive for HIV), the symptomatic infection stage (the period the immune system becomes weakened by HIV), the advanced HIV disease (AIDS) stage, and so on [2].

Although it is currently known that there is no cure for HIV infection, the ART treatment only help individuals with HIV from advancing to the next stage of the infection, thereby making them to live longer and reducing the risk of transmission. According to the United States Department of Health and Human Services [23], without proper or any antiretroviral therapy (ART), most HIV-infected individuals will eventually develop progressive immunodeficiency marked by CD4 T lymphocyte (CD4) cell depletion and leading to AIDS-defining illnesses and premature death. The primary goal of ART is to prevent HIV-associated morbidity and mortality. Proper stages of the ART administration must be followed to maximally inhibit HIV replication and sustain plasma HIV-1 RNA (viral load) below limits of quantification. This shows the need to study how to reduce the disease infection or eliminate the transmission of the disease by studying different stages of the disease, especially from high endemic countries.

Several mathematical models [6, 7, 8, 9, 11, 15, 17, 20, 22] have been developed in order to understand the disease transmission as well as to discuss the impact of treatment/intervention strategies and also discuss conditions under which transmission rate is eliminated. In this paper, we discuss transmission and treatment of the HIV/AIDS by constructiong a deterministic and stochastic differential equation describing progression of susceptible populations through n stages of infection and treatments, and uptake and dropping out of treatments. We note here that the deterministic model described in this work is the extension of the work of Granich et al. [7] and Kretzschmar et al. [15]. We analyze the dynamics of the epidemic model when the transmission rate displays Gaussian white noise fluctuations around its mean value. The effects of fluctuations on dynamics of epidemics have been widely explored in the work of Hattaf et al. (2018) [8], Horsthemke et al. [10], Keeling et al. [12], Mendez et al. [18] and Tornatore et al. [22]. According to the work of Mendez et al. [18], demographic noise or internal fluctuations are due to the discrete nature of the constituents of the system (in this case, the susceptible and infected individuals). External noise appears multiplicatively in our model and it is able to modify the mean dynamical behavior of the population [10, 18]. We assume, following the argument mabe by Mendez et al. that external fluctiations may be caused by variability in the number of contacts between infected and susceptible individuals and such random variations can be modeled by a white noise [18].

The paper is organized as follows.

In Section 2, we present a deterministic HIV epidemic model describing the transmission and spread of HIV as well as its treatment. In Section 3, the existence and stability of the equilibrium points in the absence of Antiretroviral treatments are analyzed. In Section 4, we discuss the existence and stability of the equilibrium points in the presence of Antiretroviral treatments. In Section 5, we present a Stratonovich stochastic HIV epidemic model by allowing the transmission rates to fluctuate around a mean value. The Stratonovich model is now converted into its Itô version. We also analyze the stability of the infection-free equilibrium and discuss threshold criterion for epidemic invasion in the presence and absence of noise. In Section 6, numerical simulation is presented to support our claim. The conclusion of the work is given in Section 7.

2. Deterministic Model

In order to study the transmission and spread of HIV/AIDS, as well as its treatments, we formulate a model which subdivides the total population, $N(t)$, at time t, into susceptible population, S, infected untreated population, I_k, in stage k of the infection, and the population T_k of infected individuals under the Antiretroviral treatment in stage k of infection, for $k = 1, 2, ..., n$. We formulate the deterministic model governing S, I_k, T_k, $k = 1, 2, ..., n$, as follows:

$$\begin{aligned} dS &= \left(\beta - \lambda S \sum_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) - \mu S\right) dt, \quad S(t_0) = S_0, \\ dI_1 &= \left(\lambda S \sum_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) - (\mu + \rho_1 + \tau) I_1 + \phi T_1\right) dt, \quad I_1(t_0) = I_{01}, \\ dI_k &= (\rho_{k-1} I_{k-1} - (\mu + \rho_k + \tau) I_k + \phi T_k)\ dt, \quad I_k(t_0) = I_{0k}, \\ dT_1 &= (\tau I_1 - (\mu + \gamma_1 + \phi) T_1) dt, \quad T_1(t_0) = T_{01}, \\ dT_k &= (\tau I_k + \gamma_{k-1} T_{k-1} - (\mu + \gamma_k + \phi) T_k)\ dt, \quad T_k(t_0) = T_{0k}, \end{aligned} \tag{2.1}$$

for $k = 2, ..., n$, where $\mu > 0$ is the mortality rate, ρ_k and γ_k, $k = 1, 2, ..., n$, are transition rates per year from stage k to stage $k + 1$ for untreated and treated individuals, respectively, τ and ϕ are rates per year of moving from untreated to treated population, and from treated to untreated population, respectively, ϵ quantifies the reduced infectiousness due to ART treatment, h_k is the infectivity of untreated individuals in stage k of infection per year, λ is the rate of transmission between susceptible and infected individuals and $\beta > 0$ is the recruitment into the population.

Since the population size $N = S + \sum_{j=1}^{n}(I_j + T_j)$, it follows from (2.1) that N satisfies the equation

$$dN = (\beta - \mu N - \rho_n I_n - \gamma_n T_n)\, dt, \tag{2.2}$$

and $\limsup_{t\to\infty} N(t) \leq \beta/\mu$. Hence, we consider model (2.1) in the feasible region

$$\mathcal{T} := \left\{ (S, I_1, ..., I_n, T_1, ..., T_n)^T \in \mathbb{R}_+^{2n+1} \ : \ 0 \leq S + \sum_{j=1}^{n}(I_j + T_j) = N \leq \frac{\beta}{\mu} \right\}, \tag{2.3}$$

where $\mathbb{R}_+$ denotes nonnegative real number. It can be shown that $\mathcal{T}$ is positively invariant with respect to (2.1). We can make the sizes S, I_k and T_k, $k = 1, 2, ..., n$ into percentages by setting $\beta = \mu$.

3. Existence and stability of equilibrium points without treatments

In this section, we discuss the existence and stability of equilibrium points without the introduction of Antiretroviral treatments in the system. Define

$$\begin{cases} \bar{a}_k &= \mu + \rho_k, \\ \bar{b}_k &= \mu + \gamma_k, \\ \bar{\kappa} &= \beta/\mu. \end{cases} \tag{3.1}$$

We write (2.1) (in the absence of Antiretroviral treatments) using the next-generation matrix [6] as

$$d\bar{\mathbf{x}} = (\mathcal{F}(\bar{\mathbf{x}}) - \mathcal{V}(\bar{\mathbf{x}}))\ dt, \tag{3.2}$$

where $\bar{\mathbf{x}} = \begin{pmatrix} I_1 \\ \vdots \\ I_n \\ S \end{pmatrix}$, $\mathcal{F} = \begin{pmatrix} \lambda S \sum_{j=1}^{n} h_j I_j \\ 0 \\ \vdots \\ 0 \\ 0 \end{pmatrix}$, $\mathcal{V} = \begin{pmatrix} \bar{a}_1 I_1 \\ \bar{a}_2 I_2 - \rho_1 I_1 \\ \vdots \\ \bar{a}_n I_n - \rho_{n-1} I_{n-1} \\ \lambda S \sum_{j=1}^{n} h_j I_j + \mu S - \beta \end{pmatrix}$.

We define the infection-free and endemic equilibrium points derived from untreated population by $P_0 = \begin{pmatrix} S^0 & I_1^0 & \dots & I_n^0 \end{pmatrix}^T$ and $P_1 = \begin{pmatrix} S^* & I_1^* & \dots & I_n^* \end{pmatrix}^T$, respectively. We will later give the closed form expression for P_0 and P_1 and also discuss their stability.

3.1. Infection-free equilibrium, P_0, and basic reproduction number, $R_{0,n}$, in the absence of treatments

The infection-free equilibrium P_0 of (3.2) is given by

$$P_0 = \left(S^0 = \bar{\kappa}, I_1^0 = 0, ..., I_n^0 = 0\right)^T .$$

Here, we derive an expression for the deterministic basic reproduction number, $R_{0,n}$, corresponding to (3.2). We define the basic reproduction number as the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual [5, 6]. The $n+1 \times n+1$ Jacobian matrices $D\,\mathcal{F}(P_0) = \left(\frac{\partial \mathcal{F}_i}{\partial \bar{\mathbf{x}}_j}\right)$ and $D\,\mathcal{V}(P_0) = \left(\frac{\partial \mathcal{V}_i}{\partial \bar{\mathbf{x}}_j}\right)$ of $\mathcal{F}$ and $\mathcal{V}$ in (3.2) evaluated at P_0 are partitioned as $D\,\mathcal{F}(P_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}$ and $D\,\mathcal{V}(P_0) = \begin{pmatrix} V & 0 \\ J_1 & J_2 \end{pmatrix}$, respectively, where F, V, J_1 and J_2 are given by $F = \lambda\bar{\kappa}\begin{pmatrix} h_1 & h_2 & \dots & h_n \\ 0 & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & 0 \end{pmatrix}$ and $V = \begin{pmatrix} \bar{a}_1 & 0 & 0 & 0 & \dots & 0 & 0 \\ -\rho_1 & \bar{a}_2 & 0 & 0 & \dots & 0 & 0 \\ 0 & -\rho_2 & \bar{a}_3 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \dots & \dots & -\rho_{n-1} & \bar{a}_n \end{pmatrix}$, $J_1 = \lambda\bar{\kappa}\begin{pmatrix} h_1 & h_2 & \dots & h_n \end{pmatrix}$, $J_2 = \mu$, respectively. It follows that the spectral radius, $R_{0,n}$, of the matrix FV^{-1} is given by

$$R_{0,n} = \lambda\bar{\kappa}\sum_{r=1}^{n} h_r \prod_{j=1}^{r}\left(\frac{\rho_{j-1}}{\mu + \rho_j}\right), \tag{3.3}$$

where $\rho_0 = 1$. Here, $\frac{1}{\mu+\rho_j}$ is the average duration of the infectious period at stage j, $\frac{\rho_{j-1}}{\mu+\rho_{j-1}}$ is the fraction of humans that will progress from the infectious stage $j-1$ to j, and $\lambda\bar{\kappa}h_r \prod_{j=1}^{r} \frac{\rho_{j-1}}{\mu+\rho_j}$ is the number of new infections produced by a typical individual during the time it spends in the r-th infectious stage. We see here that the reproduction number, $R_{0,n}$, depends on the transmission rate λ, the background mortality rate, μ, the recruitment rate, β, and the total infectiousness (unless the population is in percentage, in which case, $\bar{\kappa} = 1$ and the reproduction number only depends on the transmission rate and the total infectiousness).

3.1.1. Stability analysis of P_0 in the absence of Antiretroviral treatments

In this subsection, we first analyze the asymptotic stability of the infection-free quilibrium by linearizing (3.2) about P_0. We later discuss the global stability of P_0. By defining

$$\mathbf{u} = \begin{pmatrix} S - \bar{\kappa} & I_1 & I_2 & \dots & I_n \end{pmatrix}^T, \tag{3.4}$$

the linearization of (3.2) about P_0 is equivalent to

$$d\,\mathbf{u} = \mathbf{\Lambda}\,\mathbf{u}\,dt, \quad \mathbf{u}(t_0) = \mathbf{u}_0, \tag{3.5}$$

where $\mathbf{\Lambda} = \begin{pmatrix} -\mu & -\lambda\bar{\kappa}h_1 & -\lambda\bar{\kappa}h_2 & -\lambda\bar{\kappa}h_3 & -\lambda\bar{\kappa}h_4 & \dots & -\lambda\bar{\kappa}h_{n-1} & -\lambda\bar{\kappa}h_n \\ 0 & -\bar{\nu} & \lambda\bar{\kappa}h_2 & \lambda\bar{\kappa}h_3 & \lambda\bar{\kappa}h_4 & \dots & \lambda\bar{\kappa}h_{n-1} & \lambda\bar{\kappa}h_n \\ 0 & \rho_1 & -\bar{a}_2 & 0 & 0 & \dots & 0 & 0 \\ 0 & 0 & \rho_2 & -\bar{a}_3 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & \dots & \dots & \rho_{n-1} & -\bar{a}_n \end{pmatrix}$ and $\bar{\nu} = \bar{a}_1 - \lambda\bar{\kappa}h_1$. By rewriting $R_{0,n} = 1 - \frac{\bar{\nu}}{\bar{a}_1} + \lambda\bar{\kappa}\sum_{k=2}^{n} h_k \prod_{j=1}^{k} \frac{\rho_{j-1}}{\bar{a}_j}$, it follows directly that $\bar{\nu} > 0$ if $R_{0,n} < 1$.

Let r be an eigenvalue of $\mathbf{\Lambda}$. The characteristic polynomial of $\mathbf{\Lambda}$ can be written as

$$det(\mathbf{\Lambda} - rI_{n+1,n+1}) = -(r+\mu)\;\; det(\bar{\mathbf{\Lambda}} - r\mathcal{I}), \tag{3.6}$$

where $I_{n+1,n+1}$ and $\mathcal{I}$ are $n+1 \times n+1$ and $n \times n$ identity matrix, respectively, $\bar{\mathbf{\Lambda}}$ is the minor of the entry $\mathbf{\Lambda}_{1,1}$ in (3.5).

We prove the asymptotic stability of the infection-free equilibrium P_0 using relations D_{12} and J_{29} in the work of Plemmons [19]. Let $s(A)$ denotes the maximum real part of all eigenvalues of a matrix A. We shall show that $s\left(\bar{\mathbf{\Lambda}}\right) < 0$ if $R_{0,n} < 1$.

Definition 1. Let Z^n be the set of all $n \times n$ square matrix A with $a_{ij} \leq 0$ if $1 \leq i \neq j \leq n$. We call a matrix $A \in Z^n$ a Z-matrix.

Theorem 1. *The solution $\boldsymbol{u}(t) = 0$ of the system (3.5) is locally asymptotically stable if $R_{0,n} < 1$, stable if $R_{0,n} = 1$ and unstable if $R_{0,n} > 1$.*

Proof. In order to show the stability of the solution $\mathbf{u}(t) = 0$ of the system (3.5), we need to show that $s\left(\bar{\mathbf{\Lambda}}\right) < 0$ if $R_{0,n} < 1$.

Let $B = -\bar{\mathbf{\Lambda}}$. It is clear that $B \in Z^n$ is a Z-matrix. Also, we can write B in the form

$$B = \mathbf{LU}, \tag{3.7}$$

where $\mathbf{L}$ and $\mathbf{U}$ are upper and lower diagonal matrices, respectively, with positive diagonals. A rigorous computation of $\mathbf{L}$ and $\mathbf{U}$ gives

$$\mathbf{L}_{i,j} = \frac{1}{D_j}\begin{vmatrix} B_{1,1} & B_{1,2} & \dots & B_{1,j} \\ B_{2,1} & B_{2,2} & \dots & B_{2,j} \\ \vdots & \vdots & \dots & \vdots \\ B_{j-1,1} & B_{j-1,2} & \dots & B_{j-1,j} \\ B_{i,1} & B_{i,2} & \dots & B_{i,j} \end{vmatrix}, \text{ for } i \geq j \neq 1, \ \mathbf{L}_{i,1} = \frac{|B_{i,1}|}{D_1}, \text{ for } i = 1,2,...,n, \text{ and } 0 \text{ elsewhere,}$$

$$\mathbf{U}_{i,j} = \frac{1}{D_{j-1}}\begin{vmatrix} B_{1,1} & \dots & B_{1,i-1} & B_{1,j} \\ B_{2,1} & \dots & B_{2,i-1} & B_{2,j} \\ \vdots & \vdots & \vdots & \vdots \\ B_{i,1} & \dots & B_{i,i-1} & B_{i,j}, \end{vmatrix}, \text{ for } 1 \neq i \leq j, \ \mathbf{U}_{1,j} = B_{1,j}, \text{ for } j = 1,2,...,n, \text{ and } 0 \text{ elsewhere,}$$

where $D_0 := 1$, and $D_j = \begin{vmatrix} B_{1,1} & B_{1,2} & \dots & B_{1,j} \\ B_{2,1} & B_{2,2} & \dots & B_{2,j} \\ \vdots & \vdots & \dots & \vdots \\ B_{j,1} & B_{j,2} & \dots & B_{j,j} \end{vmatrix}$ for $j = 1,2,...,n$, and $|.|$ denotes determinant of matrix.

Clearly, $\mathbf{L}_{j,j} = 1$ for $j = 1,2,...,n$. If $R_{0,n} < 1$, then the diagonal $\mathbf{U}_{j,j} = \frac{D_j}{D_{j-1}} = \bar{a}_j\left(\frac{1-R_{0,j}}{1-R_{0,j-1}}\right) > 0$ for $j = 1,2,...,n$. It follows from relations D_{12} and J_{29} in [19], equation (3.7) and the fact that $\mathbf{L}_{j,j} > 0$, $\mathbf{U}_{j,j} > 0$, $j = 1,2,...,n$, that the real part of each eigenvalue of B is positive, which is equivalent to $s\left(\bar{\mathbf{\Lambda}}\right) < 0$. If $R_{0,n} = 1$, then $r = 0$ is one of the eigenvalues of $\bar{\mathbf{\Lambda}}$ since $det(\bar{\mathbf{\Lambda}}) = D_n = (1 - R_{0,n})\prod_{j=1}^{n}\bar{a}_j = 0$. If $R_{0,n} > 1$, then $det(\bar{\mathbf{\Lambda}}) < 0$. If r_1, r_2,..., r_n are eigenvalues of $\bar{\mathbf{\Lambda}}$, then $det(\bar{\mathbf{\Lambda}}) = \prod_{j=1}^{n} r_j < 0$ irrespective of whether n is even or odd. Hence, $\bar{\mathbf{\Lambda}}$ must have at least one positive eigenvalue. ■

Remark 1. We note here that the stability of the solution $\mathbf{u}(t) = 0$ of the system (3.5) is equivalent to the stability of the infection-free equilibrium P_0.

Remark 2. The characteristic polynomial of $\bar{\mathbf{\Lambda}}$ can be written in the form

$$det(\bar{\mathbf{\Lambda}} - r\mathcal{I}) = \sum_{i=0}^{n} c_i r^{n-i}, \tag{3.8}$$

where $c_0 = (-1)^n$,

$$\begin{aligned}
c_1 &= (-1)^n \left[\bar{a}_1(1 - R_{0,1}) + \sum_{i=2}^{n} \bar{a}_i \right] = (-1)^n \mathrm{trace}(\bar{\mathbf{\Lambda}}),\\
c_n &= (-1)^n (1 - R_{0,n}) \prod_{j=1}^{n} \bar{a}_j,\\
c_i &= (-1)^n \left[\prod_{j=1}^{i} \bar{a}_j (1 - R_{0,i}) + \sum_{k=1}^{i} \prod_{j=0}^{i-k} \bar{a}_j \left\{ \sum_{\substack{l_1,l_2,\dots,l_k=i-k+2\\ l_1\neq l_2,\neq\dots,\neq l_k}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_k} \right\} (1 - R_{0,i-k}) \right], \quad i = 2, 3, \dots, n,
\end{aligned}$$

and $\bar{a}_0 = 1$, $R_{0,0} = 0$. If $R_{0,n} < 1$, then $R_{0,i} \leq R_{0,n} < 1$ for $i = 1, 2, \dots, n$. Hence, all coefficients c_i, $i = 0, 1, 2, \dots, n$, are of the same sign. By Descartes' rule of sign, the matrix $\bar{\mathbf{\Lambda}}$ has no real positive eigenvalue. If $R_{0,n} = 1$, then $R_{0,j} < 1$ for all $j = 1, 2, \dots, n-1$, $c_n = 0$ and $\lambda = 0$ is one of the eigenvalues.

We will now investigate the global stability of the infection-free equilibrium P_0 in the feasible region $\mathcal{T}$.

Theorem 2. *The infection-free equilibrium P_0 is globally stable in the feasible region $\mathcal{T}$ if $R_{0,n} \leq 1$.*

Proof. Consider the Lyapunov function $V : \mathbb{R}^+_{n+1} \to \mathbb{R}^+$ defined by

$$V(S, I_1, I_2, \dots, I_n) = \left(S - S^0 - S^0 \ln \frac{S}{S^0} \right) + \sum_{k=1}^{n} \omega_k I_k,$$

where $\mathbb{R}^+$ is the set of positive real numbers and

$$\begin{aligned}
\omega_1 &= 1,\\
\omega_{k+1} &= \left(\prod_{j=1}^{k} \frac{\bar{a}_j}{\rho_j} \right) (1 - R_{0,k}), \quad \text{for } k = 1, 2, \dots, n-1.
\end{aligned}$$

It can be shown that $\omega_k \bar{a}_k - \omega_{k+1}\rho_k - \lambda S^0 h_k = 0$ for $k = 1, 2, \dots, n-1$ and $\omega_n \bar{a}_n - \lambda S^0 h_n = \left(\prod_{j=1}^{n} \frac{\bar{a}_j}{\rho_{j-1}} \right) (1 - R_{0,n}) \geq 0$ if $R_{0,n} \leq 1$. Also, if $R_{0,n} \leq 1$, then the derivative of V with respect to t along the solutions of (3.2) is given by

$$\begin{aligned}
\frac{dV}{dt} &= \beta + \mu S^0 - \beta S^0/S - \mu S + (\omega_1 - 1)\lambda S \sum_{k=1}^{n} h_k I_k - \sum_{k=1}^{n-1} \left(\omega_k \bar{a}_k - \omega_{k+1}\rho_k - \lambda S^0 h_k \right) I_k - \left(\omega_n \bar{a}_n - \lambda S^0 h_n \right) I_n\\
&\leq -\beta \left(\frac{S^0}{S} + \frac{S}{S^0} - 2 \right)\\
&\leq 0,
\end{aligned}$$

using the fact that $S^0 = \bar{\kappa} = \beta/\mu$ and $1 = \left(\frac{S^0}{S} \frac{S}{S^0} \right)^{1/2} \leq \frac{1}{2} \left(\frac{S^0}{S} + \frac{S}{S^0} \right)$ (arithmetic mean of a list of nonnegative real numbers is greater than or equal to the geometric mean of the same set [21]). If $R_{0,n} < 1$, then $\frac{dV}{dt} = 0$ if and only if $S = S^0$ and $I_n = 0$. If $R_{0,n} = 1$, then $\frac{dV}{dt} = 0$ if and only if $S = S^0$. In either case, since the equilibrium point $P_0 = P_1$ if $R_{0,n} = 1$ (this fact is shown in the next subsection), it can be easily verified that the largest invariant set of (3.2) contained in the set $\{(S, I_1, \dots, I_n)^T \in \mathcal{T} \; : \; dV/dt = 0\}$ is the singleton $\{P_0\}$. The global stability of P_0 follows from the LaSalle invariance principle [16]. ■

3.2. Existence and stability of endemic equilibrium, P_1, in the absence of treatment

The endemic equilibrium $P_1 = \left(S^*, I_1^*, ..., I_n^*\right)^T$ of the system (3.2) is given by

$$\begin{cases} S^* &= \frac{\bar{\kappa}}{R_{0,n}}, \\ I_k^* &= \beta\left(\prod_{j=1}^{k} \frac{\rho_{j-1}}{\bar{a}_j}\right)\left(1 - \frac{1}{R_{0,n}}\right), \quad k = 1, 2, ..., n. \end{cases} \tag{3.9}$$

It follows directly that the endemic equilibrium, P_1, converges to the infection-free equilibrium, P_0, as $R_{0,n}$ tends to 1.

Remark 3. We show here that S^* and I_k^*, for $k = 1, 2, ..., n$, are in the feasible region, $\mathcal{T}$, whenever they exist (that is, whenever $R_{0,n} > 1$). It is easy to show from (3.9) that $\beta - \mu S^* = \bar{a}_1 I_1^*$ and $\sum_{k=1}^{n-1} \rho_k I_k^* = \sum_{k=2}^{n} \bar{a}_k I_k^*$. Therefore, $\mu \sum_{k=2}^{n-1} I_k^* = \rho_1 I_1^* - \bar{a}_n I_n^*$ and $\mu\left(S^* + I_1^* + \sum_{k=2}^{n-1} I_k^*\right) = \beta - \bar{a}_n I_n^*$. Also, if $R_{0,n} > 1$, then $S^* > 0$, $I_k^* > 0$ for all $k = 1, 2, ..., n$. Hence, $0 < S^* + \sum_{k=1}^{n-1} I_k^* = \bar{\kappa} - \frac{\bar{a}_n}{\mu} I_n^* < \bar{\kappa}$.

The following theorems show the existence and global stability of the endemic equilibrium P_1.

Theorem 3. *The endemic equilibrium P_1 of (3.2) exists if and only if $R_{0,n} > 1$, and does not exist if $R_{0,n} \leq 1$, with the case $P_1 = P_0$ if $R_{0,n} = 1$.*

Proof. The proof follows directly from (3.9) and Remark 3. ■.

The following lemma will be useful in proving the global stability of the endemic equilibrium, P_1.

Lemma 4. *Define the sequence $\{z_k\}_1^n$ and $\{m_k\}_1^n$ by*

$$\begin{cases} z_1 &= 1, \\ z_{k+1} &= \left(\prod_{j=1}^{k} \frac{\bar{a}_j}{\rho_j}\right) - \lambda S^* \sum_{r=2}^{k} \frac{h_{r-1}}{\rho_{r-1}} \left(\prod_{j=r}^{k} \frac{\bar{a}_j}{\rho_j}\right) - \lambda S^* \frac{h_k}{\rho_k}, \quad for \ \ k = 1, 2, ..., n-1, \end{cases} \tag{3.10}$$

and

$$\begin{cases} m_1 &= \beta - \rho_1 z_2 I_1^*, \\ m_k &= \rho_{k-1} z_k I_{k-1}^* - \rho_k z_{k+1} I_k^*, \quad for \ \ k = 2, ..., n-1, \\ m_n &= \rho_{n-1} z_n I_{n-1}^*, \\ C &= \sum_{k=1}^{n} (k+1) m_k. \end{cases} \tag{3.11}$$

If $R_{0,n} > 1$, then $\{z_k\}_1^n$ and $\{m_k\}_1^n$ are positive sequences.

Proof. Assume $R_{0,n} > 1$. We know from (3.2) that S^* and I_k^* satisfy

$$\begin{cases} \beta - \mu S^* &= \bar{a}_1 I_1^*, \\ \rho_{k-1} I_{k-1}^* &= \bar{a}_k I_k^*, \quad \text{for} \ \ k = 2, ..., n. \end{cases} \tag{3.12}$$

By substituting (3.9) and (3.12) into (3.10), it follows from Remark 3 that (3.10) and (3.11) reduce to

$$\begin{cases} z_1 &= 1, \\ z_{k+1} &= \left(\prod_{j=1}^{k} \frac{\bar{a}_j}{\rho_j}\right)\left(1 - \frac{R_{0,k}}{R_{0,n}}\right) > 0, \ k = 1, 2, ..., n-1, \\ z_n &= \lambda S^* \frac{h_n}{\bar{a}_n} > 0, \end{cases} \tag{3.13}$$

and

$$\begin{cases} m_1 &= S^* \left(\mu + \lambda h_1 I_1^*\right), \\ m_k &= \lambda S^* h_k I_k^*, \ \text{ for } k = 2, ..., n, \\ C &= \beta + \mu S^* + \sum_{k=1}^{n} \bar{a}_k z_k I_k^*. \end{cases} \tag{3.14}$$

■

Theorem 5. *The endemic equilibrium P_1 of the system (3.2) is globally stable in the feasible region if $R_{0,n} > 1$.*

Proof. Assume $R_{0,n} > 1$. Define the Lyapunov function $V^* : \mathbb{R}^+_{n+1} \to \mathbb{R}^+$ by

$$V^*(S, I_1, ..., I_n) = \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + \sum_{k=1}^{n} \bar{z}_k \left(I_k - I_k^* - I_k^* \ln \frac{I_k}{I_k^*}\right), \tag{3.15}$$

where $\bar{z}_k$, $k = 1, 2, ..., n$ are positive constants. We shall show that $\bar{z}_k = z_k$, $k = 1, 2, ..., n$ as defined in (3.10) and (3.13). It follows from the fact that $c - \ln c > 1$ for $c > 0$ that $V^*(S, I_1, ..., I_n) > 0$ if $R_{0,n} > 1$. Define

$$y_0 = \frac{S}{S^*}, \ \ y_k = \frac{I_k}{I_k^*}, \ \text{ for } k = 1, 2, ..., n.$$

The derivative of V^* computed along solutions of the system (3.2) is given by

$$\begin{aligned} \frac{dV^*}{dt} &= C + (\bar{z}_1 - 1)\lambda S^* y_0 \sum_{k=1}^{n} h_k I_k^* y_k - S^*(\mu + \lambda h_1 \bar{z}_1 I_1^*) y_0 - \frac{\beta}{y_0} - \sum_{k=1}^{n-1} (\bar{a}_k \bar{z}_k - \lambda S^* h_k - \rho_k \bar{z}_{k+1}) I_k^* y_k \\ &\quad - (\bar{a}_n \bar{z}_n - \lambda S^* h_n) I_n^* y_n - \sum_{k=2}^{n} \rho_{k-1} \bar{z}_k I_{k-1}^* \frac{y_{k-1}}{y_k} - \lambda S^* \bar{z}_1 \sum_{k=2}^{n} h_k I_k^* \frac{y_0 y_k}{y_1}. \end{aligned}$$

By setting $\bar{z}_1 - 1 = 0$, $\bar{a}_k \bar{z}_k - \lambda S^* h_k - \rho_k \bar{z}_{k+1} = 0$ for $k = 1, 2, ..., n-1$, and $\bar{a}_n \bar{z}_n - \lambda S^* h_n = 0$, it follows that $0 < \bar{z}_k = z_k$ defined in (3.10) and (3.13) for $k = 1, 2, ..., n$ if $R_{0,n} > 1$. Hence

$$\begin{aligned} \frac{dV^*}{dt} &= C - S^*(\mu + \lambda h_1 z_1 I_1^*) y_0 - \frac{\beta}{y_0} - \sum_{k=2}^{n} \rho_{k-1} z_k I_{k-1}^* \frac{y_{k-1}}{y_k} - \lambda S^* z_1 \sum_{k=2}^{n} h_k I_k^* \frac{y_0 y_k}{y_1}, \\ &= -m_1 \left(y_0 + \frac{1}{y_0} - 2\right) - \sum_{k=2}^{n} m_k \left(\frac{1}{y_0} + \frac{y_0 y_k}{y_1} + \sum_{j=2}^{k} \frac{y_{j-1}}{y_j} - (k+1)\right), \end{aligned}$$

where C and m_k, $k = 1, 2, ..., n$ satisfy (3.11) and (3.14).

Using the fact that the arithmetic mean of a list of non-negative real numbers is greater than or equal to the geometric mean of the same list [21], we have $1 = \left(y_0 \frac{1}{y_0}\right)^{\frac{1}{2}} \leq \frac{1}{2}\left(y_0 + \frac{1}{y_0}\right)$ and $1 = \left(\frac{1}{y_0} \frac{y_0 y_k}{y_1} \prod_{j=2}^{k} \frac{y_{j-1}}{y_j}\right)^{\frac{1}{k+1}} \leq \frac{1}{k+1}\left(\frac{1}{y_0} + \frac{y_0 y_k}{y_1} + \sum_{j=2}^{k} \frac{y_{j-1}}{y_j}\right)$ for $k = 2, ..., n$. Equality holds if and only if $y_0 = 1$ and $y_{k-1} = y_k$ for $k = 2, ..., n$. Therefore,

$$\frac{dV^*}{dt} \leq 0,$$

and equality holds if and only if $y_0 = 1$ and $y_{k-1} = y_k$, that is, $S = S^*$, $I_{k-1}/I^*_{k-1} = I_k/I^*_k$ for $k = 2, ..., n$. It can be easily verified that the largest invariant set of (3.2) contained in the set $\{(S, I_1, ..., I_n)^T \in \mathcal{T} \ : \ dV^*/dt = 0\} = \{(S, I_1, ..., I_n)^T \in \mathcal{T} \ : \ S = S^*, I_{k-1}/I^*_{k-1} = I_k/I^*_k, \ k = 2, ..., n\}$ is the singleton $\{P_1\}$. By the LaSalle's Invariance Principle [16], it follows that P_1 is globally stable in the feasible region. ∎

Remark 4. Define $\mathbf{u}^* = \begin{pmatrix} S - S^* & I_1 - I_1^* & I_2 - I_2^* & \dots & I_n - I_n^* \end{pmatrix}^T$. The linearization of (3.2) about the endemic equilibrium P_1 is equivalent to

$$d\,\mathbf{u}^* = \mathbf{A}^*\,\mathbf{u}^*\,dt, \ \ \mathbf{u}^*(t_0) = \mathbf{u}^*_0, \tag{3.16}$$

where $\mathbf{A}^* = \begin{pmatrix} -\left(\mu + \lambda \sum_{k=1}^{n} h_k I_k^*\right) & -\lambda h_1 S^* & -\lambda h_2 S^* & -\lambda h_3 S^* & -\lambda h_4 S^* & \dots & -\lambda h_{n-1} S^* & -\lambda h_n S^* \\ \lambda \sum_{k=1}^{n} h_k I_k^* & -\bar{\bar{\nu}} & \lambda h_2 S^* & \lambda h_3 S^* & \lambda h_4 S^* & \dots & \lambda h_{n-1} S^* & \lambda h_n S^* \\ 0 & \rho_1 & -\bar{a}_2 & 0 & 0 & \dots & 0 & 0 \\ 0 & 0 & \rho_2 & -\bar{a}_3 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & \dots & \dots & \rho_{n-1} & -\bar{a}_n \end{pmatrix}$ and $\bar{\bar{\nu}} = \bar{a}_1 - \lambda h_1 S^*$. Clearly, $\bar{\bar{\nu}} = \bar{a}_1 \left(1 - \frac{R_{0,1}}{R_{0,n}}\right) \geq 0$.

We give the closed form expression for the characteristic polynomial of $\mathbf{A}^*$. Let $\bar{r}$ be eigenvalue of $\mathbf{A}^*$, then

$$det(\mathbf{A}^* - \bar{r}\mathcal{I}_{n+1,n+1}) = \sum_{i=0}^{n+1} c_i^* \bar{r}^{n+1-i} \tag{3.17}$$

where $\mathcal{I}_{n+1,n+1}$ is a $n+1 \times n+1$ identity matrix; $c_0^* = 1$,

$$\begin{aligned}
c_1^* &= \left(\sum_{k=1}^{n} \bar{a}_k\right) + \mu + \lambda\left(\sum_{k=1}^{n} h_k I_k^*\right) - \lambda h_1 S^* = \left(\sum_{k=2}^{n} \bar{a}_k\right) + \mu R_{0,n} + \bar{a}_1\left(1 - \frac{R_{0,1}}{R_{0,n}}\right) = -\text{trace}(\mathbf{A}^*), \\
c_{n+1}^* &= \left(\prod_{j=1}^{n} \bar{a}_j\right) \sum_{k=1}^{n} \lambda h_k I_k^* = det(\mathbf{A}^*), \\
c_i^* &= \left(\sum_{\substack{l_1,l_2,\dots,l_i=1 \\ l_1 \neq l_2 \neq \dots \neq l_i}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_i}\right) + \left(\mu + \lambda \sum_{k=1}^{n} h_k I_k^*\right)\left(\sum_{\substack{l_1,l_2,\dots,l_{i-1}=1 \\ l_1 \neq l_2 \neq \dots \neq l_{i-1}}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_{i-1}}\right) \\
&\quad - \left\{\sum_{k=1}^{i-1} \lambda h_k S^* \left(\left(\sum_{\substack{l_1,l_2,\dots,l_{i-k}=k+1 \\ l_1 \neq l_2 \neq \dots \neq l_{i-k}}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_{i-k}}\right) + \mu\left(\sum_{\substack{l_1,l_2,\dots,l_{i-k-1}=k+1 \\ l_1 \neq l_2 \neq \dots \neq l_{i-k-1}}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_{i-k-1}}\right)\right)\prod_{j=0}^{k-1} \rho_j\right\} - \lambda h_i S^* \prod_{j=0}^{i-1} \rho_j, \quad i = 2, 3, \dots, n.
\end{aligned}$$

If $R_{0,n} > 1$, then it follows from (3.9) that $c_1^* > 0$, $c_i^* > \left(\sum_{\substack{l_1,l_2,\dots,l_i=2 \\ l_1 \neq l_2 \neq \dots \neq l_i}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_i}\right) + \mu R_{0,n}\left(\sum_{\substack{l_1,l_2,\dots,l_{i-1}=2 \\ l_1 \neq l_2 \neq \dots \neq l_{i-1}}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}\dots\bar{a}_{l_{i-1}}\right)$ for

$i = 2,3,...,n-1$, $c_n^* > \mu(R_{0,n}-1)\left(\sum_{\substack{l_1,l_2,...,l_{n-2}=2 \\ l_1\neq l_2,\neq ...,\neq l_{n-2}}}^{n} \bar{a}_{l_1}\bar{a}_{l_2}...\bar{a}_{l_{n-2}}\right)\bar{a}_1 + \mu R_{0,n}\prod_{j=2}^{n}\bar{a}_j$ and $c_{n+1}^* > 0$. Hence, all coefficients c_j^*, $j = 0,...,n+1$ are positive. Therefore, by Descartes' rule of sign, all real eigenvalues of $\mathbf{A}^*$ are nonpositive. If $R_{0,n} = 1$, then $c_{n+1}^* = 0$ and $\bar{r} = 0$ is an eigenvalue of $\mathbf{A}^*$.

Remark 5. We briefly describe the stability of the epidemic equilibrium $\left(S^*, I_1^*\right)$ for the case $n = 1$ graphically using Figure 1 below.

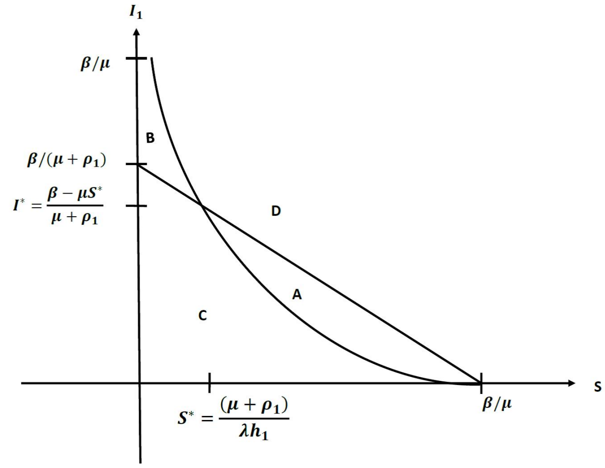

Figure 1: Graph of $I_1 = \frac{\beta-\mu S}{\lambda h_1 S}$ and $I_1 = \frac{\beta-\mu S}{\mu+\rho_1}$

In region A, $\frac{\beta-\mu S}{\lambda h_1 S} \leq I_1 \leq \frac{\beta-\mu S}{\mu+\rho_1}$ and $\frac{\mu+\rho_1}{\lambda h_1} \leq S \leq \frac{\beta}{\mu}$, $0 \leq I_1 \leq I_1^*$. So, $dS/dt = \beta - \mu S - \lambda h_1 S I_1 < 0$ and $dI_1/dt = \lambda h_1 S I_1 - (\mu+\rho_1)I_1 > 0$. Therefore , we have $R_{0,1} > 1$, S is decreasing and I_1 is increasing in region A.

In region B, $\frac{\beta-\mu S}{\mu+\rho_1} < I_1 < \frac{\beta-\mu S}{\lambda h_1 S}$, $0 < S \leq \frac{\mu+\rho_1}{\lambda h_1}$ and $I_1^* \leq I_1 \leq \frac{\beta}{\mu}$. So, $dS/dt > 0$ and $dI_1/dt < 0$. Therefore , we have $R_{0,1} > 1$, S is increasing and I_1 is decreasing in region B. Hence, the point $P_1 = \left(S^*, I_1^*\right)^T$ is a locally stable equilibrium point.

4. Existence and stability of equilibrium points in the presence of Antiretroviral treatments

In this section, we discuss the existence and stability of equilibrium points of (2.1) while ART treatment is introduced into the system. We define the infection-free and endemic equilibrium points of (2.1) by

$$\begin{aligned}
\bar{P}_0 &= \left(\bar{S}^0 \quad \bar{I}_1^0 \quad \ldots \quad \bar{I}_n^0 \quad \bar{T}_1^0 \quad \ldots \quad \bar{T}_n^0\right)^T, \\
\bar{P}_1 &= \left(\bar{S}^* \quad \bar{I}_1^* \quad \ldots \quad \bar{I}_n^* \quad \bar{T}_1^* \quad \ldots \quad \bar{T}_n^*\right)^T,
\end{aligned}$$

respectively. It follows from (2.1) that

$$\bar{S}^0 = \bar{\kappa}, \ \ \bar{I}_j^0 = 0, \ \ \bar{T}_j^0 = 0, \ \ j = 1, 2, ..., n. \tag{4.1}$$

We shall denote the reproduction number in the presence of treatment by $R_{t,n}$ and call it the elimination threshold parameter. This parameter will be used to quantify the level of treatment above which infection can no longer persist in the endemic steady state. We shall use the idea in Section 3.1 to find the closed form expression for $R_{t,n}$ and show that it convey significant amount of insight. We shall solve for the closed form expression for the endemic equilibrium, $\bar{P}_1$, in terms of $R_{t,n}$ and show that if $R_{t,n} = 1$, then there is enough treatment to avoid persistent of infection in the endemic equilibrium state (that is, $\bar{P}_1 = \bar{P}_0$).

4.1. Elimination threshold quantity, $R_{t,n}$, in the presence of treatments.

In the presence of treatments, we write (2.1) using the next-generation matrix [6] in the form

$$d\bar{\bar{\mathbf{x}}} = (\mathcal{F}(\bar{\bar{\mathbf{x}}}) - \mathcal{V}(\bar{\bar{\mathbf{x}}})) \ dt, \tag{4.2}$$

where $\bar{\bar{\mathbf{x}}} = \begin{pmatrix} I_1 \\ \vdots \\ I_n \\ T_1 \\ \vdots \\ T_n \\ S \end{pmatrix}$, $\mathcal{F} = \begin{pmatrix} \lambda S \sum_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) \\ 0 \\ \vdots \\ 0 \\ 0 \end{pmatrix}$, $\mathcal{V} = \begin{pmatrix} a_1 I_1 - \phi T_1 \\ a_2 I_2 - \rho_1 I_1 - \phi T_2 \\ \vdots \\ a_n I_n - \rho_{n-1} I_{n-1} - \phi T_n \\ b_1 T_1 - \tau I_1 \\ b_2 T_2 - \tau I_2 - \gamma_1 T_1 \\ \vdots \\ b_n T_n - \tau I_n - \gamma_{n-1} T_{n-1} \\ \lambda S \sum_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) + \mu S - \beta \end{pmatrix}$.

The $2n+1 \times 2n+1$ Jacobian matrices $D\,\mathcal{F}\left(\bar{P}_0\right) = \left(\frac{\partial \mathcal{F}_i}{\partial \bar{\mathbf{x}}_j}\right)$ and $D\,\mathcal{V}\left(\bar{P}_0\right) = \left(\frac{\partial \mathcal{V}_i}{\partial \bar{\mathbf{x}}_j}\right)$ of $\mathcal{F}$ and $\mathcal{V}$ in (4.2) evaluated at $\bar{P}_0$ are partitioned as $D\,\mathcal{F}\left(\bar{P}_0\right) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}$ and $D\,\mathcal{V}\left(\bar{P}_0\right) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}$, respectively, where F, V, J_3 and J_4 are given by

$$F = \lambda\bar{\kappa} \begin{pmatrix} h_1 & h_2 & \dots & h_n & \epsilon & \epsilon & \dots & \epsilon \\ 0 & 0 & \dots & 0 & 0 & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & 0 & 0 & 0 & \dots & 0 \end{pmatrix}, \ V = -\begin{pmatrix} M_I & \phi\mathcal{I} \\ \tau\mathcal{I} & M_T \end{pmatrix}, \ J_3 = \lambda\bar{\kappa}\begin{pmatrix} h_1 & h_2 & \dots & h_n & \epsilon & \epsilon & \dots & \epsilon \end{pmatrix}, \ J_4 = \mu,$$

and

$$
\begin{aligned}
a_k &= \mu + \rho_k + \tau, \\
b_k &= \mu + \gamma_k + \phi, \\
M_I &= \begin{pmatrix} -a_1 & 0 & 0 & 0 & \dots & 0 & 0 \\ \rho_1 & -a_2 & 0 & 0 & \dots & 0 & 0 \\ 0 & \rho_2 & -a_3 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \dots & \dots & \rho_{n-1} & -a_n \end{pmatrix}, \; M_T = \begin{pmatrix} -b_1 & 0 & 0 & 0 & \dots & 0 & 0 \\ \gamma_1 & -b_2 & 0 & 0 & \dots & 0 & 0 \\ 0 & \gamma_2 & -b_3 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \dots & \dots & \gamma_{n-1} & -b_n \end{pmatrix},
\end{aligned} \tag{4.3}
$$

$\mathcal{I}$ is a $n \times n$ identity matrix.

It follows that the spectral radius, $R_{t,n}$, of the next generation matrix FV^{-1} is given by

$$
R_{t,n} = \bar{\kappa}\lambda \sum_{k=1}^{n} \left[\frac{u_k h_k + \tau\epsilon v_k}{\prod_{j=1}^{k} \left(a_j b_j - \tau\phi \right)} \right], \tag{4.4}
$$

where u_k and v_k satisfy

$$
\begin{aligned}
u_k &= b_k \rho_{k-1} u_{k-1} + \tau\phi\gamma_{k-1} v_{k-1}, \\
v_k &= \rho_{k-1} u_{k-1} + a_k \gamma_{k-1} v_{k-1}, \quad \text{for } k = 1, 2, ..., n,
\end{aligned}
$$

and $\rho_0 = 1$, $u_0 = 1$, $\gamma_0 = 0$ and $v_0 = 0$. We note here that $a_j b_j - \tau\phi = \bar{a}_j b_j + \tau(\mu + \gamma_j) > 0$ for $j = 1, 2, ..., n$.

Remark 6. Some insights on the derivation of $R_{t,n}$ are as follows: a fraction $\frac{\rho_j}{a_j}$ of infected individuals in stage j progress to stage $j+1$, a fraction $\frac{\gamma_j}{b_j}$ of individuals receiving treatment progress from stage j to $j+1$, a fraction $\frac{\tau}{a_j}$ of infected individuals in stage j progress to compartments with individuals receiving treatment in stage j, a fraction $\frac{\phi}{b_j}$ of individual receiving treatments in stage j re-enters compartment with infected individuals in stage j. Thus, an individual introduced into compartment with infected individuals at stage 1 spends, on average $\frac{1}{b_1} \sum_{j=1}^{\infty} \left(\frac{\tau}{a_1}\right)^j \left(\frac{\phi}{b_1}\right)^{j-1} = \frac{\tau}{a_1 b_1 - \tau\phi}$ times unit in compartment of individuals receiving treatment in stage 1. Likewise, an individual introduced into compartment with treated individuals at stage 1 spends, on average $\frac{\phi}{a_1 b_1 - \tau\phi}$ times unit in compartment of infected individuals. An individual enters the infectious compartment 1 and spends $\frac{1}{a_1}$ time units there, producing on average, $\frac{\lambda h_1}{a_1}$ secondary infections. Hence, $R_{t,1} = \bar{\kappa}\lambda \left(\frac{h_1}{a_1} \frac{1}{1 - \frac{\tau}{a_1}\frac{\phi}{b_1}} + \epsilon \frac{\tau}{a_1 b_1 - \tau\phi} \right)$.

Remark 7. It follows directly that if there are no individual moving from untreatment to treatment population (that is, if $\tau = 0$), then $u_j = \prod_{k=1}^{j} b_k\rho_{k-1}$ for $j = 1, 2, ..., n$, and $R_{t,n} = R_{0,n}$.

Remark 8. We point out the error made in Kretzschmar et al. [15]. We show here that $R_{t,1} \nleq R_{0,1}$ for all values of τ and ϕ. For fixed ϕ, define $f(\tau) = \frac{R_{t,1}}{R_{0,1}}$. We have $f^{'}(\tau) = \frac{(\mu+\rho_1)b_1}{h_1}\left[\frac{\epsilon(\mu+\rho_1)-h_1(\mu+\gamma_1)}{(a_1b_1-\tau\phi)^2}\right]$. It follows that $f(\tau) \leq f(0) = 1$ if $\epsilon(\mu + \rho_1) < h_1(\mu + \gamma_1)$ (that is, if $\frac{h_1}{\epsilon} > \frac{\bar{a}_1}{\bar{b}_1}$). Hence, $R_{t,1} \leq R_{0,1}$ if $\frac{h_1}{\epsilon} > \frac{\bar{a}_1}{\bar{b}_1}$, $R_{t,1} \geq R_{0,1}$ if $\frac{h_1}{\epsilon} < \frac{\bar{a}_1}{\bar{b}_1}$ and $R_{t,1} = R_{0,1}$ if $\frac{h_1}{\epsilon} = \frac{\bar{a}_1}{\bar{b}_1}$. We define $\frac{h_1}{\epsilon}$ as the full-to-reduced infection ratio in stage 1.

4.1.1. Existence and Stability of infection-free equilibrium $\bar{P}_0$ in the presence of treatment

The following theorem shows the condition for the local stability of the infection-free equilibrium, $\bar{P}_0$. Following the same idea used to proof Theorem 1, the proof of the local asymptotic stability of $\bar{P}_0$ reduces to showing that the real part of all eigenvalues of the coefficient matrix of the linear associated system to (2.1) is negative. The coefficient matrix of the linear associated system to (2.1) is similar to that presented in (5.11) (and the same if $\sigma_1 = 0$). For this reason, we omit the proof here and direct the reader to Theorem 14 where the real part of the eigenvalues of the coefficient matrix is shown to be negative.

Theorem 6. *The infection-free equilibrium $\bar{P}_0$ of* (2.1) *is asymptotically stable if $R_{t,n} < 1$ and unstable if $R_{t,n} > 1$.*

We give the proof of the global stability of the infection-free equilibrium $\bar{P}_0$ if $R_{t,n} \leq 1$.

Theorem 7. *The infection-free equilibrium $\bar{P}_0$ of* (2.1) *is globally stable in the feasible region if $R_{t,n} \leq 1$.*

Proof. Consider the Lyapunov function $L : \mathbb{R}^+_{2n+1} \to \mathbb{R}^+$ by

$$L(S, I_1, I_2, ..., I_n, T_1, ..., T_n) = \left(S - \bar{S}^0 - \bar{S}^0 \ln \frac{S}{\bar{S}^0}\right) + \sum_{k=1}^{n} \bar{\omega}_k I_k + \sum_{k=1}^{n} \bar{q}_k T_k,$$

where $\bar{\omega}_k$ and $\bar{q}_k$ satisfy

$$\begin{array}{rcl}\begin{pmatrix}\bar{\omega}_n\\ \bar{q}_n\end{pmatrix} & = & \frac{\lambda\bar{S}^0}{a_nb_n-\tau\phi}\begin{pmatrix}h_nb_n+\tau\epsilon\\ h_n\phi+a_n\epsilon\end{pmatrix},\\ \begin{pmatrix}\bar{\omega}_{n-k}\\ \bar{q}_{n-k}\end{pmatrix} & = & \frac{1}{a_{n-k}b_{n-k}-\tau\phi}\left[\begin{pmatrix}b_{n-k}\rho_{n-k} & \gamma_{n-k}\tau\\ \phi\rho_{n-k} & \gamma_{n-k}a_{n-k}\end{pmatrix}\begin{pmatrix}\bar{\omega}_{n-k+1}\\ \bar{q}_{n-k+1}\end{pmatrix}+\lambda\bar{S}^0\begin{pmatrix}h_{n-k}b_{n-k}+\tau\epsilon\\ h_{n-k}\phi+a_{n-k}\epsilon\end{pmatrix}\right], \text{ for } k = 1,2,3,...,n-1.\end{array} \tag{4.5}$$

It can be shown that $\bar{\omega}_k\bar{a}_k - \bar{\omega}_{k+1}\rho_k - \lambda\bar{S}^0h_k - \tau\bar{q}_k = 0$, $\bar{q}_kb_k - \bar{q}_{k+1}\gamma_k - \lambda\bar{S}^0\epsilon - \phi\bar{\omega}_k = 0$ for $k = 1, 2, ..., n-1$, $\bar{\omega}_n\bar{a}_n - \tau\bar{q}_n - \lambda\bar{S}^0h_n = 0$ and $\bar{q}_nb_n - \phi\bar{\omega}_n - \lambda\bar{S}^0\epsilon = 0$. Define

$$\bar{R}_{t,n} = \bar{\kappa}\lambda\sum_{k=1}^{n}\left[\frac{\bar{u}_kh_k + \epsilon\bar{v}_k}{\prod_{j=1}^{k}\left(a_jb_j - \tau\phi\right)}\right], \tag{4.6}$$

where $\bar{u}_k$ and $\bar{v}_k$ are recurssive sequences defined by

$$\begin{aligned}\bar{u}_k &= b_k\rho_{k-1}\bar{u}_{k-1} + \phi\gamma_{k-1}\bar{v}_{k-1},\\ \bar{v}_k &= \tau\rho_{k-1}\bar{u}_{k-1} + a_k\gamma_{k-1}\bar{v}_{k-1},\ \text{for } k = 2, 3, ..., n,\end{aligned}$$

and $\bar{u}_1 = \phi$, $\bar{v}_1 = a_1$. It follows from (4.5) that

$$\begin{aligned}\begin{pmatrix}\bar{\omega}_1\\ \bar{q}_1\end{pmatrix} &= \left(\prod_{j=1}^{n-1}\left[\frac{1}{a_jb_j-\tau\phi}\begin{pmatrix}b_j\rho_j & \gamma_j\tau\\ \phi\rho_j & \gamma_ja_j\end{pmatrix}\right]\right)\begin{pmatrix}\bar{\omega}_n\\ \bar{q}_n\end{pmatrix}\\ &\quad+\lambda\bar{S}^0\sum_{k=1}^{n-2}\left(\prod_{j=1}^{k}\left[\frac{1}{a_jb_j-\tau\phi}\begin{pmatrix}b_j\rho_j & \gamma_j\tau\\ \phi\rho_j & \gamma_ja_j\end{pmatrix}\right]\right)\left[\frac{1}{a_{k+1}b_{k+1}-\tau\phi}\begin{pmatrix}h_{k+1}b_{k+1}+\tau\epsilon\\ h_{k+1}\phi+a_{k+1}\epsilon\end{pmatrix}\right]\\ &\quad+\frac{\lambda\bar{S}^0}{a_1b_1-\tau\phi}\begin{pmatrix}h_1b_1+\tau\epsilon\\ h_1\phi+a_1\epsilon\end{pmatrix}\\ &= \begin{pmatrix}R_{t,n}\\ \bar{R}_{t,n}\end{pmatrix},\end{aligned}$$

and the derivative of L computed along solution of (4.2) is

$$\begin{aligned}\frac{dL}{dt} &= \beta+\mu\bar{S}^0-\beta\bar{S}^0/S-\mu S+(\bar{\omega}_1-1)\lambda S\sum_{k=1}^{n}(h_kI_k+\epsilon T_k)-\sum_{k=1}^{n}\left(\bar{\omega}_k\bar{a}_k-\bar{\omega}_{k+1}\rho_k-\lambda\bar{S}^0h_k-\tau\bar{q}_k\right)I_k\\ &\quad-\sum_{k=1}^{n}\left(\bar{q}_kb_k-\bar{q}_{k+1}\gamma_k-\lambda\bar{S}^0\epsilon-\phi\bar{\omega}_k\right)T_k-\left(\bar{\omega}_n\bar{a}_n-\lambda\bar{S}^0h_n-\tau\bar{q}_n\right)I_n-\left(\bar{q}_n\bar{b}_n-\lambda\bar{S}^0\epsilon-\phi\bar{\omega}_n\right)T_n.\end{aligned}$$

If $R_{t,n}\le 1$, then $0<R_{t,n}\le 1$ and $0<\bar{\omega}_1\le 1$. Thus, it follows from (4.5) and (4.6) that $\bar{\omega}_k$ and $\bar{q}_k$ are positive for $k = 1, 2, ..., n$ and

$$\begin{aligned}\frac{dL}{dt} &\le -\beta\left(\frac{\bar{S}^0}{S}+\frac{S}{\bar{S}^0}-2\right),\\ &\le 0,\end{aligned}$$

using the fact that $\bar{S}^0 = \bar{\kappa} = \beta/\mu$ and $1 = \left(\frac{\bar{S}^0}{S}\frac{S}{\bar{S}^0}\right)^{1/2} \le \frac{1}{2}\left(\frac{\bar{S}^0}{S}+\frac{S}{\bar{S}^0}\right)$. If $R_{t,n}<1$, then $dL/dt = 0$ if and only if $S = \bar{S}^0$, $I_k = 0$ and $T_k = 0$ for all $k = 1, 2, ..., n$. It $R_{t,n} = 1$, then $dL/dt = 0$ if and only if $S = \bar{S}^0$. In either case, it can be shown that the largest invariant set of (4.2) contained in $\{(S, I_1, ..., I_n, T_1, ..., T_n)^T \in \mathcal{T}\ \ dL/dt = 0\}$ is the set $\{\bar{P}_0\}$. The global stability of $\bar{P}_0$ follows from the LaSalle invariance principle [16]. ■

4.1.2. Existence and stability of endemic equilibrium $\bar{P}_1$ in the presence of treatment

The endemic equilibrium $\bar{P}_1 = \begin{pmatrix}\bar{S}^* & \bar{I}_1^* & \dots & \bar{I}_n^* & \bar{T}_1^* & \dots & \bar{T}_n^*\end{pmatrix}^T$ of the system (2.1) is given by

$$\left\{\begin{aligned}\bar{S}^* &= \frac{\bar{\kappa}}{R_{t,n}},\\ \bar{I}_k^* &= \frac{\beta u_k}{\prod_{j=1}^{k}(a_jb_j-\tau\phi)}\left(1-\frac{1}{R_{t,n}}\right),\\ \bar{T}_k^* &= \frac{\tau\beta v_k}{\prod_{j=1}^{k}(a_jb_j-\tau\phi)}\left(1-\frac{1}{R_{t,n}}\right),\ \ k = 1, 2, ..., n,\end{aligned}\right. \tag{4.7}$$

where u_k and v_k are defined in (4.4). The following theorem follows directly from (4.7).

Theorem 8. *The endemic equilibrium $\bar{P}_1$ of* (2.1) *exists if and only if $R_{t,n} > 1$ and does not exit if $R_{t,n} < 1$. The endemic equilibrium becomes infection-free (that is, $\bar{P}_1 = \bar{P}_0$) if $R_{t,n} = 1$.*

Proof. It follows directly from (4.7) that $\bar{S}^* > 0$, $\bar{I}_k^* > 0$ and $\bar{T}_k^* > 0$ for $k = 1, 2, ..., n$, if $R_{t,n} > 1$.

Remark 9. From (4.7) and Theorem 8, we deduce that the level of treatment above which the infection can no longer persist in endemic state is attained when $R_{t,n} = 1$. In this case, we only have one equilibrium point, namely, $\bar{P}_0$.

We follow the same procedure used in previous theorems to discuss the global stability of the endemic equilibrium $\bar{P}_1$.

Theorem 9. *The endemic equilibrium $\bar{P}_1$ of the system* (2.1) *is globally stable if $R_{t,n} > 1$.*

Proof. The existence of the endemic equilibrium $\bar{P}_1$ follows from Theorem 8 if $R_{t,n} > 1$. Assume $R_{t,n} > 1$. Define the Lyapunov function $\bar{L} : \mathbb{R}^+_{2n+1} \to \mathbb{R}^+$ by

$$\bar{L}(S, I_1, ..., I_n, T_1, ..., T_n) = \left(S - \bar{S}^* - \bar{S}^* \ln \frac{S}{\bar{S}^*}\right) + \sum_{k=1}^{n} \bar{w}_k^* \left(I_k - \bar{I}_k^* - \bar{I}_k^* \ln \frac{I_k}{\bar{I}_k^*}\right) + \sum_{k=1}^{n} \bar{c}_k^* \left(T_k - \bar{T}_k^* - \bar{T}_k^* \ln \frac{T_k}{\bar{T}_k^*}\right), \quad (4.8)$$

where $\bar{w}_k^*$ and $\bar{c}_k^*$, $k = 1, 2, ..., n$ are positive constants to be determined later. Define

$$\bar{y}_0 = \frac{S}{\bar{S}^*}, \quad \bar{y}_k = \frac{I_k}{\bar{I}_k^*}, \text{and } \pi_k = \frac{T_k}{\bar{T}_k^*} \text{ for } k = 1, 2, ..., n.$$

We have

$$\begin{aligned}
\frac{d\bar{L}}{dt} \quad = \quad & \bar{C} + (\bar{w}_1^* - 1)\lambda \bar{S}^* \bar{y}_0 \sum_{k=1}^{n} \left(h_k \bar{I}_k^* \bar{y}_k + \epsilon \bar{T}_k^* \pi_k\right) - S^* \left(\mu + \lambda h_1 \bar{w}_1^* \bar{I}_1^*\right) \bar{y}_0 - \tfrac{\beta}{\bar{y}_0} - \sum_{k=1}^{n-1} \left(a_k \bar{w}_k^* - \lambda \bar{S}^* h_k - \rho_k \bar{w}_{k+1}^* - \tau \bar{c}_k^*\right) \bar{I}_k^* \bar{y}_k \\
& - \left(a_n \bar{w}_n^* - \lambda \bar{S}^* h_n - \tau \bar{c}_n^*\right) \bar{I}_n^* \bar{y}_n - \sum_{k=2}^{n} \rho_{k-1} \bar{w}_k^* \bar{I}_{k-1}^* \tfrac{\bar{y}_{k-1}}{\bar{y}_k} - \lambda \bar{S}^* \bar{w}_1^* \tfrac{\bar{y}_0}{\bar{y}_1} \sum_{k=2}^{n} h_k \bar{I}_k^* \bar{y}_k \\
& - \sum_{k=1}^{n-1} \left(\bar{c}_k^* b_k - \bar{c}_{k+1}^* \gamma_k - \lambda \bar{S}^* \epsilon - \bar{w}_k^* \phi\right) \bar{T}_k^* \pi_k - \left(\bar{c}_n^* b_n - \lambda \bar{S}^* \epsilon - \bar{w}_n^* \phi\right) \bar{T}_n^* \pi_n \\
& - \sum_{k=1}^{n} \phi \bar{w}_k^* \bar{T}_k^* \tfrac{\pi_k}{\bar{y}_k} - \sum_{k=1}^{n} \bar{c}_k^* \tau \bar{I}_k^* \tfrac{\bar{y}_k}{\pi_k} - \sum_{k=2}^{n} \bar{c}_k^* \gamma_{k-1} \bar{T}_{k-1}^* \tfrac{\pi_{k-1}}{\pi_k} - \lambda \bar{S}^* \bar{w}_1^* \tfrac{\bar{y}_0}{\bar{y}_1} \sum_{k=1}^{n} \epsilon \bar{T}_k^* \pi_k
\end{aligned} \quad (4.9)$$

where

$$\bar{C} = \beta + \mu \bar{S}^* + \sum_{k=1}^{n} \left(a_k \bar{w}_k^* \bar{I}_k^* + b_k \bar{c}_k^* \bar{T}_k^*\right). \quad (4.10)$$

By setting $\bar{w}_1^* - 1 = 0$, $a_k \bar{w}_k^* - \lambda \bar{S}^* h_k - \rho_k \bar{w}_{k+1}^* - \tau \bar{c}_k^* = 0$ and $\bar{c}_k^* b_k - \bar{c}_{k+1}^* \gamma_k - \lambda \bar{S}^* \epsilon - \bar{w}_k^* \phi = 0$ for $k = 1, 2, ..., n-1$, $a_n \bar{w}_n^* - \lambda \bar{S}^* h_n - \tau \bar{c}_n^* = 0$ and $\bar{c}_n^* b_n - \lambda \bar{S}^* \epsilon - \bar{w}_n^* \phi = 0$, it follows that $\bar{w}_k^*$ and $\bar{c}_k^*$ satisfy

$$\begin{aligned}
\bar{w}_1^* &= 1, \\
\bar{w}_{k+1}^* &= \left(a_k \bar{w}_k^* - \lambda \bar{S}^* h_k - \tau \bar{c}_k^*\right) / \rho_k, \quad k = 1, ..., n-1, \\
\bar{w}_n^* &= \left(\tau \bar{c}_n^* + \lambda \bar{S}^* h_n\right) / a_n,
\end{aligned} \quad (4.11)$$

$$\begin{aligned}
\bar{c}_1^* &= \tfrac{1}{\tau \bar{I}_1^*} \left(\phi \bar{T}_1^* + \lambda \bar{S}^* \epsilon \sum_{k=1}^{n} \bar{T}_k^*\right), \\
\bar{c}_{k+1}^* &= \left(b_k \bar{c}_k^* - \lambda \bar{S}^* \epsilon - \phi \bar{w}_k^*\right) / \gamma_k, \quad k = 1, ..., n-1, \\
\bar{c}_n^* &= \left(\phi \bar{w}_n^* + \lambda \bar{S}^* \epsilon\right) / b_n,
\end{aligned} \quad (4.12)$$

Hence, the derivative of $\bar{L}$ with respect to t computed along solutions of (4.2) is

$$\begin{aligned}
\frac{d\bar{L}}{dt} &= -g_1\left(\bar{y}_0 + \frac{1}{\bar{y}_0} - 2\right) - \sum_{k=2}^{n} g_k\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\bar{y}_k}{\bar{y}_1} + \sum_{j=2}^{k}\frac{\bar{y}_{j-1}}{\bar{y}_j} - (k+1)\right) \\
&\quad - \sum_{k=1}^{n} f_k\left(\frac{\pi_k}{\bar{y}_k} + \frac{\bar{y}_k}{\pi_k} - 2\right) - d_1\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\pi_1}{\bar{y}_1} + \frac{\bar{y}_1}{\pi_1} - 3\right) \\
&\quad - \sum_{k=2}^{n} d_k\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\pi_k}{\bar{y}_1} + \frac{\bar{y}_1}{\pi_1} + \sum_{j=2}^{k}\frac{\pi_{j-1}}{\pi_j} - (k+2)\right),
\end{aligned} \tag{4.13}$$

where $\bar{C}$, d_k, f_k and g_k, $k = 1, 2, ..., n$, satisfy

$$\begin{aligned}
g_1 &= \left(\mu + \lambda\bar{w}_1^* h_1 \bar{I}_1^*\right)\bar{S}^*, \\
g_k &= \rho_{k-1}\bar{w}_k^*\bar{I}_{k-1}^* - \rho_k\bar{w}_{k+1}^*\bar{I}_k^* = \lambda\bar{w}_1^*\bar{S}^* h_k\bar{I}_k^*, \text{ for } k = 2, 3, ..., n-1, \\
g_n &= \lambda\bar{w}_1^*\bar{S}^* h_n\bar{I}_n^* = \rho_{n-1}\bar{w}_n^*\bar{I}_{n-1}^*,
\end{aligned} \tag{4.14}$$

$$\begin{aligned}
d_1 &= \lambda\bar{w}_1^*\bar{S}^*\epsilon\bar{T}_1^*, \\
d_k &= \gamma_{k-1}\bar{c}_k^*\bar{T}_{k-1}^* - \gamma_k\bar{c}_{k+1}^*\bar{T}_k^* = \lambda\bar{w}_1^*\bar{S}^*\epsilon\bar{T}_k^*, \text{ for } k = 2, 3, ..., n-1, \\
d_n &= \lambda\bar{w}_1^*\bar{S}^*\epsilon\bar{T}_n^* = \gamma_{n-1}\bar{c}_n^*\bar{T}_{n-1}^*,
\end{aligned} \tag{4.15}$$

$$\begin{aligned}
f_1 &= \phi\bar{w}_1^*\bar{T}_1^* = \bar{c}_1^*\tau\bar{I}_1^* - \sum_{j=1}^{n} d_j, \\
f_k &= \phi\bar{w}_k^*\bar{T}_k^* = \bar{c}_k^*\tau\bar{I}_k^*, \text{ for } k = 2, 3, ..., n,
\end{aligned} \tag{4.16}$$

and

$$\bar{C} = \sum_{k=1}^{n}(k+1)g_k + 2\sum_{k=1}^{n} f_k + \sum_{k=1}^{n}(k+2)d_k. \tag{4.17}$$

The expressions for g_k and d_k in (4.14) and (4.15) follow by using (4.11), (4.12) and (4.16), and the fact that $\bar{S}^*$, $\bar{I}_k^*$ and $\bar{T}_k^*$ are endemic equilibrium of (2.1) that satisfy $\rho_{k-1}\bar{I}_{k-1}^* = a_k\bar{I}_k^* - \phi\bar{T}_k^*$ and $b_k\bar{T}_k^* - \tau\bar{I}_k^* = \gamma_{k-1}\bar{T}_{k-1}^*$ for $k = 2, 3, ..., n-1$. The value of $\bar{c}_1^*$ in (4.12) is computed using expression for f_1 in (4.16) and the fact that $\sum_{j=1}^{n} d_j = \lambda\bar{S}^*\sum_{j=1}^{n}\epsilon\bar{T}_j^*$ (derived by comparing coefficients of $\bar{y}_0\pi_1/\bar{y}_1$ in (4.9) and (4.13)). By substituting (4.16) into (4.11) and (4.12) and using the fact that $\bar{S}^*$, $\bar{I}_k^*$ and $\bar{T}_k^*$ are endemic equilibrium of (2.1), it follows that

$$\begin{aligned}
\bar{w}_1^* &= 1, \\
\bar{w}_{k+1}^* &= \frac{1}{\rho_k\bar{I}_k^*}\lambda\bar{S}^*\sum_{j=k+1}^{n} h_j\bar{I}_j^*, \text{ for } k = 1, 2, ..., n-1, \\
\bar{c}_1^* &= \frac{1}{\tau\bar{I}_1^*}\left(\phi\bar{T}_1^* + \lambda\bar{S}^*\sum_{j=1}^{n}\epsilon\bar{T}_j^*\right), \\
\bar{c}_{k+1}^* &= \frac{1}{\gamma_k\bar{T}_k^*}\lambda\bar{S}^*\sum_{j=k+1}^{n}\epsilon\bar{T}_j^*, \text{ for } k = 1, 2, ..., n-1.
\end{aligned} \tag{4.18}$$

Finally, by using (4.14), (4.15), (4.16) and the fact that

$$\sum_{k=1}^{n}(g_k + d_k) = \beta,$$

(derived by comparing coefficients of $1/\bar{y}_0$ in (4.9) and (4.13)), we can show that the expression for $\bar{C}$ in (4.10) and (4.17) are the same. Hence, from (4.13)-(4.16), (4.18), and the fact that the arithmetic mean of a list of non-negative real numbers is greater than or equal to the geometric mean of the same list [21], it follows that $1 = \left(\bar{y}_0\frac{1}{\bar{y}_0}\right)^{\frac{1}{2}} \leq$

$\frac{1}{2}\left(\bar{y}_0 + \frac{1}{\bar{y}_0}\right)$ and $1 = \left(\frac{1}{\bar{y}_0}\frac{\bar{y}_0\bar{y}_k}{\bar{y}_1}\prod_{j=2}^{k}\frac{\bar{y}_{j-1}}{\bar{y}_j}\right)^{\frac{1}{k+1}} \leq \frac{1}{k+1}\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\bar{y}_k}{\bar{y}_1} + \sum_{j=2}^{k}\frac{\bar{y}_{j-1}}{\bar{y}_j}\right)$ for $k = 2, ..., n$, $1 = \left(\frac{\pi_k}{\bar{y}_k}\frac{\bar{y}_k}{\pi_k}\right)^{\frac{1}{2}} \leq \frac{1}{2}\left(\frac{\pi_k}{\bar{y}_k} + \frac{\bar{y}_k}{\pi_k}\right)$, for $k = 1, 2, ..., n$, $1 = \left(\frac{1}{\bar{y}_0}\frac{\bar{y}_0\pi_1}{\bar{y}_1}\frac{\bar{y}_1}{\pi_1}\right)^{\frac{1}{3}} \leq \frac{1}{3}\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\pi_1}{\bar{y}_1} + \frac{\bar{y}_1}{\pi_1}\right)$, $1 = \left(\frac{1}{\bar{y}_0}\frac{\bar{y}_0\pi_k}{\bar{y}_1}\frac{\bar{y}_1}{\pi_1}\prod_{j=2}^{k}\frac{\pi_{j-1}}{\pi_j}\right)^{\frac{1}{k+2}} \leq \frac{1}{k+2}\left(\frac{1}{\bar{y}_0} + \frac{\bar{y}_0\pi_k}{\bar{y}_1} + \frac{\bar{y}_1}{\pi_1} + \sum_{j=2}^{k}\frac{\pi_{j-1}}{\pi_j}\right)$, for $k = 2, 3, ..., n$, and

$$\frac{d\bar{L}}{dt} \leq 0. \tag{4.19}$$

Equality holds if and only if $\bar{y}_0 = 1$, $\bar{y}_{j-1} = \bar{y}_j$, $\pi_{j-1} = \pi_j$ for $j = 2, 3, ..., n$, $\bar{y}_j = \pi_j$ for $j = 1, 2, ..., n$, that is, if $S = \bar{S}^*$, $I_{j-1}/\bar{I}^*_{j-1} = I_j/\bar{I}^*_j = T_{j-1}/\bar{T}^*_{j-1} = T_j/\bar{T}^*_j$ for $j = 2, 3, ..., n$. It can be easily verified that the largest invariant set of (4.2) contained in $\{(S, I_1, ..., I_n, T_1, ..., T_n)^T \in \mathcal{T} : d\bar{L}/dt = 0\}$ is the singleton $\{\bar{P}_1\}$. By the LaSalle's Invariance Principle [16], it follows that $\bar{P}_1$ is globally stable in the feasible region if $R_{t,n} > 1$. ■

5. Stochastic Model

In this section, we study the effect of noise on the transmission rate and infectivity, h_k, of untreated individuals in stage k. External noise appears multiplicatively in our model and it is able to modify the mean dynamical behavior of the population [10, 18]. We assume, following the argument mabe by Mendez et al. [18], that external fluctiations may be caused by variability in the number of contacts between infected and susceptible individuals and such random variations can be modeled by a white noise [18]. Let $\bar{\lambda}_k = \lambda h_k$. By allowing the transmission rate λ to fluctuate around a mean value, we introduce external fluctuations in the model as follows:

$$\bar{\lambda}_k \equiv \bar{\lambda}_k + \boldsymbol{\sigma}_k\, C(t), \tag{5.1}$$

where $C(t)$ is a noise term with zero mean, and $\boldsymbol{\sigma} > 0$ is the noise intensity, a measure of the amplitude of fluctuation. By substituting (5.1) into (2.1), we have the Stratonovich stochastic model

$$\begin{aligned}
dS &= \left(\beta - \lambda S \sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) - \mu S\right)dt - S\sum_{j=1}^{n}\sigma_j I_j \circ\ dW_j(t),\ \ S(t_0) = S_0,\\
dI_1 &= \left(\lambda S \sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) - (\mu + \rho_1 + \tau)I_1 + \phi T_1\right)dt + S\sum_{j=1}^{n}\sigma_j I_j \circ\ dW_j(t),\ \ I_1(t_0) = I_{01},\\
dI_k &= (\rho_{k-1}I_{k-1} - (\mu + \rho_k + \tau)I_k + \phi T_k)\ dt,\ \ I_k(t_0) = I_{0k},\\
dT_1 &= (\tau I_1 - (\mu + \gamma_1 + \phi)T_1)dt,\ \ T_1(t_0) = T_{01},\\
dT_k &= (\tau I_k + \gamma_{k-1}T_{k-1} - (\mu + \gamma_k + \phi)T_k)\ dt,\ \ T_k(t_0) = T_{0k},\ \ \text{for}\ \ k = 2, 3, ..., n,
\end{aligned} \tag{5.2}$$

where $W_i(t)$, $i = 1, 2, ..., n$, are standard Wiener process on a filtered probability space $(\Omega, \mathcal{F}_t, (\mathcal{F}_t)_{t\geq 0}, \mathbb{P})$, the filtration function $(\mathcal{F})_{t\geq 0}$ 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 [1], the initial process $x(t_0) = (S(t_0), I_1(t_0), ..., I_n(t_0), T_1(t_0), ..., T_n(t_0))$ is $\mathcal{F}_{t_0}$ measurable and independent of $W(t) - W(t_0)$.

We use the Stratonovich-Itô conversion theorem given in Bernardi et al [4] and Kloeden et al. [14] (stated below) to convert the Stratonovich dynamic model (5.2) to its Itô's equivalent and later give a theorem showing how the Itô's equivalent is derived.

Theorem 10. *([4, 14]) The Itô stochastic differential equation (SDE)*

$$dX = a(t,X)dt + \sum_{j=1}^{M} b^j(t,X)dW^j(t), \tag{5.3}$$

defined componentwise as

$$dX^i = a^i(t,X)dt + \sum_{j=1}^{M} b^{i,j}(t,X)dW^j(t), \quad i = 1,2,...,N,$$

having the same solution as the $N-$ dimensional Stratonovich SDE with $M-$ dimensional Wiener process

$$dX = \underline{a}(t,X)dt + \sum_{j=1}^{M} b^j(t,X) \circ dW^j(t), \tag{5.4}$$

has drift coefficient $a(t,X)$ that is defined in terms of $\underline{a}(t,X)$, componentwise, by

$$a^i(t,X) = \underline{a}^i(t,X) + \frac{1}{2}\sum_{k=1}^{N}\sum_{j=1}^{M} b^{k,j}(t,X)\frac{\partial b^{i,j}}{\partial x_k}(t,X), \quad i = 1,2,...,N. \tag{5.5}$$

The following theorem gives the Itô's equivalent of (5.2).

Theorem 11. *The Itô stochastic differential equation having the same solution as the $2n+1$-dimensional Stratonovich stochastic differential equation (5.2) is given by*

$$\begin{aligned}
dS &= \left(\beta - \lambda S \sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) - \mu S + \tfrac{1}{2} S \sum_{j=1}^{n} \sigma_j^2 I_j^2 - \tfrac{1}{2}\sigma_1^2 S^2 I_1\right) dt - S \sum_{j=1}^{n} \sigma_j I_j \, dW_j(t), \;\; S(t_0) = S_0,\\
dI_1 &= \left(\lambda S \sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) - (\mu + \rho_1 + \tau) I_1 + \phi T_1 - \tfrac{1}{2} S \sum_{j=1}^{n} \sigma_j^2 I_j^2 + \tfrac{1}{2}\sigma_1^2 S^2 I_1\right) dt + S \sum_{j=1}^{n} \sigma_j I_j \, dW_j(t), \;\; I_1(t_0) = I_{01},\\
dI_k &= (\rho_{k-1} I_{k-1} - (\mu + \rho_k + \tau) I_k + \phi T_k) \; dt, \;\; I_k(t_0) = I_{0k},\\
dT_1 &= (\tau I_1 - (\mu + \gamma_1 + \phi) T_1) dt, \;\; T_1(t_0) = T_{01},\\
dT_k &= (\tau I_k + \gamma_{k-1} T_{k-1} - (\mu + \gamma_k + \phi) T_k) \; dt, \;\; T_k(t_0) = T_{0k}, \;\; \textit{for} \;\; k = 2,3,...,n.
\end{aligned} \tag{5.6}$$

Proof. Using Theorem 10, we define $x = (S, I_1, I_2, ..., I_n, T_1, T_2, ..., T_n)$. It follows from (5.2) and (5.4) that

$$\underline{a}(t,x) = \begin{pmatrix} \beta - \lambda S \sum\limits_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) - \mu S \\ \lambda S \sum\limits_{j=1}^{n} \left(h_j I_j + \epsilon T_j\right) - (\mu + \rho_1 + \tau) I_1 + \phi T_1 \\ \rho_1 I_1 - (\mu + \rho_2 + \tau) I_2 + \phi T_2 \\ \vdots \\ \rho_{n-1} I_{n-1} - (\mu + \rho_n + \tau) I_n + \phi T_n \\ \tau I_1 - (\mu + \gamma_1 + \phi) T_1 \\ \vdots \\ \tau I_n + \gamma_{n-1} T_{n-1} - (\mu + \gamma_n + \phi) T_n \end{pmatrix},$$

$b^{1,j} = -\sigma_j S I_j$, $b^{2,j} = \sigma_j S I_j$ and $b^{i,j} = 0$ for $i \geq 3$, $j = 1, 2, ..., n$. Also, we have $\frac{\partial b^{1,j}}{\partial x_1} = \frac{\partial b^{1,j}}{\partial S} = -\sigma_j I_j$, $\frac{\partial b^{2,j}}{\partial x_1} = \sigma_j I_j$ for $j = 1, 2, ..., n$, $\frac{\partial b^{1,j}}{\partial x_2} = \frac{\partial b^{1,j}}{\partial I_1} = -\sigma_1 S$, $\frac{\partial b^{2,j}}{\partial x_2} = \sigma_1 S$ if $j = 1$ and zero otherwise, so that from (5.5),

$$\begin{aligned} a^i(t,x) &= \underline{a}^i(t,x) + \frac{1}{2} \sum_{k=1}^{2n+1} \sum_{j=1}^{n} b^{k,j}(t,x) \frac{\partial b^{i,j}}{\partial x_k}(t,x) = \underline{a}^i(t,x) + \frac{1}{2} \sum_{k=1}^{2} \sum_{j=1}^{n} b^{k,j}(t,x) \frac{\partial b^{i,j}}{\partial x_k}(t,x), \\ &= \underline{a}^i(t,x) + \frac{1}{2} \sum_{j=1}^{n} \left(b^{1,j} \frac{\partial b^{i,j}}{\partial x_1} + b^{2,j} \frac{\partial b^{i,j}}{\partial x_2} \right). \end{aligned}$$

Therefore,

$$\begin{aligned} a^1(t,x) &= \underline{a}^1(t,x) + \tfrac{1}{2} \sum_{j=1}^{n} \left(\sigma_j^2 S I_j^2\right) - \tfrac{1}{2} \sigma_1^2 S^2 I_1, \\ a^2(t,x) &= \underline{a}^2(t,x) - \tfrac{1}{2} \sum_{j=1}^{n} \left(\sigma_j^2 S I_j^2\right) + \tfrac{1}{2} \sigma_1^2 S^2 I_1, \\ a^i(t,x) &= \underline{a}^i(t,x), \quad \text{for } i = 3, 4, ..., 2n+1. \end{aligned} \tag{5.7}$$

Using (5.3) and (5.7), the Itô's equivalent of (5.2) reduces to (5.6). ■

5.1. *Existence of solution of (5.6)*

Following Theorem 3.5 of Khasminskii [13], we use Theorem 12 below to show the existence and uniqueness of solution of (5.6).

Definition 2. Let $C_{1,2}(\mathbb{R}_+ \times \mathbb{R}^{2n+1}; \mathbb{R}^+)$ denote the family of all nonnegative functions $\mathbf{V}(t,\mathbf{u})$ on $\mathbb{R}_+ \times \mathbb{R}^{2n+1}$ that are continuously differentiable with respect to t and twice continuously differentiable with respect to $\mathbf{u}$.

Definition 3. Define the domain U_n by $U_n = \{|x| < n\}$. We define the differential operator L on a function $\mathbf{V}(t,\mathbf{u}) \in C_{1,2}$ corresponding to a stochastic differential equation with drift and diffusion coefficients $\mathbf{A}(t,\mathbf{u})$ and $\mathbf{B}(t,\mathbf{u})$, respectively, by

$$L\mathbf{V}(t,\mathbf{u}) = \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial t} + \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}} \mathbf{A} + \frac{1}{2} \text{trace} \left[B^T \frac{\partial^2 \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}^2} B \right] \tag{5.8}$$

where $\frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial \mathbf{u}} = \left(\frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial u_1}, ..., \frac{\partial \mathbf{V}(t,\mathbf{u})}{\partial u_n} \right)$ 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 12. *(Khasminskii [13]) Suppose that* (5.6) *satisfies the classical existence and uniqueness theorem in every cylinder* $[a, b] \times U_R$ *and, moreover, that there exists a nonnegative function* $V \in C_{1,2}\left([t_0, T] \times \mathbb{R}_+^{2n+1} \to \mathbb{R}^+\right)$ *such that for some constant* $c > 0$

$$\begin{aligned} LV &\leq cV, \\ V_R &= \inf_{|x|>R} V(t, x) \to \infty, \quad as \;\; R \to \infty. \end{aligned} \tag{5.9}$$

Assume $x(t_0) = (S(t_0), I_1(t_0), ..., I_n(t_0), T_1(t_0), ..., T_n(t_0))$ *is independent of the processes* $W_i(t) - W_i(t_0)$*,* $i = 1, 2, ..., n$*. Then there exists a solution* $x(t) = (S(t), I_1(t), ..., I_n(t), T_1(t), ..., T_n(t))$ *of the stochastic differential equation* (5.6) *which is an almost surely continuous stochastic process and is unique up to equivalence.*

Theorem 13. *There exists a solution* $x(t) = (S(t), I_1(t), ..., I_n(t), T_1(t), ..., T_n(t))$ *of* (5.6) *which is an almost surely continuous stochastic process and is unique up to equivalence if* $x(t_0)$ *is independent of the processes* $W_i(t) - W_i(t_0)$*,* $i = 1, 2, ..., n$*.*

Proof. It is easy to show that (5.6) satisfies the classical existence and uniqueness theorem in every cylinder $[a, b] \times U_R$ (that is, the drift and diffusion coefficients of (5.6) satisfy the Lipschitz condition and linear growth, locally, in $[a, b] \times U_R$). It suffices to show that condition (5.9) is satisfied in order to prove the existence of $x(t)$ using Theorem 12. Define $x = (S, I_1, ..., I_n, T_1, ..., T_n)$ and $\mathbf{V} : [0, T] \times \mathbb{R}_+^{2n+1} \to \mathbb{R}^+$ by

$$\mathbf{V}(t, x) = \ln\left(S + \sum_{j=1}^{n}\left(I_j + T_j\right) + e^{\beta}\right).$$

It follows directly that $\mathbf{V} > 0$. Using (5.8), we have

$$\begin{aligned} L\mathbf{V} &= \frac{1}{S + \sum_{j=1}^{n}\left(I_j + T_j\right) + e^{\beta}}\Bigg(\beta - \lambda S\sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) - \mu S + \frac{1}{2}S\sum_{j=1}^{n}\sigma_j^2 I_j^2 - \frac{1}{2}\sigma_1^2 S^2 I_1 + \lambda S\sum_{j=1}^{n}\left(h_j I_j + \epsilon T_j\right) \\ &\quad -(\mu + \rho_1 + \tau)I_1 + \phi T_1 - \frac{1}{2}S\sum_{j=1}^{n}\sigma_j^2 I_j^2 + \frac{1}{2}\sigma_1^2 S^2 I_1 + \sum_{k=2}^{n}(\rho_{k-1}I_{k-1} - (\mu + \rho_k + \tau)I_k + \phi T_k) + \tau I_1 \\ &\quad -(\mu + \gamma_1 + \phi)T_1 + \sum_{k=2}^{n}(\tau I_k + \gamma_{k-1}T_{k-1} - (\mu + \gamma_k + \phi)T_k)\Bigg) \\ &\quad - \frac{1}{\left(S + \sum_{j=1}^{n}\left(I_j + T_j\right) + e^{\beta}\right)^2}\sum_{j=1}^{n}\sigma_j^2 S^2 I_j^2 \\ &\leq \frac{\beta - \mu\left(S + \sum_{j=1}^{n}\left(I_j + T_j\right)\right)}{S + \sum_{j=1}^{n}\left(I_j + T_j\right) + e^{\beta}} \\ &< \mathbf{V}. \end{aligned}$$

Define $\mathbf{V}_R = \inf_{|x|>R} \mathbf{V}(t, x)$. Since $\mathbf{V}(t, x) \geq \ln\left(|x| + e^{\beta}\right)$, it follows that $\mathbf{V}_R \to \infty$ as $R \to \infty$. The existence and uniqueness of solution $x(t) = (S, I_1, ..., I_n, T_1, ..., T_n)$ with initial condition $x(t_0)$ independent of $W_i(t) - W_i(t_0)$, $i = 1, 2, ..., n$, follow directly from Theorem 12. ■

5.2. Reproduction number $\mathcal{R}_{0,n}$ and elimination threshold $\mathcal{R}_{t,n}$ in the presence of noise

By defining $\mathcal{R}_{0,n}$ and $\mathcal{R}_{t,n}$ as the stochastic reproduction number equivalent to $R_{0,n}$ and $R_{t,n}$, respectively, we study the condition under which the system (5.6) evolves into an endemic or transient epidemic advance state by analyzing thresholds for $\mathcal{R}_{0,n}$ and $\mathcal{R}_{t,n}$. According to Tornatore et al. [22], 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. For this reason, we shall first study the conditions under which the linear associated system to (5.6) evolves into an endemic or transient epidemic advance state. Using the idea in Mendez et al. [18], we find condition under which expected infected population (with respect to linear associated system to (5.6)) becomes extinct.

Define $\Phi = \begin{pmatrix} S - \bar{\kappa} & I_1 \dots I_n & T_1 \dots T_n \end{pmatrix}^T$. The linearization of (5.6) along the infection-free equilibrium $\bar{P}_0$ is given by

$$d\,\Phi = \mathcal{A}\,\Phi\,dt + \sum_{i=1}^{n} \mathcal{G}_i\,\Phi\,dW_i(t), \quad \mathbf{u}(t_0) = \mathbf{u}_0, \tag{5.10}$$

where $\mathcal{A} = \begin{pmatrix} A_{1,1} & A_{1,2} \\ A_{2,1} & A_{2,2} \end{pmatrix}$, $A_{1,1} = \begin{pmatrix} -\mu & -\left(\lambda h_1 + \sigma_1^2\bar{\kappa}/2\right)\bar{\kappa} & -\lambda\bar{\kappa}h_2 & -\lambda\bar{\kappa}h_3 & \dots & -\lambda\bar{\kappa}h_{n-1} & -\lambda\bar{\kappa}h_n \\ 0 & -\left(\nu - \sigma_1^2\bar{\kappa}^2/2\right) & \lambda\bar{\kappa}h_2 & \lambda\bar{\kappa}h_3 & \dots & \lambda\bar{\kappa}h_{n-1} & \lambda\bar{\kappa}h_n \\ 0 & \rho_1 & -a_2 & 0 & \dots & 0 & 0 \\ 0 & 0 & \rho_2 & -a_3 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & \dots & \rho_{n-1} & -a_n \end{pmatrix}_{n+1\times n+1}$,

$A_{1,2} = \begin{pmatrix} -\lambda\bar{\kappa}\epsilon & -\lambda\bar{\kappa}\epsilon & -\lambda\bar{\kappa}\epsilon & \dots & -\lambda\bar{\kappa}\epsilon & -\lambda\bar{\kappa}\epsilon \\ \phi + \lambda\bar{\kappa}\epsilon & \lambda\bar{\kappa}\epsilon & \lambda\bar{\kappa}\epsilon & \dots & \lambda\bar{\kappa}\epsilon & \lambda\bar{\kappa}\epsilon \\ 0 & \phi & 0 & 0 & \dots & 0 \\ 0 & 0 & \phi & 0 & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \dots & 0 & \phi \end{pmatrix}_{n\times n}$, $A_{2,1} = \begin{pmatrix} 0 & \tau & 0 & \dots & 0 & 0 \\ 0 & 0 & \tau & \dots & 0 & 0 \\ 0 & 0 & 0 & \tau & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \dots & 0 & \tau \end{pmatrix}_{n\times n+1}$, $A_{2,2} = M_T$ defined in (4.3), $\nu = a_1 - \lambda h_1\bar{k}$, a_k and b_k are defined in (4.3), and $\mathcal{G}_j = \begin{pmatrix} O_j & \Gamma & O_{2n-j} \end{pmatrix}$, where O_m is a $2n+1\times m$ zero matrix and $\Gamma = \sigma_j\bar{\kappa}\begin{pmatrix} -1 & 1 & 0\dots 0 \end{pmatrix}^T_{2n+1\times 1}$.

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

$$d\mathbf{m} = \mathcal{A}\,\mathbf{m}\,dt. \tag{5.11}$$

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

$$det(\mathcal{A} - r\mathcal{I}_{2n+1\times 2n+1}) = -(r+\mu)\;\; det(\bar{\mathcal{A}} - r\mathcal{I}_{2n\times 2n}), \tag{5.12}$$

where $\bar{\mathcal{A}}$ is the minor of $\mathcal{A}_{1,1}$ in (5.10).

Using the idea presented in Mendez et al. [18] and in Section 3.1, we calculate the reproduction number $\mathcal{R}_{0,n}$ with respect to the deterministic model (5.11) in the absence of treatment (that is, case where $\mathbf{m} = \mathbb{E}\begin{pmatrix} S-\bar{\kappa} & I_1 \ldots I_n \end{pmatrix}^T$ and $d\mathbf{m} = A_{1,1}\ \mathbf{m}\ dt$) as

$$\begin{aligned} \mathcal{R}_{0,n} &= \lambda\bar{\kappa}\sum_{r=1}^{n} h_r \prod_{j=1}^{r}\left(\frac{\rho_{j-1}}{\mu+\rho_j}\right) + \frac{1}{2}\left(\frac{\sigma_1^2\bar{\kappa}^2}{\mu+\rho_1}\right), \\ &= R_{0,n} + \frac{1}{2}\left(\frac{\sigma_1^2\bar{\kappa}^2}{\mu+\rho_1}\right), \end{aligned} \tag{5.13}$$

where $R_{0,n}$ is defined in (3.3). Also, using similar idea, we calculate the elimination threshold $\mathcal{R}_{t,n}$ with respect to (5.11) in the presence of treatment as

$$\begin{aligned} \mathcal{R}_{t,n} &= \bar{\kappa}\lambda\sum_{k=1}^{n}\left[\frac{u_k h_k + \tau\epsilon v_k}{\prod_{j=1}^{k}\left(a_j b_j - \tau\phi\right)}\right] + \frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1 b_1 - \tau\phi}\right), \\ &= R_{t,n} + \frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1 b_1 - \tau\phi}\right), \end{aligned} \tag{5.14}$$

where u_k, v_k and $R_{t,n}$ are defined in (4.4).

5.3. Stability of infection-free equilibrium $\bar{P}_0$ of (5.6)

We get conditions for stochastic stability of the infection-free equilibrium $\bar{P}_0$ of (5.6). According to Tornatore et al. [22], 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. For this reason, we first study the conditions for stochastic stability of the infection-free equilibrium $\bar{P}_0$ of the linear associated system (5.10) and later use Theorem A.2 in [22] to extend the result to that of the nonlinear system (5.6).

Remark 10. We compute the determinant of $\bar{\mathcal{A}}$ as $det(\bar{\mathcal{A}}) = \left[\prod_{j=1}^{n}\left(a_j b_j - \tau\phi\right)\right](1 - \mathcal{R}_{t,n})$.

Define

$$\begin{aligned}
\overline{\mathcal{R}}_{0,n} &= \lambda\bar{\kappa}\sum_{r=1}^{n} h_r \prod_{j=1}^{r}\left(\frac{\rho_{j-1}}{\mu+\rho_j+\tau}\right) + \frac{1}{2}\left(\frac{\sigma_1^2\bar{\kappa}^2}{\mu+\rho_1+\tau}\right),\\
\overline{\mathcal{R}}_{t,n} &= \bar{\kappa}\lambda\sum_{k=1}^{n-1}\left[\frac{u_k h_k+\tau\epsilon v_k}{\prod_{j=1}^{k}\left(a_j b_j-\tau\phi\right)}\right] + \bar{\kappa}\lambda\left[\frac{h_n\rho_{n-1}u_{n-1}}{a_n\prod_{j=1}^{n-1}\left(a_j b_j-\tau\phi\right)}\right] + \frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1 b_1-\tau\phi}\right).
\end{aligned} \tag{5.15}$$

It is clear from (5.15) that $\overline{\mathcal{R}}_{0,n} < \mathcal{R}_{t,n}$ and $\overline{\mathcal{R}}_{t,n} = \mathcal{R}_{t,n-1} + \bar{\kappa}\lambda\left[\frac{h_n b_n\rho_{n-1}u_{n-1}}{a_n b_n\prod_{j=1}^{n-1}\left(a_j b_j-\tau\phi\right)}\right] \leq \mathcal{R}_{t,n}$.

Also, $det(A_{1,1}) = -(-1)^n\mu\left[\prod_{j=1}^{n} a_j\right]\left(1-\overline{\mathcal{R}}_{0,n}\right)$ and $det\left(\text{Minor of } \bar{\mathcal{A}}_{2n,2n}\right) = a_n\left[\prod_{j=1}^{n-1}\left(a_j b_j-\tau\phi\right)\right]\left(1-\overline{\mathcal{R}}_{t,n}\right)$. It follows directly from (5.10) that $\nu - \sigma_1^2\bar{\kappa}^2/2 = a_1\left(1-\lambda\bar{\kappa}h_1/a_1 - \sigma_1^2\bar{\kappa}^2/(2a_1)\right) = a_1\left(1-\overline{\mathcal{R}}_{0,1}\right) > a_1\left(1-\mathcal{R}_{t,1}\right) > 0$ if $\mathcal{R}_{t,1} < 1$.

Theorem 14. *The real part of all eigenvalues of $\mathcal{A}$ is negative if $\mathcal{R}_{t,n} < 1$.*

Proof. Using the result from (5.12), it suffices to show that the real part of all eigenvalues of $\bar{\mathcal{A}}$ is negative. Define $\mathcal{B} = -\bar{\mathcal{A}}$. We can write $\mathcal{B}$ in the form

$$\mathcal{B} = \mathcal{L}\mathcal{U}, \tag{5.16}$$

where $\mathcal{L}$ and $\mathcal{U}$ are upper and lower diagonal matrices, respectively with positive diagonals. The matrices $\mathcal{L} = \left(\mathcal{L}_{i,j}\right)$ and $\mathcal{U} = \left(\mathcal{U}_{i,j}\right)$ are computed rigorously as follows:

$$\begin{aligned}
\mathcal{L}_{i,j} &= \frac{1}{\mathcal{D}_j}\begin{vmatrix}\mathcal{B}_{1,1} & \mathcal{B}_{1,2} & \dots & \mathcal{B}_{1,j}\\ \mathcal{B}_{2,1} & \mathcal{B}_{2,2} & \dots & \mathcal{B}_{2,j}\\ \vdots & \vdots & \dots & \vdots\\ \mathcal{B}_{j-1,1} & \mathcal{B}_{j-1,2} & \dots & \mathcal{B}_{j-1,j}\\ \mathcal{B}_{i,1} & \mathcal{B}_{i,2} & \dots & \mathcal{B}_{i,j}\end{vmatrix}, \text{ for } i \geq j \neq 1,\ \ \mathcal{L}_{i,1} = \frac{|\mathcal{B}_{i,1}|}{\mathcal{D}_1} \text{ for } i = 1,2,...,2n, \text{ and } 0 \text{ elsewhere},\\
\mathcal{U}_{i,j} &= \frac{1}{\mathcal{D}_{j-1}}\begin{vmatrix}\mathcal{B}_{1,1} & \dots & \mathcal{B}_{1,i-1} & \mathcal{B}_{1,j}\\ \mathcal{B}_{2,1} & \dots & \mathcal{B}_{2,i-1} & \mathcal{B}_{2,j}\\ \vdots & \vdots & \vdots & \vdots\\ \mathcal{B}_{i,1} & \dots & \mathcal{B}_{i,i-1} & \mathcal{B}_{i,j}\end{vmatrix}, \text{ for } 1 \neq i \leq j,\ \ \mathcal{U}_{1,j} = \mathcal{B}_{1,j}, \text{ for } j = 1,2,...,2n, \text{ and } 0 \text{ elsewhere},
\end{aligned}$$

where $\mathcal{D}_0 := 1$, and $\mathcal{D}_j = \begin{vmatrix}\mathcal{B}_{1,1} & \mathcal{B}_{1,2} & \dots & \mathcal{B}_{1,j}\\ \mathcal{B}_{2,1} & \mathcal{B}_{2,2} & \dots & \mathcal{B}_{2,j}\\ \vdots & \vdots & \dots & \vdots\\ \mathcal{B}_{j,1} & \mathcal{B}_{j,2} & \dots & \mathcal{B}_{j,j}\end{vmatrix}$ for $j = 1,2,...,2n$, and can be simplified as

$$\begin{aligned}
\mathcal{D}_j &= \left[\prod_{k=1}^{j} a_k\right]\left(1-\overline{\mathcal{R}}_{0,j}\right), \text{ for } j = 1,2,...,n,\\
\mathcal{D}_{n+j} &= \left[\prod_{k=1}^{j}\left(a_k b_k-\tau\phi\right)\right]\left(\prod_{k=j+1}^{n} a_k\right)\left(1-\overline{\mathcal{R}}_{t,j+1}\right) + u_j\frac{\prod_{k=1}^{n} a_k}{\prod_{k=1}^{j}\rho_{k-1}}\left(\overline{\mathcal{R}}_{0,n}-\overline{\mathcal{R}}_{0,j+1}\right), \text{ for } j = 1,2,...,n-1,\\
\mathcal{D}_{2n} &= \left[\prod_{k=1}^{n}\left(a_k b_k-\tau\phi\right)\right]\left(1-\mathcal{R}_{t,n}\right),
\end{aligned} \tag{5.17}$$

where $\{a_k, b_k\}$ and u_k are defined in (4.3) and (4.4), respectively. If $\mathcal{R}_{t,n} < 1$, it follows from (5.15) and (5.17) that $\overline{\mathcal{R}}_{t,j} < \mathcal{R}_{t,n} < 1$, $\mathcal{D}_j > 0$ and the diagonal entries $\mathcal{U}_{j,j} = \frac{\mathcal{D}_j}{\mathcal{D}_{j-1}} > 0$ for all $j = 1,2,...,2n$. Since $\mathcal{B} \in Z^{2n}$ is a Z-matrix

$\left(\text{that is, } b_{i,j} \le 0 \text{ if } i \neq j, 1 \le i, j \le n, \text{ where } \mathcal{B} = \left(b_{i,j}\right)\right)$ and the diagonal entries $\mathcal{L}_{j,j} = \frac{\mathcal{D}_j}{\mathcal{D}_j} = 1$ for $j = 1, 2, ..., 2n$, it follows from relations D_{12} and J_{29} in [19] that the real part of each eigenvalues of matrix $\mathcal{B}$ is positive, which is in turn equivalent to $s\left(\bar{\mathcal{A}}\right) < 0$. ■

Remark 11. It follows from relation I_{25} in [19] that there exist a positive diagonal matrix $\mathcal{K}$ such that $\mathcal{K}\mathcal{A} + \mathcal{A}^T\mathcal{K}$ is negative definite. Thus, there exist a real number $z > 0$ such that $y^T\left(\mathcal{K}\mathcal{A} + \mathcal{A}^T\mathcal{K}\right)y \le -zy^Ty$ for every nonzero vector $y \in \mathbb{R}^{2n+1}$.

Let $k_j > 0$, $j = 1, 2, ..., 2n + 1$ be the diagonal entries of $\mathcal{K}$. We shall show that the trivial solution $\Phi = 0$ of (5.10) is asymptotically stable if $\mathcal{R}_{t,n} < 1$ by finding appropriate positive numbers k_j, $j = 1, 2, ..., 2n + 1$, such that

$$\Phi^T\left(\mathcal{K}\mathcal{A} + \mathcal{A}^T\mathcal{K} + \sum_{i=1}^{n}\mathcal{G}_i^T\mathcal{K}\mathcal{G}_i\right)\Phi < 0. \tag{5.18}$$

Theorem 15. *The trivial solution $\Phi = 0$ of* (5.10) *is asymptotically stable if $\mathcal{R}_{t,n} < 1$.*

Proof. Let $\Phi = (\Phi_1, \Phi_2, ..., \Phi_{2n+1})^T$ be a vector satisfying (5.10) and define $V : [0, T] \times \mathbb{R}^{2n+1} \to \mathbb{R}^+$ by

$$V(t, \Phi) = \Phi^T\mathcal{K}\Phi,$$

where $\mathcal{K}$ is the positive diagonal matrix described in Remark 11 such that $k_1 = k_2 = \frac{z}{8\sigma_1^2\bar{\kappa}^2}$, $k_j > 0$ for $j = 3, 4, ..., 2n+1$, and z is described in Remark 11. If $\mathcal{R}_{t,n} < 1$, it follows from (5.8) and (5.10) that

$$\begin{aligned} LV(t,\Phi) &= \Phi^T\left(\mathcal{K}\mathcal{A} + \mathcal{A}^T\mathcal{K}\right)\Phi + \Phi^T\left(\sum_{i=1}^{n}\mathcal{G}_i^T\mathcal{K}\mathcal{G}_i\right)\Phi \\ &\le -z\,\Phi^T\Phi + \Phi^T\left(\sum_{i=1}^{n}\mathcal{G}_i^T\mathcal{K}\mathcal{G}_i\right)\Phi = -z\sum_{j=1}^{2n+1}\Phi_j^2 + 2\sigma_1^2\bar{\kappa}^2\left(k_1 + k_2\right)\sum_{j=2}^{n+1}\Phi_j^2 \\ &= -z\,\Phi_1^2 - \frac{z}{2}\sum_{j=2}^{n+1}\Phi_j^2 - z\sum_{j=n+2}^{2n+1}\Phi_j^2 < -\frac{z}{2}\Phi^T\Phi. \end{aligned}$$

Let k_l and k_u be $\min\{k_1, ..., k_{2n+1}\}$ and $\max\{k_1, ..., k_{2n+1}\}$, respectively. Then $k_l\|\Phi\|^2 \le V(t,\Phi) \le k_u\|\Phi\|^2$. It follows from Theorem A.1 of Tornatore et al. [22] that the trivial solution of (5.10) is asymptotically stable if $\mathcal{R}_{t,n} < 1$. ■

We state the following theorem (Theorem A.2 of Tornatore et al. [22]) which shall be used to show the global stability of the trivial solution of (5.6).

Theorem 16. *(See [22], Theorem A.2) If the trivial solution $\Phi = 0$ of a linear system of stochastic differential equation with drift and diffusion coefficients $F(t, \Phi)$ and $G(t, \Phi)$, respectively, is asymptotically stable and the drift and diffusion coefficients $f(t, \Phi)$ and $g(t, \Phi)$, respectively, of its equivalent nonlinear system (the linear system derived by linearizing the nonlinear system) satisfy the inequality*

$$\|f(t,\Phi) - F(t,\Phi)\| + \|g(t,\Phi) - G(t,\Phi)\| < \varepsilon\,\|\Phi\| \tag{5.19}$$

in a sufficiently small neighbourhood of $\Phi = 0$*, with a sufficiently small constant* ε*, then the trivial solution* $\Phi(t) = 0$ *of the nonlinear system is globally asymptotically stable. Here,* $\|.\|$ *denotes the* L_2*-norm.*

Substituting $\Phi = \begin{pmatrix} S - \bar{\kappa} & I_1 \ldots I_n & T_1 \ldots T_n \end{pmatrix}^T$ into (5.6), we have

$$\begin{aligned}
d\Phi_1 &= \left(-\lambda(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \left(h_j \Phi_{j+1} + \epsilon \Phi_{n+j+1}\right) - \mu \Phi_1 + \tfrac{1}{2}(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \sigma_j^2 \Phi_{j+1}^2 - \tfrac{1}{2}\sigma_1^2 (\Phi_1 + \bar{\kappa})^2 \Phi_2 \right) dt \\
&\quad -(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \sigma_j \Phi_{j+1}\, dW_j(t), \ \ \Phi_1(t_0) = \Phi_{0,1}, \\
d\Phi_2 &= \left(\lambda(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \left(h_j \Phi_{j+1} + \epsilon \Phi_{n+j+1}\right) - a_1 \Phi_2 + \phi \Phi_{n+2} - \tfrac{1}{2}(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \sigma_j^2 \Phi_{j+1}^2 + \tfrac{1}{2}\sigma_1^2 (\Phi_1 + \bar{\kappa})^2 \Phi_2 \right) dt \\
&\quad +(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \sigma_j \Phi_{j+1}\, dW_j(t), \ \ \Phi_2(t_0) = \Phi_{0,2}, \\
d\Phi_{k+1} &= \left(\rho_{k-1}\Phi_k - a_k \Phi_{k+1} + \phi \Phi_{n+k+1}\right)\, dt, \ \ \Phi_{k+1}(t_0) = \Phi_{0,k+1}, \\
d\Phi_{n+2} &= (\tau \Phi_2 - b_1 \Phi_{n+2}) dt, \ \ \Phi_{n+2}(t_0) = \Phi_{0,n+2}, \\
d\Phi_{n+k+1} &= \left(\tau \Phi_{k+1} + \gamma_{k-1}\Phi_{n+k} - b_k \Phi_{n+k+1}\right)\, dt, \ \ \Phi_{n+k+1}(t_0) = \Phi_{0,n+k+1}, \ \ \text{for } k = 2, 3, ..., n,
\end{aligned} \tag{5.20}$$

where a_k and b_k are defined in (4.3).

Theorem 17. *The infection-free equilibrium* $\bar{P}_0$ *of the system (5.6) is globally asymptotically stable in the feasible region if* $\mathcal{R}_{t,n} < 1$.

We show that Theorem 16 is satisfied with respect to the systems (5.10) and (5.20), where F and G are the drift and diffusion coefficients of (5.10), respectively, and f and g are the drift and diffusion coefficients of (5.20), respectively.

Proof. If $\mathcal{R}_{t,n} < 1$, we only need to show that condition (5.19) is satisfied since the trivial solution $\Phi = 0$ of (5.10) is asymptotically stable. In a sufficiently small neighbourhood of $\Phi = 0$, choose $\varepsilon > 0$ sufficiently small so that $|\Phi| < \varepsilon$. We have $|f(t, \Phi) - F(t, \Phi)| + |g(t, \Phi) - G(t, \Phi)|$ reducing to

$$\begin{aligned}
&\sqrt{2\left(\lambda\Phi_1 \sum_{j=1}^{n} \left(h_j \Phi_{j+1} + \epsilon \Phi_{n+j+1}\right) - \frac{1}{2}(\Phi_1 + \bar{\kappa}) \sum_{j=1}^{n} \sigma_j^2 \Phi_{j+1}^2 + \frac{1}{2}\sigma_1^2 \Phi_2 \left(\Phi_1^2 + 2\Phi_1 \bar{\kappa}\right)\right)^2} + \sqrt{\Phi_1^2 \left(\sum_{j=1}^{n} \sigma_j \Phi_{j+1}\right)^2} \\
&\le \sqrt{6\left(2\lambda^2 \varepsilon^2 \sum_{j=1}^{n} \left(h_j^2 \Phi_{j+1}^2 + \epsilon^2 \Phi_{n+j+1}^2\right) + \frac{\varepsilon^2(\varepsilon^2 + \bar{\kappa}^2)}{2} \sum_{j=1}^{n} \sigma_j^4 \Phi_{j+1}^2 + \frac{\sigma_1^4}{2} \varepsilon^2 \left(\varepsilon^2 + 4\bar{\kappa}^2\right) \Phi_1^2\right)} + \sqrt{2}\varepsilon \sqrt{\sum_{j=1}^{n} \sigma_j^2 \Phi_{j+1}^2} \\
&\le \varepsilon \sqrt{6\underline{h}} \sqrt{\sum_{j=1}^{2n+1} \Phi_j^2} + \sqrt{2}\underline{\sigma}\varepsilon \sqrt{\sum_{j=1}^{2n+1} \Phi_j^2} \\
&\le \overline{h} \|\Phi\|,
\end{aligned}$$

where $\underline{h} = \max_{1 \le j \le n} \left\{2\lambda^2 h_j^2 + (\varepsilon^2 + \bar{\kappa}^2)\sigma_j^4, \sigma_1^4 \left(\varepsilon^2 + 4\bar{\kappa}^2\right)/2\right\}$ and $\overline{h} = \varepsilon \max\left\{\sqrt{6\underline{h}}, \ \sqrt{2}\underline{\sigma}\right\}$.

■.

Remark 12. From (5.14), if

$$1 \leq \mathcal{R}_{t,n} < 1 + \frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1b_1-\tau\phi}\right), \tag{5.21}$$

or equivalently,

$$1 - \frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1b_1-\tau\phi}\right) \leq R_{t,n} < 1, \tag{5.22}$$

then from Remark 10, we have $-\frac{1}{2}\left(\frac{b_1\sigma_1^2\bar{\kappa}^2}{a_1b_1-\tau\phi}\right)\prod_{j=1}^{n}\left(a_jb_j-\tau\phi\right) < det(\bar{\mathcal{A}}) = \left[\prod_{j=1}^{n}\left(a_jb_j-\tau\phi\right)\right](1-\mathcal{R}_{t,n}) \leq 0$. Since $det(\bar{\mathcal{A}}) = \prod_{j=1}^{2n} r_j$, where r_j, $j = 1, ..., 2n$, are the eigenvalues of $\bar{\mathcal{A}}$, then at least one eigenvalue of $\bar{\mathcal{A}}$ is positive. This causes an epidemic growth, initially, leading to transient epidemic advance. The transient epidemic advance is caused by the noise intensity, σ_1, in the rate of efficient contact in stage 1 of the infection.

6. Numerical simulations

In this section, we give simulation result for the susceptible, infected untreated and treated population satisfying (2.1), (3.2) and (5.6) using published real data estimates in the work [7, 15]. The following graph verifies the global stability criteria discussed in previous sections.

6.1. Numerical verification of global stability of equilibrium points for the deterministic model

For $i = 1, 2, ..., n$, let S_m, $I_{i,m}$, $T_{i,m}$ be simulated value of S, I_i, T_i, respectively, at time t_m with respect to (2.1). We use the Euler-Maruyama type discretization scheme [14] to discretize (2.1) on $t_0 \leq t \leq T$ for a given discretization $t_0 < t_1 < ... < t_i < ... < t_N = T$ of time interval $[t_0, T]$ with equidistance discretization times $t_i = t_0 + i\Delta t$ and time step $\Delta t = (T - t_0)/N$.

6.1.1. *Graphs showing global stability of P_0 (Figure 2 (a)) and P_1 (Figure 2 (b)) for $n = 1$ (no treatment)*

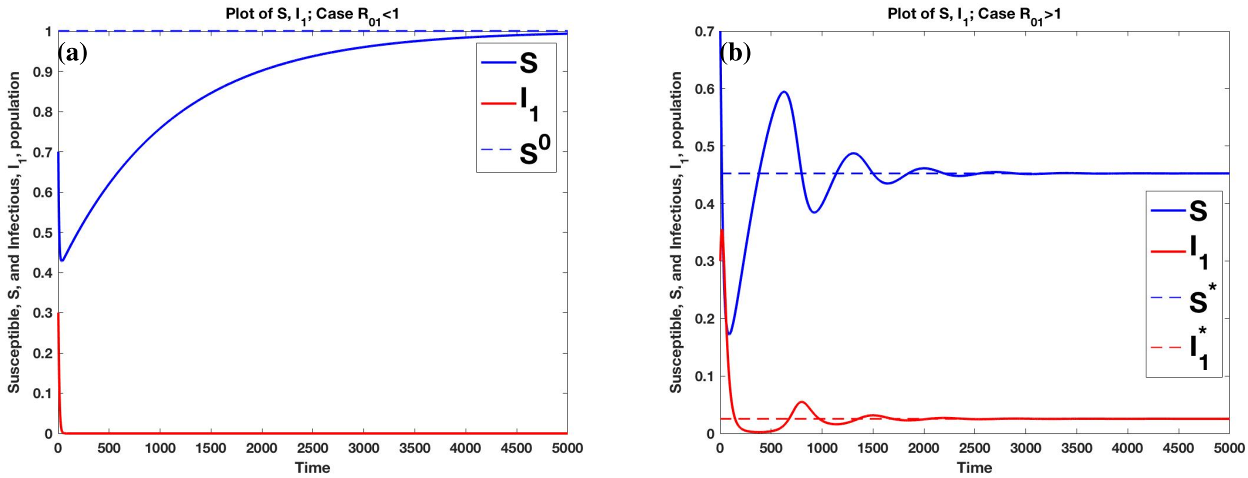

Figure 2: Graphs of deterministic trajectories of S and I_1 model for the cases $R_{0,1} < 1$ and $R_{0,1} > 1$.

Figure 2 (a) shows the trajectory of S and I_1 with initial condition $S_0 = 0.7$, $I_{01} = 0.3$, $\beta = 0.018$, $\lambda = 1.2$, $h_1 = 2.76$, $\rho_1 = 1/0.271$, $\mu = 0.018$. In this case, $R_{0,1} = 0.893$ and infection-free equilibrium $P_0 = \left(S^0 = 1, I_1^0 = 0\right)^T$. Figure 2 (b) shows the trajectory of S and I_1 with initial condition $S_0 = 0.7$, $I_{01} = 0.3$, $\beta = 0.18$, $\lambda = 3.1$, $h_1 = 2.76$, $\rho_1 = 1/0.271$, $\mu = 0.18$. In this case, $R_{0,1} = 2.2108$ and endemic equilibrium $P_1 = \left(S^* = 0.4523, I_1^* = 0.0255\right)^T$.

6.1.2. *Graphs showing global stability of P_0 (Figure 2 (a)) and P_1 (Figure 2 (b)) for $n = 2$ (no treatment)*

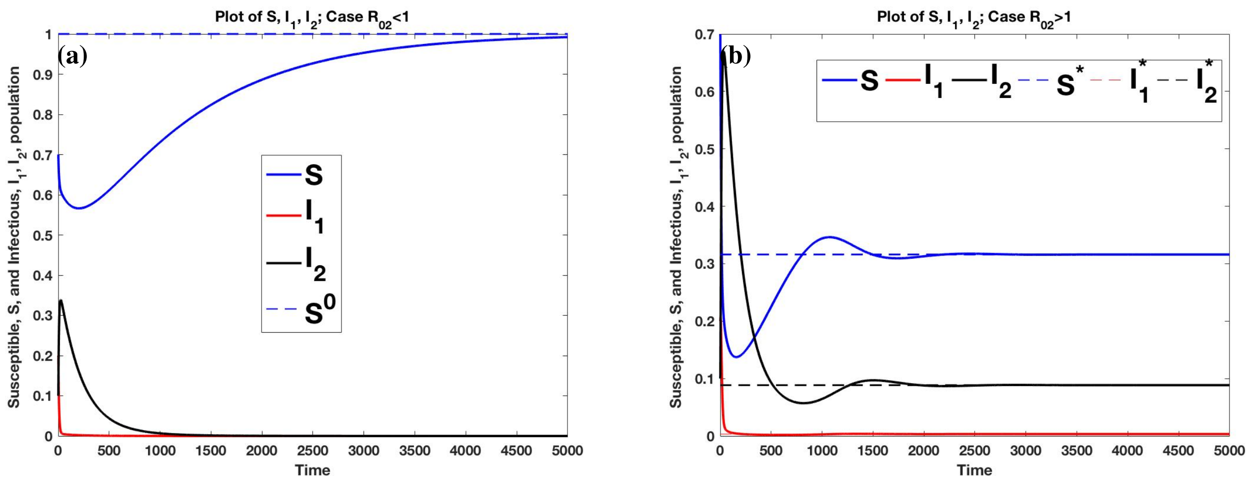

Figure 3: Graphs of deterministic trajectories of S, I_1 and I_2 for the cases $R_{0,2} < 1$ and $R_{0,2} > 1$.

Figure 3 (a) shows the trajectory of S, I_1 and I_2 with initial condition $S_0 = 0.7$, $I_{01} = 0.2$, $I_{02} = 0.1$, $\beta = 0.018$, $\lambda = 0.6$, $h_1 = 2.76$, $h_2 = 0.106$, $\rho_1 = 1/0.271$, $\rho_2 = 1/8.31$, $\mu = 0.018$. In this case, $R_{0,2} = 0.9041$ and infection-free equilibrium $P_0 = \left(S^0 = 1, I_1^0 = 0, I_2^0 = 0\right)^T$. Figure 3 (b) shows the trajectory of S, I_1 and I_2 with initial condition $S_0 = 0.7$, $I_{01} = 0.2$, $I_{02} = 0.1$, $\beta = 0.018$, $\lambda = 2.1$, $h_1 = 2.76$, $h_2 = 0.106$, $\rho_1 = 1/0.271$, $\rho_2 = 1/8.31$, $\mu = 0.018$. In this case, $R_{0,2} = 3.1644$ and endemic equilibrium $P_1 = \left(S^* = 0.316, I_1^* = 0.0033, I_2^* = 0.0886\right)^T$.

6.1.3. *Graphs showing global stability of $\bar{P}_0$ (Figure 4 (a)) and $\bar{P}_1$ (Figure 4 (b)) for $n = 1$ (with treatment)*

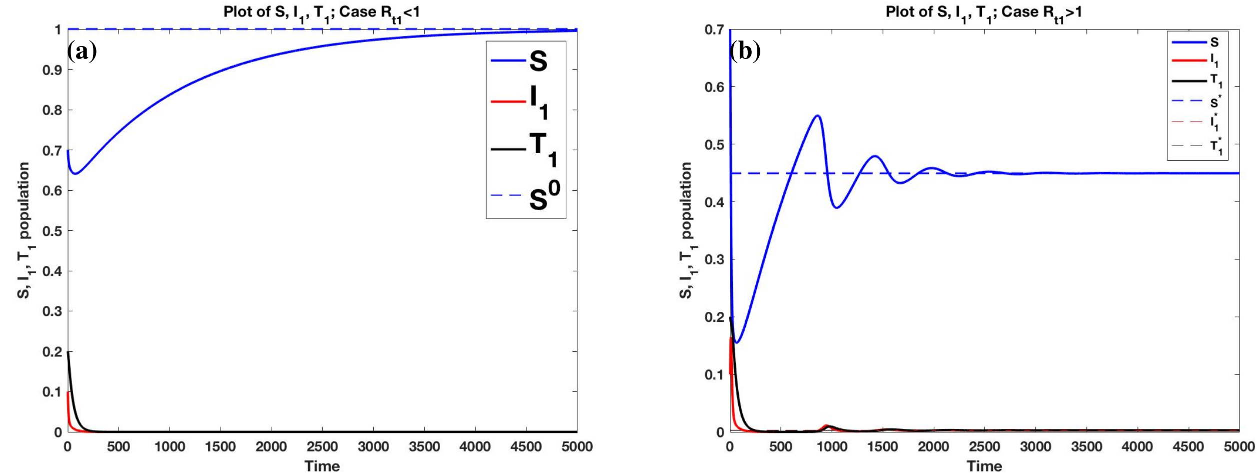

Figure 4: Graphs of deterministic trajectories of S, I_1, T_1 for the cases $R_{t,1} < 1$ and $R_{t,1} > 1$.

Figure 4 (a) shows the trajectory of S, I_1, T_1 with initial condition $S_0 = 0.7$, $I_{01} = 0.1$, $T_{01} = 0.2$, $\beta = 0.018$, $\lambda = 0.6$, $h_1 = 2.76$, $h_2 = 0.106$, $\rho_1 = 1/0.271$, $\mu = 0.018$, $\epsilon = 0.01$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$. In this case, $R_{t,1} = 0.4307$ and infection-free equilibrium $\bar{P}_0 = \left(\bar{S}^0 = 1, \bar{I}_1^0 = 0, \bar{T}_1^0 = 0\right)^T$. Figure 4 (b) shows the trajectory of S, I_1, T_1 with initial condition $S_0 = 0.7$, $I_{01} = 0.1$, $T_{01} = 0.2$, $\beta = 0.018$, $\lambda = 3.1$, $h_1 = 2.76$, $\rho_1 = 1/0.271$, $\mu = 0.018$, $\epsilon = 0.01$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$. In this case, $R_{t,1} = 2.2253$ and endemic equilibrium $\bar{P}_1 = \left(\bar{S}^* = 0.4494, \bar{I}_1^* = 0.0026, \bar{T}_1^* = 0.0028\right)^T$.

6.1.4. Graphs showing global stability of $\bar{P}_0$ (Figure 5 (a)) and $\bar{P}_1$ (Figure 5 (b)) for $n = 2$ (with treatment)

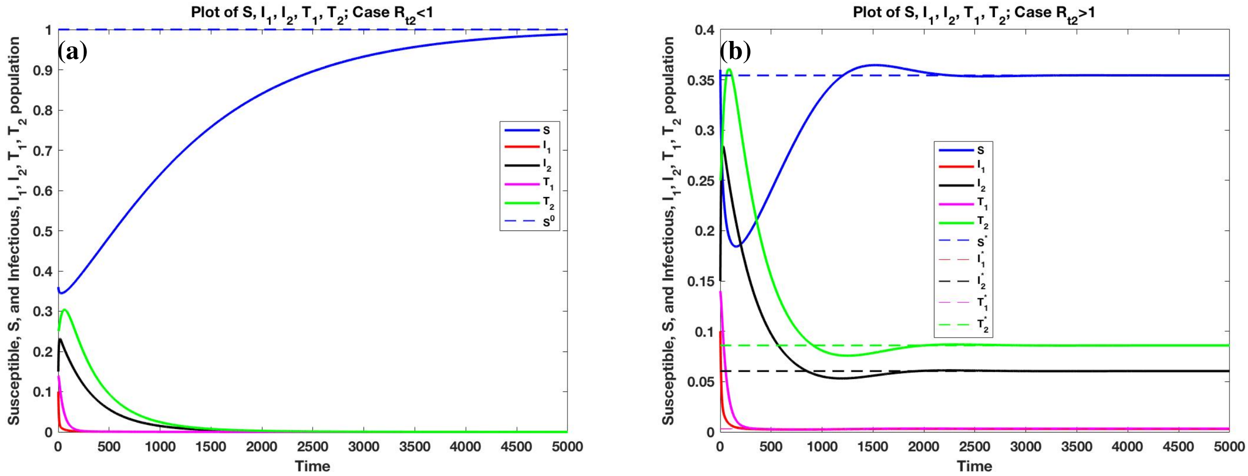

Figure 5: Graphs of deterministic trajectories of S, I_1, I_2, T_1, T_2 for the cases $R_{t,2} < 1$ and $R_{t,2} > 1$.

Figure 5 (a) shows the trajectory of S, I_1, I_2, T_1, T_2 with initial condition $S_0 = 0.36$, $I_{01} = 0.1$, $I_{02} = 0.15$, $T_{01} = 0.14$, $T_{02} = 0.25$, $\beta = 0.018$, $\lambda = 0.6$, $h_1 = 2.76$, $h_2 = 0.106$, $\rho_1 = 1/0.271$, $\rho_2 = 1/8.31$, $\mu = 0.018$, $\epsilon = 0.01$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$, $\gamma_2 = 1/54$. In this case, $R_{t,2} = 0.8062$ and infection-free equilibrium $\bar{P}_0 = \left(\bar{S}^0 = 1, \bar{I}_1^0 = 0, \bar{I}_2^0 = 0, \bar{T}_1^0 = 0, \bar{T}_2^0 = 0\right)^T$. Figure 5 (b) shows the trajectory of S, I_1, I_2, T_1, T_2 with initial condition $S_0 = 0.46$, $I_{01} = 0.1$, $I_{02} = 0.15$, $T_{01} = 0.14$, $T_{02} = 0.25$, $\beta = 0.018$, $\lambda = 2.1$, $h_1 = 2.76$, $h_2 = 0.106$, $\rho_1 = 1/0.271$, $\rho_2 = 1/8.31$, $\mu = 0.018$, $\epsilon = 0.01$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$, $\gamma_2 = 1/54$. In this case, $R_{t,2} = 2.8216$ and endemic equilibrium $\bar{P}_1 = \left(\bar{S}^* = 0.3544, \bar{I}_1^* = 0.003, \bar{I}_2^* = 0.0605, \bar{T}_1^* = 0.0033, \bar{T}_2^* = 0.086\right)^T$.

6.2. Numerical verification of global stability of $\bar{P}_0$ in stochastic model (5.6)

For $i = 1, 2, ..., n$, let S_m, $I_{i,m}$, $T_{i,m}$ be simulated value of S, I_i, T_i, respectively, at time t_m. We use the Euler-Maruyama type discretization scheme [14] to discretize (5.6) on $t_0 \le t \le T$. For a given discretization $t_0 < t_1 < ... < t_i < ... < t_N = T$ of time interval $[t_0, T]$ with equidistance discretization times $t_i = t_0 + i\Delta t$ and time step $\Delta t = (T - t_0)/N$, the Euler discretization is given by

$$\Delta x_m^i = a^i(t_m, x_m)\,\Delta t + \sum_{j=1}^{n} b^{i,j}(t_m, x_m)\,\Delta W_{j,m}, \quad x_0 = x(t_0), \tag{6.1}$$

where $x(t) = (S(t), I_1(t), ..., I_n(t), T_1(t), ..., T_n(t))$ satisfying (5.6), $x_m^i = x^i(t_m)$, $i = 1, 2, ..., 2n+1$, a (defined in (5.7)) and b are the drift and diffusion coefficients of (5.6), respectively, $\Delta x_m = x_{m+1} - x_m$, $\Delta W_{j,m} = W_{j,m+1} - W_{j,m}$, for $m = 0, 1, 2, ..., N-1$, $j = 1, 2, ..., n$. We generate random increments $\Delta W_{j,m}$ for $m = 0, 1, 2, ..., N-1$ of the Wiener process $W_k(t)$, $t \ge 0$. It is known that these increments are independent Gaussian random variables with mean $\mathbb{E}\left(\Delta W_{j,m}\right) = 0$ and variance $\mathbb{E}\left(\left(\Delta W_{j,m}\right)^2\right) = \Delta t$.

6.2.1. Transient epidemic advances: Case where $R_{t,1} < 1$ and $\mathcal{R}_{t,1} > 1$

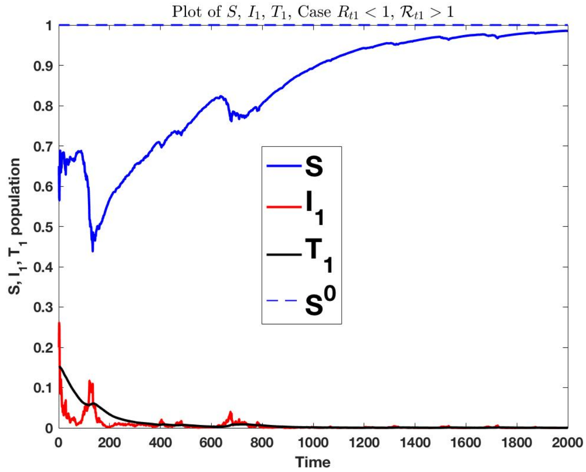

Figure 6: Graph of stochastic trajectories of S, I_1, T_1 for the case where $R_{t,1} < 1$.

Figure 6 shows the trajectory of S, I_1, T_1 with initial condition $S_0 = 0.55$, $I_{01} = 0.3$, $T_{01} = 0.15$, $\beta = 0.18$, $\lambda = 0.85$, $h_1 = 3.7$, $\rho_1 = 1/0.271$, $\mu = 0.18$, $\epsilon = 0.1$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$, $\sigma_1 = 2$. In this case, $R_{t,1} = 0.7813$, $\mathcal{R}_{t,1} = 1.2676$ and infection-free equilibrium $\bar{P}_0 = \left(\bar{S}^0 = 1, \bar{I}_1^0 = 0, \bar{T}_1^0 = 0,\right)^T$.

6.2.2. Transient epidemic advances: Case where $R_{t,2} < 1$ and $\mathcal{R}_{t,2} > 1$

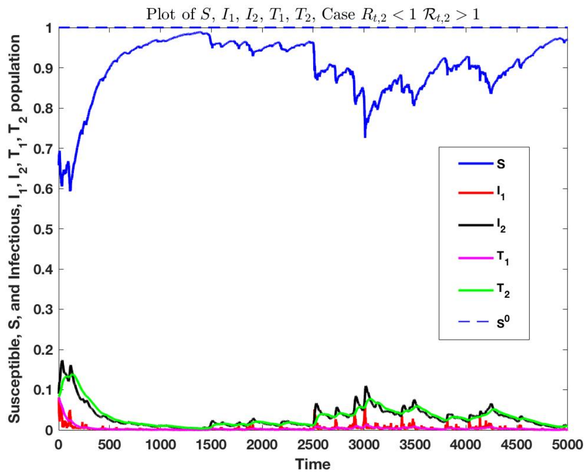

Figure 7: Graph of stochastic trajectories of S, I_1, I_2, T_1, T_2 for the case where $R_{t,2} < 1$ and $\mathcal{R}_{t,2} > 1$.

Figure 7 shows the trajectory of S, I_1, I_2, T_1, T_2 with initial condition $S_0 = 0.46$, $I_{01} = 0.08$, $I_{02} = 0.09$, $T_{01} = 0.081$, $T_{02} = 0.082$, $\beta = 0.18$, $\lambda = 0.85$, $h_1 = 2.7$, $h_2 = 0.05$, $\rho_1 = 1/0.271$, $\rho_2 = 1/8.31$, $\mu = 0.18$, $\epsilon = 0.1$, $\tau = 0.5$, $\phi = 0.32$, $\gamma_1 = 1/8.21$, $\gamma_2 = 1/54$, $\sigma_1 = 1.8$. In this case,

$R_{t,2} = 0.8094$, $\mathcal{R}_{t,2} = 1.2033$, and infection-free equilibrium $\bar{P}_0 = \left(\bar{S}^0 = 1, \bar{I}_1^0 = 0, \bar{I}_2^0 = 0, \bar{T}_1^0 = 0, \bar{T}_2^0 = 0\right)^T$.

7. Conclusion

In this paper, we present a deterministic and stochastic HIV/AIDS epidemic model describing the transmission of HIV/AIDS disease between susceptible, infected untreated population and infected individuals receiving the ART treatment. With the help of the next generation matrix method, we obtain the basic reproduction numbers $R_{0,n}$, $R_{t,n}$ and $\mathcal{R}_{t,n}$ denoting the deterministic basic reproduction number in the absence of ART treatments, deterministic basic reproduction number in the presence of ART treatments and stochastic reproduction number in the presence of ART treatment, respectively, and derive the global dynamics of the model. We discuss the stability of the infection-free and endemic equilibrium in the absence (presence) of treatments by showing that if the reproduction number $R_{0,n} \leq 1$ ($R_{t,n} \leq 1$), the infection-free equilibrium derived from untreated population (treated and untreated population) is globally asymptotically stable. Hence, the disease will be extinct. Also, we further show that if $R_{0,n} > 1$ ($R_{t,n} > 1$), the endemic equilibrium derived from untreated population (endemic equilibrium derived from both treated and untreated population) is globally asymptotically stable. This shows that there is enough treatment to avoid persistence of infection in the endemic equilibrium state if $R_{t,n} = 1$ and suggests that early treatment of AIDS is necessary. By introducing noise in the transmission rate of the disease, a theoretical treatment strategy of regular HIV testing and immediate treatment with Antiretroviral Therapy (ART) is investigated in the presence and absence of noise. We further show by studying the effect of noise in the transmission rate of the disease that transient epidemic invasion can still occur even if $R_{t,n} < 1$. Numerical simulations are presented to support our claim.

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