Epidemic Models with Age of Infection, Indirect Transmission and Incomplete Treatment *

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Abstract

An infection-age-structured epidemic model with environmental bacterial infection is investigated in this paper. It is assumed that the infective population is structured according to age of infection, and the infectivity of the treated individuals is reduced but varies with the infection-age. An explicit formula for the reproductive number $\Re_0$ of the model is obtained. By constructing a suitable Lyapunov function, the global stability of the infection-free equilibrium in the system is obtained for $\Re_0 < 1$. It is also shown that if the reproduction number $\Re_0 > 1$, then the system has a unique endemic equilibrium which is locally asymptotically stable. Furthermore, if the reproduction number $\Re_0 > 1$, the system is permanent. When the treatment

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rate and the transmission rate are both independent of infection age, the system of partial differential equations (PDEs) reduces to a system of ordinary differential equations (ODEs). In this special case, it is shown that the global dynamics of the system can be determined by the basic reproductive number.

Key words: Epidemic model, global stability, Lyapunov function, infection-age-structured.

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1 Introduction

Typhoid fever is a bacterial disease caused by Salmonella typhi. Typically the disease is transmitted through the ingestion of food or drinks contaminated by the faeces or urine of infected individuals. However, typhoid fever has also occurred from human-to-human transmission that may have been facilitated by flying insects. Symptoms include elevated temperature, headache and coughing but some individuals remain asymptomatic carriers who can still infect with the disease. The most famous example is a young cook who was responsible for infecting at least 53 people with typhoid, three of whom died from the disease [11]. Another disease with similar characteristics is cholera. The most important and common routes of transmission again are water and food contaminated with the bacterium, but human-to-human transmission is also possible [9]. This suggests the necessity of modeling both direct and environmental transmission for some groups of diseases. Infected individuals usually tend to seek effective treatment after they are diagnosed, but the treatment is incomplete and the treated individuals continue to be infectious. According to the CDC approximately 5% of people who contract typhoid continue to carry the disease after they are treated [2]. Therefore, effects of treatment after infection and environmental bacteria transmission are important factors that affect the disease dynamics and need to be considered in the prevention and control of such diseases.

Mathematical modeling has contributed significantly to our understanding of the epidemiology of typhoid and cholera [1,18]. Recently, a number of articles develop ODE models of cholera and typhoid (see, [5,6,15,24]). In [6], Gonzalez-Guzman analyzed an SIS model for the spread of typhoid by considering the direct as well as indirect transmission with shedding of bacteria from infectivity into the environment. It has been noticed that the infectiousness of an infected individual can be very different at various stages of infection. This suggests that the age of infection may be an important factor to model for some infectious diseases. To gain insights into the effects of treatment and environmentally transmitted bacteria, in this paper, we consider an infection-age-structured epidemic model with treated class and bacterial transmission. It is

assumed that the infectivity of the treated individuals is reduced and varies in a way associated with their infection age. The incorporation of an age structure leads to a model that includes PDEs, which makes it more difficult to theoretically analyze (see, [27]). Incorporating individuals' infection age in epidemic models has been done in a number of articles before. The results in those articles show that the age-structure may play an important role in the transmission dynamics of infectious diseases (see, [12,13,14,16,19,21,22,23,29]).

The organization of this paper is as follows: In the next section, a system of partial differential equations (PDEs) is introduced. We obtain an explicit formula for the reproductive number of infection, which determines the stability of the infection-free equilibrium. We investigate the existence and stability of the equilibria of the system. The global stability of the infection-free equilibrium of the system is obtained by constructing a Lyapunov function. By applying the persistence theory for infinite-dimensional systems, we show that the disease is uniformly persistent if the reproductive number $\Re_0 > 1$. In section 3 we consider the special case where the treatment rate and transmission rate are both independent of infection age. The model equations reduce to a system of ODEs. In this simplified situation, the global stability of the equilibria of system is completely analyzed. We end the paper with concluding remarks.

2 The infection-age-structured model

We consider an infection-age-structured model with bacterial transmission. The infectious disease under consideration is assumed to spread by infectivity directly as well as by flow of bacteria in the environment. The human population is divided into distinct classes of susceptibles, infectives, treated. Let $S(t)$ represent the classes of susceptible individuals. Let $i(a,t)$ be the distribution of infected individuals with infection-age a. The independent variable a is called infection-age because it measures the time that has elapsed since infection. It is time variable and therefore progresses as time. Although in practice the infection progression is different in different individuals, in epidemiological models it is customary to assume that all parameters are average of the different progression regimes of the different individuals. Hence, we assume that the infection progresses identically in all individuals and varies only with respect to time since infection.

The fact that $i(a,t)$ is the distribution of infected individuals in particular means that $\int_{a_1}^{a_2} i(a,t)da$ is the total number of infected individuals with infection-age between a_1 and a_2. We assume that a fraction of infective group is diagnosed at a rate $\sigma(a)$ and $i_c(a,t)$ represents the treated infective class. Therefore, $\int_{a_1}^{a_2} i_c(a,t)da$ is the total number of the treated infectious individuals with infection-age between a_1 and a_2. The number of toxigenic bacterial cells per ml in the environment is denoted by $B(t)$. We further assume that the infective groups $i(a,t)$, $i_c(a,t)$ move to the recov-

ered class after they recover with rates $\nu_1(a),\ \nu_2(a)$, respectively. Λ is the birth/recruitment rate of susceptible individuals. The parameters $\beta_i(a)(i=1,2)$ are the infection-age specific transmission rates. Let ρ be the infection rate by contact with environment bacterial. $\eta_i(a)(i=1,2)$ are the age-specific contribution of infected individuals to the bacteria population in the environment. μ is natural mortality rate. δ is the clearance rate of the bacteria from the environment.

With the above notation, we study the following infection-age-structured model with bacteria transmission:

$$\begin{aligned}
&\frac{dS(t)}{dt} = \Lambda - \mu S(t) - S(t)\Big(\int_0^\infty \beta_1(a)i(a,t)da + \int_0^\infty \beta_2(a)i_c(a,t)da\Big) - \rho S(t)B(t),\\
&\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} = -(\mu + \nu_1(a) + \sigma(a))i(a,t),\\
&i(0,t) = S(t)\Big(\int_0^\infty \beta_1(a)i(a,t)da + \int_0^\infty \beta_2(a)i_c(a,t)da\Big) + \rho B(t)S(t),\\
&\frac{\partial i_c(a,t)}{\partial t} + \frac{\partial i_c(a,t)}{\partial a} = \sigma(a)i(a,t) - (\mu + \nu_2(a))i_c(a,t),\\
&i_c(0,t) = 0,\\
&\frac{dB(t)}{dt} = \int_0^\infty \eta_1(a)i(a,t)da + \int_0^\infty \eta_2(a)i_c(a,t)da - \delta B(t),
\end{aligned} \tag{2.1}$$

where, the initial distributions $\psi(a)$ and $\phi(a)$ are assumed integrable and compact support in $[0,\infty)$. System (2.1) is equipped with the following initial conditions:

$$S(0) = S_0,\ i(a,0) = \varphi(a),\ i_c(a,0) = \psi(a),\ B(0) = B_0.$$

We assume that all the parameters are nonnegative, $\Lambda > 0,\ \mu > 0,\ \delta > 0, \rho > 0$. Moreover, the parameters satisfy the following assumption.

Assumption 2.1. *The parameter functions satisfy*

(1) The functions $\beta_i(a)(i=1,2)$ are bounded, uniformly continuous and with compact support.

(2) The functions $\nu_i(a), \eta_i(a),\ \sigma(a) \in L^\infty(0,\infty), i=1,2.$

(3) The functions $\varphi(a),\ \psi(a)$ are nonnegative and integrable.

Define the space of functions $X = \mathbb{R}\times L^1(0,\infty)\times L^1(0,\infty)\times\mathbb{R}$. The model (2.1) with assumption 2.1 is a well posed system of differential equations in the positive cone X_+. Rigorous justification of this fact in the framework of semigroup theory can be found in the Appendix A.

2.1 Equilibria and their stabilities

Let $\bar\eta = \max\{\bar\eta_1;\bar\eta_2\}, \bar\eta_i = esssup_{[0,\infty)}|\eta_i(a)|,\ i=1,2$. It is easy to show that the following set is positively invariant for system (2.1)

$$\mathcal{D} = \{(S,i,i_c,B)|\Big(S(t) + \int_0^\infty (i(a,t)+i_c(a,t))da\Big) \le \frac{\Lambda}{\mu},\ B(t) \le \frac{\bar\eta\Lambda}{\mu\delta}\}.$$

System (2.1) always has the disease-free equilibrium $E_0(\frac{\Lambda}{\mu}, 0, 0, 0)$. To simplify expressions, we introduce the following notations

$$\pi_1(a) = e^{-\mu a} e^{-\int_0^a (\nu_1(v)+\sigma(v))dv}, \quad \pi_2(a) = e^{-\mu a} e^{-\int_0^a \nu_2(v)dv}. \tag{2.2}$$

Let $(S^*, i^*(a), i_c^*(a), B^*)$ represent any arbitrary endemic equilibrium of the model (2.1). This equilibrium satisfies the following equations

$$\begin{aligned}
&\Lambda - \mu S^* - S^*\Big(\int_0^{+\infty} \beta_1(a) i^*(a) da + \int_0^{+\infty} \beta_2(a) i_c^*(a) da\Big) - \rho S^* B^* = 0,\\
&\frac{di^*(a)}{da} = -(\mu + \nu_1(a) + \sigma(a)) i^*(a),\\
&i^*(0) = S^*\Big(\int_0^{+\infty} \beta_1(a) i^*(a) da + \int_0^{+\infty} \beta_2(a) i_c^*(a) da\Big) + \rho B^* S^*,\\
&\frac{di_c^*(a)}{da} = \sigma(a) i^*(a) - (\mu + \nu_2(a)) i_c^*(a),\\
&i_c(0) = 0,\\
&\int_0^{+\infty} \eta_1(a) i^*(a) da + \int_0^{+\infty} \eta_2(a) i_c^*(a) da - \delta B^* = 0.
\end{aligned} \tag{2.3}$$

Solving the second and the fourth equation of system (2.3), respectively, yields

$$\begin{aligned}
&i^*(a) = i^*(0)\pi_1(a),\ i_c^*(a) = i^*(0)\pi_2(a) \int_0^a \sigma(s) e^{-\int_0^s (\nu_1(v)+\sigma(v)-\nu_2(v))dv} ds,\\
&B^* = \frac{1}{\delta} \int_0^{+\infty} \Big(\eta_1(a) i^*(a) + \eta_2(a) i_c^*(a)\Big) da.
\end{aligned} \tag{2.4}$$

Let

$$\begin{aligned}
\Re_0 \ &= \frac{\Lambda}{\mu} \int_0^{\infty} \Big[\beta_1(a)\pi_1(a) + \beta_2(a)\pi_2(a) \int_0^a \sigma(s) e^{-\int_0^s (\nu_1(v)+\sigma(v)-\nu_2(v))dv} ds\Big] da\\
&+ \frac{\rho\Lambda}{\mu\delta} \int_0^{\infty} \Big[\eta_1(a)\pi_1(a) + \eta_2(a)\pi_2(a) \int_0^a \sigma(s) e^{-\int_0^s (\nu_1(v)+\sigma(v)-\nu_2(v))dv} ds\Big] da.
\end{aligned} \tag{2.5}$$

According to Diekmann et al. [3], $\Re_0$ in (2.5) can be regarded as the basic reproduction number of the disease and explained as follows. Since the total infectivity at time t is the sum of the infectivities of each infected compartment and the bacteria compartment, we define $\Re_0 = R_i + R_{i_c} + R_B$, where

$$R_i = S_0 \int_0^{\infty} \beta_1(a)\pi_1(a) da$$

is the number of secondary cases generated by individuals in the $i-$class, and $S_0 = \frac{\Lambda}{\mu}$ is the number of susceptible individuals in the absence of the disease. The term $\pi_1(a) = e^{-\int_0^a (\mu+\nu_1(v)+\sigma(v))dv}$ is the survival probability as a function of age a in the infected $i-$class.

Since $\pi_2(a) = e^{-\int_0^a (\mu+\nu_2(v))dv}$ is the survival probability in the treatment i_c-class and $\sigma(a)$ is the rate at which infectives are selected for the treatment in i_c-class, then $\pi_2(a)\int_0^a \sigma(s)\frac{\pi_1(s)}{\pi_2(s)}ds$ is the proportion of infected individuals who move to the treated class. If we consider the infection-age specific transmission rate $\beta_2(a)$, then the contribution to $\Re_0$ from the i_c-class is

$$R_{i_c} = S_0 \int_0^\infty \beta_2(a)\pi_2(a) \int_0^a \sigma(s)\frac{\pi_1(s)}{\pi_2(s)}dsda.$$

Since $\eta_i(a)(i = 1, 2)$ are the age-specific contribution of infected individuals to the bacterial population in the environment, and δ is the clearance rate of the bacteria from the environment, therefore, the reproduction number of the infections caused by the free bacteria is

$$R_B = \frac{\rho}{\delta}S_0 \int_0^\infty \eta_1(a)\pi_1(a)da + \frac{\rho}{\delta}S_0 \int_0^\infty \eta_2(a)\pi_2(a) \int_0^a \sigma(s)\frac{\pi_1(s)}{\pi_2(s)}dsda.$$

Now we consider the existence of the endemic equilibria. From (2.3) and (2.4), we obtain that the equilibrium level of susceptible individuals S^* satisfies the following equations

$$\begin{aligned} S^* \int_0^\infty \Big[\Big(\beta_1(a) + \frac{\rho}{\delta}\eta_1(a)\Big)\pi_1(a) + \Big(\beta_2(a) + \frac{\rho}{\delta}\eta_2(a)\Big)\pi_2(a) \\ \times \int_0^a \sigma(s)e^{-\int_0^s (\nu_1(v)+\sigma(v)-\nu_2(v))dv} ds\Big]da = 1, \\ S^* = \frac{\Lambda}{\mu\Re_0}. \end{aligned} \tag{2.6}$$

Substituting (2.4) and (2.6) into the first equation of (2.3), we have

$$i^*(0) = \Lambda\Big(1 - \frac{1}{\Re_0}\Big). \tag{2.7}$$

Thus, we have the following theorem:

Theorem 1. *There exists a unique positive endemic equilibrium $E^*(S^*,\ i^*(a),\ i_c^*(a), B^*)$ if and only if $\Re_0 > 1$. The components of the equilibrium are given by (2.4) and (2.6), with $i^*(0)$ given by (2.7)*

Now we investigate the stability of the equilibria in system (2.1). We notice that for the structured model with unbounded domain, *i.e.,* $a \in [0, \infty)$, its linear stability analysis of the equilibrium is different from those of the models in ODEs, where the characteristic equation has only roots with negative real part directly leads to the conclusion that the corresponding equilibrium point is locally stable. Here we apply some analysis techniques in recent papers [4,20] to establish the local stability of equilibrium solutions of model (2.1) (see, Appendix B).

First, we consider the local stability of the infection free equilibrium $E_0(\frac{\Lambda}{\mu}, 0, 0, 0)$. Let $S(t) = \frac{\Lambda}{\mu} + x(t), i(a,t) = y(a,t),\ i_c(a,t) = y_c(a,t), B(t) = z(t)$, and linearizing system (2.1) about E_0, we

obtain the system:

$$\begin{aligned}
&\frac{dx(t)}{dt} = -\mu x(t) - \frac{\Lambda}{\mu}\Big(\int_0^{+\infty}\beta_1(a)y(a,t)da + \int_0^{+\infty}\beta_2(a)y_c(a,t)da\Big) - \frac{\Lambda\rho}{\mu}z(t),\\
&\frac{\partial y(a,t)}{\partial t} + \frac{\partial y(a,t)}{\partial a} = -(\mu + \nu_1(a) + \sigma(a))y(a,t),\\
&y(0,t) = \frac{\Lambda}{\mu}\Big(\int_0^{+\infty}\beta_1(a)y(a,t)da + \int_0^{+\infty}\beta_2(a)y_c(a,t)da\Big) + \frac{\rho\Lambda}{\mu}z(t),\\
&\frac{\partial y_c(a,t)}{\partial t} + \frac{\partial y_c(a,t)}{\partial a} = \sigma(a)y(a,t) - (\mu + \nu_2(a))y_c(a,t),\\
&y_c(0,t) = 0,\\
&\frac{dz(t)}{dt} = \int_0^{+\infty}\eta_1(a)y(a,t)da + \int_0^{+\infty}\eta_2(a)y_c(a,t)da - \delta z(t).
\end{aligned} \tag{2.8}$$

To analyze the asymptotic behavior of E_0, we look for solutions of the form $x(t) = \bar{x}e^{\lambda t}$, $y(a,t) = \bar{y}(a)e^{\lambda t}$, $y_c(a,t) = \bar{y}_c(a)e^{\lambda t}$ and $z(t) = \bar{z}e^{\lambda t}$. Thus, we can consider the following eigenvalue problem:

$$\begin{aligned}
&(\mu+\lambda)\bar{x} = -\frac{\Lambda}{\mu}\Big(\int_0^{+\infty}\beta_1(a)\bar{y}(a)da + \int_0^{+\infty}\beta_2(a)\bar{y}_c(a)da\Big) - \frac{\Lambda\rho}{\mu}\bar{z},\\
&\frac{d\bar{y}(a)}{da} = -(\lambda + \mu + \nu_1(a) + \sigma(a))\bar{y}(a),\\
&\bar{y}(0) = \frac{\Lambda}{\mu}\Big(\int_0^{+\infty}\beta_1(a)\bar{y}(a)da + \int_0^{+\infty}\beta_2(a)\bar{y}_c(a)da\Big) + \frac{\rho\Lambda}{\mu}\bar{z},\\
&\frac{d\bar{y}_c(a)}{da} = \sigma(a)\bar{y}(a) - (\mu + \nu_2(a) + \lambda)\bar{y}_c(a),\\
&\bar{y}_c(0) = 0,\\
&(\delta+\lambda)\bar{z} = \int_0^{+\infty}\eta_1(a)\bar{y}(a)da + \int_0^{+\infty}\eta_2(a)\bar{y}_c(a)da.
\end{aligned} \tag{2.9}$$

Solving Eq.(2.9), we obtain

$$\begin{aligned}
&\bar{y}(a) = y(0)e^{-\lambda a}\pi_1(a),\\
&\bar{y}_c(a) = y(0)e^{-\lambda a}\pi_2(a)\int_0^a \sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds,\\
&\bar{z} = \frac{\bar{y}(0)}{\lambda+\delta}\int_0^{\infty}\Big(\eta_1(a)e^{-\lambda a}\pi_1(a) + \eta_2(a)e^{-\lambda a}\pi_2(a)\int_0^a\sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds\Big)da.
\end{aligned} \tag{2.10}$$

Substituting (2.10) into the third equation of (2.9), we have

$$1=\frac{\Lambda}{\mu}\int_0^\infty\Big(\beta_1(a)e^{-\lambda a}\pi_1(a)+\beta_2(a)e^{-\lambda a}\pi_2(a)\int_0^a\sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds\Big)da$$
$$+\frac{\rho\Lambda}{\mu(\lambda+\delta)}\int_0^\infty\Big(\eta_1(a)e^{-\lambda a}\pi_1(a)+\eta_2(a)e^{-\lambda a}\pi_2(a)\int_0^a\sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds\Big)da. \tag{2.11}$$

Define a function $\mathcal{G}(\lambda)$ to be the right-hand side in (2.11). Obviously, $\mathcal{G}(\lambda)$ is a continuously differentiable function with $\lim_{\lambda\to\infty}\mathcal{G}(\lambda)=0$. By direct computation, it is easy to show that $\mathcal{G}'(\lambda)<0$, and therefore, $\mathcal{G}(\lambda)$ is a decreasing function. Hence, any real solution of Eq.(2.11) is negative if $\mathcal{G}(0)<1$, and positive if $\mathcal{G}(0)>1$. Thus, if $\mathcal{G}(0)>1$, the infection-free equilibrium is unstable.

Next, we show that Eq.(2.11) has no complex solutions with nonnegative real part if $\mathcal{G}(0)<1$. In fact, set

$$\begin{aligned}\mathcal{H}(a)&=\frac{\Lambda}{\mu}\Big(\beta_1(a)\pi_1(a)+\beta_2(a)\pi_2(a)\int_0^a\sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds\Big),\\ \mathcal{F}(a)&=\frac{\rho\Lambda}{\mu}\Big(\eta_1(a)\pi_1(a)+\eta_2(a)\pi_2(a)\int_0^a\sigma(s)e^{-\int_0^s(\nu_1(v)+\sigma(v)-\nu_2(v))dv}ds\Big).\end{aligned} \tag{2.12}$$

Thus, we have

$$\mathcal{G}(\lambda)=\int_0^\infty e^{-\lambda a}\mathcal{H}(a)da+\frac{1}{\lambda+\delta}\int_0^\infty e^{-\lambda a}\mathcal{F}(a)da.$$

Suppose $\mathcal{G}(0)<1$. Assume that $\lambda=a_1+b_1i$ is a complex solution of equation (2.11) with $a_1\geq 0$. Then

$$\begin{aligned}|\mathcal{G}(\lambda)|&=|\int_0^\infty e^{-\lambda a}\mathcal{H}(a)da+\frac{1}{\lambda+\delta}\int_0^\infty e^{-\lambda a}\mathcal{F}(a)da|\\ &\leq|\int_0^\infty e^{-(a_1+ib_1)a}\mathcal{H}(a)da|+\frac{1}{|a_1+ib_1+\delta|}|\int_0^\infty e^{-(a_1+ib_1)a}\mathcal{F}(a)da|\\ &=\int_0^\infty|e^{-(a_1+ib_1)a}|\mathcal{H}(a)da+\frac{1}{\sqrt{(a_1+\delta)^2+b_1^2}}\int_0^\infty|e^{-(a_1+ib_1)a}|\mathcal{F}(a)da\\ &\leq\int_0^\infty e^{-a_1a}\mathcal{H}(a)da+\frac{1}{a_1+\delta}\int_0^\infty e^{-a_1a}\mathcal{F}(a)da=|\mathcal{G}(a_1)|\leq\mathcal{G}(0)<1\end{aligned} \tag{2.13}$$

It follows from equation (2.13) that Eq.(2.11) has solutions $\lambda=a_1+ib_1$ only if $a_1<0$. Thus, every solution of (2.11) must have a negative real part. Observe that $\Re_0=\mathcal{G}(0)$. Therefore, the infection-free equilibrium E_0 is locally asymptotically stable if $\mathcal{G}(0)<1$.

Summarizing the above discussion, we have

Theorem 2. *The infection-free equilibrium E_0 is locally asymptotically stable if $\Re_0<1$ and unstable if $\Re_0>1$.*

Theorem 3. *If $\Re_0\leq 1$, the uninfected equilibrium E_0 is globally asymptotically stable.*

Proof. From Theorem 2, we know that E_0 is locally asymptotically stable for $\Re_0 < 1$. It suffices to show that E_0 is a global attractor. Let

$$i(0,t) = \omega(t).$$

Integrating the second equation in system (2.1) along the characteristic lines, we obtain

$$i(a,t) = \begin{cases} \omega(t-a)\pi_1(a), & t > a, \\ \varphi(a-t)\dfrac{\pi_1(a)}{\pi_1(a-t)}, & t < a. \end{cases} \tag{2.14}$$

Similarly, integrating the third equation in system (2.1) along the characteristic lines yields

$$i_c(a,t) = \begin{cases} \displaystyle\int_0^a \sigma(s)\omega(t-a)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}ds, & t > a, \\ \psi(a-t)\dfrac{\pi_2(a)}{\pi_2(a-t)} + \displaystyle\int_{a-t}^a \sigma(s)\varphi(s-t)\frac{\pi_1(s)}{\pi_1(a-t)}\frac{\pi_2(a)}{\pi_2(s)}ds, & t < a. \end{cases} \tag{2.15}$$

Notice that here we have used $i_c(0,t) = 0$. Let

$$\begin{aligned} q(a) \quad &= \int_a^\infty \Big(\beta_1(s) + \frac{\rho}{\delta}\eta_1(s)\Big)\pi_1(s)ds \\ &+ \int_a^\infty \Big(\beta_2(s) + \frac{\rho}{\delta}\eta_2(s)\Big)\pi_2(s)\int_0^s \sigma(u)e^{-\int_0^u (\nu_1(v)+\sigma(v)-\nu_2(v))dv}duds. \end{aligned} \tag{2.16}$$

Consider the following generic form of a Lyapunov function

$$g(x(t)) = x(t) - 1 - \ln x(t),$$

where $g(x) \geq 0$ for all $x > 0$. Furthermore $g(x)$ achieves its global minimum at one with $g(1) = 0$ and $g'(x) = 1 - \dfrac{1}{x(t)}$. Consider the following Lyapunov function

$$V(t) = g\Big(\frac{S}{S_0}\Big) + \int_0^\infty q(a)\frac{i(a,t)}{\pi_1(a)}da + \frac{\rho}{\delta}B(t). \tag{2.17}$$

Using (2.14), we rewrite equation (2.17) as follows

$$V(t) = g\Big(\frac{S}{S_0}\Big) + \int_0^\infty q(a)\omega(t-a)da + \frac{\rho}{\delta}B(t). \tag{2.18}$$

Differentiating (2.18) along the solution of system (2.1) and (2.16), we obtain

$$\begin{aligned}
\frac{dV(t)}{dt} &= \Big(1-\frac{S_0}{S(t)}\Big)\frac{S'(t)}{S_0} + \Big[q(0)\omega(t) + \int_0^\infty q'(a)\omega(t-a)da\Big] + \frac{\rho}{\delta}B'(t) \\
&= \Big(\frac{1}{S_0}-\frac{1}{S}\Big)\Big[\Lambda - \mu S - S\Big(\int_0^{+\infty}\beta_1(a)i(a,t)da + \int_0^{+\infty}\beta_2(a)i_c(a,t)da\Big) - \rho S B(t)\Big] \\
&\quad +\omega(t)\int_0^\infty \Big(\beta_1(s)+\frac{\rho}{\delta}\eta_1(s)\Big)\pi_1(s)ds \\
&\quad +\omega(t)\int_0^\infty \Big(\beta_2(s)+\frac{\rho}{\delta}\eta_2(s)\Big)\pi_2(s)\int_0^s \sigma(u)e^{-\int_0^u(\nu_1(v)+\sigma(v)-\nu_2(v))dv}duds \\
&\quad -\int_0^\infty \omega(t-a)\Big(\beta_1(a)+\frac{\rho}{\delta}\eta_1(a)\Big)\pi_1(a)da \\
&\quad -\int_0^\infty \omega(t-a)\Big(\beta_2(a)+\frac{\rho}{\delta}\eta_2(a)\Big)\pi_2(a)\int_0^a \sigma(u)e^{-\int_0^u(\nu_1(v)+\sigma(v)-\nu_2(v))dv}duda \\
&\quad +\frac{\rho}{\delta}\Big[\int_0^{+\infty}\eta_1(a)i(a,t)da + \int_0^{+\infty}\eta_2(a)i_c(a,t)da - \delta B(t)\Big]
\end{aligned} \tag{2.19}$$

Using $\Lambda = \mu S_0$, (2.14) and (2.15), we have

$$\begin{aligned}
\frac{dV(t)}{dt} &= -\frac{\mu(S(t)-S_0)^2}{S(t)S_0} - \frac{S(t)}{S_0}\Big[\int_0^\infty \Big(\beta_1(a)i(a,t)+\beta_2(a)i_c(a,t)\Big)da + \rho B(t)\Big] \\
&\quad +\int_0^\infty(\beta_1(a)i(a,t)+\beta_2(a)i_c(a,t))da + \rho B(t) + i(0,t)\int_0^\infty(\beta_1(s)+\frac{\rho}{\delta}\eta_1(s))\pi_1(s))ds \\
&\quad +i(0,t)\int_0^\infty \pi_2(s)\Big(\beta_2(s)+\frac{\rho}{\delta}\eta_2(s)\Big)\int_0^s \sigma(u)\pi_1(u)e^{-\int_0^u(\nu_1(v)+\sigma(v)-\nu_2(v))dv}duds \\
&\quad -\int_0^\infty \Big(\beta_1(a)+\frac{\rho}{\delta}\eta_1(a)\Big)i(a,t)da - \int_0^\infty \Big(\beta_2(a)+\frac{\rho}{\delta}\eta_2(a)\Big)i_c(a,t)da \\
&\quad +\frac{\rho}{\delta}\int_0^{+\infty}\Big(\eta_1(a)i(a,t)da + \eta_2(a)i_c(a,t)\Big)da - \rho B(t).
\end{aligned} \tag{2.20}$$

Using (2.14), (2,15) and (2.5), we obtain

$$\begin{aligned}
\frac{dV(t)}{dt} &= -\frac{\mu(S-S_0)^2}{SS_0} - \frac{i(0,t)}{S_0} + \frac{i(0,t)}{S_0}\Re_0 \\
&= -\frac{\mu(S-S_0)^2}{SS_0} - \frac{1}{S_0}\Big(1-\Re_0\Big)i(0,t) \le 0, \qquad \text{for} \quad \Re_0 \le 1.
\end{aligned}$$

The equality $\dfrac{dV(t)}{dt} = 0$ holds if and only if $S = S_0,\ i(0,t) = 0$. Thus, from the solutions (2.14) and (2.15) for system (2.1) along the characteristic lines, we have that $i(a,t) = 0,\ i_c(a,t) = 0$ for all $t > a$. Hence, we have $i(a,t) \to 0,\ i_c(a,t) \to 0$ when $t \to \infty$.

It is easy to show that $\{E_0\}$ is the maximal compact invariant set. From the LaSalle invariant principle ([8],Theorem 5.3.1), we have that the disease-free equilibrium E_0 of system (2.1) is globally stable for $\Re_0 \le 1$.

This completes the proof of Theorem 3.

Next, we show that the endemic equilibrium is locally stable whenever it exits.

Proposition 1. *The unique endemic equilibrium $E^*(S^*,\ i^*(a),\ i_c^*(a), B^*)$, given by (2.4) and (2.6), with $i^*(0)$ given by (2.7) is locally asymptotically stable if $\Re_0 > 1$.*

Proof. To show the local stability we linearize system (2.1) around the endemic equilibrium E^*. In particular, we take $S(t) = S^* + x(t)$, $i(a,t) = i^*(a) + y(a,t)$, $i_c(a,t) = i_c^*(a) + y_c(a,t)$, $B(t) = B^* + z(t)$. We look for solutions of the linearized system in exponential form $x(t) = xe^{\lambda t}$, $y(a,t) = y(a)e^{\lambda t}$, $y_c(a,t) = y_c(a)e^{\lambda t}$ and $z(t) = ze^{\lambda t}$. We arrive at the following linear eigenvalue problem.

$$\begin{aligned}
\lambda x &= -x(\int_0^{+\infty}(\beta_1(a)i^*(a) + \beta_2(a)i_c^*(a))da) - S^*(\int_0^{+\infty}(\beta_1(a)y(a) + \beta_2(a)y_c(a))da \\
&\quad - \rho S^* z - \rho B^* x - \mu x, \\
\frac{dy}{da} &= -(\lambda + \mu + \nu_1(a) + \sigma(a))y(a), \\
y(0) &= x(\int_0^{+\infty}(\beta_1(a)i^*(a) + \beta_2(a)i_c^*(a))da) + S^*(\int_0^{+\infty}(\beta_1(a)y(a) + \beta_2(a)y_c(a))da \\
&\quad + \rho S^* z + \rho B^* x, \\
\frac{dy_c}{da} &= -(\lambda + \mu + \nu_2(a))y_c(a) + \sigma(a)y(a), \\
y_c(0) &= 0, \\
\lambda z &= \int_0^{+\infty}(\eta_1(a)y(a) + \eta_2(a)y_c(a))da - \delta z.
\end{aligned}$$

To derive the characteristic equation, we assume the system has a nonzero solution. Solving the differential equations we obtain

$$\begin{aligned}
y(a) &= y(0)e^{-\lambda a}\pi_1(a) \\
y_c(a) &= y(0)e^{-\lambda a}\pi_2(a)\int_0^a \sigma(\tau)\frac{\pi_1(\tau)}{\pi_2(\tau)}d\tau = y(0)e^{-\lambda a}\Gamma_c(a).
\end{aligned}$$

Adding the equations for x and and for $y(0)$ we obtain $\lambda x + y(0) = -\mu x$. Solving for x, we have

$$x = -\frac{y(0)}{\lambda + \mu}.$$

Solving the last equation for z we have

$$z = \frac{\int_0^{+\infty}(\eta_1(a)y(a) + \eta_2(a)y_c(a))da}{\lambda + \delta}.$$

Denote by K the constant

$$K = \int_0^{+\infty}(\beta_1(a)i^*(a) + \beta_2(a)i_c^*(a))da.$$

Substituting x, z, $y(a)$ and $y_c(a)$ in the equation for $y(0)$ and canceling $y(0)$ we obtain the following characteristic equation:

$$\begin{aligned} 1 &= -\frac{K}{\lambda+\mu} + S^*\Big(\int_0^{+\infty}(\beta_1(a)e^{-\lambda a}\pi_1(a) + \beta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big) \\ &+\frac{\rho S^*}{\lambda+\delta}\Big(\int_0^{+\infty}(\eta_1(a)e^{-\lambda a}\pi_1(a) + \eta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big) - \frac{\rho B^*}{\lambda+\mu} \end{aligned}$$

We rewrite this equation in the following form

$$\begin{aligned} \frac{\lambda+\mu+K+\rho B^*}{\lambda+\mu} &= S^*\Big(\int_0^{+\infty}(\beta_1(a)e^{-\lambda a}\pi_1(a) + \beta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big) \\ &+\frac{\rho S^*}{\lambda+\delta}\Big(\int_0^{+\infty}(\eta_1(a)e^{-\lambda a}\pi_1(a) + \eta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big) \end{aligned}$$

It is not hard to see that for λ with $Re\lambda \geq 0$

$$\left|\frac{\lambda+\mu+K+\rho B^*}{\lambda+\mu}\right| > 1.$$

On the other hand for the right hand side we have for λ with $Re\lambda \geq 0$:

$$\begin{aligned} &S^*\Big|\Big(\int_0^{+\infty}(\beta_1(a)e^{-\lambda a}\pi_1(a) + \beta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big) \\ &+\frac{\rho}{\lambda+\delta}\Big(\int_0^{+\infty}(\eta_1(a)e^{-\lambda a}\pi_1(a) + \eta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big)\Big| \\ &\leq S^*\Big|\Big(\int_0^{+\infty}(\beta_1(a)e^{-\lambda a}\pi_1(a) + \beta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big)\Big| \\ &+S^*\frac{\rho}{|\lambda+\delta|}\Big|\Big(\int_0^{+\infty}(\eta_1(a)e^{-\lambda a}\pi_1(a) + \eta_2(a)e^{-\lambda a}\Gamma_c(a))da\Big)\Big| \\ &\leq S^*\Big(\int_0^{+\infty}(\beta_1(a)\pi_1(a) + \beta_2(a)\Gamma_c(a))da\Big)\Big| \\ &+S^*\frac{\rho}{\delta}\Big|\Big(\int_0^{+\infty}(\eta_1(a)\pi_1(a) + \eta_2(a)\Gamma_c(a))da\Big)\Big| = S^*\frac{\mu\Re_0}{\Lambda} = 1. \end{aligned}$$

Hence, for λ with $Re\lambda \geq 0$ the left hand side of the characteristic equation is strictly larger than one, while the right hand side of the characteristic equation is strictly smaller than one. Therefore the characteristic equation has no roots with non-negative real parts. We provide the justification that the semigroup corresponding to the linearized equations converges to zero in the Appendix B.

This concludes the proof of Proposition 1.

Now we investigate the disease persistence for system (2.1).

Firstly, we introduce the following notations. Set

$$\mathcal{M}_1 = \{\varphi(a) \in L^1_+(0,+\infty) | \exists t \geq 0 : \int_0^\infty \beta_1(a+t)\varphi(a)da > 0 \text{ and } \int_0^\infty \eta_1(a+t)\varphi(a)da > 0\}.$$

$$\mathcal{M}_2 = \{\psi(a) \in L^1_+(0,+\infty) | \exists t \geq 0 : \int_0^\infty \beta_2(a+t)\psi(a)da > 0 \text{ and } \int_0^\infty \eta_2(a+t)\psi(a)da > 0\}.$$

$$\mathcal{D}_0 = \mathbb{R}_+ \times \mathcal{M}_1 \times \mathcal{M}_2 \times \mathbb{R}_+. \quad X_0 = \mathcal{D} \cap \mathcal{D}_0.$$

Theorem 4. *If $\Re_0 > 1$, then there exists a constant $0 < \eta < 1$ (independent of initial conditions), such that any solution $(S(t), i(a,t), i_c(a,t), B(t))$ of (2.1) with $(S(0), \varphi(a), \psi(a), B(0)) \in X_0$ satisfies*

$$\liminf_{t\to+\infty} \Big(\int_0^\infty (\beta_1(a) i(a,t) + \beta_2(a) i_c(a,t)) da + \rho B(t) \Big) > \eta.$$

In order to prove Theorem 4, we need the following two Lemmas.

Lemma 1. *Assume that $\Re_0 > 1$, then there exists a constant $\gamma > 0$ such that any solution $(S(t), i(a,t), i_c(a,t), B(t))$ of (2.1) with $(S(0), \varphi(a), \psi(a), B(0)) \in X_0$ satisfies*

$$\limsup_{t\to+\infty} (\int_0^\infty (\beta_1(a) i(a,t) + \beta_2(a) i_c(a,t)) da + \rho B(t)) > \gamma.$$

Proof. Assume the contrary that all infected individuals die out. Thus, for every $\varepsilon > 0$ and the initial condition in X_0, we have

$$\limsup_{t\to+\infty} (\int_0^{+\infty} (\beta_1 i(a,t) + \beta_2 i_c(a,t)) da + \rho B(t)) < \varepsilon. \tag{2.21}$$

Hence, there exists $T > 0$ such that for all $t > T$, we have

$$\int_0^\infty (\beta_1 i(a,t) + \beta_2 i_c(a,t)) da + \rho B(t) < \varepsilon. \tag{2.22}$$

Consequently, from the first equation in (2.1), we have

$$S'(t) \geq \Lambda - \mu S(t) - \varepsilon S(t).$$

Therefore, we have

$$\lim_{t\to+\infty} \sup S(t) \geq \lim_{t\to+\infty} \inf S(t) \geq \frac{\Lambda}{\mu + \varepsilon}. \tag{2.23}$$

Using $\omega(t) = i(0,t)$ and the inequality above, we obtain

$$\omega(t) \geq \frac{\Lambda}{\mu+\varepsilon} \int_0^{+\infty} (\beta_1(a) i(a,t) + \beta_2(a) i_c(a,t)) da + \rho \frac{\Lambda}{\mu+\varepsilon} B(t). \tag{2.24}$$

Using expression (2.14) and (2.15), we have the following system

$$\begin{aligned}
\omega(t) &\geq \frac{\Lambda}{\mu+\varepsilon} \int_0^t (\beta_1(a)\omega(t-a)\pi_1(a) + \beta_2(a) \int_0^a \sigma(s)\omega(t-a)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)} ds) da + \rho \frac{\Lambda}{\mu+\varepsilon} B(t), \\
\frac{dB(t)}{dt} &\geq \int_0^t \eta_1(a)\omega(t-a)\pi_1(a) da + \int_0^t \eta_2(a) \int_0^a \sigma(s)\omega(t-a)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)} ds da - \delta B(t).
\end{aligned} \tag{2.25}$$

Let $\hat{\omega}(\lambda)$ be the Laplace transform of $\omega(t)$ and $\hat{B}(\lambda)$ be the Laplace transform of $B(t)$. Furthermore, we have

$$\begin{aligned}
&\hat{K}_1(\lambda)=\int_0^\infty \beta_1(a)\pi_1(a)e^{-\lambda a}da, \hat{K}_2(\lambda)=\int_0^\infty \beta_2(a)\int_0^a \sigma(s)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}dse^{-\lambda a}da,\\
&\hat{K}_3(\lambda)=\int_0^\infty \eta_1(a)\pi_1(a)e^{-\lambda a}da, \quad \hat{K}_4(\lambda)=\int_0^\infty \eta_2(a)e^{-\lambda a}\int_0^a \sigma(s)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}dsda.
\end{aligned} \tag{2.26}$$

Applying the Laplace transform of both sides in (2.25), we obtain

$$\begin{aligned}
&\hat{\omega}(\lambda)\geq \frac{\Lambda}{\mu+\varepsilon}\Big(\hat{K}_1(\lambda)\hat{\omega}(\lambda)+\hat{K}_2(\lambda)\hat{\omega}(\lambda)\Big)+\rho\frac{\Lambda}{\mu+\varepsilon}\hat{B}(\lambda),\\
&\lambda\hat{B}(\lambda)-B(0)\geq \hat{K}_3(\lambda)\hat{\omega}(\lambda)+\hat{K}_4(\lambda)\hat{\omega}(\lambda)-\delta\hat{B}(\lambda).
\end{aligned} \tag{2.27}$$

From (2.27), we have

$$\hat{\omega}(\lambda)\geq \frac{\Lambda}{\mu+\varepsilon}\Big(\hat{K}_1(\lambda)+\hat{K}_2(\lambda)+\frac{\rho}{\lambda+\delta}\hat{K}_3(\lambda)+\frac{\rho}{\lambda+\delta}\hat{K}_4(\lambda)\Big)\hat{\omega}(\lambda)+\frac{\Lambda\rho}{(\mu+\varepsilon)(\lambda+\delta)}B(0).$$

The above inequality should hold for the given $\varepsilon\approx 0$ and for any $\lambda>0$. But it is impossible since for $\varepsilon\approx 0$ and $\lambda\approx 0$, the coefficient in front $\hat{\omega}(\lambda)$ on the right hand side is approximately $\Re_0>1$. In addition, there is another positive term on the right hand side. This is a contradiction. Therefore, there exists a constant $\gamma>0$ such that any solution $(S(t),i(a,t),i_c(a,t),B(t))$ of (2.1) with $(S(0),\varphi(a),\psi(a),B(0))\in X_0$ satisfying $\limsup_{t\to+\infty}(\int_0^\infty(\beta_1(a)i(a,t)+\beta_2(a)i_c(a,t))da+\rho B(t))>\gamma$. Further, we can show that any solution $(S(t),i(a,t),i_c(a,t),B(t))$ of (2.1) is bounded below. In fact, from (2.24) and the inequality above we have that $\limsup_{t\to+\infty}\omega(t)>\frac{\Lambda\gamma}{\mu+\varepsilon}$. Hence, we have

$$\begin{aligned}
&\limsup_{t\to+\infty}\int_0^\infty \beta_1(a)i(a,t)da>\frac{\Lambda\gamma}{\mu+\varepsilon}\int_0^\infty \beta_1(a)\pi_1(a)da,\\
&\limsup_{t\to+\infty}\int_0^\infty \beta_2(a)i_c(a,t)da>\frac{\Lambda\gamma}{\mu+\varepsilon}\int_0^\infty \beta_2(a)\int_0^a \sigma(s)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}dsda.
\end{aligned} \tag{2.28}$$

In addition, it follows from the differential equation for $B(t)$ in system (2.1) that $B(t)$ is also bounded below.

This completes the proof of Lemma 1.

We now show that system (2.1) has a global compact attractor $\mathcal{M}_0$. A set K in X_+ is called a global compact attractor for the solution semiflow Ψ, if K is a maximal compact invariant set, and if for all open sets U containing K and all bounded sets B of X_+ there exists some $t_0>0$ such that $\Psi(t,B)\subseteq U$ for all $t\geq t_0$ (see [7],Section 3.4). We give the following Lemma.

Lemma 2. *Assume that $\Re_0>1$, then there exists $\mathcal{M}_0$ (a compact subset of X_0) which is a global attractor for the solution semiflow Ψ of system (2.1) in X_0.*

In order to prove Lemma 2, we need the following two results, which come from Lemma 3.2.3 and Theorem 3.4.6 in [7]. These methods and techniques have been recently employed in [20].

Lemma 3. (see, Lemma 3.2.3 in [7]) *For each $t \geq 0$, suppose $T(t) = S(t)+U(t) : X \to X$ has the property that $U(t)$ is complete continuous and there is a continuous function $k : \mathbb{R}^+ \times \mathbb{R}^+ \to \mathbb{R}^+$ such that $k(t, r) \to 0$ as $t \to 0$ and $|S(t)x| \leq k(t, r)$, if $|x| < r$. Then $T(t), t \geq 0$ is asymptotically smooth.*

Lemma 4.(see, Theorem 3.4.6 in [7]) *If $T(t) : X \to X, t \geq 0$ is asymptotically smooth point dissipative and orbits of bounded sets are bounded, then there exists a global attractor $\mathcal{M}_0$. If $T(t)$ is also one-to-one on A,then $T(t)/\ \mathcal{M}_0$ is a C^r- group. If in addition, X is a Banach space,then $\mathcal{M}_0$ is connected.*

Proof of Lemma 2. Set

$$\Psi(t; S_0, \varphi(\cdot), \psi(\cdot), B_0) = (S(t), i(\cdot, t), i_c(\cdot, t), B(t)),$$

$\Psi : [0, \infty) \times X_0 \to X_0$, with $\Psi(t, \Psi(s, .)) = \Psi(t + s, \cdot)$ for all $t, s \geq 0$ and $\Psi(0, \cdot)$ being the identity map. Our goal is to show that Ψ satisfies the assumptions of Lemma 3 and Lemma 4. To this end, we additively split the solution semiflow Ψ into two components $\Psi = \widehat{\Psi}(t, x^0) + \widetilde{\Psi}(t, x^0)$ such that $\widehat{\Psi}(t, x^0) \to 0$ as $t \to \infty$ for every $x^0 \in X_0$, and for a fixed t and any bounded set $\mathcal{M}$ in X_0, the set $\{\ \widetilde{\Psi}(t, x^0) : x^0 \in \mathcal{M}\}$ is precompact. The two summands are defined as follows:

$$\widehat{\Psi}(t, S_0, \varphi, \psi, B_0) = (0,\ \widehat{i}(\cdot, t),\ \widehat{i}_c(\cdot, t),\ 0);$$

$$\widetilde{\Psi}(t, S_0, \varphi, \psi, B_0) = (S(t),\ \widetilde{i}(\cdot, t),\ \widetilde{i}_c(\cdot, t),\ B(t)).$$

Notice that $S(t)$ and $B(t)$ satisfy system (2.1) with $i(a, t) = \widehat{i}(a, t) + \widetilde{i}(a, t)$, $i_c(a, t) = \widehat{i}_c(a, t) + \widetilde{i}_c(a, t)$. The functions $\widehat{i}(a, t)$ and $\widehat{i}_c(a, t)$ are solutions to the following systems:

$$\begin{cases} \dfrac{\partial \widehat{i}(a,t)}{\partial t} + \dfrac{\partial \widehat{i}(a,t)}{\partial a} = -(\mu + \nu_1(a) + \sigma(a))\widehat{i}(a, t), \\ \widehat{i}(0, t) = 0, \\ \widehat{i}(a, 0) = \varphi(a), \\ \dfrac{\partial \widehat{i}_c(a,t)}{\partial t} + \dfrac{\partial \widehat{i}_c(a,t)}{\partial a} = \sigma(a)\widehat{i}(a, t) - (\mu + \nu_2(a))\widehat{i}_c(a, t), \\ \widehat{i}_c(a, 0) = \psi(a). \end{cases} \tag{2.29}$$

The functions $\widetilde{i}(a,t), \widetilde{i}_c(a,t)$ are the solutions of the following equations:

$$\begin{cases} \dfrac{\partial \widetilde{i}(a,t)}{\partial t} + \dfrac{\partial \widetilde{i}(a,t)}{\partial a} = -(\mu + \nu_1(a) + \sigma(a))\widetilde{i}(a,t), \\ \widetilde{i}(0,t) = S(t)\Big(\int_0^{+\infty} \beta_1(a)\widetilde{i}(a,t)da + \int_0^{+\infty} \beta_2(a)\widetilde{i}_c(a,t)da \Big) + \rho B(t)S(t), \\ \widetilde{i}(a,0) = 0, \\ \dfrac{\partial \widetilde{i}_c(a,t)}{\partial t} + \dfrac{\partial \widetilde{i}_c(a,t)}{\partial a} = \sigma(a)\widetilde{i}(a,t) - (\mu + \nu_2(a))\widetilde{i}_c(a,t), \\ \widetilde{i}_c(0,t) = 0, \quad \widetilde{i}_c(a,0) = 0. \end{cases} \tag{2.30}$$

It is easy to show that $\widehat{i}(a,t), \widetilde{i}(a,t)$ and $\widehat{i}_c(a,t), \widetilde{i}_c(a,t)$ are nonnegative. Define by $u(t) = \int_0^{\infty} \widehat{i}(a,t)da + \int_0^{\infty} \widehat{i}_c(a,t)da$. It follows from (2.29) that $u'(t) \leq -\mu u(t)$. Therefore, this result shows that $\widetilde{\Psi}(t,x_0) \to 0$ as $t \to \infty$ for every $x_0 \in X_0$.

Now it remains to show that for a fixed t and any bounded set $\mathcal{M}$ in X_0, the set $\{\widetilde{\Psi}(t,x^0) : x^0 \in \mathcal{M}\}$ is precompact. In fact, we only need to show the set $\{\widetilde{\Psi}(t;x^0)|x^0 \in X_0, t - \text{fixed}\}$ is precompact by using Fréchet-Kolmogorov Theorem [28]. In fact, first, we have the family

$$\{\Psi(t;x^0)|x^0 \in X_0, t - \text{fixed}\} \subset X_0.$$

Notice that X_0 is bounded. Therefore, $\{\Psi(t;x^0)\}$ is bounded for different initial conditions in X_0.

Second, from (2.30), it is easy to obtain that $\widetilde{i}(a,t) = 0, \widetilde{i}_c(a,t) = 0$ for $a > t$. Hence, the third condition of the Fréchet-Kolmogorov Theorem is trivially satisfied. Finally, to see the second condition, we have to bound by a constant the L^1-norm of $\frac{\partial \widetilde{i}}{\partial a}$, $\frac{\partial \widetilde{i}_c}{\partial a}$. In fact, from (2.30), we have

$$\widetilde{i}(a,t) = \begin{cases} \widetilde{\omega}(t-a)\pi_1(a), & t > a, \\ 0, & t < a, \end{cases} \quad \widetilde{i}_c(a,t) = \begin{cases} \displaystyle\int_0^a \sigma(s)\widetilde{\omega}(t-a)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}ds, & t > a, \\ 0, & t < a, \end{cases} \tag{2.31}$$

where,

$$\widetilde{\omega}(t) = S(t)\Big(\int_0^t \beta_1(s)\widetilde{\omega}(t-s)\pi_1(s)ds + \int_0^t \beta_2(a)\int_0^a \sigma(s)\widetilde{\omega}(t-a)\pi_1(s)\frac{\pi_2(a)}{\pi_2(s)}dsda + \rho B(t) \Big). \tag{2.32}$$

Notice that for $x^0 \in X_0$, $\widetilde{\omega}(t)$ is bounded. Form Lemma 1, we know $S(t), B(t)$ are bounded. Hence, from (2.32), we have the following inequalities:

$$\begin{aligned} \widetilde{\omega}(t) &\leq m_1 \int_0^t \widetilde{\omega}(t-s)ds + M_1, \\ |\widetilde{\omega}'(t)| &\leq m_2 \int_0^t |\widetilde{\omega}'(t-s)|ds + M_2, \end{aligned} \tag{2.33}$$

where, m_i, $M_i (i = 1,2)$ are constants, which depend on the bounds of the parameters as well as the bounds of the solution.

Using Gronwall's inequality, we have

$$\widetilde{\omega}(t) \leq M_1 e^{m_1 t}, \quad \widetilde{\omega}'(t) \leq M_2 e^{m_2 t}. \tag{2.34}$$

From (2.31), we have

$$\left|\frac{\partial \widetilde{i}(a,t)}{\partial a}\right| = \begin{cases} |\widetilde{\omega}'(t-a)|\pi_1(a) + \widetilde{\omega}(t-a)|\pi_1'(a)|, & t > a, \\ 0, & t < a. \end{cases} \tag{2.35}$$

From (2.34) and (2.35), we obtain

$$\| \partial_a \widetilde{i}(a,t) \| \leq M_2 e^{m_2 t} \int_0^\infty \pi_1(a) da + M_1 e^{m_1 t} \int_0^\infty |\pi_1'(a)| da < M.$$

Since

$$\int_0^\infty |\widetilde{i}(a+h,t) - \widetilde{i}(a,t)| da \leq \| \partial_a \widetilde{i}(a,t) \| \, |h| \leq M|h|. \tag{2.36}$$

Therefore, it follows that the integral (2.36) can be made arbitrary small uniformly in the family of functions. Similarly, by the following integral inequality

$$\int_0^\infty |\widetilde{i}_c(a+h,t) - \widetilde{i}_c(a,t)| da \leq \| \partial_a \widetilde{i}_c(a,t) \| \, |h|, \tag{2.37}$$

we can show that the integral (2.37) can be made arbitrary small uniformly. Thus, all requirements of the Fréchet-Kolmogorov Theorem are satisfied. The proof of Lemma 2 is completed.

To complete our proof, we need the following definition and Lemma, which come from paper in [25]. Let $\rho : X \to [0, \infty)$ be a non-negative functional on X and $X_\rho = X \bigcap \{\rho > 0\}$: X_ρ is not necessarily forward invariant under Ψ. We consider the function

$$\sigma : [0, \infty) \times X \times [r_0, \infty) \to [0, \infty)$$

defined by

$$\sigma(t; x, r) = \rho(\Psi(t + r, r, x)), \ t \geq 0, \ x \in X, \ r \geq r_0.$$

We make the following assumption that the real-valued function $\sigma(.; x, r)$ is continuous on $[0; \infty)$ for all $x \in X; r \geq r_0$, and introduce the following notation:

$$\sigma^\infty(x, r) = \limsup_{t \to \infty} \sigma(t, x, r); \quad \sigma_\infty(x, r) = \liminf_{t \to \infty} \sigma(t, x, r).$$

Definition 1. *Ψ is called uniformly weakly$\rho-$persistence if there exists some $\varepsilon > 0$ such that $\sigma^\infty(x, r) > \varepsilon, \ \forall x \in X_\rho, r \geq r_0$; Ψ is called uniformly strongly $\rho-$persistence if there exists some $\varepsilon > 0$ such that $\sigma_\infty(x, r) > \varepsilon, \ \forall x \in X_\rho, r \geq r_0$.*

Lemma 3. *Let Φ be a continuous autonomous semiflow on a metric space X which has a compact attracting set K, i.e., a compact set K such that dist $(\Phi(t;x),K)\to 0; t\to\infty$. We further assume for any total orbit $\phi:\mathbb{R}\to X$ of Φ with relatively compact range: If $s\in\mathbb{R}$ and $\rho(\phi(s))>0$, then $\rho(\phi(t))>0$ for all $t>s$. Then Φ is uniformly strongly ρ-persistent whenever it is uniformly weakly ρ-persistent.*

Proof of Theorem 4. Here we apply Lemma 3 to complete our proof. Consider the solution semiflow Ψ on X_0. Define a function $\rho: X_0\to\mathbb{R}_+$ as follows

$$\rho(\Phi(t,x^0))=\int_0^\infty \beta_1(a)i(a,t)da+\int_0^\infty \beta_2(a)i_c(a,t)da+\rho B(t). \tag{2.38}$$

Lemma 1 implies that the semiflow is uniformly weakly $\rho-$ persistent. Lemma 2 shows that the solution semiflow has a global compact attractor $\mathcal{M}_0$. Since the solution semiflow is nonnegative for all times $t\in\mathbb{R}_+$, we have that for any s, with $t>s$, using (2.25), we can obtain

$$\int_0^\infty \beta_1(a)i(a,t)da+\int_0^\infty \beta_2(a)i_c(a,t)da+\rho B(t)\geq \rho B(s)e^{\delta(t-s)}.$$

Therefore, $\int_0^\infty \beta_1(a)i(a,t)da+\int_0^\infty \beta_2(a)i_c(a,t)da+\rho B(t)>0$ for all $t>s$, provided $B(s)>0$. It follows from Lemma 3 that the solution semiflow is uniformly strongly $\rho-$ persistent. Hence, there exists a constant η such that

$$\lim\inf_{t\to+\infty}\rho(\Phi(t,x^0))\geq\eta.$$

This completes the proof of Theorem 4.

Remark: The set X_0 may not be the largest set on which persistence occurs. For instance, persistence may occur if $\phi(a)=\psi(a)=0$, but $S(0)>0$ and $B(0)>0$. However, that point is not in X_0.

3 ODE system with environmental transmission

To gain further insights into the global transmission dynamics of the disease governed by system (2.1), we assume in this section that the infection rate of the disease and the treatment rate are independent of the infection and treatment stages. We define these constant rates as $\beta_1(a)=\beta_1,\beta_2(a)=\beta_2,\nu_1(a)=\nu_1,\nu_2(a)=\nu_2,\sigma(a)=\sigma,\eta_1(a)=\eta_1,\eta_2(a)=\eta_2$.

Let the total infectives be $I(t):=\int_0^\infty i(a,t)da$, and the total treated individuals be $I_c(t):=\int_0^\infty i_c(a,t)da$. Integrating the equations for $i(a,t)$ and $i_c(a,t)$ in system (2.1) with respect to a and using the initial conditions $i(t,0)$ and $i_c(t,0)$ we reduce the system of PDEs to the following

system of ODEs:

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \mu S(t) - \beta_1 S(t)I(t) - \beta_2 I_c(t)S(t) - \rho S(t)B(t),\\
\frac{dI(t)}{dt} &= \beta_1 S(t)I(t) + \beta_2 I_c(t)S(t) + \rho B(t)S(t) - (\mu+\nu_1+\sigma)I(t),\\
\frac{dI_c(t)}{dt} &= \sigma I(t) - (\mu+\nu_2)I_c(t),\\
\frac{dB(t)}{dt} &= \eta_1 I(t) + \eta_2 I_c(t) - \delta B(t).
\end{aligned} \tag{3.1}$$

Using the next generation approach and Theorem 2 in [25], it is easy to obtain the basic reproduction number of system (3.1):

$$R_0 = \frac{\Lambda(\beta_1\delta(\mu+\nu_2) + \beta_2\delta\sigma + \rho(\eta_1(\mu+\nu_2)+\eta_2\sigma))}{\mu(\mu+\nu_1+\sigma)(\mu+\nu_2)\delta}.$$

System (3.1) always has the infection-free equilibrium $E_0(\frac{\Lambda}{\mu}, 0, 0, 0)$. Direct calculation shows that when $R_0 > 1$, system (3.1) has a unique endemic equilibrium $E^*(S^*, I^*, I_c^*, B^*)$, where

$$\begin{aligned}
&S^* = \frac{\Lambda}{\mu R_0}, \quad I_c = \frac{\sigma}{\mu+\nu_2}I, \quad B^* = \frac{\eta_1(\mu+\nu_2)+\eta_2\sigma}{\delta(\mu+\nu_2)}I,\\
&I = \frac{\Lambda}{\mu+\nu_1+\sigma}\Big(1 - \frac{1}{\mathcal{R}_0}\Big).
\end{aligned} \tag{3.2}$$

For system (3.1), it is easy to show the uniform persistence of solutions. By constructing Lyapunov functions, we can show global stability of the equilibria.

Define the following set:

$$\Omega = \{(S, I, I_c, B) \in \mathbb{R}_+^4 \big| S + I + I_c \le \frac{\Lambda}{\mu}, \quad B \le \frac{\bar{\eta}\Lambda}{\mu\delta}\},$$

where $\bar{\eta} = \max\{\eta_1, \eta_2\}$.

Theorem 5. *For system (3.1), the infection-free equilibrium E_0 is globally stable on the set Ω if $R_0 < 1$; the endemic equilibrium E^* is globally stable in the set Ω if $R_0 > 1$.*

Proof. First we prove the global stability of the infection-free equilibrium E_0. Define the function

$$V_1(t) = I(t) + \frac{\Lambda(\beta_2\delta + \rho\eta_2)}{\mu(\mu+\nu_2)\delta}I_c(t) + \frac{\rho\Lambda}{\mu\delta}B(t).$$

Along the solution of (3.1), directly calculating the derivative of $V_1(t)$, we have

$$\begin{aligned}
\frac{dV_1(t)}{dt} &= (\beta_1 I(t) + \beta_2 I_c(t) + \rho B(t))S(t) - (\mu+\nu_1+\sigma)I(t)\\
&\quad + \frac{\Lambda\sigma(\beta_2\delta+\rho\eta_2)}{\mu(\mu+\nu_2)\delta}I(t) - \frac{\Lambda(\beta_2\delta+\rho\eta_2)}{\mu\delta}I_c(t)\\
&\quad + \frac{\rho\Lambda\eta_1}{\mu\delta}I(t) + \frac{\rho\Lambda\eta_2}{\mu\delta}I_c(t) - \frac{\rho\Lambda}{\mu}B(t).
\end{aligned} \tag{3.3}$$

Since $S(t) \leq \frac{\Lambda}{\mu}$ for $(S, I, I_c, B) \in \Omega$, we have

$$\begin{aligned} \frac{dV_1(t)}{dt} &\leq \Big(\frac{\beta_1\Lambda}{\mu} + \frac{\Lambda\sigma(\beta_2\delta + \rho\eta_2)}{\mu(\mu+\nu_2)\delta} + \frac{\rho\Lambda\eta_1}{\mu\delta} - (\mu+\nu_1+\sigma)\Big)I(t) \\ &= (\mu+\nu_1+\sigma)(R_0-1)I(t) \leq 0, \quad \text{for} \quad R_0 < 1. \end{aligned} \tag{3.4}$$

It is obvious that if $R_0 < 1$, we have $\dfrac{dV_1(t)}{dt} = 0$ if and only if $I(t) = 0$. From (3.1), it is easy to obtain that $I_c(t) = B(t) = 0$, and $S(t) = \Lambda/\mu$. Thus, the invariant set of system (3.1) on the set $\{(S, I, I_cB) \in \Omega : dV_1/dt = 0\}$ is the singleton $\{E_0\}$. Therefore, it follows from LaSalle invariance principle (see, [8],Theorem 5.3.1) that E_0 is globally stable if $R_0 < 1$.

Now we show the global asymptotic stability of the endemic equilibrium $E^*(S^*, I^*, I_c^*, B^*)$. Set

$$x_1 = \frac{S}{S^*}, \quad x_2 = \frac{I}{I^*}, \quad x_3 = \frac{I_c}{I_c^*}, \quad x_4 = \frac{B}{B^*}.$$

Thus, system (3.1) can be rewritten the following form

$$\begin{aligned} \frac{dx_1(t)}{dt} &= x_1\Big[\frac{\Lambda}{S^*}\Big(\frac{1}{x_1} - 1\Big) - \beta_1 I^*(x_2-1) - \beta_2 I_c^*(x_3-1) - \rho B^*(x_4-1)\Big], \\ \frac{dx_2(t)}{dt} &= x_2\Big[\beta_1 S^*(x_1-1) + \frac{\beta_2 S^* I_c^*}{I^*}\Big(\frac{x_1x_3}{x_2} - 1\Big) + \frac{\rho S^* B^*}{I^*}\Big(\frac{x_1x_4}{x_2} - 1\Big)\Big], \\ \frac{dx_3(t)}{dt} &= \frac{\sigma I^*}{I_c^*}x_3\Big(\frac{x_2}{x_3} - 1\Big), \\ \frac{dx_4(t)}{dt} &= \frac{\eta_1 I^*}{B^*}x_4\Big(\frac{x_2}{x_4} - 1\Big) + \frac{\eta_2 I_c^*}{B^*}x_4\Big(\frac{x_3}{x_4} - 1\Big). \end{aligned} \tag{3.5}$$

Consider the following Lyapunov function:

$$\begin{aligned} V_2(x_1, x_2, x_3, x_4) &= S^*(x_1 - 1 - \ln x_1) + a_1 I^*(x_2 - 1 - \ln x_2) + a_2 I_c^*(x_3 - 1 - \ln x_3) \\ &+ a_3 B^*(x_4 - 1 - \ln x_4)], \end{aligned} \tag{3.6}$$

where $a_i > 0, i = 1, 2, 3$ are to be determined later. Thus, the derivative of function $V_2(t)$ with respect to time along the solutions of (3.5) is given by:

$$\begin{aligned} \frac{dV_2(t)}{dt} &= S^*(x_1-1)\frac{x_1'}{x_1} + a_1 I^*(x_2-1)\frac{x_2'}{x_2} + a_2 I_c^*(x_3-1)\frac{x_3'}{x_3} + a_3 I_c^*(x_4-1)\frac{x_4'}{x_4} \\ &= (x_1-1)\Big[\Lambda\Big(\tfrac{1}{x_1} - 1\Big) - \beta_1 S^* I^*(x_2-1) - \beta_2 S^* I_c^*(x_3-1) - \rho S^* B^*(x_4-1)\Big] \\ &\quad + a_1(x_2-1)\Big[\beta_1 S^* I^*(x_1-1) + \beta_2 S^* I_c^*\Big(\frac{x_1x_3}{x_2} - 1\Big) + \rho S^* B^*\Big(\frac{x_1x_4}{x_2} - 1\Big)\Big] \\ &\quad + a_2\sigma I^*(x_3-1)\Big(\frac{x_2}{x_3} - 1\Big) + a_3(x_4-1)\Big(\eta_1 I^*\Big(\frac{x_2}{x_4} - 1\Big) + \eta_2 I_c^*\Big(\frac{x_3}{x_4} - 1\Big)\Big). \end{aligned} \tag{3.7}$$

Thus, we have

$$\begin{aligned}\frac{dV_2(t)}{dt} &= 2\Lambda - \beta_1 S^* I^* - \beta_2 S^* I_c^* - \rho S^* B^* + a_1\beta_1 S^* I^* + a_1\beta_2 S^* I_c^* + a_1\rho S^* B^* + a_2\sigma I^* + a_3\eta_1 I^* \\ &+a_3\eta_2 I_c^* - x_1(\Lambda - \beta_1 S^* I^* - \beta_2 S^* I_c^* - \rho S^* B^* + a_1\beta_1 S^* I^*) - \frac{\Lambda}{x_1} - x_2(a_1\beta_1 S^* I^* \\ &+a_1\beta_2 S^* I_c^* + a_1\rho S^* B^* - \beta_1 S^* I^* - a_2\sigma I^* - a_3\eta_1 I^*) - x_1x_2(\beta_2 S^* I^* - a_1\beta_2 S^* I^*) \\ &-x_3(a_2\sigma I^* - a_3\eta_2 I_c^* - \beta_2 S^* I_c^*) - x_1x_3(\beta_2 S^* I_c^* - a_1\beta_2 S^* I_c^*) - x_4(a_3\eta_1 I^* + a_3\eta_2 I_c^* \\ &-\rho S^* B^*) - x_1x_4(\rho S^* B^* - a_1\rho S^* B^*) - a_1\beta_2 S^* I_c^* \frac{x_1x_3}{x_2} - a_1\rho S^* B^* \frac{x_1x_4}{x_2} - a_2\sigma I^* \frac{x_2}{x_3} \\ &-a_3\eta_1 I^* \frac{x_2}{x_4} - a_3\eta_2 I_c \frac{x_3}{x_4}.\end{aligned} \tag{3.8}$$

Choose the constants $a_1 = 1$, $a_2 = \frac{1}{\sigma I^*}(\frac{\rho\eta_2}{\delta} S^* I_c^* + \beta_2 S^* I_c^*)$, $a_3 = \frac{\rho}{\delta} S^*$. Using the fact that S^*, I^*, I_c^*, B^* satisfy the equilibrium equations, we have

$$\begin{aligned}\frac{dV_2(t)}{dt} &= 2\Lambda + \beta_2 S^* I_c^* + a_3\eta_1 I^* + 2a_3\eta_2 I_c^* - x_1(\mu S^* + \beta_1 S^* I^*) - \frac{\Lambda}{x_1} \\ &\quad -\beta_2 S^* I_c^* \frac{x_1x_3}{x_2} - \rho S^* B^* \frac{x_1x_4}{x_2} - a_2\sigma I^* \frac{x_2}{x_3} - a_3\eta_1 I^* \frac{x_2}{x_4} - a_3\eta_2 I_c^* \frac{x_3}{x_4} \ . \\ &= F(x_1, x_2, x_3, x_4)\end{aligned} \tag{3.9}$$

Motivated by [10,17], we define the function $P(x_1, x_2, x_3, x_4) = \sum_{k=1}^{4} P_k(x_1, x_2, x_3, x_4)$,where

$$\begin{aligned}P_1(x_1, x_2, x_3, x_4) &= b_1\Big(2 - x_1 - \frac{1}{x_1}\Big), \\ P_2(x_1, x_2, x_3, x_4) &= b_2\Big(3 - \frac{x_2}{x_3} - \frac{x_1x_3}{x_2} - \frac{1}{x_1}\Big), \\ P_3(x_1, x_2, x_3, x_4) &= b_3\Big(3 - \frac{x_2}{x_4} - \frac{x_1x_4}{x_2} - \frac{1}{x_1}\Big), \\ P_4(x_1, x_2, x_3, x_4) &= b_4\Big(4 - \frac{x_2}{x_3} - \frac{x_3}{x_4} - \frac{x_1x_4}{x_2} - \frac{1}{x_1}\Big).\end{aligned} \tag{3.10}$$

Let the coefficients for the same terms between $F(x_1, x_2, x_3, x_4)$ and $\sum_{k=1}^{4} P_k$ be equal. This yields the following equations

$$\begin{aligned}&2b_1 + 3b_2 + 3b_3 + 4b_4 = 2\Lambda + \beta_2 S^* I_c^* + a_3\eta_1 I^* + 2a_3\eta_2 I_c^* \\ &b_1 + b_2 + b_3 + b_4 = \Lambda, \quad b_2 + b_4 = a_2\sigma I^* \\ &b_3 + b_4 = \rho S^* B^*.\end{aligned} \tag{3.11}$$

Consequently, we can solve for $b_1, \ldots, b_4$:

$$b_1 = \mu S^* + \beta_1 S^* I^*, \quad b_2 = \beta_2 S^* I_c^*, \quad b_3 = a_3\eta_1 I^*, \quad b_4 = a_3\eta_2 I_c^*.$$

It is easy to verify that equations (3.11) are compatible, and b_1, b_2, b_3 and b_4 are all nonnegative. Thus, we have

$$\begin{aligned}\frac{dV_2(t)}{dt} &= (\mu S^* + \beta_1 S^* I^*)\Big(2 - x_1 - \frac{1}{x_1}\Big) + \beta_2 S^* I_c^*\Big(3 - \frac{x_2}{x_3} - \frac{x_1 x_3}{x_2} - \frac{1}{x_1}\Big) \\ &+ \frac{\eta_1}{\sigma}\Big(\frac{\rho\eta_2}{\delta} S^* I_c^* + \beta_2 S^* I_c^*\Big)\Big(3 - \frac{x_2}{x_4} - \frac{x_1 x_4}{x_2} - \frac{1}{x_1}\Big), \\ &+ \frac{\eta_2 I_c^*}{\sigma I^*}\Big(\frac{\rho\eta_2}{\delta} S^* I_c^* + \beta_2 S^* I_c^*\Big)\Big(4 - \frac{x_2}{x_3} - \frac{x_3}{x_4} - \frac{x_1 x_4}{x_2} - \frac{1}{x_1}\Big)\end{aligned} \tag{3.12}$$

Since the arithmetic mean is greater than or equal to the geometric mean, we have

$$\begin{aligned} &x_1 + \frac{1}{x_1} \geq 2, \quad \frac{x_2}{x_3} + \frac{x_1 x_3}{x_2} + \frac{1}{x_1} \geq 3, \\ &\frac{x_2}{x_4} + \frac{x_1 x_4}{x_2} + \frac{1}{x_1} \geq 3, \quad \frac{x_2}{x_3} - \frac{x_3}{x_4} + \frac{x_1 x_4}{x_2} + \frac{1}{x_1} \geq 4. \end{aligned} \tag{3.13}$$

Thus, it follows from (3.12) and (3.13) that $\dfrac{dV_2(t)}{dt} \leq 0$ in Ω. The equality $\dfrac{dV_2(t)}{dt} = 0$ holds if and only if $x_1 = x_2 = x_3 = x_4 = 1$. That is, $S(t) = S^*, I(t) = I^*, I_c(t) = I_c^*, B(t) = B^*$ in Ω. The maximal compact invariant set in

$$\{S(t), I(t), I_c(t), B(t)) \in \Omega : \frac{dV_2(t)}{dt}\Big|_{(3.5)} = 0\}$$

is $\{E^*\}$ when $R_0 > 1$. From the LaSalle invariance principle [8], we have that the unique endemic equilibrium E^* of the system (3.1) is globally asymptotically stable for $R_0 > 1$.

4 Concluding remarks

In this paper, we first formulate a partial differential equations (PDEs) model describing the transmission dynamics of an infectious disease with treatment and environmental bacterial infection. An explicit formula for the reproduction number is obtained in the age-since-infection structured case. By means of a suitable Lyapunov function and the LaSalle invariance principle, we have shown that if the reproductive number $\Re_0$ is less than or equal to unity, the disease-free equilibrium of system (2.1) is globally asymptotically stable and the disease dies out while the endemic equilibrium is not feasible. On the other hand, if the reproductive number $\Re_0$ is greater than unity, then system (2.1) has a unique endemic equilibrium which is locally asymptotically stable whenever it exists. Furthermore if $\Re_0$ is greater than unity, then system (2.1) is permanent, therefore the disease becomes endemic. Since the endemic equilibrium is unique and locally stable, we conjecture that this endemic equilibrium is globally stable for $\Re_0 > 1$. When the treatment rate and the transmission rate are both independent of the infection age, the system of partial differential equations (PDEs) reduces to a system of ordinary differential equations (ODEs). The

global stability of the equilibria of the reduced system (3.1) is completely determined by its basic reproductive number R_0. Hence, to control the disease, a strategy should be devised to reduce the reproduction number to below unity.

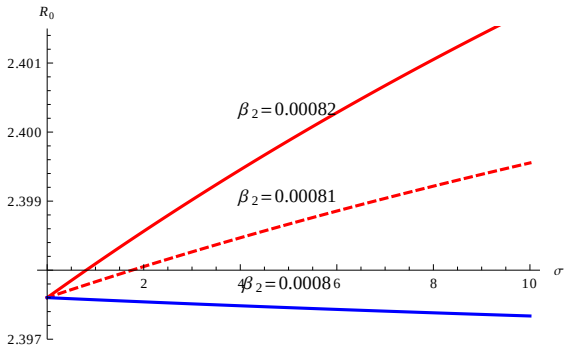

Figure 1: The reproduction number R_0 of system (3.1) as a function of the treatment rate σ for three different values of β_2. Clearly for larger values of β_2 the reproduction number is an increasing function of σ.

Examining the reproduction number more closely, however, reveals that the treatment incorporated in this model may not be sufficient to achieve the goal of reducing the reproduction number below one. In particular, it can be shown that the reproduction number may, in fact, increase with treatment (see Figure 1). Increase in R_0 of system (3.1) with treatment occurs if and only if

$$\frac{\beta_2\delta + \eta_2\rho}{\mu + \nu_2} > \frac{\beta_1\delta + \rho\eta_1}{\mu + \nu_1},$$

or in other words, if transmission through treated individuals plays more important role compared to transmission through infectious but not yet treated individuals. The trend of the reproduction number to increase (or decrease) is sustained for all values of the treatment. Consequently, once the reproduction number starts increasing with treatment, it will be impossible to reduce it below one independently how intensive the treatment becomes. The main reason for the increase in the reproduction number is the fact that treatment is incomplete so if it does not reduce the transmission rate and the shedding rate of treated individuals significantly, it may in fact hurt elimination efforts. But even if the reproduction number R_0 in system (3.1) is decreasing with treatment, it may not decrease below one, since

$$\lim_{\sigma\to\infty} R_0 = \frac{\Lambda(\beta_2\delta + \eta_2\rho)}{\mu(\mu + \nu_2)\delta} = R_\infty.$$

So, if $R_\infty > 1$, incomplete treatment cannot be used as elimination control strategy at all. In summary, incomplete treatment can be effective for directly and indirectly transmitted bacteria

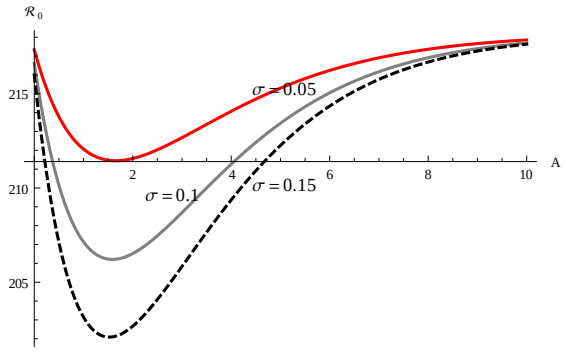

Figure 2: The reproduction number R_0 as a function of the delay in treatment A for three different values of the treatment rate σ.

if it reduces sufficiently both the direct transmission rate and the environmental shedding of the treated individuals.

Age-structure does not seem to play a significant role in the dynamics of the model. However, it may have epidemiological consequences. To understand the impact of age structure on the reproduction number, we consider the case of delayed treatment. Suppose treatment does not commence at the moment of infection but after some period of time A. The simplest way to model such a scenario is to take $\sigma(a)$ to be the following step function.

$$\sigma(a) = \begin{cases} 0, & 0 \leq a < A; \\ \\ \sigma, & a > A. \end{cases}$$

We assume all other parameters independent of age. In this case, the reproduction number $\Re_0$ takes the form

$$\Re_0 = \frac{\Lambda}{\mu}\left(\beta_1 + \frac{\rho}{\delta}\eta_1\right)\frac{1 - e^{-(\mu+\nu_1)A}}{\mu + \nu_1} + \frac{\Lambda}{\mu}\left(\beta_1 + \frac{\rho}{\delta}\eta_1\right)\frac{e^{-(\mu+\nu_1+\sigma)A}}{\mu + \nu_1 + \sigma} + \frac{\Lambda}{\mu}\left(\beta_2 + \frac{\rho}{\delta}\eta_2\right)\frac{\sigma e^{-(\mu+\nu_1)A}}{(\mu + \nu_1 + \sigma)(\mu + \nu_2)}.$$

Plotting the reproduction number as a function of the delay in treatment A (see Figure 2) reveals that small delays of treatment are actually beneficial to the control of the disease. The reproduction number first decreases for small delays but then increases. Consequently, there is some optimal delay in treatment A^* for which the reproduction number is smallest. In addition, the level of treatment after the delay σ also impacts the reproduction number. Clearly the larger the value of σ the smaller the reproduction number and the bigger the effect of the delay in initial decrease of the reproduction number.

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Appendix

A. Wellposedness. Here we apply the approach used by Martcheva and Thieme in [20] to show that system (2.1) is well posed. In order to take into account the boundary condition, we extend the state space and let

$$\hat{Z} = \mathbb{R} \times L^1(0,\infty) \times \mathbb{R} \times L^1(0,\infty).$$

Let $\hat{A} : D(\hat{A}) \subset \hat{Z} \to \hat{Z}$ the linear operator and is defined by

$$\hat{A}\begin{pmatrix} 0 \\ \varphi_1 \\ 0 \\ \varphi_2 \end{pmatrix} = \begin{pmatrix} -\varphi_1(0) \\ -(\mu+\nu_1+\sigma)\varphi_1 - \varphi_1' \\ -\varphi_1(0) \\ \sigma\varphi_1 - (\mu+\nu_2)\varphi_2 - \varphi_2' \end{pmatrix}$$

with

$$D(\hat{A}) = \{0\} \times W^{1,1}(0,\infty) \times \{0\} \times W^{1,1}(0,\infty).$$

Let $\hat{i}(t) = \begin{pmatrix} 0 \\ i(t,.) \\ 0 \\ i_c(t,.) \end{pmatrix}$. By the above definition, system (2.1) can be rewritten as the following ordinary differential equation coupled with a non-density defined Cauchy problem

$$\begin{cases} \dfrac{dS(t)}{dt} = -\mu S(t) + F_1(S(t), \hat{i}(t), B(t)), \\ \dfrac{d\hat{i}(t)}{dt} = \hat{A}\hat{i}(t) + F_2(S(t), \hat{i}(t), B(t)), \\ \dfrac{dB(t)}{dt} = -\delta B(t) + F_3(S(t), \hat{i}(t), B(t)), \end{cases} \tag{A.1}$$

where

$$F_1(S(t),\hat{i}(t),B(t)) = \Lambda - S(t)\Big(\int_0^{+\infty}\beta_1(a)i(a)da + \int_0^{+\infty}\beta_2(a)i_c(a)da\Big) - \rho B(t),$$

$$F_2(S(t),\hat{i}(t),B(t)) = \begin{pmatrix} S(t)\Big(\int_0^{+\infty}\beta_1(a)i(a)da + \int_0^{+\infty}\beta_2(a)i_c(a)da\Big) + \rho B(t)S(t) \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$F_3(S(t),\hat{i}(t),B(t)) = \int_0^{+\infty}\eta_1(a)i(a)da + \int_0^{+\infty}\eta_2(a)i_c(a)da.$$

Set

$$Z = \mathbb{R}\times\mathbb{R}\times L^1(0,+\infty)\times\mathbb{R}\times L^1(0,+\infty)\times\mathbb{R}.$$

$$Z_+ = \mathbb{R}_+\times\mathbb{R}_+\times L^1(0,+\infty)\times\mathbb{R}_+\times L^1(0,+\infty)\times\mathbb{R}_+.$$

Let $A : D(A)\subset Z\to Z$ be the linear operator defined by

$$A\begin{pmatrix} S \\ \begin{pmatrix} 0 \\ i \\ 0 \\ i_c \end{pmatrix} \\ B \end{pmatrix} = \begin{pmatrix} -\mu S \\ \hat{A}\begin{pmatrix} 0 \\ i \\ 0 \\ i_c \end{pmatrix} \\ -\delta B \end{pmatrix} = \begin{bmatrix} -\mu & 0 & 0 \\ 0 & \hat{A} & 0 \\ 0 & 0 & 0 \end{bmatrix}\begin{pmatrix} S \\ \begin{pmatrix} 0 \\ i \\ 0 \\ i_c \end{pmatrix} \\ B \end{pmatrix}.$$

with

$$D(A) = \mathbb{R}\times D(\hat{A})\times\mathbb{R}.$$

Thus, $\overline{D(A)} = \mathbb{R}\times\{0\}\times L^1(0,\infty)\times\{0\}\times L^1(0,\infty)\times\mathbb{R}$ is not dense in Z. We consider $F : \overline{D(A)}\to Z$ the nonlinear map defined by

$$F\begin{pmatrix} S \\ \begin{pmatrix} 0 \\ i \end{pmatrix} \\ \begin{pmatrix} 0 \\ i_c \end{pmatrix} \\ B \end{pmatrix} = \begin{pmatrix} F_1(S(t), \hat{i}(t), B(t)) \\ F_2(S(t), \hat{i}(t), B(t)) \\ F_3(S(t), \hat{i}(t), B(t)) \end{pmatrix}.$$

Set $Z_0 := \overline{D(A)}, Z_+^0 := \overline{D(A)} \bigcap Z_+$. Thus, system (A.1) can be rewritten as the following abstract Cauchy problem:

$$\frac{du(t)}{dt} = Au(t) + F(u(t)), \text{ for } \quad t \geq 0 \text{ with } u(0) = x \in \overline{D}(A). \tag{A.2}$$

In general, the differential equation may not have a strong solution. Thus, we solve (A.1) in integrated form

$$U(t)x = x + A\int_0^t U(s)xds + \int_0^t F(U(s))xds, \forall t \geq 0. \tag{A.3}$$

Let $\bar{\eta} = \max\{\bar{\eta_1}; \bar{\eta_2}\}, \bar{\eta_i} = esssup_{[0,\infty)}|\eta_i(a)|, \ i = 1, 2$. From system(2.1), it is easy to obtain that

$$S(t) + \int_0^\infty (i(a,t) + i_c(a,t))da\Big) \leq \frac{\Lambda}{\mu}, \ B(t) \leq \frac{\bar{\eta}\Lambda}{\mu\delta}. \tag{A.4}$$

Using the fact that the non-linearities are Lipschitz continuous on bounded set, by using (A.4) and by applying the results used in paper [20], we have the following result

Theorem A.1 *The system of equations (2.1) represented by the integral equation (A.2) has a unique continuous solution with values in Z_+^0. Moreover, the map $\Psi : [0,\infty) \times Z_+^0 \to Z_+^0$ defined by $\Psi(t,x) = U(t)$ is a continuous semiflow, i.e., the map Ψ is continuous and $\Psi(t, \Psi(s,.)) = \Psi(t+s,)$ and $\Psi(0,)$ is the identity map.*

B. Connection between the real part of the eigenvalues and the stability of the equilibrium.

To establish the local stability of model (2.1), we use the approach taken in [20].

Definition B.1. *$T(t)$ is called quasi-compact if $T(t) = T_1(t) + T_2(t)$ with operator families $T_1(t), T_2(t)$, where $T_1(t) \to 0$, as $t \to 0$, $T_2(t)$ is eventually compact, that is, there exists $t_0 > 0$ such that $T_2(t)$ is a compact operator for all $t > t_0$.*

Lemma B.1. *Let $T(t)$ be a quasi-compact C_0-semigroup and $\bar{B}$ its infinitesimal generator. Then $e^{\delta t}||T(t)|| \to 0$ as $t \to +\infty$ for $\delta > 0$ if and only if all eigenvalues of $\bar{B}$ have strictly negative real part.*

Set $S(t) = S^* + x(t),\ i(a,t) = i^*(a) + y(a,t),\ i_c(a,t) = i_c^*(a) + y(a,t),\ B(t) = B^* + Z(t)$, where $u^* = (S^*, i^*(a), i_c^*(a), B^*)$ is any equilibrium of system (2.1).

Thus, the linearized problem for the above perturbations can read

$$\chi'(t) = \mathcal{A}\chi(t) + F'(u^*)\chi(t), \quad \chi(0) = \chi^0. \tag{B.1}$$

We rewrite the linearized problem (B.1) in the following form

$$\chi'(t) = \mathcal{B}\chi(t) + \mathcal{K}\chi(t), \quad \chi(0) = \chi^0,$$

where $\mathcal{B} : Z^0 \to Z$ is defined as follows

$$\mathcal{B}\chi = \begin{pmatrix} -\mu x \\ -(\frac{\partial}{\partial a} + \mu + v_1(a) + \sigma(a))y \\ -(\frac{\partial}{\partial a} + \mu + v_2(a))y_c + \sigma(a)y \\ -\delta z \\ -y(0) \\ -y_c(0) \end{pmatrix}$$

The operator $\mathcal{K} : Z^0 \to Z$ is defined as follows

$$\mathcal{K}\chi = \begin{pmatrix} [-x(\int_0^{+\infty}(\beta_1(a)i^*(a) + \beta_2(a)i_c^*(a))da) - S^*(\int_0^{+\infty}(\beta_1(a)y(a,t) + \beta_2(a)y_c(a,t))da) \\ -\rho S^* z(t) - \rho B^* x(t)] \\ 0 \\ 0 \\ \int_0^{+\infty}\eta_1(a)y(a,t)da + \int_0^{+\infty}\eta_2(a)y_c(a,t)da \\ \{x[\int_0^{+\infty}(\eta_1(a)i^*(a) + \eta_2(a)i_c^*(a)da] + S^*[\int_0^{+\infty}(\beta_1(a)y(a,t) + \beta_2(a)y_c(a,t))da] \\ +\rho S^* z(t) + \rho B^* x(t)\} \\ 0 \end{pmatrix}$$

In the following, we observe that the powers of the resolvent of $\mathcal{B}$ satisfy the Hille-Yosida estimate

Theorem B. *The operator $\mathcal{B}$ is a closed linear operator such that $\lambda - \mathcal{B}$ has bounded inverse for $\lambda > -\mu_0$, where $\mu_0 = \min\{\mu, \delta\}$ and*

$$||(\lambda - \mathcal{B})^{-n}|| \leq \frac{1}{(\lambda + \mu_0)^n}$$

for all positive integers n.

Proof. For an element $f \in Z_+^0$ with coordinates $f = (f_1, f_2, f_3, f_4, \xi_1, \xi_2)$, we consider the equation $(\lambda - \mathcal{B})v = f$ with $\lambda > -\mu_0$. This results in the following system

$$\begin{cases} (\lambda + \mu)x = f_1, \\ \dfrac{dy}{da} = -(\mu + v_1(a) + \sigma(a))y(a) + f_2, \\ y(0) = \xi_1, \\ \dfrac{dy_c}{da} = -(\mu + v_2(a))y_c(a) + \sigma(a)y(a) + f_3, \\ y_c(0) = \xi_2, \\ (\lambda + \delta)z = f_4. \end{cases} \tag{B.2}$$

Clearly, $x \geq 0$ and $z \geq 0$. The system $(B.1)$ for $y(a)$ and $y_c(a)$ can be explicity solved. Thus, we have

$$y(a) = \xi_1 e^{-\lambda a}\pi_1(a) + \int_0^a e^{-\lambda(a-s)}\frac{\pi_1(a)}{\pi_1(s)}f_2(s)ds,$$
$$y_c(a) = \xi_2 e^{-\lambda a}\pi_2(a) + \int_0^a e^{-\lambda(a-s)}\frac{\pi_2(a)}{\pi_2(s)}(\sigma(s)y(s) + f_3(s))ds.$$

Thus, we have $y(a) \geq 0$ and $y_c(a) \geq 0$. In addition, $y(a), y_c(a) \in L^1[a, \infty)$. Thus, all the solutions of the system $(B.2)$ are nonnegative. Adding the equations for $y(a), y_c(a)$, dropping ν_1 and ν_2 and integrating the inequality in the age variable and adding all equations, we obtain for $\lambda > -\mu_0$ ($\mu_0 = \max\{\mu, \delta\}$):

$$|x| + ||y|| + ||y_c|| + |y| \leq \frac{1}{\lambda + \mu_0}(|f_1| + ||f_2|| + ||f_3|| + |f_4| + |\xi_1| + |\xi_2|)$$

Hence, for $f \in Z_+^0$, we have

$$||(\lambda - \mathcal{B})^{-1}f|| \leq \frac{1}{(\lambda + \mu_0)}||f||.$$

Notice that if $f \in Z$, we have $||(\lambda - \mathcal{B})^{-1}f|| \leq ||(\lambda - \mathcal{B})^{-1}|||f|$. Therefore, our conclusion follows.

Thus, the part of $\mathcal{B}$ in Z^0 is a densely defined operator whose resolvents satisfy the Hille-Yosida estimates and is the generator of a C_0-semigroup on Z^0, $\mathcal{S}(t)$. The Hille-Yosida estimate in addition implies that

$$||\mathcal{S}(t)|| \leq e^{-\mu_0 t}.$$

Therefore, from the above discussion, we know that the nonlinear semiflow $\Psi(t,x)$ of the solutions of (2.1) satisfies the following properties:

If all eigenvalues of $A + F'(u^*)$ have strictly negative real part, then there exists $\omega < 0$ and constants $k > 0$ and $\delta > 0$ such that

$$||\Psi(t, x^0) - u^*|| \leq ke^{\omega t}||x^0 - u^*||, \qquad (B.3)$$

for all $x^0 \in Z^0_+ / \{0\}$ with $||x^0 - u^*|| \leq \delta$.

Inequality (B.3) implies that if u^* is an equilibrium such that all eigenvalues of $A + F'(u^*)$ have negative real part then u^* is locally asymptotically stable, that is, trajectories which start sufficiently close to the steady state u^* remain close and return to the steady state when time tends to infinity.

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