Research Article
Dynamic of a TB-HIV Coinfection Epidemic Model with Latent Age

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A coepidemic arises when the spread of one infectious disease stimulates the spread of another infectious disease. Recently, this has happened with human immunodeficiency virus (HIV) and tuberculosis (TB). The density of individuals infected with latent tuberculosis is structured by age since latency. The host population is divided into five subclasses of susceptibles, latent TB, active TB (without HIV), HIV infectives (without TB), and coinfection class (infected by both TB and HIV). The model exhibits three boundary equilibria, namely, disease free equilibrium, TB dominated equilibrium, and HIV dominated equilibrium. We discuss the local or global stabilities of boundary equilibria. We prove the persistence of our model. Our simple model of two synergistic infectious disease epidemics illustrates the importance of including the effects of each disease on the transmission and progression of the other disease. We simulate the dynamic behaviors of our model and give medicine explanations.

1. Introduction

Coepidemics—the related spread of two or more infectious diseases—have afflicted mankind for centuries. Worldwide, there were an estimated 1.37 million coinfected HIV and TB patients globally in 2007. Around 80 percent of patients live in sub-Saharan Africa. 456000 people died of HIV-associated TB in 2007. HIV/AIDS and tuberculosis (TB) are commonly called the "deadly duo" and referred to as HIV/TB, despite biological differences. HIV is a retrovirus that is transmitted primarily by homosexual and heterosexual contact, needle sharing, and from mother to child. The disease eventually progresses to AIDS as the immune system weakens. HIV can be treated with highly active antiheroical therapy (HAART), but there is presently no cure [1]. Virtually all HIV-infected individuals can transmit the virus to others, and an infected individual's chance of spreading the virus generally increases as the disease progresses and damages the immune system [2]. Tuberculosis is caused by mycobacterium tuberculosis bacteria and is spread through the air. Some TB infections are "latent," meaning that a person has the TB-causing bacteria but it is dormant. A person with latent TB is not sick and is not infectious. However, latent TB can progress to "active" TB. "Active" TB infection means that the TB bacteria are

multiplying and spreading in the body. A person with active TB in their lungs or throat can transmit the bacteria to others. Symptoms of active TB include a cough that lasts several weeks, weight loss, loss of appetite, fever, night sweats, and coughing up blood.

HIV weakens the immune system and so people are more susceptible to catching TB if they are exposed. At least one-third of people living with HIV worldwide are infected with TB and are 20–30 times more likely to develop TB than those without HIV. TB bacteria accelerate the progression of HIV to AIDS. Persons coinfected with TB and HIV may spread the disease not only to the other HIV-infected persons, but also to members of the general population who do not participate in any of the high risk behaviors associated with HIV. People living with HIV and displaying early diagnosis need treatment in time. If TB is present, they should receive TB preventive treatment (IPT). The treatments are not expensive. Therefore, it is essential that adequate attention must be paid to study the transmission dynamics of HIV-TB coinfection in the population. Current treatment for HIV is known as highly active antiretroviral therapy (HAART) [3].

Some authors have developed simulation models to investigate HIV-TB co-epidemic dynamics [4–7]. West and
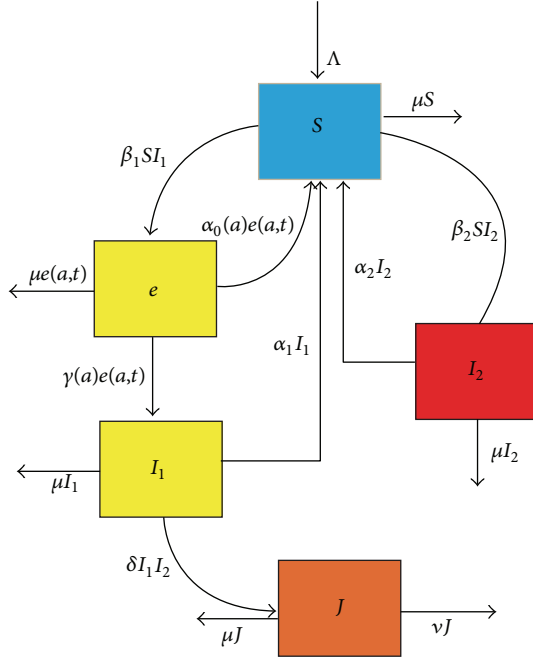
FIGURE 1: The flow diagram of the model (1). Two yellow rectangulars denote the individuals infected by latent tuberculosis and active tuberculosis. The red rectangular denotes the individuals infected by HIV. The orange rectangular denotes the individuals coinfected by TB and HIV.

Thompson [8] developed models which reflect the transmission dynamics of both TB and HIV and discussed the magnitude and duration of the effect that the HIV epidemic may have on TB. Naresh and Tripathi [9] presented a model for HIV-TB coinfection with constant recruitment of susceptibles and found that TB will be eradicated from the population if more than 90 percent TB infectives are recovered due to effective treatment. Naresh et al. [10] studied the effect of tuberculosis on the spread of HIV infection in a logistically growing human population. They found that as the number of TB infectives decreases due to recovery, the number of HIV infectives also decreases and endemic equilibrium tends to TB free equilibrium. Long et al. [11] discussed two synergistic infectious disease epidemics illustrating the importance of including the effects of each disease on the transmission and progression of the other disease.

However, these models may exclude coinfection, may greatly simplify infection dynamics, and may include few disease states (e.g., the important distinction between latent and active TB was absent). They assume that HIV treatment is unavailable. Bifurcation will appear in some models [12, 13]. We perform the additional latent age, analyze the coexistence equilibria, and extend the model to include disease recovery in this paper. At the same time, we obtain the persistence of the system and global stabilities of the equilibria under some conditions.

This paper is organized as follows. In Section 2, we introduce the TB-HIV coinfection model. In Section 3, we introduce the reproduction numbers of TB and HIV R_1, R_2 and discuss the existence of the equilibria. The values of the disease-free equilibrium, the two boundary equilibria, and the coexistence equilibrium are given explicitly. Section 4 focuses on local and global stabilities of the equilibria. In Section 5, we discuss the persistence of the system in suitable period. In Section 6, we simulate and illustrate our results. We give some biological explanations in this section. In Section 7, we conclude our results and discuss the defect of our model.

2. The Model Formulation

Two diseases mentioned in the introduction are spreading in a population of total size $N(t)$. We classify the total population into four classes: the susceptible $S(t)$; the individuals infected by the tuberculosis, $e(a,t)$ and $I_1(t)$ denotes the latent TB class which has no infectious ability and active TB class who can infect the susceptible class, respectively; the individuals infected by HIV $I_2(t)$; the individuals coinfected by tuberculosis and HIV $J(t)$. The individuals infected with active TB infect the susceptible and then develop into the latent individuals at β_1. The individuals infected by HIV infect the susceptible and become the individuals infected by HIV at β_2. An individual already infected with TB can be coinfected with HIV at δ and thus become jointly infected individuals $J(t)$.

Figure 1 presents a schematic flow diagram of the mathematical model as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - \beta_1 S I_1 - \beta_2 S I_2$$
$$+ \int_0^\infty \alpha_0(a) e(a,t) \, da + \alpha_1 I_1 + \alpha_2 I_2,$$
$$\frac{\partial e(a,t)}{\partial a} + \frac{\partial e(a,t)}{\partial t} = -(\mu + \gamma(a) + \alpha_0(a)) e(a,t),$$
$$e(0,t) = \beta_1 S I_1,$$
$$\frac{dI_1}{dt} = \int_0^\infty \gamma(a) e(a,t) \, da - \mu I_1 - \delta I_1 I_2 - \alpha_1 I_1,$$
$$\frac{dI_2}{dt} = \beta_2 S I_2 - (\mu + \alpha_2) I_2,$$
$$\frac{dJ}{dt} = \delta I_1 I_2 - (\mu + \nu) J,$$
$$(1)$$

where μ is natural death rate and Λ is birth rate. $\gamma(a)$ is rate of endogenous reactivation of latent TB. We assume that the individuals separately infected by TB and HIV are not lethal but the coinfection can lead to the extra death at ν. Specifically, we assume that jointly infected individuals do not recover. Individuals infected with latent TB, active TB, or HIV alone may be potentially treated at rates $\alpha_0(a), \alpha_1$, and α_2, respectively.

Assumption 1. Suppose that

(a) $\Lambda, \mu, \delta, \alpha_1, \alpha_2, \beta_1, \beta_2 \in (0, +\infty)$;

(b) $\nu \in [0, +\infty)$;

(c) $\gamma(a), \alpha_0(a) \in C_{B,U}([0, +\infty), R) \cap C_+([0, +\infty), R)$ and for each $a \geq 0$, where $C_{BU}(R)$ denotes the space of bounded and uniformly continuous map from $[0, +\infty)$ into R.

We assume (1) with the initial conditions:

$$S(0) = S_0 \geq 0, \qquad e(a, 0) = e_0(a) \in L^1_+(0, +\infty),$$

$$I_1(0) = I_{10} \geq 0, \qquad I_2(0) = I_{20} \geq 0, \qquad (2)$$

$$J(0) = J_0 \geq 0.$$

Set

$$X = R \times Y \times R^2, \qquad X_+ = R_+ \times Y_+ \times R_2^+,$$

$$X_0 = R \times Y_0 \times R^2, \qquad X_{0+} = X_0 \cap X_+. \qquad (3)$$

with

$$Y = R \times L^1(0, +\infty), \qquad Y_+ = [0, +\infty) \times L^1_+(0, +\infty),$$

$$Y_0 = \{0\} \times L^1(0, +\infty). \qquad (4)$$

Let $D(\mathscr{A}) = R \times Z \times R^2$, with $Z = \{0_R\} \times W^{1,1}(0, \infty)$, for each $x = (S, 0_R, e, I_1, I_2) \in X_0$. Define $\mathscr{A} : D(\mathscr{A}) \subset X_0 \subset X \to X$ and $\mathscr{F} : X_0 \to X$ by

$$\mathscr{A}x$$

$$= \begin{pmatrix} -\mu S \\ -e(0) \\ -\dfrac{de(\cdot)}{da} - (\mu + \alpha_0(\cdot) + \gamma(\cdot))e(\cdot) \\ -\mu I_1 - \alpha_1 I_1 \\ -\mu I_2 - \alpha_2 I_2 \\ -(\mu + \nu)J \end{pmatrix} \quad \text{if } x \in D(\mathscr{A}),$$

$$(5)$$

$$\mathscr{F}(x)$$

$$= \begin{pmatrix} \mu - \beta_1 SI_1 - \beta_2 SI_2 + \int_0^\infty \alpha_0(a)e(a)\,da + \alpha_1 I_1 + \alpha_2 I_2 \\ \beta_1 SI_1 \\ 0_{L^1} \\ \int_0^\infty \gamma(a)e(a)\,da - \delta I_1 I_2 \\ \beta_2 SI_2 \\ \delta I_1 I_2 \end{pmatrix}. \qquad (6)$$

Rewrite problem (1) as an abstract Cauchy problem

$$\frac{du_x(t)}{dt} = \mathscr{A}u_x(t) + \mathscr{F}(u_x(t)), \quad t \geq 0, \ u_x(0) = x \in X_{0+}. \qquad (7)$$

It is well known that $\mathscr{A}$ is a Hille-Yosida operator. More precisely, we have $(-\mu, +\infty) \subset \rho(\mathscr{A})$ and for each $\lambda > -\mu$,

$$\left\|(\lambda - \mathscr{A})^{-1}\right\| \leq \frac{1}{\lambda + \mu}. \qquad (8)$$

By applying the results in Magal et al. [14–16], we obtain the following proposition.

Lemma 1. *There exists a uniquely determined semiflow $\{U(t)\}_{t \geq 0}$ on X_{0+}, such that for each $x = (S_0, 0, e_0, I_{10}, I_{20}, J_0)^T \in X_{0+}$, there exists a unique continuous map $U \in C([0, +\infty), X_{0+})$ which is an integrated solution of the Cauchy problem (1), that is to say that*

$$\int_0^t U(s)x\,ds \in D(\mathscr{A}), \quad \forall t \geq 0,$$

$$U(t)x = x + \mathscr{A}\int_0^t U(s)x\,ds + \int_0^t \mathscr{F}(U(s)x)\,ds, \quad \forall t \geq 0. \qquad (9)$$

The total population size $N(t)$ is the sum of all individuals in all classes

$$N = S(t) + \int_0^{+\infty} e(a, t)\,da + I_1(t) + I_2(t) + J(t). \qquad (10)$$

The total population size satisfies the equation $N'(t) = \Lambda - \mu N - \nu J$. We introduce the notation

$$\pi(a) = \exp\left(-\int_0^a (\alpha_0(\tau) + \gamma(\tau))\,d\tau\right), \qquad (11)$$

To understand the biological meaning of the quantity $\pi(a)$ we note that $\pi(a)e^{-\mu a}$ is the probability to remain infected with TB time units after infection. In addition, we define the quantity

$$B = \int_0^{+\infty} \alpha_0(a)\pi(a)e^{-\mu a}\,da, \qquad (12)$$

which gives the probability of treatment since the individuals can leave TB infectious period via treatment.

$$C = \int_0^{+\infty} \gamma(a)\pi(a)e^{-\mu a}\,da, \qquad (13)$$

which gives the probability of progression since the individuals can leave TB infectious period via progression. Since individuals can only leave the latent TB infected class through treatment, progression, or death, the sum of the probabilities of recovery, progression, and death equals one, that is,

$$\int_0^\infty \alpha_0(a)\pi(a)e^{-\mu a}\,da + \int_0^\infty \gamma(a)\pi(a)e^{-\mu a}\,da$$

$$+ \mu \int_0^\infty \pi(a)e^{-\mu a}\,da = 1. \qquad (14)$$

It immediately follows that $B + C < 1$.

3. Equilibria of the Model with Coinfection

We introduce the reproduction numbers of the two diseases. The reproduction number of TB is

$$R_1 = \frac{\Lambda \beta_1 C}{\mu(\mu + \alpha_1)}, \qquad (15)$$

and the reproduction number of HIV is

$$R_2 = \frac{\Lambda \beta_2}{\mu(\mu + \alpha_2)}. \tag{16}$$

We note that the coinfection rate δ does not affect the reproduction numbers since coinfection does not lead to additional infections. Setting the derivatives with respect to time to zero we obtain a system of algebraic equations and one ODE for the equilibria of (1). For convenience we consider s, e, i_1, i_2, j as the equilibria of the model. Therefore equilibria satisfy the following equations:

$$\Lambda - \beta_1 s i_1 - \beta_2 s i_2 - \mu s$$
$$+ \int_0^{+\infty} \alpha_0(a) e(a, t)\, da + \alpha_1 i_1 + \alpha_2 i_2 = 0,$$

$$\frac{de}{da} = -\alpha_0(a) e - \mu e - \gamma(a) e,$$

$$e(0) = \beta_1 s i_1, \tag{17}$$

$$\int_0^{+\infty} \gamma(a) e(a)\, da - \mu i_1 - \delta i_1 i_2 - \alpha_1 i_1 = 0,$$

$$\beta_2 s i_2 - (\mu + \alpha_2) i_2 = 0,$$

$$\delta i_1 i_2 - (\mu + \nu) j = 0.$$

The ODE in the system can be solved to result in

$$e(a) = e(0) \pi(a) e^{-\mu a}. \tag{18}$$

Substituting for i in the integrals, one obtains

$$\int_0^{+\infty} \alpha_0(a) e(a)\, da = e(0) \int_0^{+\infty} \alpha_0(a) \pi(a) e^{-\mu a} da = e(0) B,$$

$$\int_0^{+\infty} \gamma(a) e(a)\, da = e(0) \int_0^{+\infty} \gamma(a) \pi(a) e^{-\mu a} da = e(0) C. \tag{19}$$

With this notation the system for the equilibria becomes

$$\Lambda - \beta_1 s i_1 - \beta_2 s i_2 - \mu s$$
$$+ e(0) B + \alpha_1 i_1 + \alpha_2 i_2 = 0,$$

$$\frac{de}{da} = -\alpha_0(a) e - \mu e - \gamma(a) e,$$

$$e(0) = \beta_1 s i_1, \tag{20}$$

$$e(0) C - \mu i_1 - \delta i_1 i_2 - \alpha_1 i_1 = 0,$$

$$\beta_2 s i_- (\mu + \alpha_2) i_2 = 0,$$

$$\delta i_1 i_2 - (\mu + \nu) j = 0.$$

This system has three boundary equilibria.

(1) The disease-free equilibrium $E_0 = (\Lambda/\mu, 0, 0, 0, 0)$. The disease-free equilibrium always exists.

(2) The TB dominated equilibrium exists if and only if $R_1 > 1$. The steady distribution of infectives in the TB equilibrium is given by

$$s_1 = \frac{\Lambda}{\mu R_1}, \qquad e = e(0) \pi(a) e^{-\mu a},$$

$$i_1 = \frac{\Lambda(1 - 1/R_1)}{(1 - B)\mu/C + (1 - B - C)\alpha_1/C}, \tag{21}$$

$$e(0) = \beta_1 s_1 i_1.$$

Thus, the equilibrium is

$$E_1 = (s_1, e, i_1, 0, 0). \tag{22}$$

(3) The HIV dominated equilibrium exists if and only if $R_2 > 1$ and is given by

$$E_2 = (s_2, 0, 0, i_2, 0), \tag{23}$$

where $s_2 = 1/R_2$, $i_2 = 0$, $e_2 = 0$, $i_2 = (\Lambda/\mu)(1 - 1/R_2)$, $j_2 = 0$.

(4) The coexistence equilibrium exists if and only if $R_1 > R_2$, and $[1 - (1/R_2 + \mu(\mu + \alpha_1)/\Lambda\delta)][(\Lambda\beta_1/\mu\alpha_1 R_2)(1 - B) - 1] > 0$ and it is given by

$$E_2 = (s, e, i_1, i_2, j), \tag{24}$$

where $s = \Lambda/\mu R_2$, $e = e(0)\pi(a)e^{-\mu a}$, $e(0) = \beta_1 s i_1$, $i_1 = (\Lambda/\alpha_1)(1 - (1/R_2 + \mu(\mu + \alpha_1)/\Lambda\delta))/((\Lambda\beta_1/\mu\alpha_1 R_2)(1 - B) - 1)$, $i_2 = ((\mu + \delta)/\delta)(R_1/R_2 - 1)$, $j = \delta i_1 i_2/(\mu + \nu)$.

Notice that the values of the two dominance equilibria do not depend on the coinfection. These exact same equilibria are present even if $\delta = 0$.

4. Stability of Equilibria

In this section we investigate local and global stabilities of equilibria. In particular, we derive conditions for the stability of the disease-free equilibrium, of the TB dominance equilibrium and of the HIV dominance equilibrium. The stability of equilibria determines whether both diseasess will be eliminated, one of the diseases will be dominated, and both diseases will persist or not.

To investigate the stability of the equilibria, we linearize the model (1). In particular, let $x(t)$, $y(a, t)$, $z(t)$, $u(t)$, and $w(t)$ be the perturbations, respectively, of $s, e(a), i_1, i_2, j$. That is, $S = x + s$, $e = y + e$, $I_1 = z + i_1$, $I_2 = u + i_2$, $J = w + j$. Thus the perturbations satisfy a linear system. Further we consider the eigenvalue problem for the linearized system. We will denote the eigenvector again with $x, y(a), z, u$, and

w. These satisfy the following linear eigenvalue problem (here s, e, i_1, i_2, and j are the corresponding equilibria):

$$\lambda x = -\beta_1 s z - \beta_1 i_1 x - \beta_2 s u - \beta_2 i_2 x - \mu x$$
$$+ \int_0^\infty \alpha_0(a) y(a) da + \alpha_1 z + \alpha_2 u,$$
$$y'(a) = -\lambda y - \alpha_0(a) y - \mu y - \gamma(a) y,$$
$$y(0) = \beta_1 s z + \beta_1 i_1 x, \qquad (25)$$
$$\lambda z = \int_0^\infty \gamma(a) y(a) da - \mu z - \delta i_2 z - \delta i_1 u - \alpha_1 z,$$
$$\lambda u = \beta_2 s u + \beta_2 i_2 x - (\mu + \alpha_2) u,$$
$$\lambda w = \delta i_2 z + \delta i_1 u - (\mu + \nu) w.$$

In the following we discuss local stability of the equilibria through the characteristic equation (25). Since the last equation has no relation with the other equations in (1) and (25), we just discuss the first four equations of them in the following.

4.1. Stability of the Disease-Free Equilibrium. For the disease-free equilibrium we have $e(0) = i_1 = i_2 = j = 0$, and $s = \Lambda/\mu$. Thus the system above simplifies to the following system:

$$\lambda x = -\beta_1 s z - \beta_2 s u - \mu s$$
$$+ \int_0^\infty \alpha_0(a) y(a) da + \alpha_1 z + \alpha_2 u,$$
$$y'(a) = -\lambda y - \alpha_0(a) y - \mu y - \gamma(a) y,$$
$$y(0) = \beta_1 s z, \qquad (26)$$
$$\lambda z = \int_0^\infty \gamma(a) y(a) da - \mu z - \delta i_2 z - \delta i_1 u - \alpha_1 z,$$
$$\lambda u = \beta_2 s u - (\mu + \alpha_2) u.$$

From this system we will establish the following result regarding the local stability of the disease-free equilibrium E_0.

Theorem 2. *If $R_1 < 1$ and $R_2 < 1$, then the disease-free equilibrium E_0 is locally asymptotically stable. If $R_1 > 1$ or $R_2 > 1$ then the disease-free equilibrium E_0 is unstable.*

Proof. To see this, from the second to last equation we have $\lambda u = [\beta_2 s - (\mu + \alpha_2)] u$, where either $\lambda = \beta_2 s - (\mu + \alpha_2)$, or $u = 0$. This eigenvalue $\lambda = (\mu + \alpha_2)(R_2 - 1) < 0$, if and only if $R_2 < 1$. Thus, if $R_2 > 1$, the disease-free equilibrium E_0 is unstable because this eigenvalue is positive. Further, from the second equation we have that the remaining eigenvalues satisfying the equation,

$$y(a) = y(0) e^{-(\lambda + \mu)a} \pi(a) = \beta_1 s z e^{-(\lambda + \mu)a} \pi(a). \qquad (27)$$

Further, from the fourth equation we have that the remaining eigenvalues satisfying the equation, also referred to as the

characteristic equation, $\lambda z = \beta_1 s \int_0^\infty \gamma(a)\pi(a) e^{-(\lambda + \mu)a} da\, z - (\mu + \alpha_1) z$. This eigenvalue $\lambda = (\mu + \alpha_1)(\beta_1 s/(\mu + \alpha_1)) \int_0^\infty \gamma(a)\pi(a) e^{-(\lambda + \mu)a} da - 1)$, or $z = 0$.

We denote the left hand side of the equation above by $\mathscr{F}_1(\lambda) = \lambda$, and $\mathscr{F}_2(\lambda) = (\mu + \alpha_1)(R_1(\lambda) - 1)$, where $R_1(\lambda) = (\beta_1 s/(\mu + \alpha_1)) \int_0^\infty \gamma(a)\pi(a) e^{-(\lambda + \mu)a} da$, and

$$R_1'(\lambda) < 0, \qquad \lim_{t \to +\infty} R_1(\lambda) = 0, \qquad \lim_{t \to -\infty} R_1(\lambda) = +\infty. \qquad (28)$$

If $\mathscr{F}_1(\lambda) = \mathscr{F}_2(\lambda)$ has a root with Re $\lambda \geq 0$, then Re $\mathscr{F}_1(\lambda) \geq 0$. But $|\mathscr{F}_2(\lambda)| \leq (\mu + \alpha_1)(R_1 - 1) < 0$, when $R_1 < 1$. This is a contradiction.

Thus, if both $R_1 < 1$ and $R_2 < 1$ all eigenvalues have negative real part and the disease-free equilibrium E_0 is locally asymptotically stable. If only $R_1 > 1$ then if we consider $\mathscr{F}_1(\lambda) = \mathscr{F}_2(\lambda)$ for λ is real, we see that $\mathscr{F}_2(\lambda)$ is a decreasing function of λ approaching zero as λ approaches infinity. Since $\mathscr{F}_2(0) = (\mu + \alpha_1)(R_1 - 1) > 0$ and $\mathscr{F}_1(0) = 0$ that implies that there is a positive eigenvalue $\lambda^* > 0$ and the disease-free equilibrium E_0 is unstable. This concludes the proof. □

In what follows, we show that the diseases vanish if $R_1 < 1$, $R_2 < 1$.

Theorem 3. *If $R_i < 1$, $i = 1, 2$, then E_0 is a global attractor, that is, $\lim_{t \to \infty} e(a, t) = 0$, $I_1 \to 0$, $I_2 \to 0$, $J \to 0$ as $t \to \infty$.*

Proof. Since $N'(t) = \Lambda - \mu N - \nu J \leq \Lambda - \mu N$, then $N^\infty \leq \Lambda/\mu$. Hence $S^\infty \leq \Lambda/\mu$. Let $\mathscr{B}(t) = e(0, t)$. Integrating this inequality along the characteristic lines we have

$$e(a, t) = \begin{cases} \mathscr{B}(t - a) \pi(a) e^{-\mu a}, & t < a, \\ e_0(a - t) \dfrac{\pi(a)}{\pi(a - t)} e^{-\mu t}, & t \geq a. \end{cases} \qquad (29)$$

Since $\mathscr{B}(t) = \beta_1 S I_1 \leq \beta_1 \Lambda I_1/\mu$ and

$$I_1' \leq \beta_1 \frac{\Lambda}{\mu} \int_0^t \gamma(a) I_1(t - a) \pi(a) e^{-\mu a} da \qquad (30)$$
$$+ F_1(t) - \mu I_1 - \alpha_1 I_1,$$

where $F_1(t) = \int_t^\infty \gamma(a) e_0(a - t)(\pi(a)/\pi(a - t)) e^{-\mu t} da$ and $\lim_{t \to \infty} F_1(t) = 0$, from the equation for I_1 then we have the following inequality:

$$I_1 \leq I_1(0) e^{-(\mu + \alpha_1)t}$$
$$+ \beta_1 \frac{\Lambda}{\mu} \int_0^t e^{-(\mu + \alpha_1)\tau} \int_0^{t - \tau} \gamma(a) I_1(t - a) \pi(a) e^{-\mu a} da\, d\tau$$
$$+ \int_0^t e^{-(\mu + \alpha_1)\tau} F_1(t - \tau) d\tau, \qquad (31)$$

where $\gamma(a)$ is bounded and the integral of $F_1(t)$ goes to zero as $t \to \infty$. Consequently, taking a limsup of both sides as $t \to \infty$ we obtain

$$I_1^\infty \leq R_1 I_1^\infty. \tag{32}$$

Since $R_1 < 1$, this inequality can only be satisfied if $I_1^\infty \to 0$, as $t \to \infty$.

Since $\mathscr{B}(t) \leq \beta_1(\Lambda/\mu)I_1$, it is easy to obtain $\mathscr{B}(t) \to 0$, as $t \to \infty$.

From the equation I_2 then we have the following inequality:

$$I_2' \leq \beta_2 \frac{\Lambda}{\mu} I_2 - (\mu + \alpha_2) I_2. \tag{33}$$

Solving the inequality we get

$$I_2 \leq I_2(0) e^{-(\mu+\alpha_2)t} + \beta_2 \frac{\Lambda}{\mu} \int_0^\infty I_2(t-\tau) e^{-(\mu+\alpha_2)\tau} d\tau. \tag{34}$$

Consequently, taking a limsup of both sides we obtain

$$I_2^\infty \leq R_2 I_2^\infty. \tag{35}$$

If $R_2 < 1$, then $I_2(t) \to 0$, as $t \to \infty$.

From the fluctuations lemma, we can choose sequence t_n such that $S(t_n) \to S_\infty$ and $S'(t_n) \to 0$ when $t_n \to +\infty$. It follows from the first equation of (1) that we have $S_\infty \geq \Lambda/\mu$. Then $\Lambda/\mu \leq S_\infty \leq S^\infty \leq \Lambda/\mu$. Hence $S \to \Lambda/\mu$ when $t \to \infty$. This completes the theorem. □

4.2. Stability of the TB Dominated Equilibrium. In this subsection we discuss stabilities of the equilibrium E_1 and derive conditions for domination of TB. We show that the equilibrium E_1 can lose stability, and dominance of the TB is possible in the form of sustained oscillation. In this case $i_2 = 0$, $j = 0$, $s = \Lambda/(\mu R_1)$, $i_1 = \Lambda(1 - 1/R_1)/((1 - B)\mu/C + (1 - B - C)\alpha_1/C)$, $e(a) = e(0)\pi(a)e^{-\mu a}$.

The eigenvalue problem takes the form

$$\lambda x = -\beta_1 sz - \beta_1 i_1 x - \beta_2 su - \mu s$$
$$+ \int_0^\infty \alpha_0(a) y(a) da + \alpha_1 z + \alpha_2 u,$$
$$y'(a) = -\lambda y - \alpha_0(a) y - \mu y - \gamma(a) y,$$
$$y(0) = \beta_1 sz + \beta_1 i_1 x, \tag{36}$$
$$\lambda z = \int_0^\infty \gamma(a) y(a) da - \mu z - \delta i_1 u - \alpha_1 z,$$
$$\lambda u = \beta_2 su - (\mu + \alpha_2) u.$$

From the last equation we have

$$\lambda = (\mu + \alpha_2)\left(\frac{R_2}{R_1} - 1\right), \quad \text{or } u = 0. \tag{37}$$

Hence $R_1 > R_2$ the partial characteristic root of (36) is negative. Substituting

$$y(a) = y(0) \pi(a) e^{-(\lambda+\mu)a}, \quad y(0) = \beta_1 sz + \beta_1 i_1 x \tag{38}$$

in the first and fourth equations and cancelling x, z, we arrive at the following characteristic equation:

$$(\lambda + \mu + \alpha_1 - \beta_1 sC(\lambda))(\lambda + \mu + \beta_1 i_1(1 - B(\lambda)))$$
$$- \beta_1 i_1 C(\lambda)(\alpha_1 + \beta_1 s(B(\lambda) - 1)) = 0. \tag{39}$$

Substituting the formula

$$1 - B(\lambda) = C(\lambda) + (\lambda + \mu) E(\lambda), \tag{40}$$

where

$$E(\lambda) = \int_0^\infty \pi(a) e^{-(\lambda+\mu)a} \tag{41}$$

into (39), we obtain the equivalent characteristic equation with (39) as follows:

$$\frac{(\lambda + \mu + \alpha_1)(1 + \beta_1 i_1 E(\lambda)) + \beta_1 i_1 C(\lambda)}{\mu + \alpha_1} = \frac{C(\lambda)}{C}. \tag{42}$$

It is easy to see if (42) has the roots with Re $\lambda > 0$, the left side mode of (42) is larger than 1, while the right side mode of (42) is less than 1, which leads to a contradiction. Hence the characteristic roots of (42) have negative real parts, then the TB dominated equilibrium E_1 is locally asymptotically stable.

Therefore we are ready to establish the first result.

Theorem 4. *Let $R_1 > 1$ and $R_1 > R_2$. Then, the TB dominated equilibrium E_1 is locally asymptotically stable.*

For all $x = (S, 0_R, e, I_1, I_2, J) \in X_0$, we define $P_S : X_0 \to R$, $P_{I_1}, P_{I_2} : X_0 \to R$ and $P_{I_{12}} : X_0 \to R$ by

$$P_S(x) = S, \qquad P_{I_1}(x) = I_1, \qquad P_{I_2}(x) = I_2. \tag{43}$$

Set

$$M_{I_{12}} = X_{0+}, \qquad M_{I_{120}} = \left\{x \in M_{I_{12}} \mid P_{I_1} x \neq 0, P_{I_2} x \neq 0\right\},$$

$$\partial M_{I_{120}} = \frac{M_{I_{12}}}{M_{I_{120}}}, \qquad M_{I_1} = \partial M_{I_{120}},$$

$$M_{I_{10}} = \left\{x \in M_{I_1} \mid P_{I_1} x \neq 0, P_{I_2} x = 0\right\}, \qquad \partial M_{I_{10}} = \frac{M_{I_1}}{M_{I_{10}}},$$

$$M_{I_2} = \partial M_{I_{10}}, \qquad M_{I_{20}} = \left\{x \in M_{I_2} \mid P_{I_2} x \neq 0, P_{I_1} x \neq 0\right\},$$

$$\partial M_{I_{20}} = \frac{M_{I_2}}{M_{I_{20}}}, \qquad M_S = \partial M_{I_{20}} \tag{44}$$

(see Figure 2).

Lemma 5. *If $R_1 > 1$, $\liminf I_1(t) \geq \varepsilon$ in $M_{I_{20}}$.*

Proof. Let $x = (S_0, 0_R, e, 0_R, 0_R) \in M_{I_{10}}$. We assume there is a $t_0 > 0$ such that $I_1 < \varepsilon$ for all $t \geq t_0$. From the first equation of (1) in $M_{I_{10}}$, it is easy to get

$$\frac{dS}{dt} \geq \Lambda - \varepsilon\beta_1 S - \mu S,$$
$$S(0) = S_0. \tag{45}$$

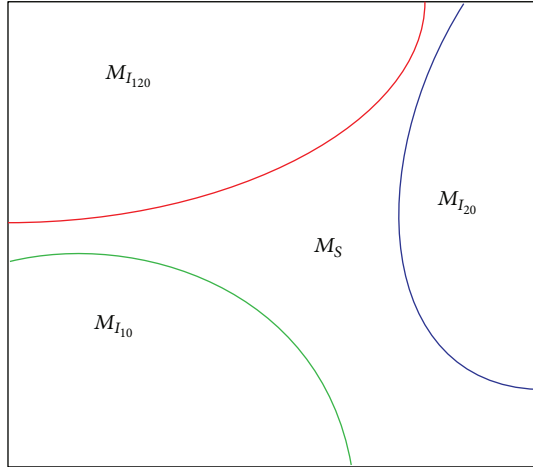FIGURE 2: Zoning the area.

We solve them as follows:

$$S(t) \geq \frac{\Lambda\left(1 - e^{-(\mu+\beta_1\varepsilon)t}\right)}{\mu} \doteq S^*(t). \tag{46}$$

And $S^*(t) \to \Lambda/\mu$, as $t \to +\infty$. Since $R_1 > 1$, there exists $\delta > 0$ and $T_1 > 0$ which satisfy $\beta_1(\Lambda/\mu) \int_0^\delta e^{-(\mu+\alpha_1)s} \int_0^{T_1} \gamma(a)\pi(a)e^{-\mu a} da\, ds > 1$. From the second and third equations of (1), and integrating them from the characteristic line $t - a = c$, we obtain

$$e(a,t) = \begin{cases} \beta_1 S(t-a) I_1(t-a) \pi(a) e^{-\mu a}, & t \geq a, \\ e_0(a-t) \dfrac{\pi(a)}{\pi(a-t)} e^{-\mu t}, & t < a. \end{cases} \tag{47}$$

From the fourth equation of (1), we get

$$I_1'(t) = \beta_1 \int_0^t \gamma(a) S(t-a) I_1(t-a) \pi(a) e^{-\mu a} da$$
$$+ \beta_1 \int_t^\infty \gamma(a) e_0(a-t) \frac{\pi(a)}{\pi(a-t)} e^{-\mu t} da \tag{48}$$
$$- (\mu + \alpha_1) I_1.$$

Solving it, we have

$$I_1(t) \geq \beta_1 \frac{\Lambda}{\mu} \int_0^t e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{t-s} \gamma(a) I_1(t-s-a) \pi(a) e^{-\mu a} da\, ds, \quad \forall t \geq t_0. \tag{49}$$

There exist a $T_1 > 0$, such that

$$I_1(t + T_1)$$
$$\geq \beta_1 \frac{\Lambda}{\mu} \int_0^{t+T_1} e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{t+T_1-s} \gamma(a) I_1(t-s-a) \pi(a) e^{-\mu a} da\, ds, \tag{50}$$
$$\geq \beta_1 \frac{\Lambda}{\mu} \int_0^t e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{T_1} \gamma(a) I_1(t-s-a) \pi(a) e^{-\mu a} da\, ds, \quad \forall t \geq t_0.$$

Thus, for $t \geq \delta$, we have

$$I_1(t + T_1)$$
$$\geq \beta_1 \frac{\Lambda}{\mu} \int_0^\delta e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{T_1} \gamma(a) I_1(t-s-a) \pi(a) e^{-\mu a} da\, ds, \quad \forall t \geq t_0. \tag{51}$$

By Assumption 1, there exists $t_1 \geq 0$, such that $I_1(t+T_1) \geq 0$, for all $t + T_1 \geq t_1$. Hence, there exists $\xi > 0$, such that $I_1(t + T_1) \geq \xi$, for all $t + T_1 \in [2t_1, 2t_1 + \delta]$. Set

$$t_2 = \sup\{t + T_1 \geq 2t_1 + \delta : I_1(l) \geq \xi, \ \forall l \in [2t_1 + \delta, t]\}. \tag{52}$$

Assuming that $t_2 < \infty$, it follows that

$$I_1(t_2) \geq \beta_1 \frac{\Lambda}{\mu} \int_0^\delta e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{T_1} \gamma(a) I_1(t-s-a) \pi(a) e^{-\mu a} da\, ds,$$
$$\geq \beta_1 \frac{\Lambda}{\mu} \int_0^\delta e^{-(\mu+\alpha_1)s} \tag{53}$$
$$\times \int_0^{T_1} \gamma(a) \pi(a) e^{-\mu a} da\, ds\, \xi.$$

Thus, $I_1(t_2) > \xi$. By the continuity for $t \to I_1(t)$, it follows that there exists an $\varepsilon_1 > 0$, such that $I_1(t) \geq \xi$, for all $t \in [t_2, t_2 + \varepsilon_1]$ which contradicts the definition of t_2. Therefore, $I_1(t) \geq \xi$, for all $t > 2t_1$. Denote $I_{1\infty} = \liminf_{t\to+\infty} I_1(t) \geq \xi > 0$. Using (51), it follows that $I_{1\infty} \geq I_{1\infty}\beta_1(\Lambda/\mu) \int_0^\delta e^{-(\mu+\alpha_1)s} \int_0^{T_1} \gamma(a)\pi(a)e^{-\mu a} da\, ds$, which is impossible. Thus, $I_1(t) \geq \varepsilon$. □

Theorem 6. *If $R_1 > 1$, system (1) is permanent in $M_{I_{10}}$. Moreover there exists $A_{I_{10}}$ a compact subset of $M_{I_{10}}$ which is a global attractor for $\{U(t)\}_{t\geq 0}$ in $M_{I_{10}}$.*

Proof. Suppose that $x = (S(t), 0, e, I_1, 0, 0) \in M_{I_{10}}$ be any solution of (1). From the first equation of (1), we have

$$S'(t) > \mu - (\beta_1 + \mu) S(t). \tag{54}$$

Consider the comparison equation.

$$u'(t) = \mu - (\beta_1 + \mu) u(t),$$
$$u(0) = S(0). \tag{55}$$

Similarly, (55) exists as a positive unique steady state. So we have $S(t) \geq u^* - \varepsilon_1 \doteq m_1$, for t large enough, where $u^* = \mu/(\mu + \beta_1)$. From the second and third equations of (1) and Volterra's formulation, we have $e(a,t) \geq \beta_1 m_1 \pi(a) e^{-\mu a} \doteq m_2$, for t large enough. $\qquad\square$

4.3. Stability of the HIV Dominated Equilibrium. In this subsection we establish that the equilibrium E_2 is locally stable whenever it exists. In this case $e(0) = 0$, $i_1 = 0$, $j = 0$, $s = \Lambda/\mu R_2$, $i_2 = (\Lambda/\mu)(1 - 1/R_2)$. The linear eigenvalue problem becomes

$$\lambda x = -\beta_1 s z - \beta_2 s u - \beta_2 i_2 x - \mu x$$
$$+ \int_0^\infty \alpha_0(a) y(a) \, da + \alpha_1 z + \alpha_2 u,$$
$$y'(a) = -\lambda y - \alpha_0(a) y - \mu y - \gamma(a) y,$$
$$y(0) = \beta_1 s z, \tag{56}$$
$$\lambda z = \int_0^{+\infty} \gamma(a) y(a) \, da - \mu z - \delta i_2 z - \alpha_1 z,$$
$$\lambda u = \beta_2 s u + \beta_2 i_2 x - (\mu + \alpha_2) u.$$

From the equation for $y(a)$ we have

$$y(a) = y(0) \pi(a) e^{-(\lambda+\mu)a}. \tag{57}$$

Substituting $y(a)$ in the equation for the initial condition $y(0)$ and assuming that $y(0) \neq 0$ we obtain the following characteristic equation:

$$\lambda + \delta i_2 = \beta_1 s \int_0^\infty \gamma(a) \pi(a) e^{-(\lambda+\mu)a} da - (\mu + \alpha_1)$$
$$= (\mu + \alpha_1) \left(\frac{R_1(\lambda)}{R_2} - 1 \right). \tag{58}$$

Denoting the left hand side of the equation above by $\mathcal{F}_1(\lambda) = \lambda + \delta i_2$, and $\mathcal{F}_2(\lambda) = (\mu + \alpha_1)((R_1(\lambda)/R_2) - 1)$, and also noting that

$$R_1'(\lambda) < 0, \qquad \lim_{t \to +\infty} R_1(\lambda) = 0, \qquad \lim_{t \to -\infty} R_1(\lambda) = +\infty, \tag{59}$$

it is easy to see that $\mathcal{F}_1(\lambda)$ is an increasing function with λ. Note that $\mathcal{F}_1(0) = \delta I_2 \geq 0$. But $\mathcal{F}_2(0) \leq (\mu + \alpha_1)((R_1/R_2) - 1) < 0$, when $R_1 < R_2$. Therefore the characteristic roots of this equation have only negative real part. Furthermore, for $y(0) = y(a) = 0$, and $z = 0$,

$$\lambda x = -\beta_2 s u - \beta_2 i_2 x - \mu x + \alpha_2 u,$$
$$\lambda u = \beta_2 s u + \beta_2 i_2 x - (\mu + \alpha_2) u. \tag{60}$$

We express x from the first equation

$$x = \frac{(-\beta_2 s + \alpha_2) u}{\lambda + \mu + \beta_2 i_2}, \tag{61}$$

and substitute it into the second equation. In addition, assuming that u is nonzero, we cancel it and obtain the following characteristic equation:

$$\lambda + \mu + \alpha_2 = \beta_2 s + \frac{\beta_2 i_2 (-\beta_2 s + \alpha_2)}{\lambda + \mu + \beta_2 i_2}, \tag{62}$$

that is,

$$(\lambda + \mu)(\lambda + \mu + \alpha_2 + \beta_2 i_2 - \beta_2 s) = 0. \tag{63}$$

Noticing that $\beta_2 s = \mu + \alpha_2$, we obtain the following eigenvalues: $\lambda = -\mu$ and $\lambda = -\beta_2 i_2$, which are both negative. Consequently, the equilibrium E_2 is locally asymptotically stable.

Therefore, we have the following theorem for equilibrium E_2.

Theorem 7. *Let $R_2 > 1$. Assume that tuberculosis cannot invade the equilibrium of HIV, that is, $R_1 < R_2$. Then the equilibrium E_2 is locally asymptotically stable.*

Lemma 8. *If $R_2 > 1$, then $\liminf I_2(t) \geq \varepsilon$ in $M_{I_{20}}$.*

Proof. Let $x = (S_0, 0_R, 0_L^1, 0_R, I_2, 0_R) \in M_{I_{20}}$. We assume there is a $t_0 > 0$ such that $I_2 < \varepsilon$ for all $t \geq t_0$. From the first equation of (1) in $M_{I_{20}}$, it is easy to get

$$\frac{dS}{dt} \geq \Lambda - \varepsilon \beta_2 S - \mu S,$$
$$S(0) = S_0. \tag{64}$$

We solve them,

$$S(t) \geq \frac{\Lambda \left(1 - e^{-(\mu + \beta_2 \varepsilon)t}\right)}{\mu} \doteq S^*(t). \tag{65}$$

Then $S(t) \geq S^*(t)$, and $S(t) \to \Lambda/\mu$, as $t \to +\infty$. From the fourth of equation (1), $\exists t_0 > 0$, we have

$$I_2'(t) \geq \beta_2 \frac{\Lambda}{\mu} I_2(t) - (\mu + \alpha_2) I_2(t), \quad \forall t \geq t_0. \tag{66}$$

Solving it, we have

$$I_2(t) \geq \beta_2 \frac{\Lambda}{\mu} \int_0^t e^{-(\mu+\alpha_2)(t-s)} I_2(t-s) \, ds. \tag{67}$$

We do $\liminf$ on both side of (67), and denote $I_{2\infty} = \liminf_{t \to +\infty} I_2(t) > 0$, thus

$$I_{2\infty} \geq R_2 I_{2\infty}, \tag{68}$$

which is impossible. Thus, $I_2(t) \geq \varepsilon$. $\qquad\square$

Theorem 9. *If $R_2 > 1$, system (1) is permanent in $M_{I_{20}}$. Moreover there exists $A_{I_{20}}$ a compact subset of $M_{I_{20}}$ which is a global attractor for $\{U(t)\}_{t\geq 0}$ in $M_{I_{20}}$.*

Proof. Suppose that $x = (S(t), 0, 0, I_2(t), 0) \in M_{I_{20}}$ be any solution of (1). From the first equation of (1), we have

$$S'(t) > \Lambda - (\beta_2 + \mu) S(t). \quad (69)$$

Consider the comparison equation

$$u'(t) = \Lambda - (\beta_2 + \mu) u(t),$$
$$u(0) = S(0). \quad (70)$$

Similarly, (70) exists as a positive unique solution. So we have $S(t) \geq u^* - \varepsilon_1 \doteq m_2$, for t large enough, where $u^* = \Lambda/(\beta_2 + \mu)$. $\square$

4.4. Stability of Coexistence Equilibrium E_*. In this subsection we establish that the equilibrium E_* is locally stable whenever it exists. In this case $s = \Lambda/\mu R_2$, $e = e(0)\pi(a)e^{-\mu a}$, $e(0) = \beta_1 s i_1$, $i_1 = (\Lambda/\alpha_1)((1 - (1/R_2 + \mu(\mu + \alpha_1)/\Lambda\delta))/((\Lambda\beta_1/\mu\alpha_1 R_2)(1-B)-1))$, $i_2 = ((\mu+\delta)/\delta)(R_1/R_2 - 1)$, $j = \delta i_1 i_2/(\mu + \nu)$. The characteristic equations at the coexistence equilibrium are as follows:

$$(\lambda + \mu + \alpha_1 + \delta i_2 - \beta_1 s C(\lambda))$$
$$\times \left(\lambda + \beta_1 i_1 + \beta_2 i_2 + \mu - \beta_1 i_1 B(\lambda) + \frac{\beta_2 i_2 \mu}{\lambda}\right) \quad (71)$$
$$= (\beta_1 s B(\lambda) - \beta_1 s)\left(\beta_1 i_1 - \frac{\delta \beta_2 i_1 i_2}{\lambda}\right).$$

Theorem 10. *If $R_1 > R_2$, $[1 - (1/R_2 + (\mu(\mu + \alpha_1)/\Lambda\delta))][((\lambda\beta_1/\mu\alpha_1 R_2)(1 - B)) - 1] > 0$, and the characteristic equation (71) has only negative real parts roots, then the coexistence equilibrium E_* is locally asymptotically stable.*

5. Persistence of the System

In this section, we consider persistence of the system in $M_{I_{120}}$ when $\nu = 0$. It is easy to check if the system (1) is dissipative and the dynamical system is asymptotically smooth. $M_{I_{120}}$, $M_{I_{10}}$, $M_{I_{20}}$, and M_s are positively invariant. Define

$$\partial\Gamma = M_{I_{10}} \cup M_{I_{20}} \cup M_s,$$
$$\partial\Gamma = M_{I_{120}}. \quad (72)$$

Assuming the boundary equilibria of (1) are globally asymptotically stable, we have

$$\widetilde{A}_{\partial M_{I_{120}}} := \cup_{(S_0, e_0(\cdot), I_1, I_2, J) \in \partial\Gamma} \omega\left((S_0, e_0(\cdot), I_1, I_2, J)\right)$$
$$= \{E_0, E_1, E_2\}. \quad (73)$$

By the above conclusions, it follows that $\widetilde{A}_{\partial M_{I_{120}}}$ is isolated and has an acyclic covering $M = \{E_0, E_1, E_2\}$. Since the orbit

of any bounded set is bounded, and from Theorem 4.2 in [17], we only need to show that E_0, E_1, E_2 are ejective in $M_{I_{120}}$ if globally stable conditions of E_0, E_1, E_2 are not satisfied. Therefore, we have the following lemmas.

Lemma 11. *Let Assumption 1 be satisfied and let E_0 be globally asymptotically stable. If $R_1 > 1$, then E_0 is ejective in $M_{I_{120}}$ for $\{U_{I_{12}}(t)\}_{t\geq 0}$.*

Proof. Let $\delta > 0$, $T_1 > 0$ and $\varepsilon \in (0, 1)$ satisfy

$$\beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon\right) \int_0^\delta e^{-(\mu+\alpha_1)s} \int_0^{T_1} \gamma(a) \pi_1(a) e^{-\mu a} da\, ds > 1. \quad (74)$$

Let $x = (S_0, 0_R, I_{10}, I_{20}, J_0) \in M_{I_{120}}$ with $\|x - x_S\| < \varepsilon$. Assume that

$$\|U(t) x - x_s\| \leq \varepsilon, \quad t \geq 0. \quad (75)$$

Defining $S(t) = P_S U(t)x$, and $I_1(t) = P_{I_1} U(t)x$, for all $t \geq 0$. from (75) it follows that

$$S(t) \geq \frac{\Lambda}{\mu} - \varepsilon, \quad \forall t \geq 0. \quad (76)$$

From the second and third equations of (1), and integrating them from the characteristic line $t - a = c$, we obtain

$$e(a,t) \geq \begin{cases} \beta_1 \left(\dfrac{\Lambda}{\mu} - \varepsilon\right) I_1(t-a) \pi_1(a) e^{-\mu a}, & t \geq a, \\ e_0(a-t) \dfrac{\pi_1(a)}{\pi_1(a-t)} e^{-\mu t}, & t < a, \end{cases} \quad (77)$$

where from the fourth equation of (1), we get

$$I_1'(t) \geq \beta_1 \frac{\Lambda}{\mu} \int_0^t I_1(t-a) \pi_1(a) e^{-\mu a} da$$
$$+ \beta_1 \int_t^\infty \gamma(a) e_0(a-t) \frac{\pi_1(a)}{\pi_1(a-t)} e^{-\mu t} da \quad (78)$$
$$- (\mu + \alpha_1) I_1.$$

Solving it, we have

$$I_1(t) \geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon\right) \int_0^t e^{-(\mu+\alpha_1)s}$$
$$\times \int_0^{t-s} \gamma(a) I_1(t-s-a) \pi_1(a) e^{-\mu a} da\, ds, \quad \forall t \geq 0. \quad (79)$$

There exist a $T_1 > 0$, such that

$$I_1 (t + T_1)$$

$$\geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon \right) \int_0^{t+T_1} e^{-(\mu+\alpha_1)s}$$

$$\times \int_0^{t+T_1-s} \gamma(a) I_1 (t - s - a) \pi_1 (a) e^{-\mu a} da\, ds, \tag{80}$$

$$\geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon \right) \int_0^t e^{-(\mu+\alpha_1)s}$$

$$\times \int_0^{T_1} \gamma(a) I_1 (t - s - a) \pi_1 (a) e^{-\mu a} da\, ds, \quad \forall t \geq 0.$$

Thus, for $t \geq \delta$, we have

$$I_1 (t + T_1)$$

$$\geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon \right) \int_0^\delta e^{-(\mu+\alpha_1)s} \tag{81}$$

$$\times \int_0^{T_1} \gamma(a) I_1 (t - s - a) \pi_1 (a) e^{-\mu a} da\, ds, \quad \forall t \geq 0.$$

By Assumption 1, there exists $t_1 \geq 0$, such that $I_1(t+T_1) \geq 0$, for all $t + T_1 \geq t_1$. Hence, there exists $\xi > 0$, such that $I_1(t + T_1) \geq \xi$, for all $t + T_1 \in [2t_1, 2t_1 + \delta]$. Set

$$t_2 = \sup \{ t + T_1 \geq 2t_1 + \delta : I(l) \geq \xi, \quad \forall l \in [2t_1 + \delta, t] \}. \tag{82}$$

Assume that $t_2 < \infty$. Then

$$I_1 (t_2) \geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon \right) \int_0^\delta e^{-(\mu+\alpha_1)s}$$

$$\times \int_0^{T_1} \gamma(a) I_1 (t - s - a) \pi_1 (a) e^{-\mu a} da\, ds, \tag{83}$$

$$\geq \beta_1 \left(\frac{\Lambda}{\mu} - \varepsilon \right) \int_0^\delta e^{-(\mu+\alpha_1)s}$$

$$\times \int_0^{T_1} \gamma(a) \pi_1 (a) e^{-\mu a} da\, ds\, \xi.$$

Thus, $I_1(t_2) > \xi$. By the continuity for $t \rightarrow I_1(t)$, it follows that there exists an $\varepsilon_2 > 0$, such that $I_1(t) \geq \xi$, for all $t \in [t_2, t_2 + \varepsilon_2]$ which contradicts the definition of t_2. Therefore, $I_1(t) \geq \xi$, for all $t > 2t_1$. Denote $I_{1\infty} = \liminf_{t \to +\infty} I_1(t) \geq \xi > 0$. Using (81), it follows that $I_{1\infty} \geq I_{1\infty} \beta_1 (\Lambda/\mu - \varepsilon) \int_0^\delta e^{-(\mu+\alpha_1)s} \int_0^{T_1} \gamma(a) I_1(t - s - a) \pi_1(a) e^{-\mu a} da\, ds$, which is impossible. □

Lemma 12. *Let Assumption 1 be satisfied and let E_1 and E_2 be globally asymptotically stable. Then one has the following.*

(i) *If $R_1 > 1$, then $x_{I_1} = E_1$ is ejective in $M_{I_{120}}$.*

(ii) *If $R_2 > 1$, then $x_{I_2} = E_2$ is ejective in $M_{I_{120}}$.*

Theorem 13. *Let Assumption 1 be satisfied and let E_0, E_1, and E_2 be globally asymptotically stable. Assume $R_1 > 1$, $R_2 > 1$. Then there exists $\varepsilon > 0$ such that for all $x \in M_{I_{120}}$,*

$$\liminf \| P_{I_{12}} U(t) x \| \geq \varepsilon. \tag{84}$$

Proof. It is a consequence of Theorem 4.2 in [18] applied with $\Omega(\partial M_{I_{120}}) = \{E_0\} \cup \{E_1\} \cup \{E_2\}$. Using Lemma 12, the result follows. □

6. Simulation

In this section, we use (1) to examine how the prevalence of HIV impacts on TB dynamics. We also present some numerical results on the stability of E_0 (the disease-free equilibrium), E_1 (the TB dominated equilibrium), and E_2 (the HIV dominated equilibrium). We perform a numerical analysis to exhibit the TB impact on HIV under different treatments with (1). We now give three examples to illustrate the main results mentioned in the above section.

Example 14. In (1), we set $\Lambda = 2$, $\mu = 0.6$, $\delta = 73.13$, $\beta_1 = 0.49$, $\beta_2 = 0.15$, $\nu = 0.9$,

$$\gamma(a) = \begin{cases} 0.02 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases}$$

$$\alpha_0(a) = \begin{cases} 0.1 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases} \tag{85}$$

$\alpha_1 = 0.01$, $\alpha_2 = 0.03$. We have $R_1 = 0.07438 < 1$ and $R_2 = 0.79365 < 1$, which satisfy the conditions of Theorems 2 and 3. E_0 should be globally asymptotically stable (see Figure 3(a)). In this case, both TB and HIV will be eliminated.

Example 15. In (1), $\Lambda = 2$, $\mu = 1$, $\delta = 4$, $\beta_1 = 50.49$, $\beta_2 = 0.15$, $\nu = 0.9$,

$$\gamma(a) = \begin{cases} 0.1 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases}$$

$$\alpha_0(a) = \begin{cases} 0.1 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases} \tag{86}$$

$\alpha_1 = 0.01$, $\alpha_2 = 0.03$. We have $R_1 = 34.48770 > 1 > R_2 = 0.79365$, which satisfy the conditions of Theorem 4. E_1 should be globally asymptotically stable (see Figure 3(b)). In this case, TB is dominated in the coinfected dynamics.

Example 16. In (1), $\Lambda = 2$, $\mu = 0.6$, $\delta = 0.0073$, $\beta_1 = 0.49$, $\beta_2 = 4.15$, $\nu = 0.9$,

$$\gamma(a) = \begin{cases} 0.1 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases}$$

$$\alpha_0(a) = \begin{cases} 0.1 & a \geq 1.49 \\ 0 & 0 \leq a \leq 1.49, \end{cases} \tag{87}$$
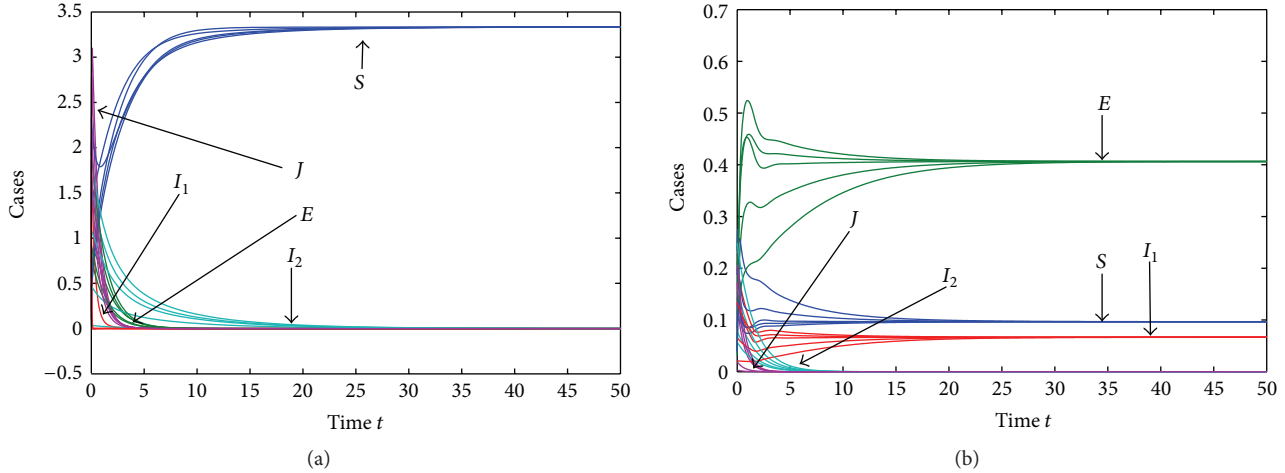
(a)

(b)

FIGURE 3: (a) show that E_0 is globally asymptotically stable. (b) shows that E_1 is globally asymptotically stable.
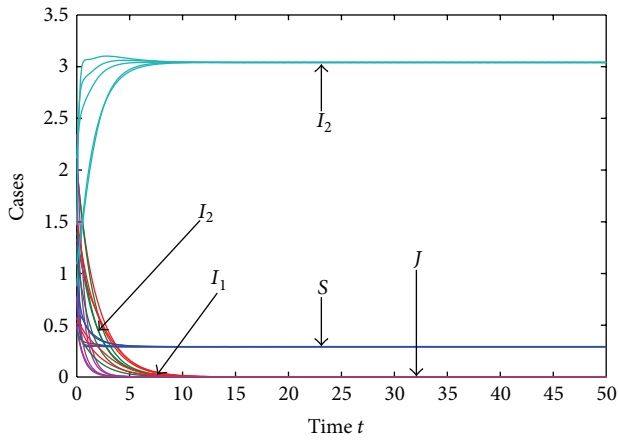

FIGURE 4: shows that E_2 is globally asymptotically stable.

$\alpha_1 = 0.01$, $\alpha_2 = 0.03$. We have $R_2 = 11.37566 > 1 > R_1 = 0.33470$, which satisfies the conditions of Theorem 7. E_2 should be globally asymptotically stable (see left of Figure 4). In this case, HIV is dominated in the coinfected dynamics.

6.1. Effect of Treatment Parameter α_i, $i=0,1,2$. We examined hypothetical treatment to gain insight into the underlying co-epidemic dynamics. We considered nine treatment scenarios: no treatment $\alpha_0 = 0$ (latent TB treatment) (IPT), $\alpha_0 = 0.5$ (latent TB treatment) (IPT), $\alpha_0 = 1$ (latent TB treatment) (IPT), no treatment $\alpha_2 = 0$, $\alpha_2 = 0.5$ (HAART), and $\alpha_2 = 1$ (HAART), where α_i, $i = 0,1$ denotes the fraction of the eligible population receiving the corresponding treatment.

First, we considered the effect of each type of treatment in isolation (e.g., IPT for individuals with treatment for latent or active TB, but not AIDS). Exclusively treating people with latent TB reduced the number of new active TB cases, which subsequently decreased the number of new latent TB infections (Figure 5(a)). However, latent TB treatment had an adverse effect on the HIV epidemic: the number of new

HIV cases increased because individuals coinfected with HIV and latent TB lived longer (due to latent TB treatment) and thus could infect more people with HIV(see Figure 5(c)). Similarly, active TB treatment reduced the number of people with infectious TB, which subsequently reduced the number of new latent and active TB cases (Figure 5(b)). Once again, new HIV cases increased due to longer life expectancy among those who were coinfected with HIV. Hence, the coinfected people have same effect of people infected by latent TB and active TB.

Second, we considered the effect of each type of treatment in isolation (e.g., HAART for individuals with AIDS, but no treatment for latent or active TB). The provision of HAART significantly slowed the HIV epidemic (Figure 6(c)). However, exclusively treating HIV-infected individuals with HAART adversely affects the TB epidemic (Figures 6(a) and 6(b)). Because HAART reduces AIDS-related mortality, treated individuals have a longer time to potentially infect others with TB, especially in the absence of any TB treatment. Thus, the numbers of new latent and active TB cases increased as more people were given HAART. However, the coinfected people have the same effect of people infected by HIV (see Figure 6(d)).

7. Discussion

We have developed a mathematical model for modelling the coepidemics, calculated the basic reproduction number, the disease-free equilibrium, the dominated equilibria (defined as a state where one disease is eradicated, while the other disease remains endemic), and got the conditions for local and global stability. We presented the sufficient conditions for the local stability of the TB dominated equilibrium in Theorem 4. We also obtained the persistence. In the case of the HIV dominated equilibrium, we presented the sufficient condition for the local stability in Theorem 7. We also obtained the persistence of (1). We simulated and illustrated our analyzed results in Section 6.
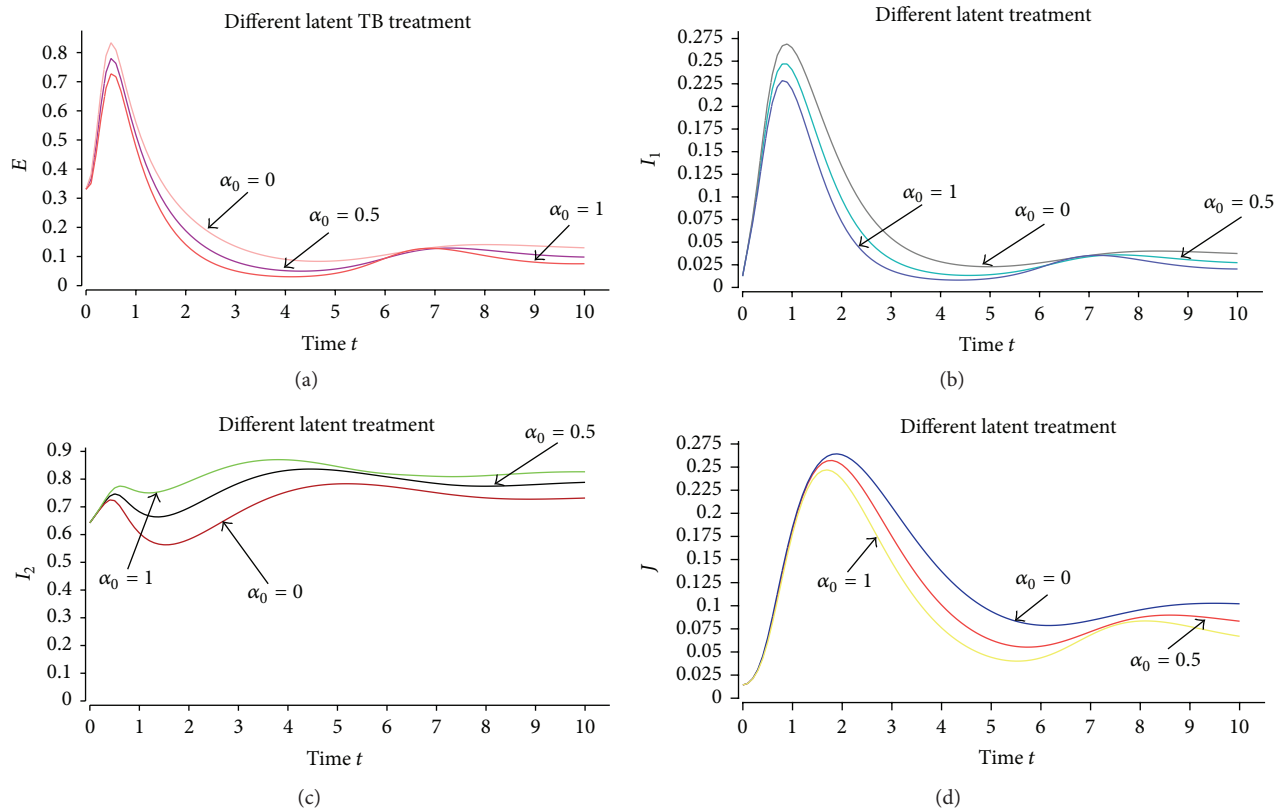
Figure 5: We take different latent TB treatments while we take no treatment of HAART and active TB.
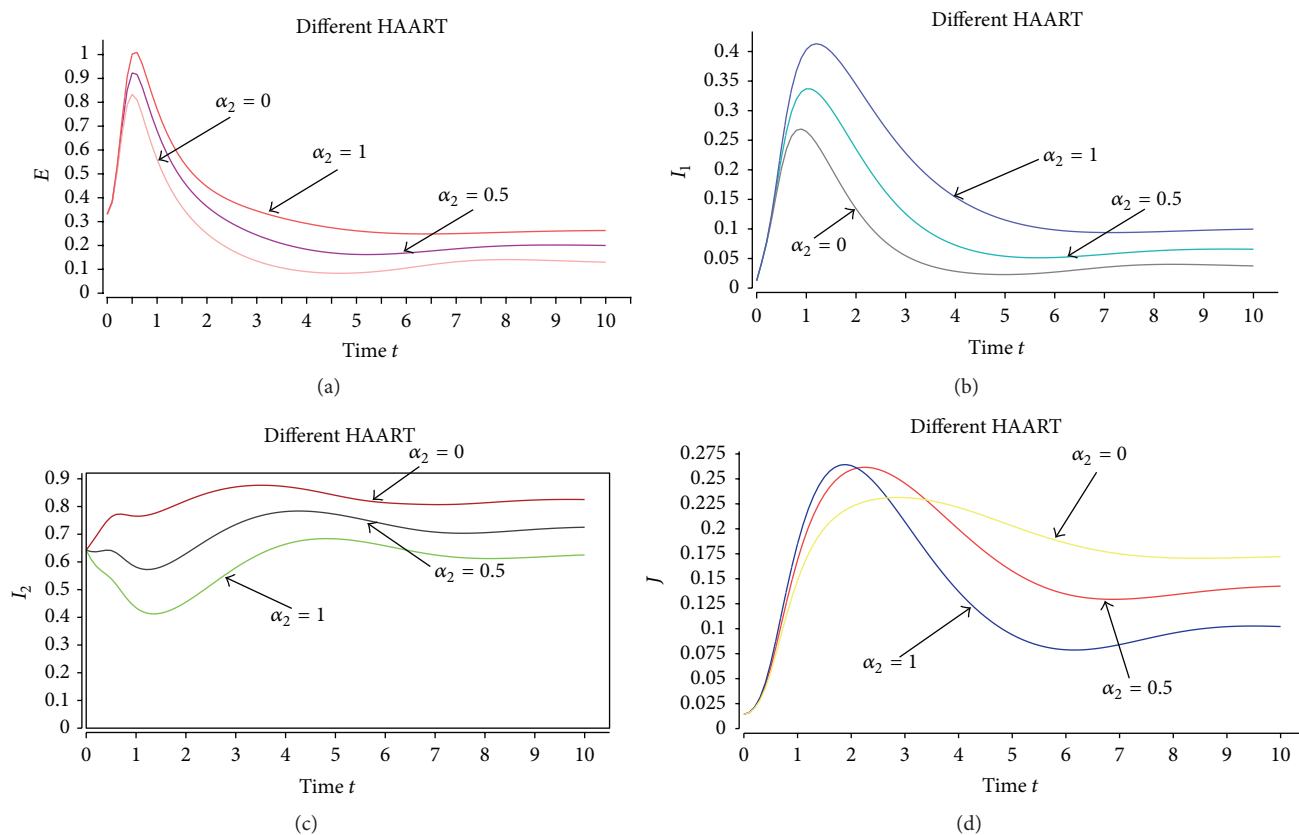

Figure 6: We take different HAART while we take no treatment of IPT.

Our models have several limitations. We simplified the complicated infection dynamics of TB and HIV to develop a tractable framework, which helped us gain insights about the basic reproduction number and equilibria. We assumed uniform patterns within compartments, that is, the mixing between compartments is homogeneous. To appropriately guide policy recommendations, our coepidemic model would need to be significantly expanded. We also apply a coepidemic model to describe the HIV coinfected with other diseases, such as HIV and hepatitis C (HCV). Some 50%–90% of HIV-infected injection drug users are coinfected with HCV [19]. The successful HIV treatment may be adversely impacted by the presence of HCV, and HCV may cause liver damage to occur more quickly in HIV-infected individuals [19]. Modelling this kind of coinfection may play particularly important role on evaluating interventions time targeted to injection drug.

Unfortunately, we are unable yet to study the models that introduce a discrete delay and an impulsive perturbation in our model. We will explore them in the future.

Acknowledgments

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