RESEARCH Open Access

CrossMark

Global dynamics of a tuberculosis transmission model with age of infection and incomplete treatment

Rui Xu^{1*}, Xiaohong Tian¹ and Fengqin Zhang²

*Correspondence: rxu88@163.com
¹Institute of Applied Mathematics,
Shijiazhuang Mechanical
Engineering College, Shijiazhuang,
Hebei 050003, P.R. China
Full list of author information is
available at the end of the article

Abstract

In this paper, a mathematical model describing tuberculosis transmission with incomplete treatment and continuous age structure for latently infected and infectious individuals is investigated. It is assumed in the model that the treated individuals may enter either the latent compartment due to the remainder of Mycobacterium tuberculosis or the infectious compartment due to the treatment failure. It is shown that the global transmission dynamics of the disease is fully determined by the basic reproduction number. The asymptotic smoothness of the semi-flow generated by the system is established. By analyzing the corresponding characteristic equations, the local stability of a disease-free steady state and an endemic steady state of the model is established. By using the persistence theory for infinite dimensional system, the uniform persistence of the system is established when the basic reproduction number is greater than unity. By means of suitable Lyapunov functionals and LaSalle's invariance principle, it is proven that if the basic reproduction number is less than unity, the disease-free steady state is globally asymptotically stable; if the basic reproduction number is greater than unity, the endemic steady state is globally asymptotically stable.

MSC: 37N25; 92B05; 37B25

Keywords: tuberculosis; age structure; stability; Lyapunov functional; LaSalle's

invariance principle

1 Introduction

Tuberculosis (TB) is a bacterial disease caused by Mycobacterium tuberculosis, and is usually acquired through airborne infection from active TB cases [1]. According to the World Health Organization, one third of the world's population is infected, either latently or actively, with tuberculosis. Tuberculosis infection remains a leading cause of death from an infectious disease [2].

It is well known that, for tuberculosis, recovered individuals may relapse with reactivation of latent infection and revert back to the infective class. This recurrence of disease is an important feature of tuberculosis, including human and bovine [3, 4], and herpes [3, 5]. For human tuberculosis, incomplete treatment can lead to relapse, but relapse can also occur in patients who took a full course of treatment and were declared cured [6]. Mathematical models of tuberculosis have contributed to the understanding of tubercu-



losis epidemics and the potential impact of control strategies (see, for example, [7-23]). In [23], Yang *et al.* considered the following tuberculosis model:

$$\dot{S}(t) = \Lambda - \mu S(t) - \beta S(t)I(t),$$

$$\dot{L}(t) = \beta S(t)I(t) - (\mu + \nu)L(t) + (1 - k)\delta T(t),$$

$$\dot{I}(t) = \nu L(t) + k\delta T(t) - (\mu + \gamma + \mu_T)I(t),$$

$$\dot{T}(t) = \gamma I(t) - (\mu + \delta)T(t).$$
(1.1)

In (1.1), S(t) represents the number of individuals who are not previously exposed to the Mycobacterium tuberculosis at time t, L(t) represents the number of latently infected individuals who have been infected with Mycobacterium tuberculosis at time t, but have no clinical illness and noninfectious, I(t) represents the number of active infectious tuberculosis cases at time t, T(t) is the number of individuals who are being treated at time t.

The assumptions of model (1.1) are made as follows [23].

- (A1) Λ is the constant rate of recruitment into the susceptible population. β is the rate that an infectious case will successfully transmit the infection to a susceptible individual. $\beta I(t)$ represents the per-capita force of infection at time t being defined as the per-susceptible risk of becoming infected with Mycobacterium tuberculosis.
- (A2) Latently infected individuals either develop tuberculosis slowly at an average rate ν or die at a natural death rate μ before developing tuberculosis.
- (A3) Active infectious tuberculosis die, either because of tuberculosis at average rate μ_T , or because of natural death at an average rate μ . γ is the per-capita treatment rate for the infectious individuals.
- (A4) δ is the rate coefficient at which a treated individual leaves treated compartment. $k(0 \le k \le 1)$ is the fraction of the drug-resistant individuals in the treated compartment. Here, k reflects the failure of treatment, k = 0 means that all the treated individuals will become latent, and k = 1 means that the treatment fails and all the treated individuals will still be infectious.

We note that system (1.1) is formulated as ordinary differential equations with distinct variables to describe the population size of compartments such as susceptible, exposed, infectious and treated. It is assumed that all individuals within a compartment behave identically, regardless of how much time they have spent in the compartment. For instance, infectious individuals are assumed to be equally infectious during their periodic infectivity and the waiting times in each compartment are assumed to be exponentially distributed [24]. However, laboratory studies suggest that the infectivity of infectious individuals be different at the differential age of infection [25]. For TB infection, the TB bacteria need to develop in the lung to be transmissible through coughing, and their transmissibility depends on their progression in the lung as well as the strength of a host's immune system. Active TB has the highest possibility of developing within the first 2-5 years of infection, while most TB infections remain latent for a long period of time until immune compromise occurs due to aging or co-infection with other illnesses such as HIV (see, for example, [26–28]).

In [24], by including the duration that an individual has spent in the exposed and infectious compartments as variables, McCluskey considered the following epidemiological

model with continuous age structure for both the exposed and the infectious classes:

$$\dot{S}(t) = \Lambda - \mu_S S(t) - S(t) \int_0^\infty \beta(a) i(a, t) \, da,$$

$$\frac{\partial e(a, t)}{\partial t} + \frac{\partial e(a, t)}{\partial a} = -(\mu(a) + \gamma(a)) e(a, t),$$

$$\frac{\partial i(a, t)}{\partial t} + \frac{\partial i(a, t)}{\partial a} = -\nu(a) i(a, t),$$
(1.2)

with boundary conditions

$$e(0,t) = S(t) \int_0^\infty \beta(a)i(a,t) da,$$

$$i(0,t) = \int_0^\infty \gamma(a)e(a,t) da.$$
(1.3)

In (1.2), e(a,t) and i(a,t) represent the numbers of the exposed and infectious populations at time t, respectively, where a is the duration for which individuals have been in the exposed and infectious compartments, respectively. Individuals who have been in the exposed compartment for duration a, progress to the infectious compartment at rate $\gamma(a)$ and are removed from the infectious compartment at rate $\mu(a)$. Individuals who have been in the infectious compartment for duration a are removed at rate $\nu(a)$, and infect susceptible individuals at transmission rate $\beta(a)$. Recently, interest has been growing in the modeling and analysis on infectious disease dynamics with class age structure (see, for example, [18, 29–35]).

Motivated by the work of Yang *et al.* [23] and McCluskey [24], in the present paper, we are concerned with the effects of incomplete treatment and age structure for latently infected and infectious individuals on the transmission dynamics of tuberculosis. To this end, we consider the following differential equation system:

$$\dot{S}(t) = A - \mu S(t) - S(t) \int_{0}^{\infty} \beta(a)i(a,t) da,$$

$$\frac{\partial e(\theta,t)}{\partial t} + \frac{\partial e(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))e(\theta,t), \quad \theta > 0,$$

$$\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} = -(\mu_{1}(a) + \gamma(a))i(a,t), \quad a > 0,$$

$$\dot{T}(t) = \int_{0}^{\infty} \gamma(a)i(a,t) da - (\mu_{2} + \delta)T(t),$$
(1.4)

with boundary conditions

$$e(0,t) = S(t) \int_0^\infty \beta(a)i(a,t) da + (1-p)\delta T(t),$$

$$i(0,t) = \int_0^\infty \nu(\theta)e(\theta,t) d\theta + p\delta T(t),$$
(1.5)

and initial condition

$$X_0 := (S(0), e(\cdot, 0), i(\cdot, 0), T(0)) = (S^0, e_0(\cdot), i_0(\cdot), T^0) \in \mathcal{X}, \tag{1.6}$$

Parameters	Description
A	The recruitment rate of individuals into the community by birth or immigration
μ	Per capita natural death rate of the population
θ	The duration for which individuals have been in the latent compartment
а	Age of infection, i.e., the time that has lapsed since the individual became infectious
$\mu_1(a)$	The rate at which individuals are removed from the infectious compartment
β (a)	The transmission rate of the infectious individuals at age of infection <i>a</i>
$\gamma(a)$	The rate that an infectious individual with age of infection <i>a</i> recovers from the disease
$\nu(\theta)$	The rate at which individuals who have been in the exposed compartment for duration θ , progress
	to the infectious compartment
δ	The rate at which a treated individual leaves the treated compartment
р	The proportion of the newly infected to develop tuberculosis directly
1 – p	The proportion of the newly infected to enter the latent class
μ_2	The death rate of the treated individuals

Table 1 The definition of the parameters in system (1.4)

where $\mathscr{X} = \mathbb{R}^+ \times L^1_+(0,\infty) \times L^1_+(0,\infty) \times \mathbb{R}^+$, $L^1_+(0,\infty)$ is the set of all integrable functions from $(0,\infty)$ into $\mathbb{R}^+ = [0,\infty)$. In system (1.4), S(t) represents the number of individuals who are susceptible to tuberculosis disease, that is, who are not yet infected at time $t; e(\theta,t)$ represents the density of individuals in latent stage (who are infected with the disease but not yet infective) at time t; i(a,t) represents the density of infective individuals with age of infection a at time t; T(t) represents the number of individuals who are being treated at time t. The definitions of all parameters and variables in system (1.4) are listed in Table 1. In the sequel, we further make the following assumptions.

- (H1) β and ν are Lipschitz continuous on \mathbb{R}^+ with Lipschitz coefficients L_{β} and L_{ν} , respectively.
- (H2) $\beta, \gamma, \nu \in L^1_+(0, \infty)$, $\bar{\beta}, \bar{\gamma}$ and $\bar{\nu}$ are the essential supremums of β, γ and ν , respectively. There are positive constants ν_0 and γ_0 such that $\nu_0 = \min_{\theta \geq 0} \nu(\theta)$ and $\gamma_0 = \min_{\theta \geq 0} \gamma(\theta)$, respectively.
- (H3) There is a positive constant μ_0 satisfying $\mu_0 = \min\{\mu, \mu_2\}$, $\mu_1(a)$ is a bounded function on \mathbb{R}^+ satisfying $\mu_1(a) \ge \mu_0$ for all $a \ge 0$.

Using the theory of age-structured dynamical systems introduced in [36, 37], one can show that system (1.4) has a unique solution $(S(t), e(\cdot, t), i(\cdot, t), T(t))$ satisfying the boundary conditions (1.5) and the initial condition (1.6). Moreover, it is easy to show that all solutions of system (1.4) with the boundary conditions (1.5) and the initial condition (1.6) are defined on $[0, +\infty)$ and remain positive for all $t \ge 0$. Furthermore, $\mathscr X$ is positively invariant and system (1.4) exhibits a continuous semi-flow $\Phi : \mathbb R^+ \times \mathscr X \to \mathscr X$, namely,

$$\Phi_t(X_0) = \Phi(t, X_0) := (S(t), e(\cdot, t), i(\cdot, t), T(t)), \quad t \ge 0, X_0 \in \mathcal{X}. \tag{1.7}$$

Given a point $(x, \varphi_1, \varphi_2, z) \in \mathcal{X}$, we have the norm $\|(x, \varphi_1, \varphi_2, z)\|_{\mathcal{X}} := x + \int_0^\infty \varphi_1(a) da + \int_0^\infty \varphi_2(a) da + z$.

The primary goal of this work is to carry out a complete mathematical analysis of system (1.4) with the boundary conditions (1.5) and the initial condition (1.6), and establish its global dynamics. The organization of this paper is as follows. In the next section, we establish the asymptotic smoothness of the semi-flow generated by system (1.4). In Section 3, we calculate the basic reproduction number and discuss the existence of feasible steady states of system (1.4) with the boundary conditions (1.5). In Section 4, by analyzing the corresponding characteristic equations, we study the local asymptotic stability of a

disease-free steady state and an endemic steady state of system (1.4). In Section 5, we show that if the basic reproduction number is greater than unity, system (1.4) is uniformly persistent. In Section 6, we are concerned with the global stability of each of feasible steady states of system (1.4) by means of Lyapunov functionals and LaSalle's invariance principle. A brief discussion is given in Section 7 to conclude this work.

2 Boundedness and asymptotic smoothness

In order to address the global dynamics of system (1.4) with the boundary conditions (1.5), in this section, we are concerned with the asymptotic smoothness of the semi-flow $\{\Phi(t)\}_{t>0}$ generated by system (1.4).

2.1 Boundedness of solutions

In this subsection, we verify the boundedness of semi-flow $\{\Phi(t)\}_{t\geq 0}$.

Proposition 2.1 Let Φ_t be defined as in (1.7). Then the following statements hold.

- (i) $\frac{d}{dt} \|\Phi_t(X_0)\|_{\mathscr{X}} \leq A \mu_0 \|\Phi_t(X_0)\|_{\mathscr{X}}$ for all $t \geq 0$;
- (ii) $\|\Phi_t(X_0)\|_{\mathscr{X}} \leq \max\{A/\mu_0, \|X_0\|_{\mathscr{X}}\}\$ for all $t \geq 0$;
- (iii) $\limsup_{t\to+\infty} \|\Phi_t(X_0)\|_{\mathscr{X}} \leq A/\mu_0$;
- (iv) Φ_t is point dissipative: there is a bounded set that attracts all points in \mathscr{X} .

Proof Let $\Phi_t(X_0) = \Phi(t, X_0) := (S(t), e(\cdot, t), i(\cdot, t), T(t))$ be any nonnegative solution of system (1.4) with the boundary conditions (1.5) and the initial condition (1.6). Denote $\|X_0\|_{\mathscr{X}} = S^0 + \int_0^\infty e_0(\theta) \, d\theta + \int_0^\infty i_0(a) \, da + T^0$.

Define

$$\|\Phi(t,X_0)\|_{\mathscr{X}} = S(t) + \int_0^\infty e(\theta,t) \, d\theta + \int_0^\infty i(a,t) \, da + T(t).$$
 (2.1)

We derive from system (1.4) that

$$\frac{d}{dt} \| \Phi(t, X_0) \|_{\mathcal{X}} = A - \mu S(t) - S(t) \int_0^\infty \beta(a) i(a, t) \, da$$

$$+ \int_0^\infty \frac{\partial e(\theta, t)}{\partial t} \, d\theta + \int_0^\infty \frac{\partial i(a, t)}{\partial t} \, da$$

$$+ \int_0^\infty \gamma(a) i(a, t) \, da - (\mu_2 + \delta) T(t). \tag{2.2}$$

On substituting $\frac{\partial e(\theta,t)}{\partial t} + \frac{\partial e(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))e(\theta,t)$, $\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} = -(\mu_1(a) + \gamma(a))i(a,t)$ into (2.2), it follows that

$$\frac{d}{dt} \| \Phi(t, X_0) \|_{\mathcal{X}} = A - \mu S(t) - S(t) \int_0^\infty \beta(a) i(a, t) \, da$$

$$- \int_0^\infty \frac{\partial e(\theta, t)}{\partial \theta} \, d\theta - \int_0^\infty (\mu + \nu(\theta)) e(\theta, t) \, d\theta$$

$$- \int_0^\infty \frac{\partial i(a, t)}{\partial a} \, da - \int_0^\infty (\mu_1(a) + \gamma(a)) i(a, t) \, da$$

$$+ \int_0^\infty \gamma(a) i(a, t) \, da - (\mu_2 + \delta) T(t)$$

$$= A - \mu S(t) - S(t) \int_0^\infty \beta(a)i(a,t) da$$

$$- e(\theta,t)|_0^\infty - \int_0^\infty (\mu + \nu(\theta))e(\theta,t) d\theta$$

$$- i(a,t)|_0^\infty - \int_0^\infty (\mu_1(a) + \gamma(a))i(a,t) da$$

$$+ \int_0^\infty \gamma(a)i(a,t) da - (\mu_2 + \delta)T(t). \tag{2.3}$$

We have from (1.5) and (2.3)

$$\frac{d}{dt} \| \Phi(t, X_0) \|_{\mathscr{X}} \le A - \mu S(t) - \mu \int_0^\infty e(\theta, t) \, d\theta - \int_0^\infty \mu_1(a) i(a, t) \, da - \mu_2 T(t) \\
\le A - \mu_0 \| \Phi(t, X_0) \|_{\mathscr{X}}. \tag{2.4}$$

The variation of constants formula implies

$$\|\Phi(t,X_0)\|_{\mathscr{X}} \le \frac{A}{\mu_0} - e^{-\mu_0 t} \left\{ \frac{A}{\mu_0} - \|X_0\|_{\mathscr{X}} \right\},\tag{2.5}$$

which yields

$$\left\|\Phi(t, X_0)\right\|_{\mathscr{X}} \le \max\left\{\frac{A}{\mu_0}, \|X_0\|_{\mathscr{X}}\right\} \tag{2.6}$$

for all $t \ge 0$. This completes the proof.

The following results are direct consequences of Proposition 2.1.

Proposition 2.2 If $X_0 \in \mathcal{X}$ and $||X_0||_{\mathcal{X}} \leq K$ for some $K \geq A/\mu_0$, then

$$S(t) \le K, \qquad \int_0^\infty e(\theta, t) d\theta \le K, \qquad \int_0^\infty i(a, t) da \le K, \qquad T(t) \le K,$$
 (2.7)

for all $t \ge 0$.

Proposition 2.3 *Let* $C \in \mathcal{X}$ *be bounded. Then*

- (1) $\Phi_t(C)$ is bounded;
- (2) Φ_t is eventually bounded on C.

2.2 Asymptotic smoothness

In this subsection, we show the asymptotic smoothness of the semi-flow $\{\Phi(t)\}_{t\geq 0}$.

Let $(S(t), e(\cdot, t), i(\cdot, t), T(t))$ be a solution of system (1.4) with the boundary conditions (1.5) and the initial condition (1.6). Integrating the second and the third equations of system (1.4) along the characteristic line t - a = const., respectively, we have

$$e(\theta, t) = \begin{cases} L_1(t - \theta)\phi_1(\theta), & 0 \le \theta < t, \\ e_0(\theta - t)\frac{\phi_1(\theta)}{\phi_1(\theta - t)}, & 0 \le t \le \theta, \end{cases}$$

$$(2.8)$$

and

$$i(a,t) = \begin{cases} L_2(t-a)\phi_2(a), & 0 \le a < t, \\ i_0(a-t)\frac{\phi_2(a)}{\phi_2(a-t)}, & 0 \le t \le a, \end{cases}$$
 (2.9)

where

$$\phi_1(\theta) = e^{-\int_0^{\theta} (\mu + \nu(s)) \, ds}, \qquad \phi_2(a) = e^{-\int_0^{a} (\mu_1(s) + \gamma(s)) \, ds}, \tag{2.10}$$

and

$$L_1(t) = S(t)A_1(t) + (1-p)\delta T(t), \qquad L_2(t) = A_2(t) + p\delta T(t),$$
 (2.11)

here

$$A_{1}(t) = \int_{0}^{\infty} \beta(a)i(a,t) da,$$

$$A_{2}(t) = \int_{0}^{\infty} \nu(\theta)e(\theta,t) d\theta.$$
(2.12)

Proposition 2.4 The functions $A_1(t)$ and $A_2(t)$ are Lipschitz continuous on \mathbb{R}^+ .

Proof Let $K \ge \max\{A/\mu_0, \|X_0\|_{\mathscr{X}}\}$. By Proposition 2.1 we have $\|\Phi_t\|_{\mathscr{X}} \le K$ for all $t \ge 0$. Fix t > 0 and h > 0. Then

$$A_{1}(t+h) - A_{1}(t) = \int_{0}^{\infty} \beta(a)i(a,t+h) da - \int_{0}^{\infty} \beta(a)i(a,t) da$$

$$= \int_{0}^{h} \beta(a)i(a,t+h) da + \int_{h}^{\infty} \beta(a)i(a,t+h) da$$

$$- \int_{0}^{\infty} \beta(a)i(a,t) da.$$
(2.13)

On substituting (2.9) into (2.13), it follows that

$$A_{1}(t+h) - A_{1}(t) = \int_{0}^{h} \beta(a)L_{2}(t+h-a)\phi_{2}(a) da$$
$$+ \int_{h}^{\infty} \beta(a)i(a,t+h) da - \int_{0}^{\infty} \beta(a)i(a,t) da.$$
(2.14)

By Proposition 2.2, we have $L_2(t) \le (\bar{\nu} + p\delta)K$. Noting that $\phi_2(a) \le 1$, it follows from (2.14) that

$$\begin{aligned} \left| A_{1}(t+h) - A_{1}(t) \right| \\ &\leq \bar{\beta}(\bar{\nu} + p\delta)Kh + \left| \int_{h}^{\infty} \beta(a)i(a,t+h) \, da - \int_{0}^{\infty} \beta(a)i(a,t) \, da \right| \\ &= \bar{\beta}(\bar{\nu} + p\delta)Kh + \left| \int_{0}^{\infty} \beta(\sigma + h)i(\sigma + h, t + h) \, d\sigma - \int_{0}^{\infty} \beta(a)i(a,t) \, da \right|. \end{aligned} \tag{2.15}$$

We have from (2.9)

$$i(a+h,t+h) = i(a,t)\frac{\phi_2(a+h)}{\phi_2(a)} = i(a,t)e^{-\int_a^{a+h}(\mu_1(s)+\gamma(s))\,ds},$$
(2.16)

for all $a \ge 0, t \ge 0, h \ge 0$. Hence, (2.15) can be rewritten as

$$\left| A_{1}(t+h) - A_{1}(t) \right| \leq \bar{\beta}(\bar{\nu} + p\delta)Kh
+ \left| \int_{0}^{\infty} \beta(a+h)i(a,t)e^{-\int_{a}^{a+h}(\mu_{1}(s)+\gamma(s))ds} da - \int_{0}^{\infty} \beta(a)i(a,t) da \right|
\leq \bar{\beta}(\bar{\nu} + p\delta)Kh + \int_{0}^{\infty} \beta(a+h)\left(1 - e^{-\int_{a}^{a+h}(\mu_{1}(s)+\gamma(s))ds}\right)i(a,t) da
+ \int_{0}^{\infty} \left| \beta(a+h) - \beta(a) \right| i(a,t) da.$$
(2.17)

Noting that $1 - e^{-x} \le x$ for $x \ge 0$, it follows from (2.17) that

$$|A_1(t+h) - A_1(t)| \le K [\bar{\beta}(\bar{\nu} + p\delta + \bar{\mu}_1 + \bar{\gamma}) + L_{\beta}]h,$$
 (2.18)

here the fact that $\beta(a)$ is Lipschitz continuous on \mathbb{R}^+ was used.

In a similar way, we have

$$|A_2(t+h) - A_2(t)| \le K \left[\bar{\nu} \left(\bar{\beta} K + (1-p)\delta + \mu + \bar{\nu} \right) + L_{\nu} \right] h. \tag{2.19}$$

This completes the proof.

Proposition 2.5 The functions $L_1(t)$ and $L_2(t)$ are Lipschitz continuous on \mathbb{R}^+ .

Proof Let $K \ge \max\{A/\mu_0, \|X_0\|_{\mathscr{X}}\}$. By Proposition 2.1 we have $\|\Phi_t\|_{\mathscr{X}} \le K$ for all $t \ge 0$. Fix $t \ge 0$ and h > 0. Then

$$\begin{aligned}
|L_{1}(t+h) - L_{1}(t)| &\leq |S(t+h)A_{1}(t+h) - S(t)A_{1}(t)| \\
&+ (1-p)\delta |T(t+h) - T(t)| \\
&\leq A_{1}(t+h)|S(t+h) - S(t)| + S(t)|A_{1}(t+h) - A_{1}(t)| \\
&+ (1-p)\delta |T(t+h) - T(t)| \\
&\leq \bar{\beta}K(A + \mu K + \bar{\beta}K^{2})h + K^{2}[\bar{\beta}(\bar{\nu} + p\delta + \bar{\mu}_{1} + \bar{\gamma}) + L_{\beta}]h \\
&+ \delta K(1-p)(\bar{\gamma} + \mu_{2} + \delta)h \\
&:= M_{L_{1}}h.
\end{aligned} (2.20)$$

Similarly, one has

$$\left| L_{2}(t+h) - L_{2}(t) \right| \leq K \left[\bar{\nu} \left(\bar{\beta} K + (1-p)\delta + \mu + \bar{\nu} \right) + L_{\nu} \right] h + p \delta K (\bar{\gamma} + \mu_{2} + \delta) h
:= M_{L_{2}} h.$$
(2.21)

This completes the proof.

We now state two theorems introduced in [38] (Theorems 2.46 and B.2) which are useful in proving the asymptotic smoothness of the semi-flow Φ .

Theorem 2.1 The semi-flow $\Phi: \mathbb{R}^+ \times \mathscr{X}_+ \to \mathscr{X}_+$ is asymptotically smooth if there are maps $\Theta, \Psi : \mathbb{R}^+ \times \mathscr{X}_+ \to \mathscr{X}_+$ such that $\Phi(t,x) = \Theta(t,X) + \Psi(t,X)$ and the following hold for any bounded closed set $C \subset \mathcal{X}_+$ that is forward invariant under Φ :

- (1) $\lim_{t\to+\infty} \operatorname{diam} \Theta(t,\mathcal{C}) = 0$;
- (2) there exists $t_C \ge 0$ such that $\Psi(t, C)$ has compact closure for each $t \ge t_C$.

Theorem 2.2 Let C be a subset of $L^1(\mathbb{R}^+)$. Then C has compact closure if and only if the following assumptions hold:

- (i) $\sup_{f \in \mathcal{C}} \int_0^\infty |f(a)| da < \infty$;
- (ii) $\lim_{r\to\infty}\int_r^\infty |f(a)|\,da=0$ uniformly in $f\in\mathcal{C}$;
- (iii) $\lim_{h\to 0^+} \int_0^\infty |f(a+h)-f(a)| da = 0$ uniformly in $f \in \mathcal{C}$; (iv) $\lim_{h\to 0^+} \int_0^h |f(a)| da = 0$ uniformly in $f \in \mathcal{C}$.

We are now ready to state and prove a result on the asymptotic smoothness of the semiflow Φ generated by system (1.4).

Theorem 2.3 The semi-flow Φ generated by system (1.4) is asymptotically smooth.

Proof To verify the conditions (1) and (2) in Theorem 2.1, we first decompose the semi-flow Φ into two parts: for $t \geq 0$, let $\Psi(t, X_0) := (S(t), \tilde{e}(\cdot, t), \tilde{i}(\cdot, t), T(t)), \Theta(t, X_0) :=$ $(0, \tilde{\phi}_e(\cdot, t), \tilde{\phi}_i(\cdot, t), 0)$, where

$$\tilde{e}(\theta,t) = \begin{cases}
L_{1}(t-\theta)\phi_{1}(\theta), & 0 \leq \theta \leq t, \\
0, & 0 \leq t < \theta,
\end{cases}$$

$$\tilde{\phi}_{e}(\theta,t) = \begin{cases}
0, & 0 \leq \theta \leq t, \\
e_{0}(\theta-t)\frac{\phi_{1}(\theta)}{\phi_{1}(\theta-t)}, & 0 \leq t < \theta,
\end{cases}$$

$$\tilde{i}(a,t) = \begin{cases}
L_{2}(t-a)\phi_{2}(a), & 0 \leq a \leq t, \\
0, & 0 \leq t < a,
\end{cases}$$

$$\tilde{\phi}_{i}(a,t) = \begin{cases}
0, & 0 \leq a \leq t, \\
i_{0}(a-t)\frac{\phi_{2}(a)}{\phi_{2}(a-t)}, & 0 \leq t < a.
\end{cases}$$
(2.23)

Clearly, we have $\Phi = \Theta + \Psi$ for $t \ge 0$.

Let \mathcal{C} be a bounded subset of \mathscr{X} and $K > A/\mu_0$ the bound for \mathcal{C} . Let $\Phi(t, X_0) =$ $(S(t), e(\cdot, t), i(\cdot, t), T(t))$, where $X_0 = (S^0, e_0(\cdot), i_0(\cdot), T^0) \in \mathcal{C}$. Then

$$\|\tilde{\phi}_{e}(\cdot,t)\|_{L^{1}} = \int_{0}^{\infty} |\tilde{\phi}_{e}(\theta,t)| d\theta$$

$$= \int_{t}^{\infty} e_{0}(\theta-t) \frac{\phi_{1}(\theta)}{\phi_{1}(\theta-t)} d\theta.$$
(2.24)

Letting $\theta - t = \sigma$, it follows from (2.24) that

$$\begin{split} \|\tilde{\phi}_{e}(\cdot,t)\|_{L^{1}} &= \int_{0}^{\infty} e_{0}(\sigma) \frac{\phi_{1}(\sigma+t)}{\phi_{1}(\sigma)} d\sigma \\ &= \int_{0}^{\infty} e_{0}(\sigma) e^{-\int_{\sigma}^{\sigma+t}(\mu+\nu(s)) ds} d\sigma \\ &\leq e^{-(\mu+\nu_{0})t} \int_{0}^{\infty} e_{0}(\sigma) d\sigma \\ &\leq K e^{-(\mu+\nu_{0})t}, \end{split}$$

$$(2.25)$$

yielding $\lim_{t\to+\infty} \|\tilde{\phi}_e(\cdot,t)\|_{L^1} = 0$. In a similar way, one can prove that $\|\tilde{\phi}_i(\cdot,t)\|_{L^1} \leq Ke^{-(\mu_0+\gamma_0)t}$ and hence

$$\lim_{t \to +\infty} \|\tilde{\phi}_i(\cdot, t)\|_{L^1} = 0. \tag{2.26}$$

Accordingly, $\Theta(t, X_0)$ approaches $\mathbf{0} \in \mathcal{X}$ with exponential decay and hence, $\lim_{t \to +\infty} \text{diam } \Theta(t, \mathcal{C}) = 0$ and the assumption (1) in Theorem 2.1 holds.

In the following we show that $\Psi(t, \mathcal{C})$ has compact closure for each $t \geq t_{\mathcal{C}}$ by verifying the assumptions (i)-(iv) of Theorem 2.2.

From Proposition 2.2 we see that S(t) and T(t) remain in the compact set [0,K]. Next, we show that $\tilde{e}(\theta,t)$ and $\tilde{i}(a,t)$ remain in a pre-compact subset of L^1_+ independent of X_0 . It is easy to show that

$$\tilde{e}(\theta, t) \le \bar{L}_1 e^{-(\mu + \nu_0)\theta}, \qquad \tilde{i}(a, t) \le \bar{L}_2 e^{-(\mu_0 + \gamma_0)a},$$
(2.27)

where

$$\bar{L}_1 = \bar{\beta}K^2 + (1-p)\delta K, \qquad \bar{L}_2 = \bar{\nu}K + p\delta K.$$
 (2.28)

Therefore, the assumptions (i), (ii) and (iv) of Theorem 2.2 follow directly. We need only to verify that (iii) of Theorem 2.2 holds. Since we are concerned with the limit as $h \to 0$, we assume that $h \in (0,t)$. In this case, we have

$$\int_{0}^{\infty} \left| \tilde{e}(\theta + h, t) - \tilde{e}(\theta, t) \right| d\theta$$

$$= \int_{0}^{t-h} \left| L_{1}(t - \theta - h)\phi_{1}(\theta + h) - L_{1}(t - \theta)\phi_{1}(\theta) \right| d\theta$$

$$+ \int_{t-h}^{t} L_{1}(t - \theta)\phi_{1}(\theta) d\theta$$

$$\leq \int_{0}^{t-h} L_{1}(t - \theta - h) \left| \phi_{1}(\theta + h) - \phi_{1}(\theta) \right| d\theta$$

$$+ \int_{0}^{t-h} \left| L_{1}(\theta - t - h) - L_{1}(\theta - t) \right| \phi_{1}(\theta) d\theta$$

$$+ \int_{t-h}^{t} L_{1}(t - \theta)\phi_{1}(\theta) d\theta. \tag{2.29}$$

It follows from (2.28) and (2.29) that

$$\int_{0}^{\infty} \left| \tilde{e}(\theta + h, t) - \tilde{e}(\theta, t) \right| d\theta \leq \bar{L}_{1} \int_{0}^{t-h} \phi_{1}(\theta) \left(1 - e^{-\int_{\theta}^{\theta + h} (\mu + \nu(s)) ds} \right) d\theta
+ M_{L_{1}} h \int_{0}^{t-h} \phi_{1}(\theta) d\theta + \bar{L}_{1} \int_{t-h}^{t} \phi_{1}(\theta) d\theta
\leq \bar{L}_{1} \int_{0}^{t-h} \phi_{1}(\theta) \int_{\theta}^{\theta + h} \left(\mu + \nu(s) \right) ds d\theta + M_{L_{1}} h + \bar{L}_{1} h
\leq \left[(\mu + \bar{\nu}) \bar{L}_{1} + M_{L_{1}} + \bar{L}_{1} \right] h.$$
(2.30)

In a similar way, we have

$$\int_{0}^{\infty} \left| \tilde{i}(a+h,t) - \tilde{i}(a,t) \right| da \le \left[(\bar{\mu}_{1} + \bar{\gamma})\bar{L}_{2} + M_{L_{2}} + \bar{L}_{2} \right] h. \tag{2.31}$$

Hence, the condition (iii) of Theorem 2.2 holds. By Theorem 2.1, the asymptotic smoothness of the semi-flow Φ generated by system (1.4) follows. This completes the proof. \Box

The following result is immediate from Theorem 2.33 in [38] and Theorem 2.3.

Theorem 2.4 There exists a global attractor A of bounded sets in \mathcal{X} .

3 Steady states and basic reproduction number

In this section, we establish the existence of feasible steady states of system (1.4) with the boundary conditions (1.5).

Clearly, system (1.4) always has a disease-free steady state $E_1(A/\mu, 0, 0, 0)$. If system (1.4) admits an endemic steady state $(S^*, e^*(\theta), i^*(a), T^*)$, then it must satisfy the following equations:

$$A - \mu S^* - S^* \int_0^\infty \beta(a) i^*(a) \, da = 0,$$

$$\frac{de^*(\theta)}{d\theta} = -(\mu + \nu(\theta)) e^*(\theta),$$

$$\frac{di^*(a)}{da} = -(\mu_1(a) + \gamma(a)) i^*(a),$$

$$\int_0^\infty \gamma(a) i^*(a) \, da = (\mu_2 + \delta) T^*,$$

$$e^*(0) = S^* \int_0^\infty \beta(a) i^*(a) \, da + (1 - p) \delta T^*,$$

$$i^*(0) = \int_0^\infty \nu(\theta) e^*(\theta) \, d\theta + p \delta T^*.$$
(3.1)

It follows from the second and the third equations of (3.1) that

$$e^*(\theta) = e^*(0)\phi_1(\theta), \qquad i^*(a) = i^*(0)\phi_2(a).$$
 (3.2)

We derive from the fourth equation of (3.1) that

$$T^* = \frac{\int_0^\infty \gamma(a)i^*(a) \, da}{\mu_2 + \delta}.\tag{3.3}$$

It follows from the fifth equation of (3.1) and (3.3) that

$$e^*(0) = S^*i^*(0) \int_0^\infty \beta(a)\phi_2(a) \, da + \frac{(1-p)\delta}{\mu_2 + \delta}i^*(0) \int_0^\infty \gamma(a)\phi_2(a) \, da. \tag{3.4}$$

We obtain from the sixth equation of (3.1) and (3.3) that

$$i^{*}(0) = e^{*}(0) \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta + \frac{p\delta}{\mu_{2} + \delta} i^{*}(0) \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da.$$
 (3.5)

On substituting (3.4) into (3.5), we have

$$1 = \int_0^\infty \nu(\theta)\phi_1(\theta) d\theta \left[S^* \int_0^\infty \beta(a)\phi_2(a) da + \frac{(1-p)\delta}{\mu_2 + \delta} \int_0^\infty \gamma(a)\phi_2(a) da \right]$$

+
$$\frac{p\delta}{\mu_2 + \delta} \int_0^\infty \gamma(a)\phi_2(a) da,$$
 (3.6)

yielding

$$S^* = \frac{\mu_2 + \delta - \delta[(1-p)\int_0^\infty \nu(\theta)\phi_1(\theta) d\theta + p]\int_0^\infty \gamma(a)\phi_2(a) da}{(\mu_2 + \delta)\int_0^\infty \nu(\theta)\phi_1(\theta) d\theta \int_0^\infty \beta(a)\phi_2(a) da}.$$
(3.7)

Since

$$\int_0^\infty \nu(\theta)\phi_1(\theta)\,d\theta \leq \int_0^\infty \nu(\theta)e^{-\int_0^\theta \nu(s)\,ds}\,d\theta = 1 - e^{-\int_0^\infty \nu(s)\,ds} < 1$$

and

$$\int_{0}^{\infty} \gamma(a)\phi_{2}(a) da \leq \int_{0}^{\infty} \gamma(a)e^{-\int_{0}^{a} \gamma(s) ds} da = 1 - e^{-\int_{0}^{\infty} \gamma(s) ds} < 1,$$

we have $S^* > 0$.

On substituting (3.7) into the first equation of (3.1), it follows that

$$i^*(0) = \frac{\mu}{S^* \int_0^\infty \nu(\theta) \phi_1(\theta) d\theta (\int_0^\infty \beta(a) \phi_2(a) da)^2} (\mathcal{R}_0 - 1), \tag{3.8}$$

where

$$\mathcal{R}_{0} = \frac{A}{\mu} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + \frac{\delta}{\mu_{2} + \delta} \left[(1 - p) \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta + p \right] \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da.$$
(3.9)

 \mathcal{R}_0 is called the basic reproduction number representing the average number of new infections generated by a single newly infectious individual during the full infectious period [39].

In conclusion, if $\mathcal{R}_0 > 1$, in addition to the disease-free steady state E_1 , system (1.4) has a unique endemic steady state $E^*(S^*, e^*(\theta), i^*(a), T^*)$, where

$$S^{*} = \frac{\mu_{2} + \delta - [(1 - p)\delta \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta + p\delta] \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da}{(\mu_{2} + \delta) \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \beta(a)\phi_{2}(a) da},$$

$$e^{*}(\theta) = \frac{\mu[(\mu_{2} + \delta)S^{*} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + \delta(1 - p)]\phi_{1}(\theta)}{(\mu_{2} + \delta)S^{*} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta(\int_{0}^{\infty} \beta(a)\phi_{2}(a) da)^{2}} (\mathcal{R}_{0} - 1),$$

$$i^{*}(a) = \frac{\mu\phi_{2}(a)}{S^{*} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta(\int_{0}^{\infty} \beta(a)\phi_{2}(a) da)^{2}} (\mathcal{R}_{0} - 1),$$

$$T^{*} = \frac{\mu \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da}{(\mu_{2} + \delta)S^{*} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta(\int_{0}^{\infty} \beta(a)\phi_{2}(a) da)^{2}} (\mathcal{R}_{0} - 1).$$
(3.10)

4 Local stability

In this section, we study the local stability of each of feasible steady states of system (1.4) with the boundary conditions (1.5).

We first consider the local stability of the disease-free steady state $E_1(A/\mu, 0, 0, 0)$. Let $S(t) = x_1(t) + A/\mu$, $e(\theta, t) = y_1(\theta, t)$, $i(a, t) = z_1(a, t)$, $T(t) = w_1(t)$. Linearizing system (1.4) at the steady state E_1 , it follows from (1.4) and (1.5) that

$$\dot{x}_{1}(t) = -\mu x_{1}(t) - \frac{A}{\mu} \int_{0}^{\infty} \beta(a)z_{1}(a,t) da,$$

$$\frac{\partial y_{1}(\theta,t)}{\partial t} + \frac{\partial y_{1}(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))y_{1}(\theta,t),$$

$$\frac{\partial z_{1}(a,t)}{\partial t} + \frac{\partial z_{1}(a,t)}{\partial a} = -(\mu_{1}(a) + \gamma(a))z_{1}(a,t),$$

$$\dot{w}_{1}(t) = \int_{0}^{\infty} \gamma(a)z_{1}(a,t) da - (\mu_{2} + \delta)w_{1}(t),$$

$$y_{1}(0,t) = \frac{A}{\mu} \int_{0}^{\infty} \beta(a)z_{1}(a,t) da + (1-p)\delta w_{1}(t),$$

$$z_{1}(0,t) = \int_{0}^{\infty} \nu(\theta)y_{1}(\theta,t) d\theta + p\delta w_{1}(t).$$
(4.1)

Looking for solutions of system (4.1) of the form $x_1(t) = x_{11}e^{\lambda t}$, $y_1(\theta, t) = y_{11}(\theta)e^{\lambda t}$, $z_1(a, t) = z_{11}(a)e^{\lambda t}$, $w_1(t) = w_{11}e^{\lambda t}$, where $x_{11}, y_{11}(\theta), z_{11}(a)$ and w_{11} will be determined later, we obtain the following linear eigenvalue problem:

$$(\lambda + \mu)x_{11} = -\frac{A}{\mu} \int_{0}^{\infty} \beta(a)z_{11}(a) da,$$

$$y'_{11}(\theta) = -(\lambda + \mu + \nu(\theta))y_{11}(\theta),$$

$$z'_{11}(a) = -(\lambda + \mu_{1}(a) + \gamma(a))z_{11}(a),$$

$$(\lambda + \mu_{2} + \delta)w_{11} = \int_{0}^{\infty} \gamma(a)z_{11}(a) da,$$

$$y_{11}(0) = \frac{A}{\mu} \int_{0}^{\infty} \beta(a)z_{11}(a) da + (1 - p)\delta w_{11},$$

$$z_{11}(0) = \int_{0}^{\infty} \nu(\theta)y_{11}(\theta) d\theta + p\delta w_{11}.$$
(4.2)

It follows from the second and the third equations of system (4.2) that

$$y_{11}(\theta) = y_{11}(0)e^{-\int_0^{\theta} (\lambda + \mu + \nu(s)) ds}$$
(4.3)

and

$$z_{11}(a) = z_{11}(0)e^{-\int_0^a (\lambda + \mu_1(s) + \gamma(s)) ds}.$$
(4.4)

We obtain from the fourth equation of system (4.2) that

$$w_{11} = \frac{\int_0^\infty \gamma(a) z_{11}(a) \, da}{\lambda + \mu_2 + \delta}.$$
 (4.5)

On substituting (4.5) into the fifth and the sixth equations of system (4.2), one obtains

$$y_{11}(0) = \frac{A}{\mu} \int_0^\infty \beta(a) z_{11}(a) \, da + \frac{(1-p)\delta}{\lambda + \mu_2 + \delta} \int_0^\infty \gamma(a) z_{11}(a) \, da \tag{4.6}$$

and

$$z_{11}(0) = y_{11}(0) \int_0^\infty \nu(\theta) \phi_1(\theta) d\theta + \frac{p\delta}{\lambda + \mu_2 + \delta} \int_0^\infty \gamma(a) z_{11}(a) da.$$
 (4.7)

We derive from (4.6) and (4.7) that

$$z_{11}(0) = \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \left[\frac{A}{\mu} \int_{0}^{\infty} \beta(a)z_{11}(a) da + \frac{(1-p)\delta}{\lambda + \mu_{2} + \delta} \int_{0}^{\infty} \gamma(a)z_{11}(a) da \right] + \frac{p\delta}{\lambda + \mu_{2} + \delta} \int_{0}^{\infty} \gamma(a)z_{11}(a) da.$$
(4.8)

On substituting (4.4) into (4.8), we obtain the characteristic equation of system (1.4) at the disease-free steady state E_1 of the form

$$f(\lambda) = 1, (4.9)$$

where

$$f(\lambda) = \frac{A}{\mu} \int_0^\infty v(\theta) \phi_1(\theta) d\theta \int_0^\infty \beta(a) e^{-\int_0^a (\lambda + \mu_1(s) + \gamma(s)) ds} da$$

$$+ \frac{\delta}{\lambda + \mu_2 + \delta} \left[(1 - p) \int_0^\infty v(\theta) \phi_1(\theta) d\theta + p \right]$$

$$\times \int_0^\infty \gamma(a) e^{-\int_0^a (\lambda + \mu_1(s) + \gamma(s)) ds} da. \tag{4.10}$$

Clearly, we have $f(0) = \mathcal{R}_0$. It is easy to show that $f'(\lambda) < 0$ and $\lim_{\lambda \to +\infty} f(\lambda) = 0$. Hence, $f(\lambda)$ is a decreasing function. Clearly, if $\mathcal{R}_0 > 1$, then $f(\lambda) = 1$ has a unique positive root. Hence, if $\mathcal{R}_0 > 1$, the steady state E_1 is unstable.

We now claim that if $\mathcal{R}_0 < 1$, the steady state E_1 is locally asymptotically stable. Otherwise, equation (4.9) has at least one root $\lambda_1 = a_1 + ib_1$ satisfying $a_1 \ge 0$. It follows that

$$\begin{split} \left| f(\lambda_1) \right| &\leq \frac{A}{\mu} \int_0^\infty \nu(\theta) \phi_1(\theta) \, d\theta \int_0^\infty \beta(a) e^{-\int_0^a (\mu_1(s) + \gamma(s)) \, ds} \, da \\ &\quad + \frac{\delta}{\mu_2 + \delta} \bigg[(1 - p) \int_0^\infty \nu(\theta) \phi_1(\theta) \, d\theta + p \bigg] \int_0^\infty \gamma(a) e^{-\int_0^a (\mu_1(s) + \gamma(s)) \, ds} \, da \\ &\quad = \mathscr{R}_0 < 1, \end{split}$$

a contradiction. Hence, if $\mathcal{R}_0 < 1$, all roots of equation (4.9) have negative real parts. Accordingly, the steady state E_1 is locally asymptotically stable if $\mathcal{R}_0 < 1$.

We now study the local stability of the endemic steady state $E^*(S^*, e^*(\theta), i^*(a), T^*)$ of system (1.4).

Letting $S(t) = x(t) + S^*$, $e(\theta, t) = y(\theta, t) + e^*(\theta)$, $i(a, t) = z(a, t) + i^*(a)$, $T(t) = w(t) + T^*$, and linearizing system (1.4) at the steady state E^* , it follows that

$$\dot{x}(t) = -\left(\mu + \int_{0}^{\infty} \beta(a)i^{*}(a) da\right)x(t) - S^{*} \int_{0}^{\infty} \beta(a)z(a,t) da,$$

$$\frac{\partial y(\theta,t)}{\partial t} + \frac{\partial y(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))y(\theta,t),$$

$$\frac{\partial z(a,t)}{\partial t} + \frac{\partial z(a,t)}{\partial a} = -(\mu_{1}(a) + \gamma(a))z(a,t),$$

$$\dot{w}(t) = \int_{0}^{\infty} \gamma(a)z(a,t) da - (\mu_{2} + \delta)w(t),$$

$$y(0,t) = x(t) \int_{0}^{\infty} \beta(a)i^{*}(a) da + S^{*} \int_{0}^{\infty} \beta(a)z(a,t) da + (1-p)\delta w(t),$$

$$z(0,t) = \int_{0}^{\infty} \nu(\theta)y(\theta,t) d\theta + p\delta w(t).$$
(4.11)

Looking for solutions of system (4.11) of the form $x(t) = x_1 e^{\lambda t}$, $y(\theta, t) = y_1(\theta) e^{\lambda t}$, $z(a, t) = z_1(a)e^{\lambda t}$, $z(a)e^{\lambda t}$, where $z_1, y_1(\theta), z_1(a)$ and z_1 will be determined later, we obtain the following linear eigenvalue problem:

$$\left(\lambda + \mu + \int_{0}^{\infty} \beta(a)i^{*}(a) da\right) x_{1} = -S^{*} \int_{0}^{\infty} \beta(a)z_{1}(a) da,$$

$$y'_{1}(\theta) = -(\lambda + \mu + \nu(\theta))y_{1}(\theta),$$

$$z'_{1}(a) = -(\lambda + \mu_{1}(a) + \gamma(a))z_{1}(a),$$

$$(\lambda + \mu_{2} + \delta)w_{1} = \int_{0}^{\infty} \gamma(a)z_{1}(a) da,$$

$$y_{1}(0) = x_{1} \int_{0}^{\infty} \beta(a)i^{*}(a) da + S^{*} \int_{0}^{\infty} \beta(a)z_{1}(a) da + (1 - p)\delta w_{1},$$

$$z_{1}(0) = \int_{0}^{\infty} \nu(\theta)y_{1}(\theta) d\theta + p\delta w_{1}.$$
(4.12)

It follows from the second and the third equations of system (4.12) that

$$y_1(\theta) = y_1(0)e^{-\int_0^\theta (\lambda + \mu + \nu(s)) ds}$$

$$\tag{4.13}$$

and

$$z_1(a) = z_1(0)e^{-\int_0^a (\lambda + \mu_1(s) + \gamma(s)) ds}.$$
(4.14)

We derive from the first equation of system (4.12) that

$$x_{1} = -\frac{S^{*} \int_{0}^{\infty} \beta(a) z_{1}(a) da}{\lambda + \mu + \int_{0}^{\infty} \beta(a) i^{*}(a) da}.$$
(4.15)

It follows from the fourth equation of system (4.12) that

$$w_1 = \frac{\int_0^\infty \gamma(a) z_1(a) \, da}{\lambda + \mu_2 + \delta}.\tag{4.16}$$

We have from the fifth equation of system (4.12), (4.15) and (4.16)

$$y_1(0) = \frac{S^*(\lambda + \mu) \int_0^\infty \beta(a) z_1(a) \, da}{\lambda + \mu + \int_0^\infty \beta(a) i^*(a) \, da} + \frac{(1 - p)\delta}{\lambda + \mu_2 + \delta} \int_0^\infty \gamma(a) z_1(a) \, da. \tag{4.17}$$

On substituting (4.16) into the sixth equation of system (4.12), one has

$$z_{1}(0) = y_{1}(0) \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) d\theta + \frac{p\delta}{\lambda + \mu_{2} + \delta} \int_{0}^{\infty} \gamma(a) z_{1}(a) da.$$
 (4.18)

It follows from (4.17) and (4.18) that

$$z_{1}(0) = \frac{S^{*}(\lambda + \mu)}{\lambda + \mu + \int_{0}^{\infty} \beta(a)i^{*}(a) da} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \beta(a)z_{1}(a) da$$
$$+ \frac{\delta}{\lambda + \mu_{2} + \delta} \left[(1 - p) \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta + p \right] \int_{0}^{\infty} \gamma(a)z_{1}(a) da. \tag{4.19}$$

On substituting (4.14) into (4.19), we obtain the characteristic equation of system (1.4) at the steady state E^* of the form

$$f_1(\lambda) = 1, \tag{4.20}$$

where

$$f_{1}(\lambda) = \frac{S^{*}(\lambda + \mu)}{\lambda + \mu + \int_{0}^{\infty} \beta(a)i^{*}(a) da} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \beta(a)e^{-\int_{0}^{a}(\lambda + \mu_{1}(s) + \gamma(s)) ds} da$$

$$+ \frac{\delta}{\lambda + \mu_{2} + \delta} \left[(1 - p) \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta + p \right]$$

$$\times \int_{0}^{\infty} \gamma(a)e^{-\int_{0}^{a}(\lambda + \mu_{1}(s) + \gamma(s)) ds} da. \tag{4.21}$$

We now claim that if $\mathcal{R}_0 > 1$, all roots of equation (4.20) have negative real parts. Otherwise, equation (4.20) has at least one root $\lambda_2 = a_2 + b_2$ i satisfying $a_2 \ge 0$. In this case, we have

$$\begin{split} \left| f_{1}(\lambda_{2}) \right| &\leq \frac{S^{*} |\lambda_{2} + \mu|}{|\lambda_{2} + \mu + \int_{0}^{\infty} \beta(a) i^{*}(a) \, da|} \\ &\times \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) \, d\theta \left| \int_{0}^{\infty} \beta(a) e^{-\int_{0}^{a} (\lambda_{2} + \mu_{1}(s) + \gamma(s)) \, ds} \, da \right| \\ &+ \frac{\delta}{|\lambda_{2} + \mu_{2} + \delta|} \left[(1 - p) \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) \, d\theta + p \right] \\ &\times \left| \int_{0}^{\infty} \gamma(a) e^{-\int_{0}^{a} (\lambda_{2} + \mu_{1}(s) + \gamma(s)) \, ds} \, da \right| \\ &< S^{*} \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) \, d\theta \int_{0}^{\infty} \beta(a) \phi_{2}(a) \, da \\ &+ \frac{\delta}{\mu_{2} + \delta} \left[(1 - p) \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) \, d\theta + p \right] \int_{0}^{\infty} \gamma(a) \phi_{2}(a) \, da \\ &= 1, \end{split} \tag{4.22}$$

a contradiction. Therefore, if $\mathcal{R}_0 > 1$, then the endemic steady state E^* is locally asymptotically stable.

In conclusion, we have the following result.

Theorem 4.1 For system (1.4) with the boundary conditions (1.5), if $\mathcal{R}_0 < 1$, the disease-free steady state $E_1(A/\mu, 0, 0, 0)$ is locally asymptotically stable; if $\mathcal{R}_0 > 1$, E_1 is unstable and an endemic steady state $E^*(S^*, e^*(\theta), i^*(a), T^*)$ exists and is locally asymptotically stable.

5 Uniform persistence

In this section, we establish the uniform persistence of the semi-flow $\{\Phi(t)\}_{t\geq 0}$ generated by system (1.4) when the basic reproduction number is greater than unity.

Define

$$\bar{a}_1 = \inf \left\{ a : \int_a^\infty \beta(u) \, du = 0 \right\}, \qquad \bar{a}_2 = \inf \left\{ a : \int_a^\infty \gamma(u) \, du = 0 \right\},$$

$$\bar{\theta} = \inf \left\{ \theta : \int_\theta^\infty \nu(u) \, du = 0 \right\}.$$

Noting that $\beta(\cdot)$, $\gamma(\cdot)$, $\nu(\cdot) \in L^1_+(0,\infty)$, we have $\bar{a}_1 > 0$, $\bar{a}_2 > 0$, $\bar{\theta} > 0$. Denote

$$\mathcal{X} = L^1_+(0, +\infty) \times L^1_+(0, +\infty) \times \mathbb{R}^+, \qquad \bar{a} = \max\{\bar{a}_1.\bar{a}_2\}$$

$$\tilde{\mathcal{Y}} = \left\{ \left(e(\cdot, t), i(\cdot, t), T(t) \right)^\top \in \mathcal{X} : \int_0^{\bar{\theta}} e(\theta, t) \, d\theta > 0 \text{ or } \int_0^{\bar{a}} i(a, t) \, da > 0 \text{ or } T(t) > 0 \right\},$$

and

$$\mathcal{Y} = \mathbb{R}^+ \times \tilde{\mathcal{Y}}, \qquad \partial \mathcal{Y} = \mathscr{X} \setminus \mathcal{Y}, \qquad \partial \tilde{\mathcal{Y}} = \mathcal{X} \setminus \tilde{\mathcal{Y}}.$$

Theorem 5.1 The subsets \mathcal{Y} and $\partial \mathcal{Y}$ are both positively invariant under the semi-flow $\{\Phi(t)\}_{t\geq 0}$, namely, $\Phi(t,\mathcal{Y})\subset \mathcal{Y}$ and $\Phi(t,\partial \mathcal{Y})\subset \partial \mathcal{Y}$ for $t\geq 0$. The disease-free steady state $E_1(A/\mu,0,0,0)$ is globally asymptotically stable for the semi-flow $\{\Phi(t)\}_{t\geq 0}$ restricted to $\partial \mathcal{Y}$.

Proof Let $(S^0, e_0(\cdot), i_0(\cdot), T^0) \in \mathcal{Y}$. Then $(e_0(\cdot), i_0(\cdot), T^0) \in \tilde{\mathcal{Y}}$. Denote

$$L(t) = \int_0^\infty e(\theta, t) d\theta + \int_0^\infty i(a, t) da + T(t).$$

It follows from (1.4), (1.5), (2.8) and (2.9) that

$$\begin{split} \frac{d}{dt}L(t) &= S(t) \int_0^\infty \beta(a)i(a,t) \, da - \mu \int_0^\infty e(\theta,t) \, d\theta - \int_0^\infty \mu_1(a)i(a,t) \, da - \mu_2 T(t) \\ &\geq -\mu \int_0^\infty e(\theta,t) \, d\theta - \int_0^\infty \mu_1(a)i(a,t) \, da - \mu_2 T(t) \\ &\geq -\max\{\mu,\mu_2,\mu_{1_{\max}}\}L(t), \end{split}$$

where $\mu_{1_{\text{max}}} = \text{ess sup}_{a \in [0,\infty)}$. This yields

$$L(t) \ge e^{-\max\{\mu,\mu_2,\mu_{1_{\max}}\}}L(0).$$

Hence, we have $\Phi(t, \mathcal{Y}) \subset \mathcal{Y}$.

Using a similar argument as in the proof of Lemma 3.2 in [40], one can show that $\partial \mathcal{Y}$ is positively invariant under the semi-flow $\{\Phi(t)\}$.

Let $(S^0, e_0(\cdot), i_0(\cdot), T^0) \in \partial \mathcal{Y}$. Then $(e_0(\cdot), i_0(\cdot), T^0) \in \partial \tilde{\mathcal{Y}}$. We consider the following system:

$$\frac{\partial e(\theta,t)}{\partial t} + \frac{\partial e(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))e(\theta,t),$$

$$\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} = -(\mu_1(a) + \gamma(a))i(a,t),$$

$$\dot{T}(t) = \int_0^\infty \gamma(a)i(a,t) da - (\mu_2 + \delta)T(t),$$

$$e(0,t) = S(t) \int_0^\infty \beta(a)i(a,t) da + (1-p)\delta T(t),$$

$$i(0,t) = \int_0^\infty \nu(\theta)e(\theta,t) d\theta + p\delta T(t),$$

$$e(\theta,0) = e_0(\theta), \qquad i(a,0) = i_0(a), \qquad T(0) = 0.$$
(5.1)

Since $\limsup_{t\to +\infty} S(t) \leq A/\mu$, by the comparison principle, we have

$$e(a,t) \le \hat{e}(a,t), \qquad i(a,t) \le \hat{i}(a,t), \qquad T(t) \le \hat{T}(t),$$

$$(5.2)$$

where $\hat{e}(a,t)$, $\hat{i}(a,t)$ and $\hat{T}(t)$ satisfy

$$\frac{\partial \hat{e}(\theta,t)}{\partial t} + \frac{\partial \hat{e}(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))\hat{e}(\theta,t),$$

$$\frac{\partial \hat{i}(a,t)}{\partial t} + \frac{\partial \hat{i}(a,t)}{\partial a} = -(\mu_1(a) + \gamma(a))\hat{i}(a,t),$$

$$\frac{d\hat{T}(t)}{dt} = \int_0^\infty \gamma(a)\hat{i}(a,t) da - (\mu_2 + \delta)\hat{T}(t),$$

$$\hat{e}(0,t) = \frac{A}{\mu} \int_0^\infty \beta(a)\hat{i}(a,t) da + (1-p)\delta\hat{T}(t),$$

$$\hat{i}(0,t) = \int_0^\infty \nu(\theta)\hat{e}(\theta,t) d\theta + p\delta\hat{T}(t),$$

$$\hat{e}(\theta,0) = e_0(\theta), \qquad \hat{i}(a,0) = i_0(a), \qquad \hat{T}(0) = 0.$$
(5.3)

Solving the first and the second equations of system (5.3), we have

$$\hat{e}(\theta, t) = \begin{cases} \hat{L}_1(t - \theta)\phi_1(\theta), & 0 \le \theta < t, \\ e_0(\theta - t)\frac{\phi_1(\theta)}{\phi_1(\theta - t)}, & 0 \le t \le \theta, \end{cases}$$

$$(5.4)$$

and

$$\hat{i}(a,t) = \begin{cases} \hat{L}_2(t-a)\phi_2(a), & 0 \le a < t, \\ i_0(a-t)\frac{\phi_2(a)}{\phi_2(a-t)}, & 0 \le t \le a, \end{cases}$$
(5.5)

where

$$\hat{L}_1(t) := \hat{e}(0, t) = \frac{A}{\mu} \int_0^\infty \beta(a) \hat{i}(a, t) \, da + (1 - p) \delta \hat{T}(t)$$
 (5.6)

and

$$\hat{L}_2(t) := \hat{i}(0,t) = \int_0^\infty \nu(\theta) \hat{e}(\theta,t) d\theta + p\delta \hat{T}(t). \tag{5.7}$$

On substituting (5.4) and (5.5) into the third, the fourth and the fifth equations of (5.3), it follows that

$$\frac{d\hat{T}(t)}{dt} = \int_{0}^{t} \gamma(a)\hat{L}_{2}(t-a)\phi_{2}(a) da - (\mu_{2} + \delta)\hat{T}(t) + G_{1}(t),$$

$$\hat{L}_{1}(t) = \frac{A}{\mu} \int_{0}^{t} \beta(a)\hat{L}_{2}(t-a)\phi_{2}(a) da + (1-p)\delta\hat{T}(t) + G_{2}(t),$$

$$\hat{L}_{2}(t) = \int_{0}^{t} \nu(\theta)\hat{L}_{1}(t-\theta)\phi_{1}(\theta) d\theta + p\delta\hat{T}(t) + G_{3}(t),$$

$$G_{1}(t) = \int_{t}^{\infty} \gamma(a)i_{0}(a-t)\frac{\phi_{2}(a)}{\phi_{2}(a-t)} da,$$

$$G_{2}(t) = \frac{A}{\mu} \int_{t}^{\infty} \beta(a)i_{0}(a-t)\frac{\phi_{2}(a)}{\phi_{2}(a-t)} da,$$

$$G_{3}(t) = \int_{t}^{\infty} \nu(\theta)e_{0}(\theta-t)\frac{\phi_{1}(\theta)}{\phi_{1}(\theta-t)} d\theta.$$
(5.8)

Since $(e_0(\cdot), i_0(\cdot), T^0) \in \partial \tilde{\mathcal{Y}}$, we have $G_i(t) \equiv 0$ (i = 1, 2, 3) for all $t \geq 0$. It therefore follows from (5.8) that

$$\frac{d\hat{T}(t)}{dt} = \int_{0}^{t} \gamma(a)\hat{L}_{2}(t-a)\phi_{2}(a) da - (\mu_{2} + \delta)\hat{T}(t),$$

$$\hat{L}_{1}(t) = \frac{A}{\mu} \int_{0}^{t} \beta(a)\hat{L}_{2}(t-a)\phi_{2}(a) da + (1-p)\delta\hat{T}(t),$$

$$\hat{L}_{2}(t) = \int_{0}^{t} \nu(\theta)\hat{L}_{1}(t-\theta)\phi_{1}(\theta) d\theta + p\delta\hat{T}(t),$$

$$\hat{T}(0) = 0.$$
(5.9)

It is easy to show that system (5.9) has a unique solution $\hat{L}_1(t) = 0$, $\hat{L}_2(t) = 0$, $\hat{T}(t) = 0$. We obtain from (5.4) $\hat{e}(\theta, t) = 0$ for $0 \le \theta < t$. For $\theta \ge t$, we have

$$\|\hat{e}(\theta,t)\|_{L^1} = \|e_0(\theta-t)\frac{\phi_1(\theta)}{\phi_1(\theta-t)}\|_{L^1} \le e^{-\mu_0 t} \|e_0\|_{L^1},$$

which yields $\lim_{t\to +\infty} \hat{e}(\theta,t) = 0$. Similarly, one has $\lim_{t\to +\infty} \hat{i}(a,t) = 0$. By comparison principle, it follows that $\lim_{t\to +\infty} e(\theta,t) = 0$, $\lim_{t\to +\infty} i(a,t) = 0$ and T(t) = 0 as $t\to +\infty$. We obtain from the first equation of system (1.4) that $\lim_{t\to +\infty} S(t) = A/\mu$. This completes the proof.

Theorem 5.2 If $\mathcal{R}_0 > 1$, then the semi-flow $\{\Phi(t)\}_{t\geq 0}$ generated by system (1.4) is uniformly persistent with respect to the pair $(\mathcal{Y}, \partial \mathcal{Y})$; that is, there exists an $\varepsilon > 0$ such that $\lim_{t\to +\infty} \|\Phi(t,x)\|_{\mathscr{X}} \geq \varepsilon$ for $x \in \mathcal{Y}$. Furthermore, there is a compact subset $\mathcal{A}_0 \subset \mathcal{Y}$ which is a global attractor for $\{\Phi(t)\}_{t\geq 0}$ in \mathcal{Y} .

Proof Since the disease-free steady state $E_1(A/\mu, 0, 0, 0)$ is globally asymptotically stable in $\partial \mathcal{Y}$, applying Theorem 4.2 in [41], we need only to show that

$$W^s(E_1) \cap \mathcal{Y} = \emptyset$$
,

where

$$W^{s}(E_1) = \left\{ x \in \mathcal{Y} : \lim_{t \to +\infty} \Phi(t, x) = E_1 \right\}.$$

Otherwise, there exists a solution $y \in \mathcal{Y}$ such that $\Phi(t, y) \to E_1$ as $t \to \infty$. In this case, one can find a sequence $\{y_n\} \subset \mathcal{Y}$ such that

$$\|\Phi(t,y_n)-\bar{y}\|_{\mathscr{X}}<\frac{1}{n},\quad t\geq 0,$$

where $\bar{y} = (A/\mu, 0, 0, 0)$.

Denote $\Phi(t, y_n) = (S_n(t), e_n(\cdot, t), i_n(\cdot, t), T_n(t))$ and $y_n = (S_n(0), e_n(\cdot, 0), i_n(\cdot, 0), T_n(0))$. Since $\mathcal{R}_0 > 1$, one can choose n sufficiently large satisfying $S_0 - \frac{1}{n} > 0$ and

$$\left(S_0 - \frac{1}{n}\right) \int_0^\infty \beta(a)\phi_2(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta
+ \frac{\delta}{\mu_2 + \delta} \left[p + (1 - p) \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta\right] \int_0^\infty \gamma(a)\phi_2(a) \, da > 1,$$
(5.10)

where $S_0 = A/\mu$. For such an n > 0, there exists a $T_1 > 0$ such that, for $t > T_1$,

$$S_0 - \frac{1}{n} < S_n(t) < S_0 + \frac{1}{n}. \tag{5.11}$$

Consider the following auxiliary system:

$$\frac{\partial \tilde{e}(\theta,t)}{\partial t} + \frac{\partial \tilde{e}(\theta,t)}{\partial \theta} = -(\mu + \nu(\theta))\tilde{e}(\theta,t),$$

$$\frac{\partial \tilde{i}(a,t)}{\partial t} + \frac{\partial \tilde{i}(a,t)}{\partial a} = -(\mu_1(a) + \gamma(a))\tilde{i}(a,t),$$

$$\frac{\partial \tilde{t}(t)}{\partial t} = \int_0^\infty \gamma(a)\tilde{i}(a,t) da - (\mu_2 + \delta)\tilde{T}(t),$$

$$\tilde{e}(0,t) = \left(S_0 - \frac{1}{n}\right) \int_0^\infty \beta(a)\tilde{i}(a,t) da + (1-p)\delta\tilde{T}(t),$$

$$\tilde{i}(0,t) = \int_0^\infty \nu(\theta)\tilde{e}(\theta,t) d\theta + p\delta\tilde{T}(t).$$
(5.12)

It is easy to show that if $\mathcal{R}_0 > 1$, system (5.12) has a unique steady state $E_0(0,0,0)$. Looking for solutions of system (5.12) of the form

$$\tilde{e}(\theta,t) = \tilde{e}_1(\theta)e^{\lambda t}, \qquad \tilde{i}(a,t) = \tilde{i}_1(a)e^{\lambda t}, \qquad \tilde{T}(t) = \tilde{T}_1e^{\lambda t}, \tag{5.13}$$

where the functions $\tilde{e}_1(\theta)$, $\tilde{i}_1(a)$ and the constant \tilde{T}_1 will be determined later, we obtain the following linear eigenvalue problem:

$$\tilde{e}'_{1}(\theta) = -(\lambda + \mu + \nu(\theta))\tilde{e}_{1}(\theta),$$

$$\tilde{i}'_{1}(a) = -(\lambda + \mu_{1}(a) + \gamma(a))\tilde{i}_{1}(a),$$

$$\int_{0}^{\infty} \gamma(a)\tilde{i}_{1}(a) da = (\lambda + \mu_{2} + \delta)\tilde{T}_{1},$$

$$\tilde{e}_{1}(0) = \left(S_{0} - \frac{1}{n}\right) \int_{0}^{\infty} \beta(a)\tilde{i}_{1}(a) da + (1 - p)\delta\tilde{T}_{1},$$

$$\tilde{i}_{1}(0) = \int_{0}^{\infty} \nu(\theta)\tilde{e}_{1}(\theta) d\theta + p\delta\tilde{T}_{1}.$$
(5.14)

It follows from the first, the second and the third equations of system (5.14) that

$$\tilde{e}_1(\theta) = \tilde{e}_1(0)e^{-\int_0^\theta (\lambda + \mu + \nu(s)) ds},\tag{5.15}$$

$$\tilde{i}_1(a) = \tilde{i}_1(0)e^{-\int_0^a (\lambda + \mu_1(s) + \gamma(s)) \, ds},\tag{5.16}$$

and

$$\tilde{T}_1 = \frac{\int_0^\infty \gamma(a)\tilde{i}_1(a)\,da}{\lambda + \mu_2 + \delta}.\tag{5.17}$$

On substituting (5.15)-(5.17) into the fourth and the fifth equations of (5.14), we obtain the characteristic equation of system (5.14) at the steady state E_0 of the form

$$f_2(\lambda) = 1, (5.18)$$

where

$$f_{2}(\lambda) = \left(S_{0} - \frac{1}{n}\right) \int_{0}^{\infty} \beta(a)e^{-\int_{0}^{a}(\lambda + \mu_{1}(s) + \gamma(s)) ds} da \int_{0}^{\infty} \nu(\theta)e^{-\int_{0}^{\theta}(\lambda + \mu + \nu(s)) ds} d\theta$$

$$+ \frac{\delta}{\lambda + \mu_{2} + \delta} \int_{0}^{\infty} \gamma(a)e^{-\int_{0}^{a}(\lambda + \mu_{1}(s) + \gamma(s)) ds} da$$

$$\times \left[p + (1 - p)\int_{0}^{\infty} \nu(\theta)e^{-\int_{0}^{\theta}(\lambda + \mu + \nu(s)) ds} d\theta\right]. \tag{5.19}$$

Clearly, we have

$$f_2(0) = \left(S_0 - \frac{1}{n}\right) \int_0^\infty \beta(a)\phi_2(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta$$
$$+ \frac{\delta}{\mu_2 + \delta} \left[p + (1 - p) \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta\right] \int_0^\infty \gamma(a)\phi_2(a) \, da > 1$$

and

$$\lim_{\lambda\to+\infty}f_2(\lambda)=0.$$

Hence, if $\mathcal{R}_0 > 1$, then equation (5.18) has at least one positive root λ_0 . This implies that the solution $(\tilde{e}(\cdot,t),\tilde{i}(\cdot,t),\tilde{T}(t))$ of system (5.12) is unbounded. By comparison principle, the solution $\Phi(t,y_n)$ of system (1.4) is unbounded, which contradicts Proposition 2.2. Therefore, the semi-flow $\{\Phi(t)\}_{t\geq 0}$ generated by system (1.4) is uniformly persistent. Furthermore, there is a compact subset $\mathcal{A}_0 \subset \mathcal{Y}$ which is a global attractor for $\{\Phi(t)\}_{t\geq 0}$ in \mathcal{Y} . This completes the proof.

6 Global stability

In this section, we are concerned with the global asymptotic stability of each of feasible steady states of system (1.4) with the boundary conditions (1.5) and the initial condition (1.6). The strategy of proofs is to use suitable Lyapunov functionals and LaSalle's invariance principle.

We first state and prove a result on the global asymptotic stability of the disease-free steady state $E_1(A/\mu, 0, 0, 0)$ of system (1.4).

Theorem 6.1 If $\mathcal{R}_0 < 1$, the disease-free steady state $E_1(A/\mu, 0, 0, 0)$ of system (1.4) is globally asymptotically stable.

Proof Let $(S(t), e(\theta, t), i(a, t), T(t))$ be any positive solution of system (1.4) with the boundary conditions (1.5). Denote $S_0 = A/\mu$.

Define

$$V_{1}(t) = S(t) - S_{0} - S_{0} \ln \frac{S(t)}{S_{0}} + \int_{0}^{\infty} F_{1}(\theta)e(\theta, t) d\theta + \int_{0}^{\infty} F_{2}(a)i(a, t) da + kT(t),$$
(6.1)

where the positive constant k and the nonnegative kernel functions $F_1(\theta)$ and $F_2(a)$ will be determined later.

Calculating the derivative of $V_1(t)$ along positive solutions of system (1.4), it follows that

$$\frac{d}{dt}V_{1}(t) = \left(1 - \frac{S_{0}}{S(t)}\right) \left[A - \mu S(t) - S(t) \int_{0}^{\infty} \beta(a)i(a,t) da\right]
+ \int_{0}^{\infty} F_{1}(\theta) \frac{\partial e(\theta,t)}{\partial t} d\theta + \int_{0}^{\infty} F_{2}(a) \frac{\partial i(a,t)}{\partial t} da
+ k \left[\int_{0}^{\infty} \gamma(a)i(a,t) da - (\mu_{2} + \delta)T(t)\right].$$
(6.2)

On substituting $A = \mu S_0$, $\frac{\partial e(\theta,t)}{\partial t} = -(\mu + \nu(\theta))e(\theta,t) - \frac{\partial e(\theta,t)}{\partial \theta}$ and $\frac{\partial i(a,t)}{\partial t} = -(\mu_1(a) + \gamma(a))i(a,t) - \frac{\partial i(a,t)}{\partial a}$ into equation (6.2), one obtains

$$\frac{d}{dt}V_{1}(t) = \left(1 - \frac{S_{0}}{S(t)}\right) \left[-\mu\left(S(t) - S_{0}\right)\right]
- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S_{0} \int_{0}^{\infty} \beta(a)i(a,t) da
- \int_{0}^{\infty} F_{1}(\theta) \left[\left(\mu + \nu(\theta)\right)e(\theta,t) + \frac{\partial e(\theta,t)}{\partial \theta}\right] d\theta
- \int_{0}^{\infty} F_{2}(a) \left[\left(\mu_{1}(a) + \gamma(a)\right)i(a,t) + \frac{\partial i(a,t)}{\partial a}\right] da
+ k \left[\int_{0}^{\infty} \gamma(a)i(a,t) da - (\mu_{2} + \delta)T(t)\right].$$
(6.3)

Using integration by parts, we derive from (6.3) that

$$\frac{d}{dt}V_{1}(t) = \left(1 - \frac{S_{0}}{S(t)}\right) \left[-\mu\left(S(t) - S_{0}\right)\right]
- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S_{0} \int_{0}^{\infty} \beta(a)i(a,t) da
- F_{1}(\theta)e(\theta,t)|_{0}^{\infty} + \int_{0}^{\infty} \left[F'_{1}(\theta) - \left(\mu + \nu(\theta)\right)F_{1}(\theta)\right]e(\theta,t) d\theta
- F_{2}(a)i(a,t)|_{0}^{\infty} + \int_{0}^{\infty} \left[F'_{2}(a) - \left(\mu_{1}(a) + \gamma(a)\right)F_{2}(a)\right]i(a,t) da
+ k \int_{0}^{\infty} \gamma(a)i(a,t) da - k(\mu_{2} + \delta)T(t).$$
(6.4)

Choose

$$F_{1}(\theta) = A_{1} \int_{\theta}^{\infty} \nu(u) e^{-\int_{\theta}^{u} (\mu + \nu(s)) ds} du,$$

$$F_{2}(a) = \int_{a}^{\infty} \left(S_{0} \beta(u) + k \gamma(u) \right) e^{-\int_{a}^{u} (\mu + \gamma(s) + \alpha(s)) ds} du,$$

$$(6.5)$$

where

$$A_1 = \frac{1}{\int_0^\infty \nu(\theta)\phi_1(\theta) d\theta}.$$
 (6.6)

Direct calculations show that

$$F_1(0) = 1, \qquad \lim_{\theta \to \infty} F_1(\theta) = 0,$$

$$F'_1(\theta) = (\mu + \nu(\theta))F_1(\theta) - A_1\nu(\theta),$$
(6.7)

and

$$F_{2}(0) = S_{0} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + k \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da,$$

$$F'_{2}(a) = (\mu_{1}(a) + \gamma(a))F_{2}(a) - (S_{0}\beta(a) + k\gamma(a)),$$

$$\lim_{a \to \infty} F_{2}(a) = 0.$$
(6.8)

We therefore obtain from (6.4)-(6.8)

$$\frac{d}{dt}V_{1}(t) = \left(1 - \frac{S_{0}}{S(t)}\right) \left[-\mu\left(S(t) - S_{0}\right)\right]
- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S_{0} \int_{0}^{\infty} \beta(a)i(a,t) da
+ F_{1}(0)e(0,t) - A_{1} \int_{0}^{\infty} \nu(\theta)e(\theta,t) d\theta
+ F_{2}(0)i(0,t) - k_{1} \int_{0}^{\infty} \left(S_{0}\beta(a) + k\gamma(a)\right)i(a,t) da
+ k \int_{0}^{\infty} \gamma(a)i(a,t) da - k(\mu_{2} + \delta)T(t)
= \left(1 - \frac{S_{0}}{S(t)}\right) \left[-\mu\left(S(t) - S_{0}\right)\right]
+ (1 - p)\delta T(t) - k(\mu_{2} + \delta)T(t) - A_{1} \int_{0}^{\infty} \nu(\theta)e(\theta,t) d\theta
+ \left(S_{0} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + k \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da\right)
\times \left(\int_{0}^{\infty} \nu(\theta)e(\theta,t) d\theta + p\delta T(t)\right).$$
(6.9)

Choosing *k* satisfying $k(\mu_2 + \delta) = (1 - p)\delta + A_1p\delta$, we have from (6.9)

$$\frac{d}{dt}V_{1}(t) = \left(1 - \frac{S_{0}}{S(t)}\right) \left[-\mu\left(S(t) - S_{0}\right)\right]
+ \left(S_{0} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + k \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da - A_{1}\right)
\times \left(\int_{0}^{\infty} \nu(\theta)e(\theta, t) d\theta + p\delta T(t)\right)
= -\mu \frac{(S(t) - S_{0})^{2}}{S(t)} + A_{1}(\mathcal{R}_{0} - 1)\left(\int_{0}^{\infty} \nu(\theta)e(\theta, t) d\theta + p\delta T(t)\right).$$
(6.10)

Clearly, if $\mathcal{R}_0 < 1$, $V_1'(t) \le 0$ holds and $V_1'(t) = 0$ implies that $S(t) = S_0$, $e(\theta, t) = 0$, T(t) = 0. Hence, the largest invariant subset of $\{V_1'(t) = 0\}$ is the singleton $E_1(S_0, 0, 0, 0)$. By Theorem 4.1, we see that if $\mathcal{R}_0 < 1$, the steady state E_1 is locally asymptotically stable. Therefore, the global asymptotic stability of E_1 follows from LaSalle's invariance principle. This completes the proof.

We are now in a position to state and prove a result on the global asymptotic stability of the endemic steady state $E^*(S^*, e^*(\theta), i^*(a), T^*)$ of system (1.4) with the boundary conditions (1.5).

Theorem 6.2 If $\mathcal{R}_0 > 1$, the endemic steady state $E^*(S^*, e^*(\theta), i^*(a), T^*)$ of system (1.4) with the boundary conditions (1.5) is globally asymptotically stable.

Proof Let (S(t), e(a, t), i(a, t), T(t)) be any positive solution of system (1.4) with the boundary conditions (1.5).

Define

$$V_{2}(t) = S^{*}G\left(\frac{S(t)}{S^{*}}\right) + \int_{0}^{\infty} f_{1}(\theta)e^{*}(\theta)G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\right)d\theta$$
$$+ \int_{0}^{\infty} f_{2}(a)i^{*}(a)G\left(\frac{i(a,t)}{i^{*}(a)}\right)da + k_{1}T^{*}G\left(\frac{T(t)}{T^{*}}\right), \tag{6.11}$$

where the function $G(x) = x - 1 - \ln x$ for x > 0, the constant $k_1 > 0$ and the nonnegative kernel functions $f_1(\theta)$ and $f_2(a)$ will be determined later.

Calculating the derivative of $V_2(t)$ along positive solutions of system (1.4) with the boundary conditions (1.5), it follows that

$$\frac{d}{dt}V_{2}(t) = \left(1 - \frac{S^{*}}{S(t)}\right) \left[A - \mu S(t) - S(t) \int_{0}^{\infty} \beta(a)i(a,t) da\right]
+ \int_{0}^{\infty} f_{1}(\theta) \left(1 - \frac{e^{*}(\theta)}{e(\theta,t)}\right) \frac{\partial e(\theta,t)}{\partial t} d\theta
+ \int_{0}^{\infty} f_{2}(a) \left(1 - \frac{i^{*}(a)}{i(a,t)}\right) \frac{\partial i(a,t)}{\partial t} da
+ k_{1} \left(1 - \frac{T^{*}}{T(t)}\right) \left[\int_{0}^{\infty} \gamma(a)i(a,t) da - (\mu_{2} + \delta)T(t)\right].$$
(6.12)

On substituting $A = \mu S^* + S^* \int_0^\infty \beta(a) i^*(a) \, da$, $\frac{\partial e(\theta,t)}{\partial t} = -\frac{\partial e(\theta,t)}{\partial \theta} - (\mu + \nu(\theta)) e(\theta,t)$ and $\frac{\partial i(a,t)}{\partial t} = -\frac{\partial i(a,t)}{\partial a} - (\mu_1(a) + \gamma(a)) i(a,t)$ into equation (6.12), we derive that

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} + S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(1 - \frac{S^{*}}{S(t)}\right)$$

$$- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S^{*} \int_{0}^{\infty} \beta(a)i(a,t) da$$

$$- \int_{0}^{\infty} f_{1}(\theta) \left(1 - \frac{e^{*}(\theta)}{e(\theta,t)}\right) \left(\frac{\partial e(\theta,t)}{\partial \theta} + (\mu + \nu(\theta))e(\theta,t)\right) d\theta$$

$$- \int_{0}^{\infty} f_{2}(a) \left(1 - \frac{i^{*}(a)}{i(a,t)}\right) \left(\frac{\partial i(a,t)}{\partial a} + (\mu_{1}(a) + \gamma(a))i(a,t)\right) da$$

$$+ k_{1} \int_{0}^{\infty} \gamma(a)i(a,t) da - k_{1}(\mu_{2} + \delta)T(t)$$

$$- k_{1} \frac{T^{*}}{T(t)} \int_{0}^{\infty} \gamma(a)i(a,t) da + k_{1}(\mu_{2} + \delta)T^{*}.$$
(6.13)

Note that

$$\frac{d}{d\theta}e^*(\theta) = -(\mu + \nu(\theta))e^*(\theta) \tag{6.14}$$

and

$$\frac{d}{da}i^{*}(a) = -(\mu_{1}(a) + \gamma(a))i^{*}(a). \tag{6.15}$$

Direct calculations show that

$$\frac{\partial}{\partial \theta} G\left(\frac{e(\theta, t)}{e^*(\theta)}\right) = \frac{1}{e^*(\theta)} \left(1 - \frac{e^*(\theta)}{e(\theta, t)}\right) \left[\frac{\partial e(\theta, t)}{\partial \theta} + \left(\mu + \nu(\theta)\right)e(\theta, t)\right]$$
(6.16)

and

$$\frac{\partial}{\partial a}G\left(\frac{i(a,t)}{i^*(a)}\right) = \frac{1}{i^*(a)}\left(1 - \frac{i^*(a)}{i(a,t)}\right)\left[\frac{\partial i(a,t)}{\partial a} + \left(\mu_1(a) + \gamma(a)\right)i(a,t)\right]. \tag{6.17}$$

We obtain from (6.13), (6.16) and (6.17) that

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} + S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(1 - \frac{S^{*}}{S(t)}\right)$$

$$-S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S^{*} \int_{0}^{\infty} \beta(a)i(a,t) da$$

$$-\int_{0}^{\infty} f_{1}(\theta)e^{*}(a) \frac{\partial}{\partial \theta} G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\right) d\theta$$

$$-\int_{0}^{\infty} f_{2}(a)i^{*}(a) \frac{\partial}{\partial a} G\left(\frac{i(a,t)}{i^{*}(a)}\right) da$$

$$+ k_{1} \int_{0}^{\infty} \gamma(a)i(a,t) da - k_{1}(\mu_{2} + \delta)T(t)$$

$$-k_{1} \frac{T^{*}}{T(t)} \int_{0}^{\infty} \gamma(a)i(a,t) da + k_{1}(\mu_{2} + \delta)T^{*}.$$
(6.18)

Using integration by parts, we have from (6.18)

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} + S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(1 - \frac{S^{*}}{S(t)}\right)
- S(t) \int_{0}^{\infty} \beta(a)i(a, t) da + S^{*} \int_{0}^{\infty} \beta(a)i(a, t) da
- f_{1}(\theta)e^{*}(\theta)G\left(\frac{e(\theta, t)}{e^{*}(\theta)}\right)\Big|_{0}^{\infty}
+ \int_{0}^{\infty} G\left(\frac{e(\theta, t)}{e^{*}(\theta)}\right)\Big[f'_{1}(\theta)e^{*}(\theta) + f_{1}(\theta)e^{*}'(\theta)\Big] d\theta
- f_{2}(a)i^{*}(a)G\left(\frac{i(a, t)}{i^{*}(a)}\right)\Big|_{0}^{\infty}
+ \int_{0}^{\infty} G\left(\frac{i(a, t)}{i^{*}(a)}\right)\Big[f'_{2}(a)i^{*}(a) + f_{2}(a)i^{*}'(a)\Big] da
+ k_{1} \int_{0}^{\infty} \gamma(a)i(a, t) da - k_{1}(\mu_{2} + \delta)T(t)
- k_{1} \frac{T^{*}}{T(t)} \int_{0}^{\infty} \gamma(a)i(a, t) da + k_{1}(\mu_{2} + \delta)T^{*}.$$
(6.19)

On substituting (6.16) and (6.17) into (6.19), it follows that

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} + S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(1 - \frac{S^{*}}{S(t)}\right) \\
- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S^{*} \int_{0}^{\infty} \beta(a)i(a,t) da \\
- f_{1}(\theta)e^{*}(\theta)G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\right)\Big|_{0}^{\infty} \\
+ \int_{0}^{\infty} G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\right) \Big[f'_{1}(\theta) - (\mu + \nu(\theta))f_{1}(\theta)\Big]e^{*}(\theta) d\theta \\
- f_{2}(a)i^{*}(a)G\left(\frac{i(a,t)}{i^{*}(a)}\right)\Big|_{0}^{\infty} \\
+ \int_{0}^{\infty} G\left(\frac{i(a,t)}{i^{*}(a)}\right) \Big[f'_{2}(a) - (\mu_{1}(a) + \gamma(a))f_{2}(a)\Big]i^{*}(a) da \\
+ k_{1} \int_{0}^{\infty} \gamma(a)i(a,t) da - k_{1}(\mu_{2} + \delta)T(t) \\
- k_{1} \frac{T^{*}}{T(t)} \int_{0}^{\infty} \gamma(a)i(a,t) da + k_{1}(\mu_{2} + \delta)T^{*}. \tag{6.20}$$

Choose

$$f_{1}(\theta) = A_{1} \int_{\theta}^{\infty} \nu(u) e^{-\int_{\theta}^{u} (\mu + \nu(s)) ds} du,$$

$$f_{2}(a) = \int_{a}^{\infty} \left(S^{*} \beta(u) + k_{1} \gamma(u) \right) e^{-\int_{a}^{u} (\mu_{1}(s) + \gamma(s)) ds} du,$$
(6.21)

where A_1 is determined in (6.6). Direct calculations show that

$$f_1(0) = 1, \qquad \lim_{\theta \to \infty} f_1(\theta) = 0,$$

$$f'_1(\theta) = (\mu + \nu(\theta))f_1(\theta) - A_1\nu(\theta),$$
(6.22)

and

$$f_{2}(0) = S^{*} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + k_{1} \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da,$$

$$f'_{2}(a) = (\mu_{1}(a) + \gamma(a))f_{2}(a) - (S^{*}\beta(a) + k_{1}\gamma(a)),$$

$$\lim_{a \to \infty} f_{2}(a) = 0.$$
(6.23)

On substituting (6.22) and (6.23) into (6.20), we have

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} + S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(1 - \frac{S^{*}}{S(t)}\right) \\
- S(t) \int_{0}^{\infty} \beta(a)i(a,t) da + S^{*} \int_{0}^{\infty} \beta(a)i(a,t) da \\
+ e(0,t) - e^{*}(0) - e^{*}(0) \ln \frac{e(0,t)}{e^{*}(0)} \\
- A_{1} \int_{0}^{\infty} \nu(\theta) \left(e(\theta,t) - e^{*}(\theta) - e^{*}(\theta) \ln \frac{e(\theta,t)}{e^{*}(\theta)}\right) d\theta \\
+ \left(S^{*} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da + k_{1} \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da\right) \\
\times \left(i(0,t) - i^{*}(0) - i^{*}(0) \ln \frac{i(0,t)}{i^{*}(0)}\right) \\
- \int_{0}^{\infty} \left(S^{*}\beta(a) + k_{1}\gamma(a)\right) \left(i(a,t) - i^{*}(a) - i^{*}(a) \ln \frac{i(a,t)}{i^{*}(a)}\right) da \\
+ k_{1} \int_{0}^{\infty} \gamma(a)i(a,t) da - k_{1}(\mu_{2} + \delta)T(t) \\
- k_{1} \frac{T^{*}}{T(t)} \int_{0}^{\infty} \gamma(a)i(a,t) da + k_{1}(\mu_{2} + \delta)T^{*}. \tag{6.24}$$

Choose $k_1 > 0$ satisfying

$$k_{1}(\mu_{2}+\delta) = p\delta\left(S^{*}\int_{0}^{\infty}\beta(a)\phi_{2}(a)\,da + k_{1}\int_{0}^{\infty}\gamma(a)\phi_{2}(a)\,da\right) + (1-p)\delta. \tag{6.25}$$

We derive from (1.5), (6.24) and (6.25) that

$$\begin{split} \frac{d}{dt}V_2(t) &= -\frac{\mu(S(t) - S^*)^2}{S(t)} + S^* \int_0^\infty \beta(a)i^*(a) \, da \left(1 - \frac{S^*}{S(t)}\right) \\ &- e^*(0) \ln \frac{e(0,t)}{e^*(0)} + A_1 \int_0^\infty \nu(\theta)e^*(\theta) \ln \frac{e(\theta,t)}{e^*(\theta)} \, d\theta \\ &- \left(S^* \int_0^\infty \beta(a)i^*(a) \, da + k_1 \int_0^\infty \gamma(a)i^*(a) \, da\right) \ln \frac{i(0,t)}{i^*(0)} \end{split}$$

$$+ \int_{0}^{\infty} \left(S^{*} \beta(a) + k_{1} \gamma(a) \right) i^{*}(a) \ln \frac{i(a,t)}{i^{*}(a)} da$$

$$- k_{1} \int_{0}^{\infty} \gamma(a) i^{*}(a) \frac{i(a,t) T^{*}}{i^{*}(a) T(t)} da + k_{1} (\mu_{2} + \delta) T^{*}.$$
(6.26)

It follows from the fourth equation of equations (3.1) and (6.26) that

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)}
- S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da\left(\frac{S^{*}}{S(t)} - 1 - \ln\frac{S^{*}}{S(t)}\right)
- k_{1} \int_{0}^{\infty} \gamma(a)i^{*}(a) \left(\frac{i(a,t)T^{*}}{i^{*}(a)T(t)} - 1 - \ln\frac{i(a,t)T^{*}}{i^{*}(a)T(t)}\right) da
+ A_{1} \int_{0}^{\infty} \nu(\theta)e^{*}(\theta) \ln\frac{e(\theta,t)}{e^{*}(\theta)} \frac{e^{*}(0)}{e(0,t)} d\theta
+ S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) \ln\frac{i(a,t)}{i^{*}(a)} \frac{S(t)}{S^{*}} \frac{i^{*}(0)}{i(0,t)} da
+ k_{1} \int_{0}^{\infty} \gamma(a)i^{*}(a) da \ln\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}}.$$
(6.27)

On substituting (3.4) into (6.27), one has

$$\frac{d}{dt}V_{2}(t) = -\frac{\mu(S(t) - S^{*})^{2}}{S(t)} \\
-S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \left(\frac{S^{*}}{S(t)} - 1 - \ln \frac{S^{*}}{S(t)}\right) \\
-k_{1} \int_{0}^{\infty} \gamma(a)i^{*}(a) \left(\frac{i(a,t)T^{*}}{i^{*}(a)T(t)} - 1 - \ln \frac{i(a,t)T^{*}}{i^{*}(a)T(t)}\right) da \\
+A_{1}S^{*} \int_{0}^{\infty} \beta(a)i^{*}(a) da \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) \ln \frac{e(\theta,t)}{e^{*}(\theta)} \frac{e^{*}(0)}{e(0,t)} d\theta \\
+A_{1} \frac{(1-p)\delta}{\mu_{2} + \delta} \int_{0}^{\infty} \gamma(a)i^{*}(a) da \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) \ln \frac{e(\theta,t)}{e^{*}(\theta)} \frac{e^{*}(0)}{e(0,t)} d\theta \\
+A_{1}S^{*} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \beta(a)i^{*}(a) \ln \frac{i(a,t)}{i^{*}(a)} \frac{S(t)}{S^{*}} \frac{i^{*}(0)}{i(0,t)} da \\
+k_{1}A_{1} \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta \int_{0}^{\infty} \gamma(a)i^{*}(a) da \ln \frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}}. \tag{6.28}$$

It follows from (6.25) and (6.28) that

$$\begin{split} \frac{d}{dt}V_2(t) &= -\frac{\mu(S(t) - S^*)^2}{S(t)} \\ &- S^* \int_0^\infty \beta(a)i^*(a) \, da \bigg(\frac{S^*}{S(t)} - 1 - \ln \frac{S^*}{S(t)} \bigg) \\ &- k_1 \int_0^\infty \gamma(a)i^*(a) \bigg(\frac{i(a,t)T^*}{i^*(a)T(t)} - 1 - \ln \frac{i(a,t)T^*}{i^*(a)T(t)} \bigg) \, da \\ &+ A_1 S^* \int_0^\infty \int_0^\infty \beta(a)i^*(a) \nu(\theta) \phi_1(\theta) \ln \frac{S(t)}{S^*} \frac{i(a,t)}{i^*(a)} \frac{e^*(0)}{e(0,t)} \, d\theta \, da \end{split}$$

$$\begin{split} &+A_{1}S^{*}\int_{0}^{\infty}\int_{0}^{\infty}\beta(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\ln\frac{e(\theta,t)}{e^{*}(\theta)}\frac{i^{*}(0)}{i(0,t)}d\theta\,da\\ &+A_{1}\frac{(1-p)\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\gamma(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\ln\frac{T(t)}{T^{*}}\frac{e^{*}(0)}{e(0,t)}d\theta\,da\\ &+A_{1}\frac{(1-p)\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\gamma(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\ln\frac{e(\theta,t)}{T^{*}}\frac{i^{*}(0)}{e(0,t)}d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}S^{*}\int_{0}^{\infty}\beta(a)\phi_{2}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)\,d\theta\\ &\times\int_{0}^{\infty}\gamma(a)i^{*}(a)\,da\ln\frac{i^{*}(0)}{i(0,t)}\frac{T(t)}{T^{*}}\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}k_{1}\int_{0}^{\infty}\gamma(a)\phi_{2}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)\,d\theta\\ &\times\int_{0}^{\infty}\gamma(a)i^{*}(a)\,da\ln\frac{i^{*}(0)}{i(0,t)}\frac{T(t)}{T^{*}}\\ &=-\frac{\mu(S(t)-S^{*})^{2}}{S(t)}-S^{*}\int_{0}^{\infty}\beta(a)i^{*}(a)\,daG\left(\frac{S^{*}}{S(t)}\right)\\ &-k_{1}\int_{0}^{\infty}\gamma(a)i^{*}(a)\,da\int_{0}^{\infty}\gamma(\theta)\phi_{1}(\theta)\,d\theta\left(\frac{S(t)}{S^{*}}\frac{i(a,t)}{i^{*}(a)}\frac{e^{*}(0)}{e(0,t)}\right)\,da\\ &-A_{1}S^{*}\int_{0}^{\infty}\beta(a)i^{*}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\frac{i^{*}(0)}{i(0,t)}\right)\,d\theta\\ &-A_{1}\frac{(1-p)\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\gamma(a)i^{*}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\frac{i^{*}(0)}{i(0,t)}\right)\,d\theta\\ &-A_{1}\frac{1(1-p)\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\gamma(a)i^{*}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)G\left(\frac{e(\theta,t)}{e^{*}(\theta)}\frac{i^{*}(0)}{i(0,t)}\right)\,d\theta\\ &\times\int_{0}^{\infty}\gamma(a)i^{*}(a)\,daG\left(\frac{i^{*}(0)}{i(0,t)}\frac{T(t)}{T^{*}}\right)\\ &-A_{1}\frac{p\delta}{\mu_{2}+\delta}k_{1}\int_{0}^{\infty}\gamma(a)\phi_{2}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)\,d\theta\\ &\times\int_{0}^{\infty}\gamma(a)i^{*}(a)\,daG\left(\frac{i^{*}(0)}{i(0,t)}\frac{T(t)}{T^{*}}\right)\\ &+A_{1}S^{*}\int_{0}^{\infty}\beta(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\left(\frac{S(t)}{S^{*}}\frac{i(a,t)}{i^{*}(a)}\frac{e^{*}(0)}{e^{*}(0,t)}\right)\,d\theta\,da\\ &+A_{1}S^{*}\int_{0}^{\infty}\beta(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\left(\frac{e(\theta,t)}{S^{*}}\frac{i^{*}(0)}{i(0,t)}-1\right)\,d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\beta(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\left(\frac{e(\theta,t)}{S^{*}}\frac{i^{*}(0)}{i(0,t)}-1\right)\,d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\gamma(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\left(\frac{e(\theta,t)}{S^{*}}\frac{i^{*}(0)}{i(0,t)}-1\right)\,d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\gamma(a)i^{*}(a)v(\theta)\phi_{1}(\theta)\left(\frac{e(\theta,t)}{S^{*}}\frac{i^{*}(0)}{i(0,t)}-1\right)\,d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\int_{0}^{\infty}\beta(a)\phi_{2}(a)\,da\int_{0}^{\infty}v(\theta)\phi_{1}(\theta)\left(\frac{e(\theta,t)}{S^{*}}\frac{i^{*}(0)}{i(0,t)}-1\right)\,d\theta\,da\\ &+A_{1}\frac{p\delta}{\mu_{2}+\delta}\int_{0}^{\infty}\beta(a)\phi$$

$$\times \int_{0}^{\infty} \gamma(a) i^{*}(a) da \left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}} - 1 \right)
+ A_{1} \frac{p\delta}{\mu_{2} + \delta} k_{1} \int_{0}^{\infty} \gamma(a) \phi_{2}(a) da \int_{0}^{\infty} \nu(\theta) \phi_{1}(\theta) d\theta
\times \int_{0}^{\infty} \gamma(a) i^{*}(a) da \left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}} - 1 \right).$$
(6.29)

After some algebra, we have from (1.5)

$$A_{1}S^{*} \int_{0}^{\infty} \int_{0}^{\infty} \beta(a)i^{*}(a)\nu(\theta)\phi_{1}(\theta) \left(\frac{S(t)}{S^{*}} \frac{i(a,t)}{i^{*}(a)} \frac{e^{*}(0)}{e(0,t)} - 1\right) d\theta da$$

$$+ A_{1}S^{*} \int_{0}^{\infty} \int_{0}^{\infty} \beta(a)i^{*}(a)\nu(\theta)\phi_{1}(\theta) \left(\frac{e(\theta,t)}{e^{*}(\theta)} \frac{i^{*}(0)}{i(0,t)} - 1\right) d\theta da$$

$$+ A_{1} \frac{(1-p)\delta}{\mu_{2} + \delta} \int_{0}^{\infty} \int_{0}^{\infty} \gamma(a)i^{*}(a)\nu(\theta)\phi_{1}(\theta) \left(\frac{T(t)}{T^{*}} \frac{e^{*}(0)}{e(0,t)} - 1\right) d\theta da$$

$$+ A_{1} \frac{(1-p)\delta}{\mu_{2} + \delta} \int_{0}^{\infty} \int_{0}^{\infty} \gamma(a)i^{*}(a)\nu(\theta)\phi_{1}(\theta) \left(\frac{e(\theta,t)}{e^{*}(\theta)} \frac{i^{*}(0)}{i(0,t)} - 1\right) d\theta da$$

$$+ A_{1} \frac{p\delta}{\mu_{2} + \delta} S^{*} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta$$

$$\times \int_{0}^{\infty} \gamma(a)i^{*}(a) da \left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}} - 1\right)$$

$$+ A_{1} \frac{p\delta}{\mu_{2} + \delta} k_{1} \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta$$

$$\times \int_{0}^{\infty} \gamma(a)i^{*}(a) da \left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}} - 1\right)$$

$$= \left(A_{1} - S^{*} \int_{0}^{\infty} \beta(a)\phi_{2}(a) da - k_{1} \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da\right) i^{*}(0)$$

$$= 0. \tag{6.30}$$

It therefore follows from (6.29) and (6.30) that

$$\begin{split} \frac{d}{dt}V_2(t) &= -\frac{\mu(S(t)-S^*)^2}{S(t)} - S^* \int_0^\infty \beta(a)i^*(a) \, daG\bigg(\frac{S^*}{S(t)}\bigg) \\ &- k_1 \int_0^\infty \gamma(a)i^*(a)G\bigg(\frac{i(a,t)T^*}{i^*(a)T(t)}\bigg) \, da \\ &- A_1 S^* \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta \int_0^\infty \beta(a)i^*(a)G\bigg(\frac{S(t)}{S^*}\frac{i(a,t)}{i^*(a)}\frac{e^*(0)}{e(0,t)}\bigg) \, da \\ &- A_1 S^* \int_0^\infty \beta(a)i^*(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta)G\bigg(\frac{e(\theta,t)}{e^*(\theta)}\frac{i^*(0)}{i(0,t)}\bigg) \, d\theta \\ &- A_1 \frac{(1-p)\delta}{\mu_2 + \delta} \int_0^\infty \gamma(a)i^*(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta \, G\bigg(\frac{T(t)}{T^*}\frac{e^*(0)}{e(0,t)}\bigg) \\ &- A_1 \frac{(1-p)\delta}{\mu_2 + \delta} \int_0^\infty \gamma(a)i^*(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta) \, G\bigg(\frac{e(\theta,t)}{e^*(\theta)}\frac{i^*(0)}{i(0,t)}\bigg) \, d\theta \\ &- A_1 \frac{p\delta}{\mu_2 + \delta} S^* \int_0^\infty \beta(a)\phi_2(a) \, da \int_0^\infty \nu(\theta)\phi_1(\theta) \, d\theta \end{split}$$

$$\times \int_{0}^{\infty} \gamma(a)i^{*}(a) daG\left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}}\right)
-A_{1} \frac{p\delta}{\mu_{2} + \delta} k_{1} \int_{0}^{\infty} \gamma(a)\phi_{2}(a) da \int_{0}^{\infty} \nu(\theta)\phi_{1}(\theta) d\theta
\times \int_{0}^{\infty} \gamma(a)i^{*}(a) daG\left(\frac{i^{*}(0)}{i(0,t)} \frac{T(t)}{T^{*}}\right).$$
(6.31)

The function $G(x) = x - 1 - \ln x \ge 0$ for all x > 0 and G(x) = 0 holds iff x = 1. Hence, $V_2'(t) \le 0$ holds if $\mathcal{R}_0 > 1$. It is readily seen from (6.31) that $V_2'(t) = 0$ if and only if

$$S(t) = S^*, \qquad \frac{i(a,t)T^*}{i^*(a)T(t)} = 1, \qquad \frac{S(t)}{S^*} \frac{i(a,t)}{i^*(a)} \frac{e^*(0)}{e(0,t)} = 1,$$

$$\frac{T(t)}{T^*} \frac{e^*(0)}{e(0,t)} = 1, \qquad \frac{e(\theta,t)}{e^*(\theta)} \frac{i^*(0)}{i(0,t)} = 1, \qquad \frac{i^*(0)}{i(0,t)} \frac{T(t)}{T^*} = 1,$$

$$(6.32)$$

for all $\theta \ge 0$, $a \ge 0$. It is easy to verify that the largest invariant subset of $\{V_2'(t) = 0\}$ is the singleton E^* . By Theorem 4.1, we see that if $\mathcal{R}_0 > 1$, E^* is locally asymptotically stable. Therefore, using LaSalle's invariance principle, we see that if $\mathcal{R}_0 > 1$, the global asymptotic stability of E^* follows. This completes the proof.

7 Discussion

In this work, a tuberculosis infection model with incomplete treatment and age structure for latently infected and infectious individuals has been investigated. By calculations, the basic reproduction number has been established. A complete mathematical analysis has been performed to show that the global dynamics of system (1.4) with boundary conditions (1.5) is completely determined by the basic reproduction number. By constructing suitable Lyapunov functionals and using LaSalle's invariance principle, it has been shown that if the basic reproduction number is less than unity, the disease-free steady state is globally asymptotically stable and the disease dies out; if the basic reproduction number is greater than unity, the endemic steady state is globally asymptotically stable and the disease persists. The global stability of the endemic steady state rules out any possibility for the existence of Hopf bifurcations and sustained oscillations in system (1.4).

From the expression of \mathcal{R}_0 , we see that the recruitment rate A, the per-capita natural death rate μ , the rate δ at which a treated individual leaves the treated compartment, the death rate μ_2 of the treated individuals, the transmission rate $\beta(a)$ of the infectious individuals, the proportion p of the newly infected to develop tuberculosis directly, the proportion 1-p of the newly infected to enter the latent class, the rate $v(\theta)$ at which individuals who have been in the exposed compartment for duration θ , progress to the infectious compartment, the remove rate $\mu_1(a)$ of infectious compartment and the recovery rate $\gamma(a)$ do affect the value of the basic reproduction number. To control the disease, a strategy should reduce the basic reproduction number to below unity. From the expression of the basic reproduction number, deceasing the recruitment rate, the transmission rate of the infectious individuals and the rate of a treated individual leaving the treated compartment and increasing the per-capita natural death rate and the death rate of the treated individuals are helpful in controlling measles by decreasing the basic reproduction number.

Acknowledgements

The authors wish to thank the editor and the reviewers for their valuable comments and suggestions that greatly improved the presentation of this work. This work was supported by the National Natural Science Foundation of China (Nos. 11371368, 11071254, 11371313), the Natural Science Foundation of Hebei Province (No. A2014506015) and the Natural Science Foundation of Young Scientist of Hebei Province (No. A2013506012).

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

The main idea of this paper was proposed by RX. RX and XT carried out the theoretical calculation and drafted the manuscript. FZ participated in the theoretical calculation and helped to draft the manuscript. All authors read and approved the final manuscript.

Author details

¹Institute of Applied Mathematics, Shijiazhuang Mechanical Engineering College, Shijiazhuang, Hebei 050003, P.R. China. ²Department of Applied Mathematics, Yuncheng University, Yuncheng, Shanxi 044000, P.R. China.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 31 March 2017 Accepted: 25 July 2017 Published online: 17 August 2017

References

- Brewer, TF, Heymann, SJ: To control and beyond: moving towards eliminating the global tuberculosis threat.
 J. Epidemiol. Community Health 58, 822-825 (2004)
- World Health Organization: Global tuberculosis report 2016, WHO report 2016, World Health Organization, Geneva (2016)
- 3. Chin, J: Control of Communicable Diseases Manual. American Public Health Association, Washington (1999)
- 4. Martin, SW: Livestock Disease Eradication: Evaluation of the Cooperative State-Federal Bovine Tuberculosis Eradication Program. National Academy Press, Washington (1994)
- VanLandingham, KE, Marsteller, HB, Ross, GW, Hayden, FG: Relapse of herpes simplex encephalitis after conventional acyclovir therapy. JAMA 259, 1051-1053 (1988)
- 6. van den Driessche, P, Wang, L, Zou, X: Modeling diseases with latency and relapse. Math. Biosci. Eng. 4, 205-219
- Aparicio, JP, Capurro, AF, Castillo-Chavez, C: Transmission and dynamics of tuberculosis on generalized households. J. Theor. Biol. 206, 327-341 (2000)
- 8. Aparicio, JP, Capurro, AF, Castillo-Chavez, C: Markers of disease evolution: the case of tuberculosis. J. Theor. Biol. 215, 227-237 (2002)
- 9. Aparicio, JP, Castillo-Chavez, C: Mathematical modelling of tuberculosis epidemics. Math. Biosci. Eng. **6**, 209-237 (2009)
- Blower, SM, McLean, AR, Porco, TC, Small, PM, Hopwell, PC, Sanchez, MA, Moss, AR: The intrinsic transmission dynamics of tuberculosis epidemics. Nat. Med. 1, 815-821 (1995)
- Blower, SM, Small, PM, Hopewell, PC: Control strategies for tuberculosis epidemics: new models for old problems. Science 273, 497-500 (1996)
- 12. Blower, SM, Tom, C: Modeling the emergence of the 'hot zones' tuberculosis and the amplification dynamics of drug resistance. Nat. Med. 10, 1111-1116 (2004)
- 13. Castillo-Chavez, C, Feng, Z: To treat or not to treat: the case of tuberculosis. J. Math. Biol. 35, 629-656 (1997)
- 14. Castillo-Chavez, C, Song, B: Dynamical models of tuberculosis and their applications. Math. Biosci. Eng. 1(2), 361-404 (2004)
- 15. Dye, C, Williams, BG: Criteria for the control of drug-resistant tuberculosis. Proc. Natl. Acad. Sci. USA **97**, 8180-8185 (2000)
- Feng, Z, Castillo-Chavez, C, Capurro, AF: A model for tuberculosis with exogenous reinfection. Theor. Popul. Biol. 57, 235-247 (2000)
- 17. Feng, Z, Huang, W, Castillo-Chavez, C: On the role of variable latent periods in mathematical models for tuberculosis. J. Dyn. Differ. Equ. 13, 425-452 (2001)
- Feng, Z, lannelli, M, Milner, FA: A two-strain tuberculosis model with age of infection. SIAM J. Appl. Math. 62, 1634-1656 (2002)
- 19. Miller, B: Preventive therapy for tuberculosis. Med. Clin. North Am. 77, 1263-1275 (1993)
- 20. Ozcaglar, C, Shabbeer, A, Vandenberg, SL, Yener, B, Bennett, KP: Epidemiological models of Mycobacterium tuberculosis complex infections. Math. Biosci. 236, 77-96 (2012)
- Rodrigues, P, Gomes, MGM, Rebelo, C: Drug resistance in tuberculosis: a reinfection model. Theor. Popul. Biol. 71, 196-212 (2007)
- 22. Ted, C, Megan, M: Modeling epidemics of multidrug resistant M. tuberculosis of heterogeneous fitness. Nat. Med. 10, 1117-1121 (2004)
- 23. Yang, Y, Li, J, Ma, Z, Liu, L: Global stability of two models with incomplete treatment for tuberculosis. Chaos Solitons Fractals 43, 79-85 (2010)
- 24. McCluskey, CC: Global stability for an SEI epidemiological model with continuous age-structure in the exposed and infectious classes. Math. Biosci. Eng. 9, 819-841 (2012)
- 25. Yang, J, Qiu, Z, Li, X: Global stability of an age-structured cholera model. Math. Biosci. Eng. 11, 641-665 (2014)

- 26. Corbett, E, Watt, C, Walker, N, Maher, D, Williams, B, Raviglione, M, Dye, C: The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch. Intern. Med. 163, 1009-1021 (2003)
- 27. Guo, H, Li, MY, Shuai, Z: Global dynamics of a general class of multistage models for infectious diseases. SIAM J. Appl. Math. 72, 261-279 (2012)
- 28. Lawn, S, Wood, R, Wilkinson, R: Changing concepts of 'latent tuberculosis infection' in patients living with HIV infection. Clin. Dev. Immunol. 2011, 980594 (2011)
- Brauer, F, Shuai, Z, van den Driessche, P: Dynamics of an age-of-infection cholera model. Math. Biosci. Eng. 10, 1335-1349 (2013)
- 30. Chen, Y, Yang, J, Zhang, F: The global stability of an SIRS model with infection age. Math. Biosci. Eng. 11, 449-469 (2014)
- Duan, X, Yuan, S, Li, X: Global stability of an SVIR model with age of vaccination. Appl. Math. Comput. 226, 528-540 (2014)
- 32. Duan, X, Yuan, S, Qiu, Z, Ma, J: Global stability of an SVEIR epidemic model with ages of vaccination and latency. Comput. Math. Appl. 68, 288-308 (2014)
- Ducrot, A, Magal, P: Travelling wave solutions for an infection-age structured epidemic model with external supplies. Nonlinearity 24, 2891-2911 (2011)
- 34. Magal, P, McCluskey, CC, Webb, GF: Lyapunov functional and global asymptotic stability for an infection-age model. Appl. Anal. 89, 1109-1140 (2010)
- 35. Yang, J, Li, X, Martcheva, M: Global stability of a DS-DI epidemic model with age of infection. J. Math. Anal. Appl. 385, 655-671 (2012)
- 36. lannelli, M: Mathematical Theory of Age-Structured Population Dynamics. Applied Mathematics Monographs, vol. 7, Comitato Nazionale per le Scienze Matematiche, Consiglio Nazionale delle Ricerche (C.N.R.), pp. 1-41. Giardini, Pisa (1995)
- 37. Webb, G: Theory of Nonlinear Age-Dependent Population Dynamics. Dekker, New York (1985)
- 38. Smith, HL, Thieme, HR: Dynamical Systems and Population Persistence. AMS, Providence (2011)
- 39. van den Driessche, P, Watmough, J: Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math. Biosci. 180, 29-48 (2002)
- 40. Browne, C: Immune response in virus model structured by cell infection-age. Math. Biosci. Eng. 13, 887-909 (2013)
- 41. Hale, JK, Waltman, P: Persistence in infinite dimensional systems. SIAM J. Math. Anal. 20, 388-395 (1989)

Submit your manuscript to a SpringerOpen journal and benefit from:

- ► Convenient online submission
- ► Rigorous peer review
- ▶ Open access: articles freely available online
- ► High visibility within the field
- ► Retaining the copyright to your article

Submit your next manuscript at ▶ springeropen.com