Global dynamics of an age-structured cholera model with multiple transmissions, saturation incidence and imperfect vaccination

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ABSTRACT
In this paper, an age-structured cholera model with multiple transmissions, saturation incidence and imperfect vaccination is proposed. In the model, we consider both the infection age of infected individuals and the biological age of Vibrio cholerae in the aquatic environment. Asymptotic smoothness is verified as a necessary argument. By analysing the characteristic equations, the local stability of disease-free and endemic steady states is established. By using Lyapunov functionals and LaSalle’s invariance principle, it is proved that the global dynamics of the model can be completely determined by basic reproduction number. The study of optimal control helps us seek cost-effective solutions of time-dependent vaccination strategy against cholera outbreaks. Numerical simulations are carried out to illustrate the corresponding theoretical results.

1. Introduction
Cholera is an acute disease caused by Vibrio cholerae O-group 1 or O-group 139, which can give rise to acute diarrhoea and vomit. The World Health Organization (WHO) estimates that there are 1.3–4 million cholera cases per year with about 21,000–143,000 deaths all over the world. Beginning in April 2017, a major cholera epidemic occurred in Yemen, with about 500,000 reported cases and 2000 deaths [29]. In order to better understand the transmission dynamics of cholera and provide some valuable insights on the prevention and control, some cholera models have been proposed (see, for example, [15, 19, 24, 25, 30]). In [25], Tien and Earn pointed out that new infections arise both through exposure to contaminated water (indirect transmission), as well as by human-to-human transmission pathway (direct transmission).

In [10], Hartley et al. found that short-lived, hyperinfectious state of vibrios decay in a matter of hours into a state of lower infectiousness and incorporated this hyperinfectious state into a cholera model to provide a much better fit with the observed epidemic pattern of cholera. Besides, Neilan et al. [18] formulated a mathematical model to include two...
classes of bacterial concentrations, one is hyperinfectious and another is less-infectious. Furthermore, in [17], Mukandavire et al. considered that human-to-human transmission is assumed to be a very fast transmission process with a lower infectious dose as a result of immediate water or food contamination by hyperinfectious vibrios from freshly passed human stool. Besides, Mukandavire et al. pointed out that if vibrios have been in the environment for a sufficiently long period (anywhere from 5 to 18 h), they are no longer hyperinfectious [17], namely, in a hypoinfectious state.

However, it was assumed in the models mentioned above that direct and indirect transmission rates, recovery rate of infected individuals, the contribution rate of each infected individual to the concentration of \( V. cholerae \) and net death rate of \( V. cholerae \) are invariant with time. In [1], Brauer et al. considered the following age-structured choleramodel:

\[
\begin{align*}
\frac{dS(t)}{dt} &= A - \mu S(t) - S(t) \int_0^\infty \beta_1(a) i(a,t) \, da - S(t) \int_0^\infty \beta_2(b) p(b,t) \, db, \\
\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} &= -\theta(a)i(a,t), \quad a > 0, \\
\frac{\partial p(b,t)}{\partial t} + \frac{\partial p(b,t)}{\partial b} &= -\delta_b(b)p(b,t), \quad b > 0,
\end{align*}
\]

with the boundary conditions

\[
\begin{align*}
i(0,t) &= S(t) \int_0^\infty \beta_1(a) i(a,t) \, da + S(t) \int_0^\infty \beta_2(b) p(b,t) \, db, \quad t > 0, \\
p(0,t) &= \int_0^\infty \xi(a)i(a,t) \, da, \quad t > 0,
\end{align*}
\]

where corresponding variables and parameters in system (1) are described in Table 1. System (1) was also investigated by Yang and Qiu [26] and Wang and Zhang [27].

It was assumed in [1] that incidence rates are bilinear, which regards the infection rate per density of infected individuals or per concentration of \( V. cholerae \) as a constant. Actually, incidence rate is influenced by the inhibition effect from behavioural change of susceptible individuals and the crowding effect of vibrios. In [4], Capasso and Serio introduced a saturation incidence rate \( \beta I/(1 + \alpha I) \), where \( \beta I \) measures the infection force of the disease and \( 1/(1 + \alpha I) \) measures the inhibition effect and the crowding effect. There have been several works on cholera models with saturation incidence in the literature (see, for example, [5,20]). As for the infection rate for per concentration of \( V. cholerae \), experimental studies [21] indicated that the probability of infection depends on the concentration of vibrios in the contaminated water. In [6], Codeço introduced a new form \( \beta P/(k + P) \) to measure the effect of saturation, where \( \beta \) is the contact rate with contaminated water and \( P/(k + P) \) is the probability of individuals to develop cholera. This saturation incidence form has been used in some cholera models (see, for example, [19,24,30,31]).

To prevent and control cholera, some preventive strategies, such as vaccination, have been widely used in several cholera outbreaks and gained great efficiencies. The availability of effective oral cholera vaccines have renewed interests in the use of vaccines for cholera control with overwhelming evidence supporting their effectiveness in endemic settings [22]. In 2010, WHO recommended the use of vaccines in cholera endemic settings and preemptively during outbreaks. In [19], Posny et al. presented a cholera epidemiological
model with three types of control measures: vaccination, treatment and sanitation, which is described by the following system:

\[
\begin{align*}
\frac{dS(t)}{dt} &= \mu N - (1 - \rho) \left[ \frac{\beta_e P(t)}{k + P(t)} + \beta_h I(t) \right] S(t) - (\phi + \mu) S(t), \\
\frac{dV(t)}{dt} &= \phi S(t) - \sigma (1 - \rho) \left[ \frac{\beta_e P(t)}{k + P(t)} + \beta_h I(t) \right] V(t) - \mu V(t), \\
\frac{dI(t)}{dt} &= (1 - \rho) \left[ \frac{\beta_e P(t)}{k + P(t)} + \beta_h I(t) \right] (S(t) + \sigma V(t)) - (\tau + \gamma + \mu) I(t), \\
\frac{dR(t)}{dt} &= (\tau + \gamma) I(t) - \mu R(t), \\
\frac{dP(t)}{dt} &= \xi I(t) - (\delta + \nu) P(t),
\end{align*}
\]

where \( S(t), V(t), I(t) \) and \( R(t) \) denote the densities of susceptible individuals, vaccinated individuals, infected individuals and recovered individuals, respectively. While, \( P(t) \) denotes the concentration of \( V.\ cholerae \). \( N \) is the total population and all individuals are born and die naturally at rate \( \mu \). Susceptible or vaccinated individuals acquire cholera infection either by ingesting environmental vibrios from contaminated aquatic reservoirs or through human-to-human transmission, at rates \( \lambda_e = (1 - \rho)\beta_e P/(k + P) \) and \( \lambda_h = (1 - \rho)\beta_h I \), respectively. Here, \( \rho = \epsilon p \) is the sanitation-induced preventability to cholera infection which is a product of the sanitation efficacy \( \epsilon \) and compliance \( p \). Susceptible individuals are vaccinated at a rate \( \phi \), while, the vaccine has a degree of losing protection efficacy that is denoted by \( \sigma \). Infected individuals are treated at a rate \( \tau \), and some recover
naturally at a rate $\gamma$. Infected individuals contribute to $V.\ \text{cholerae}$ in the aquatic environment at a rate $\xi$, and vibrios have a net death rate $\delta$. In addition, water sanitation leads to the death of vibrios at a rate $\nu$.

Motivated by the works of Posny et al. [19], Brauer et al. [1] and Capasso and Serio [4], in the present paper, we are concerned with both human-to-human and environment-to-human transmissions, saturation incidence and imperfect vaccination on the transmission dynamics of cholera. To this end, we consider the following differential equations:

$$\frac{dS(t)}{dt} = A - (\mu + \phi) S(t) - S(t) \left( \int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db \right),$$

$$\frac{dV(t)}{dt} = \phi S(t) - \mu V(t) - \sigma V(t) \left( \int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db \right),$$

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

$$\frac{dR(t)}{dt} = \int_0^\infty \gamma(a)i(a,t) \, da - \mu R(t),$$

$$\frac{\partial p(b,t)}{\partial t} + \frac{\partial p(b,t)}{\partial b} = -\delta_p p(b,t),$$

with the boundary conditions

$$i(0,t) = (S(t) + \sigma V(t)) \left( \int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db \right), \quad t > 0,$$

$$p(0,t) = \int_0^\infty \xi(a)i(a,t) \, da, \quad t > 0,$$

and the initial condition

$$S(0) = S_0 > 0, \quad V(0) = V_0 > 0, \quad i(a,0) = i_0(a) \in L^1_+(0,\infty),$$

$$R(0) = R_0 > 0, \quad p(b,0) = p_0(b) \in L^1_+(0,\infty),$$

where $L^1_+(0,\infty)$ is the space of functions on $(0,\infty)$ that are positive and Lebesgue integrable. In system (3), the infection rate of infected individuals is given by saturation infection rate $\beta_1(a)i(a,t)/[1 + \alpha i(a,t)]$, where $\alpha$ is the saturation infection rate coefficient. Besides, the infection rate for per concentration of $V.\ \text{cholerae}$ takes the form $\beta_2(b)p(b,t)/[k + p(b,t)]$, where $k$ is the concentration of $V.\ \text{cholerae}$ in contaminated water that yields 50% chance of catching cholera. Corresponding flowchart of cholera transmission in system (3) is depicted in Figure 1. Variables and parameters in system (3) are described in Table 1. Thereinto, $A, \mu, \alpha$ and $k$ are nonnegative and bounded, while $\phi$ and $\sigma$ are nonnegative and less than unity. Denote function space $X = \mathbb{R}^+ \times \mathbb{R}^+ \times L^1_+(0,\infty) \times \mathbb{R}^+ \times L^1_+(0,\infty)$, equipped with the norm

$$\| (x,y,\psi,z,\zeta) \|_X = x + y + \int_0^\infty \psi(a) \, da + z + \int_0^\infty \zeta(b) \, db.$$
Figure 1. Flowchart of cholera transmission in system (3).

\( \mathcal{X} \), which takes the form \( \Phi(t, x_0) = \Phi_t(x_0) = (S(t), V(t), i(\cdot, t), R(t), p(\cdot, t)), t \geq 0, x_0 = (S_0, V_0, i_0(\cdot), R_0, p_0(\cdot)) \in \mathcal{X} \) with

\[
\| \Phi_t(x_0) \|_{\mathcal{X}} = \| (S(t), V(t), i(\cdot, t), R(t), p(\cdot, t)) \|_{\mathcal{X}} = S(t) + V(t) + \int_{0}^{\infty} i(a, t) \, da + R(t) + \int_{0}^{\infty} p(b, t) \, db.
\]  

(6)

This paper is organized as follows. In Section 2, some preliminaries are given for later analysis. In Section 3, we investigate the asymptotic smoothness of the semi-flow \( \{\Phi(t)\}_{t \geq 0} \). Next, we study the existence of disease-free and endemic steady states and calculate basic reproduction number in Section 4. In Section 5, the local asymptotic stability of each of steady states is established by analysing the distribution of roots of characteristic equations. In Section 6, we discuss the global asymptotic stability of each of steady states by using suitable Lyapunov functionals and LaSalle’s invariance principle. We carry out a study of optimal control to seek cost-effective solutions of control strategies for cholera in Section 7. In Section 8, we present numerical simulations to illustrate theoretical results and obtain the optimal control solution by Forward-Backward Sweep Method. The paper ends with a conclusion in Section 9.

2. Preliminaries

Before analysing the global dynamics of system (3), we make the following reasonable assumptions based on biological significance, which hold throughout the paper.

(H1) \( \beta_1(a), \beta_2(b), \theta(a), \gamma(a), \delta_p(b), \xi(a) \in L^1_{+}(0, \infty) \), with essential upper bounds \( \bar{\beta}_1, \bar{\beta}_2, \bar{\theta}, \bar{\gamma}, \bar{\delta}_p, \bar{\xi} \), respectively, i.e.,

\[
\bar{\beta}_1 = \text{ess. sup}_{a \in (0, \infty)} \beta_1(a) < \infty, \quad \bar{\beta}_2 = \text{ess. sup}_{b \in (0, \infty)} \beta_2(b) < \infty, \quad \bar{\theta} = \text{ess. sup}_{a \in (0, \infty)} \theta(a) < \infty,
\]

\[
\bar{\gamma} = \text{ess. sup}_{a \in (0, \infty)} \gamma(a) < \infty, \quad \bar{\delta}_p = \text{ess. sup}_{b \in (0, \infty)} \delta_p(b) < \infty, \quad \bar{\xi} = \text{ess. sup}_{a \in (0, \infty)} \xi(a) < \infty;
\]

(H2) There exists a \( \mu_0 \) such that \( \delta_p(b) > \mu \geq \mu_0 > 0 \), for all \( b \geq 0 \).
Denote
\[ \rho_1(a) = \exp \left( - \int_0^a \theta(e) \, de \right), \quad \rho_2(b) = \exp \left( - \int_0^b \delta_p(e) \, de \right), \]
\[ f_1(t) = \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + a i(a, t)} \, da, \quad f_2(t) = \int_0^\infty \frac{\beta_2(b) p(b, t)}{k + p(b, t)} \, db. \]

From [28], solving the PDE parts of system (3) along the characteristic lines \( t - a = \text{const.} \) and \( t - b = \text{const.} \) yields

\[
i(a, t) = \begin{cases} 
\rho_1(a) (S(t - a) + \sigma V(t - a)) (f_1(t - a) + f_2(t - a)), & t > a \geq 0, \\
\frac{\rho_1(a)}{\rho_1(a - t)} i_0(a - t), & a \geq t \geq 0,
\end{cases}
\]

(7)

\[ p(b, t) = \begin{cases} 
\rho_2(b) \int_0^\infty \xi(a) i(a, t - b) \, da, & t > b \geq 0, \\
\frac{\rho_2(b)}{\rho_2(b - t)} p_0(b - t), & b \geq t \geq 0.
\end{cases}
\]

(8)

Denote
\[ \Omega = \left\{ (x, y, \psi, z, \xi) \in \mathcal{X} \mid \| (x, y, \psi, z, \xi) \|_{\mathcal{X}} \leq \frac{A}{\tilde{\mu}_0} \right\}, \]

where \( \tilde{\mu}_0 = \mu_0 / (1 + \tilde{\xi} / \mu_0) \).

**Proposition 2.1:** For system (3), we have

(a) \( \Omega \) is positively invariant for \( \Phi \), that is, \( \Phi(t, x_0) \in \Omega \), for \( \forall t \geq 0, x_0 \in \Omega \);
(b) \( \Phi \) is point dissipative and \( \Omega \) attracts all points in \( \mathcal{X} \).

**Proof:** From (6), we obtain that

\[ \frac{d}{dt} \| \Phi_t(x_0) \|_{\mathcal{X}} = \frac{d}{dt} \| S(t) \|_{\mathcal{X}} + \frac{d}{dt} \| V(t) \|_{\mathcal{X}} + \frac{d}{dt} \int_0^\infty i(a, t) \, da + \frac{d}{dt} \int_0^\infty p(b, t) \, db. \]

It follows from (7) that

\[ \frac{d}{dt} \int_0^\infty i(a, t) \, da = \frac{d}{dt} \int_0^t \rho_1(a) (S(t - a) + \sigma V(t - a)) (f_1(t - a) + f_2(t - a)) \, da \\
+ \frac{d}{dt} \int_t^\infty \frac{\rho_1(a)}{\rho_1(a - t)} i_0(a - t) \, da \\
= \frac{d}{dt} \int_0^t \rho_1(t - \tau) (S(\tau) + \sigma V(\tau)) (f_1(\tau) + f_2(\tau)) \, d\tau \\
+ \frac{d}{dt} \int_0^\infty \frac{\rho_1(t + \tau)}{\rho_1(\tau)} i_0(\tau) \, d\tau \\
= \rho_1(0) (S(t) + \sigma V(t)) (f_1(t) + f_2(t)). \]
\[ + \int_0^t (S(t - a) + \sigma V(t - a)) \left( f_1(t - a) + f_2(t - a) \right) \frac{d}{da} \rho_1(a) \, da \\
+ \int_t^\infty \frac{i_0(a - t)}{\rho_1(a - t)} \, d\rho_1(a) \, da. \]

Noting that \( \rho_1(0) = 1 \) and \( d\rho_1(a)/da = -\theta(a)\rho_1(a) \), we have
\[
\frac{d}{dt} \int_0^\infty i(a, t) \, da = (S(t) + \sigma V(t)) \left( f_1(t) + f_2(t) \right) - \int_0^\infty \theta(a)i(a, t) \, da. \tag{9} \]

Similarly, we obtain
\[
\frac{d}{dt} \int_0^\infty p(b, t) \, db = \int_0^\infty \xi(a)i(a, t) \, da - \int_0^\infty \delta_p(b)p(b, t) \, db. \tag{10} \]

From (9) and the first two equations of (3), we get
\[
\frac{d}{dt} \left( S(t) + V(t) + \int_0^\infty i(a, t) \, da + R(t) \right) \\
= A - \mu S(t) - \mu V(t) - \int_0^\infty (\mu + \delta_i) i(a, t) \, da - \mu R(t) \\
\leq A - \mu_0 \left( S(t) + V(t) + \int_0^\infty i(a, t) \, da + R(t) \right). \tag{11} \]

It follows from the variation of constants formula that
\[
S(t) + V(t) + \int_0^\infty i(a, t) \, da + R(t) \\
\leq \frac{A}{\mu_0} - e^{-\mu_0 t} \left[ \frac{A}{\mu_0} - \left( S(0) + V(0) + \int_0^\infty i(a, 0) \, da + R(0) \right) \right]. \tag{12} \]

Hence, for any solution of (3) satisfying \( x_0 \in \Omega \), the following inequality holds
\[
S(t) + V(t) + \int_0^\infty i(a, t) \, da + R(t) \leq \frac{A}{\mu_0}. \tag{12} \]

From (10) and (12), we have
\[
\frac{d}{dt} \int_0^\infty p(b, t) \, db \leq \xi \int_0^\infty i(a, t) \, da - \mu_0 \int_0^\infty p(b, t) \, db \leq \frac{A\xi}{\mu_0} - \mu_0 \int_0^\infty p(b, t) \, db. \]

Similarly, by the variation of constants formula, we obtain that
\[
\int_0^\infty p(b, t) \, db \leq \frac{A\xi}{\mu_0^2} - e^{-\mu_0 t} \left( \frac{A\xi}{\mu_0^2} - \int_0^\infty p(b, 0) \, db \right). \tag{13} \]

Adding (11) and (13) yields
\[
S(t) + V(t) + \int_0^\infty i(a, t) \, da + R(t) + \int_0^\infty p(b, t) \, db \
\]
\[
\begin{align*}
\leq & \frac{A}{\mu_0} \left( 1 + \frac{\tilde{\xi}}{\mu_0} \right) - e^{-\mu_0 t} \left[ \frac{A}{\mu_0} \left( 1 + \frac{\tilde{\xi}}{\mu_0}\right) - \|x_0\|_X \right] \\
= & \frac{A}{\mu_0} - e^{-\mu_0 t} \left( \frac{A}{\mu_0} - \|x_0\|_X \right),
\end{align*}
\]  

which implies that \( \Phi(t, x_0) \in \Omega \) holds for \( \forall t \geq 0, x_0 \in \Omega \). Moreover, it follows from (14) that \( \limsup_{t \to \infty} \|\Phi_t(x_0)\|_X \leq A/\tilde{\mu}_0 \) for any \( x_0 \in X \). Therefore, \( \Phi \) is point dissipative and \( \Omega \) attracts all points in \( X \). This completes the proof. 

From the proof of Proposition 2.1, it is not difficult to verify the following result that will be useful in next section.

**Corollary 2.1:** If \( x_0 \in X \) and \( \|x_0\|_X \leq K \) for some constant \( K \geq A/\tilde{\mu}_0 \), then the following statements hold for \( t \geq 0 \):

1. \( 0 \leq S(t, V(t), \int_0^\infty i(a, t) \, da, R(t), \int_0^\infty p(b, t) \, db \leq K; \)
2. \( i(0, t) \leq (1 + \sigma)(\beta_1 + \tilde{\beta}_2/k)K^2, p(0, t) \leq \tilde{\xi} K; \)
3. \( S(t), V(t), f_1(t) \) and \( f_2(t) \) are Lipschitz continuous on \( \mathbb{R}^+ \) with Lipschitz coefficients \( M_S, M_V, M_1 \) and \( M_2 \), respectively. Then, the following inequalities hold,

\[
\begin{align*}
|S(t_1) - S(t_2)| &\leq M_S |t_1 - t_2|, \\
|V(t_1) - V(t_2)| &\leq M_V |t_1 - t_2|, \\
|f_1(t_1) - f_1(t_2)| &\leq M_1 |t_1 - t_2|, \\
|f_2(t_1) - f_2(t_2)| &\leq M_2 |t_1 - t_2|,
\end{align*}
\]

for \( \forall t_1, t_2 \in \Pi \), in which \( \Pi \) denotes an interval defined on \( \mathbb{R}^+ \).

### 3. Asymptotic smoothness

Noting that system (3) is an infinite dimensional dynamical system, the asymptotic smoothness of solutions is the prerequisite before discussing the stability of each of steady states. Hence, in this section, we investigate the asymptotic smoothness of the semi-flow \( \{\Phi(t)\}_{t \geq 0} \) generated by system (3).

**Definition 3.1:** ([23]) For any nonempty and closed bounded set \( B \subset X \) for which \( \Phi(t, B) \subset B \), there is a compact set \( B_0 \subset B \) such that \( B_0 \) attracts \( B \). Then semi-flow \( \Phi(t, x_0) : \mathbb{R}^+ \times X \to X \) is asymptotically smooth.

The following lemmas are useful in proving the asymptotic smoothness of the semi-flow \( \{\Phi(t)\}_{t \geq 0} \).

**Lemma 3.1:** ([23]) The semi-flow \( \Phi(t, x_0) = \phi(t, x_0) + \varphi(t, x_0) : \mathbb{R}^+ \times X \to X \) is asymptotically smooth in \( X \) if the following two conditions hold:

1. There exists a continuous function \( u : \mathbb{R}^+ \times \mathbb{R}^+ \to \mathbb{R}^+ \) such that \( u(t, h) \to 0 \) as \( t \to \infty \) and \( \|\phi_1(x_0)\|_X \leq u(t, h) \) if \( \|x_0\|_X \leq h; \)
2. For \( t \geq 0, \varphi(t, x_0) \) is completely continuous.
**Lemma 3.2:** ([23]) Let $\mathcal{K}$ be a subset of $L^1(\mathbb{R}^+)$. Then $\mathcal{K}$ has compact closure if and only if the following conditions hold:

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

From Proposition 3.13 in [28], we can obtain the following theorem by applying Lemmas 3.1 and 3.2.

**Theorem 3.1:** The semi-flow $\{\Phi(t)\}_{t \geq 0}$ generated by system (3) is asymptotically smooth.

**Proof:** Decompose $\Phi(t, x_0) : \mathbb{R}^+ \times \mathcal{X} \to \mathcal{X}$ into the following two operators $\phi(t, x_0)$, $\varphi(t, x_0) : \mathbb{R}^+ \times \mathcal{X} \to \mathcal{X}$,

$$
\phi(t, x_0) := (0, 0, i_1(\cdot, t), 0, p_1(\cdot, t)), \quad \varphi(t, x_0) := (S(t), V(t), i_2(\cdot, t), R(t), p_2(\cdot, t)),
$$

where

$$
i_1(a, t) := \begin{cases} 0, & t > a \geq 0, \\ i(a, t), & a \geq t \geq 0, \\ i(a, t), & t > a \geq 0, \quad p_1(b, t) := \begin{cases} 0, & t > b \geq 0, \\ p(b, t), & b \geq t \geq 0, \\ \end{cases}
\end{cases}
$$

$$
i_2(a, t) := \begin{cases} 0, & a \geq t \geq 0, \\ i(a, t), & t > a \geq 0, \\ 0, & a \geq t \geq 0, \quad p_2(b, t) := \begin{cases} 0, & t > b \geq 0, \\ p(b, t), & b \geq t \geq 0, \\ \end{cases}
\end{cases}
$$

For $h > 0$, let $u(t, h) = e^{-\mu_0 t}$. It is obvious that $\lim_{t \to \infty} u(t, h) = 0$. From (7) and (8), we have

$$
i_1(a, t) := \begin{cases} 0, & t > a \geq 0, \\ \frac{\rho_1(a)}{\rho_1(a-t)} i_0(a-t), & a \geq t \geq 0, \\
\end{cases}
$$

$$
p_1(b, t) := \begin{cases} 0, & t > b \geq 0, \\ \frac{\rho_2(b)}{\rho_2(b-t)} p_0(b-t), & b \geq t \geq 0. \\
\end{cases}
$$

For $x_0 \in \Omega$ and $\|x_0\|_{\mathcal{X}} \leq h$, we obtain that

$$
\|\Phi_t(x_0)\|_{\mathcal{X}} = 0 + 0 + \int_0^\infty i_1(a, t) \, da + 0 + \int_0^\infty p_1(b, t) \, db
$$

$$
= \int_0^\infty \frac{\rho_1(a)}{\rho_1(a-t)} i_0(a-t) \, da + \int_t^\infty \frac{\rho_2(b)}{\rho_2(b-t)} p_0(b-t) \, db
$$

$$
= \int_0^\infty \frac{\rho_1(t+\tau)}{\rho_1(\tau)} i_0(\tau) \, d\tau + \int_0^\infty \frac{\rho_2(t+\tau)}{\rho_2(\tau)} p_0(\tau) \, d\tau
$$
\[ = \int_0^\infty i_0(\tau) \exp\left(-\int_\tau^{t+\tau} \theta(\nu) \, d\nu\right) \, d\tau + \int_0^\infty p_0(\tau) \exp\left(-\int_\tau^{t+\tau} \delta_p(\nu) \, d\nu\right) \, d\tau. \]

From (H2), it follows that
\[ \|\phi_t(x_0)\|_{\mathcal{X}} \leq e^{-\mu_0 t} \left( 0 + \int_0^\infty i_0(\tau) \, d\tau + 0 + \int_0^\infty p_0(\tau) \, d\tau \right) \]
\[ = e^{-\mu_0 t} \|x_0\|_{\mathcal{X}} \leq h e^{-\mu_0 t} \Delta u(t, h). \]

This completes the proof of (I) in Lemma 3.1. From (7), we have
\[ i_2(a, t) := \begin{cases} \rho_1(a) \left(S(t - a) + \sigma V(t - a) \right) \left(f_1(t - a) + f_2(t - a)\right), & t > a \geq 0, \\ 0, & a \geq t \geq 0. \end{cases} \tag{16} \]

It follows from (1) and (2) in Corollary 2.1 that, for any solution of system (3) with \(x_0 \in \Omega,\)
\[ \rho_1(a) \left(S(t - a) + \sigma V(t - a)\right) \left(f_1(t - a) + f_2(t - a)\right) \leq \rho_1(a)(1 + \sigma)(\bar{\beta}_1 + \bar{\beta}_2/k)K^2, \]
where \(K\) is defined in Corollary 2.1. It is obvious that (i), (ii) and (iv) in Lemma 3.2 hold. Denote \(F(t) = S(t) + \sigma V(t)\). It follows that
\[ \int_0^\infty |i_2(a + h, t) - i_2(a, t)| \, da \\
\[ = \int_0^{t-h} |i(a + h, t) - i(a, t)| \, da + \int_{t-h}^t |0 - i(a, t)| \, da \\
\[ \leq \int_0^{t-h} |\rho_1(a+h) - \rho_1(a)| F(t - a - h)f_1(t - a - h) \, da \\
\[ + \int_0^{t-h} |\rho_1(a+h) - \rho_1(a)| F(t - a - h)f_2(t - a - h) \, da \\
\[ + \int_0^{t-h} \rho_1(a) \left|F(t - a - h)f_1(t - a - h) - F(t - a)f_1(t - a)\right| \, da \\
\[ + \int_0^{t-h} \rho_1(a) \left|F(t - a - h)f_2(t - a - h) - F(t - a)f_2(t - a)\right| \, da \\
\[ + \int_{t-h}^t |\rho_1(a)F(t - a)(f_1(t - a)+f_2(t - a))| \, da. \tag{17} \]

Note that
\[ \int_0^{t-h} |\rho_1(a+h) - \rho_1(a)| \, da = \int_0^{t-h} \rho_1(a) \, da - \int_0^{t-h} \rho_1(a + h) \, da \\
\[ = \int_0^{t-h} \rho_1(a) \, da - \int_h^t \rho_1(a) \, da \]
\[ \int_0^{t-h} \rho_1(a) \, da - \int_h^t \rho_1(a) \, da - \int_{t-h}^t \rho_1(a) \, da \leq \int_0^h \rho_1(a) \, da \leq h. \]

It follows from (1) and (2) in Corollary 2.1 that

\[ \int_0^{t-h} |\rho_1(a + h) - \rho_1(a)| F(t - a - h)f_1(t - a - h) \, da \]
\[ + \int_0^{t-h} |\rho_1(a + h) - \rho_1(a)| F(t - a - h)f_2(t - a - h) \, da \leq (1 + \sigma)(\bar{\beta}_1 + \bar{\beta}_2/k)K^2h, \] (18)

and

\[ \int_{t-h}^t |\rho_1(a)F(t - a)(f_1(t - a) + f_2(t - a))| \, da \leq (1 + \sigma)(\bar{\beta}_1 + \bar{\beta}_2/k)K^2h. \] (19)

According to (3) in Corollary 2.1, we have

\[ \int_0^{t-h} \rho_1(a) \left| F(t - a - h)f_1(t - a - h) - F(t - a)f_1(t - a) \right| \, da \]
\[ + \int_0^{t-h} \rho_1(a) \left| F(t - a - h)f_2(t - a - h) - F(t - a)f_2(t - a) \right| \, da \]
\[ \leq \frac{(1 + \sigma)K(M_1 + M_2) + (\bar{\beta}_1 + \bar{\beta}_2/k)K(M_S + \sigma M_V)}{\mu_0} h. \] (20)

Finally, it follows from (17)–(20) that

\[ \int_0^{\infty} |i_2(a + h, t) - i_2(a, t)| \, da \]
\[ \leq \left[ 2(1 + \sigma)(\bar{\beta}_1 + \bar{\beta}_2/k)K^2 + \frac{(1 + \sigma)K(M_1 + M_2) + (\bar{\beta}_1 + \bar{\beta}_2/k)K(M_S + \sigma M_V)}{\mu_0} \right] h. \]

It is not difficult to find that the right side of the above inequality converges uniformly to 0 as \( h \to 0 \). Hence, for \( t \geq 0, \varphi(t, \cdot) \) maps any bounded sets of \( \Omega \) into sets with compact closure in \( X \). Similarly, we can obtain that \( \rho_2(b, t) \) satisfies similar conditions in Lemma 3.2. Hence, the semi-flow \( \{\Phi(t)\}_{t \geq 0} \) is asymptotically smooth. \( \square \)

4. The existence of steady states

It is easy to see that system (3) always has a disease-free steady state \( E_0(S^0, V^0, 0, 0, 0) \), where

\[ S^0 = \frac{A}{\mu + \phi}, \quad V^0 = \frac{\phi A}{\mu(\mu + \phi)}. \]
If system (3) has an endemic steady state \( E^*(S^*, V^*, i^*(-), R^*, p^*(-)) \), where \( S^* > 0, V^* > 0, \int_0^\infty i^*(a) \, da > 0, R^* > 0 \) and \( \int_0^\infty p^*(b) \, db > 0 \), it must satisfy the following equations:

\[
A - (\mu + \phi)S^* - S^* \left( \int_0^\infty \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b)p^*(b)}{k + p^*(b)} \, db \right) = 0, \tag{21a}
\]

\[
\phi S^* - \mu V^* - \sigma V^* \left( \int_0^\infty \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b)p^*(b)}{k + p^*(b)} \, db \right) = 0, \tag{21b}
\]

\[
\frac{di^*(a)}{da} = -\theta(a)i^*(a), \tag{21c}
\]

\[
\int_0^\infty \gamma(a)i^*(a) \, da - \mu R^* = 0, \tag{21d}
\]

\[
\frac{dp^*(b)}{db} = -\delta_p(b)p^*(b), \tag{21e}
\]

\[
i^*(0) = (S^* + \sigma V^*) \left( \int_0^\infty \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b)p^*(b)}{k + p^*(b)} \, db \right), \tag{21f}
\]

\[
p^*(0) = \int_0^\infty \xi(a)i^*(a) \, da. \tag{21g}
\]

From (21a), (21b) and (21f), we obtain that \( i^*(0) = A - \mu S^* - \mu V^* \). Then solving (21c) yields

\[
i^*(a) = i^*(0)\rho_1(a) = (A - \mu S^* - \mu V^*)\rho_1(a). \tag{22}
\]

It follows from (21) and (22) that

\[
p^*(0) = (A - \mu S^* - \mu V^*) \int_0^\infty \xi(a)\rho_1(a) \, da. \tag{23}
\]

According to (23), solving (21e) yields

\[
p^*(b) = p^*(0)\rho_2(b) = (A - \mu S^* - \mu V^*)\rho_2(b) \int_0^\infty \xi(a)\rho_1(a) \, da. \tag{24}
\]

Substituting (22) and (24) into (21a) and (21b), we have

\[
f(S^* + V^*) := A - \mu (S^* + V^*) - (S^* + \sigma V^*)[A - \mu (S^* + V^*)]N(S^* + V^*) = 0, \tag{25}
\]

where

\[
N(S^* + V^*) = \int_0^\infty \frac{\beta_1(a)\rho_1(a)}{1 + \alpha \rho_1(a) [A - \mu (S^* + V^*)]} \, da + \int_0^\infty \frac{c\beta_2(b)\rho_2(b)}{k + c\rho_2(b) [A - \mu (S^* + V^*)]} \, db,
\]
and

\[ c = \int_{0}^{\infty} \xi(a) \rho_1(a) \, da. \]

Noting that \( 0 < S^* + V^* < A/\mu \), namely, \( A - \mu S^* - \mu V^* \neq 0 \), Equation (25) becomes

\[ g(S^* + V^*) := (S^* + \sigma V^*) N(S^* + V^*) - 1 = 0. \]

(26)

Obviously, \( g \) belongs to a two-variable function. In order to establish the existence of the endemic steady state, we have to prove that there is a unique positive solution to the following system of two equations:

\[
\begin{align*}
(x + \sigma y) N(x + y) - 1 &= 0, \\
A - (\mu + \phi) x - x (A - \mu (x + y)) N(x + y) &= 0,
\end{align*}
\]

where \( N \) is the same function defined in Equation (25) and \( x + y \leq A/\mu \). Then

\[ y = \frac{\phi x^2}{(\mu - \mu \sigma - \phi \sigma) x + A \sigma} \overset{\Delta}{=} \varphi(x). \]

Let \( h(x) \overset{\Delta}{=} (x + \sigma \varphi(x)) N(x + \varphi(x)), x \in [0, A/(\mu + \phi)] \). This can be seen that \( h(0) = 0 \) and \( h(x) \) is a monotone increasing function because of

\[
N'(x + \varphi(x)) = \int_{0}^{\infty} \frac{\alpha \mu \beta_1(a) (\rho_1(a))^2}{[1 + \alpha \rho_1(a) (A - \mu x - \mu \varphi(x))]^2} \, da \\
+ \int_{0}^{\infty} \frac{\mu c^2 \beta_2(b) (\rho_2(b))^2}{[k + c \rho_2(b) (A - \mu x - \mu \varphi(x))]^2} \, db > 0.
\]

It is sufficient to prove that \( h(x) = 1 \) has a unique positive solution if \( h(A/(\mu + \phi)) > 1 \). We therefore obtain the basic reproduction number as follows

\[
R_0 = h \left( \frac{A}{\mu + \phi} \right) = \frac{\mu + \sigma \phi}{\mu + \phi} \left( \frac{A}{\mu} \int_{0}^{\infty} \beta_1(a) \rho_1(a) \, da + \frac{c A}{k \mu} \int_{0}^{\infty} \beta_2(b) \rho_2(b) \, db \right),
\]

which represents the average number of new infections generated by a single newly infectious individual during the full infectious period. Thus, if \( R_0 > 1 \), system (3) has a unique endemic steady state \( E^* (S^*, V^*, i^*(\cdot), R^*, p^*(\cdot)) \).

5. Local asymptotic stability

In this section, we are concerned with the local stability of disease-free and endemic steady states to system (3) by analysing the distribution of roots of characteristic equations.

**Theorem 5.1:** If \( R_0 < 1 \), the disease-free steady state \( E_0 \) is locally asymptotically stable; if \( R_0 > 1 \), \( E_0 \) is unstable.
Proof: First, letting \( u_1(t) = S(t) - S^0 \), \( u_2(t) = V(t) - V^0 \), \( u_3(a, t) = i(a, t) \), \( u_4(t) = R(t) \), \( u_5(b, t) = p(b, t) \) and linearizing system (3) at \( E_0 \), we obtain

\[
\begin{align*}
\frac{du_1(t)}{dt} &= - (\mu + \phi) u_1(t) - S^0 \left( \int_0^\infty \beta_1(a) u_3(a, t) \, da + \int_0^\infty \frac{\beta_2(b) u_5(b, t)}{k} \, db \right), \\
\frac{du_2(t)}{dt} &= \phi u_1(t) - \mu u_2(t) - \sigma V^0 \left( \int_0^\infty \beta_1(a) u_3(a, t) \, da + \int_0^\infty \frac{\beta_2(b) u_5(b, t)}{k} \, db \right), \\
\frac{\partial u_3(a, t)}{\partial t} + \frac{\partial u_3(a, t)}{\partial a} &= - \theta(a) u_3(a, t), \\
\frac{du_4(t)}{dt} &= \int_0^\infty \gamma(a) u_3(a, t) \, da - \mu u_4(t), \\
\frac{\partial u_5(b, t)}{\partial t} + \frac{\partial u_5(b, t)}{\partial b} &= - \delta_p(b) u_5(b, t), \\
u_3(0, t) &= (S^0 + \sigma V^0) \left( \int_0^\infty \beta_1(a) u_3(a, t) \, da + \int_0^\infty \frac{\beta_2(b) u_5(b, t)}{k} \, db \right), \\
u_5(0, t) &= \int_0^\infty \xi(a) u_3(a, t) \, da.
\end{align*}
\]

Substituting \( u_1(t) = \bar{u}_1 e^{\lambda t}, u_2(t) = \bar{u}_2 e^{\lambda t}, u_3(a, t) = \bar{u}_3(a) e^{\lambda t}, u_4(t) = \bar{u}_4 e^{\lambda t}, u_5(b, t) = \bar{u}_5(b) e^{\lambda t} \) into (27), where \( \bar{u}_1, \bar{u}_2, \bar{u}_3(a), \bar{u}_4 \) and \( \bar{u}_5(b) \) will be determined later and \( (\bar{u}_1, \bar{u}_2, \bar{u}_3, \bar{u}_4, \bar{u}_5) \in X \), we have

\[
\begin{align*}
\lambda \bar{u}_1 &= - (\mu + \phi) \bar{u}_1 - S^0 \left( \int_0^\infty \beta_1(a) \bar{u}_3(a) \, da + \int_0^\infty \frac{\beta_2(b) \bar{u}_5(b)}{k} \, db \right), \quad (28a) \\
\lambda \bar{u}_2 &= \phi \bar{u}_1 - \mu \bar{u}_2 - \sigma V^0 \left( \int_0^\infty \beta_1(a) \bar{u}_3(a) \, da + \int_0^\infty \frac{\beta_2(b) \bar{u}_5(b)}{k} \, db \right), \quad (28b) \\
\frac{d\bar{u}_3(a)}{da} &= - (\lambda + \theta(a)) \bar{u}_3(a), \quad (28c) \\
\lambda \bar{u}_4 &= \int_0^\infty \gamma(a) \bar{u}_3(a) \, da - \mu \bar{u}_4, \quad (28d) \\
\frac{d\bar{u}_5(b)}{db} &= - (\lambda + \delta_p(b)) \bar{u}_5(b), \quad (28e) \\
\bar{u}_3(0) &= (S^0 + \sigma V^0) \left( \int_0^\infty \beta_1(a) \bar{u}_3(a) \, da + \int_0^\infty \frac{\beta_2(b) \bar{u}_5(b)}{k} \, db \right), \\
\bar{u}_5(0) &= \int_0^\infty \xi(a) \bar{u}_3(a) \, da. \quad (28f)
\end{align*}
\]
From (28a), (28b) and (28f), we have \( \tilde{u}_3(0) = -(\lambda + \mu)(\tilde{u}_1 + \tilde{u}_2) \). Then, integrating (28c) from 0 to \( a \) yields

\[
\tilde{u}_3(a) = -(\lambda + \mu)(\tilde{u}_1 + \tilde{u}_2) \exp \left[ -\int_0^a (\lambda + \theta(\varepsilon)) \, d\varepsilon \right].
\] (29)

According to (28g), integrating (28e) from 0 to \( b \) yields

\[
\tilde{u}_5(b) = -\exp \left[ -\int_0^b (\lambda + \delta_\rho(\varepsilon)) \, d\varepsilon \right] \times \int_0^\infty \xi(a)(\lambda + \mu)(\tilde{u}_1 + \tilde{u}_2) \exp \left[ -\int_0^a (\lambda + \theta(\varepsilon)) \, d\varepsilon \right] \, da.
\] (30)

Substituting (29) and (30) into (28a) and (28b), we obtain the characteristic equation at \( E_0 \) as follows

\[
(\lambda + \mu) - \frac{\mu + \sigma \phi}{\mu + \phi} (\lambda + \mu) \left( \frac{A}{\mu} \int_0^\infty e^{-a_\lambda \beta_1(a)\rho_1(a)} \, da \\
+ \frac{A}{k\mu} \int_0^\infty e^{-a_\lambda \xi(a)\rho_1(a)} \, da \int_0^\infty e^{-b_\lambda \beta_2(b)\rho_2(b)} \, db \right) = 0.
\] (31)

It is clear that (31) has a negative real root \( \lambda = -\mu \) and other roots are determined by the following equation:

\[
\frac{\mu + \sigma \phi}{\mu + \phi} \left( \frac{A}{\mu} \int_0^\infty e^{-a_\lambda \beta_1(a)\rho_1(a)} \, da \\
+ \frac{A}{k\mu} \int_0^\infty e^{-a_\lambda \xi(a)\rho_1(a)} \, da \int_0^\infty e^{-b_\lambda \beta_2(b)\rho_2(b)} \, db \right) = 1.
\] (32)

Now, we claim that all roots of (32) have negative real parts if \( \mathcal{R}_0 < 1 \). If not, there exists a root \( \lambda_1 = x_1 + iy_1 \) with \( x_1 \geq 0 \). In this case, substituting \( \lambda_1 \) into (32), we obtain

\[
\frac{\mu + \sigma \phi}{\mu + \phi} \left( \frac{A}{\mu} \int_0^\infty e^{-a_\lambda \beta_1(a)\rho_1(a)} \, da \\
+ \frac{A}{k\mu} \int_0^\infty e^{-a_\lambda \xi(a)\rho_1(a)} \, da \int_0^\infty e^{-b_\lambda \beta_2(b)\rho_2(b)} \, db \right) = 1.
\] (33)

It follows that

\[
\left| \frac{\mu + \sigma \phi}{\mu + \phi} \left( \frac{A}{\mu} \int_0^\infty e^{-a_\lambda \beta_1(a)\rho_1(a)} \, da \\
+ \frac{A}{k\mu} \int_0^\infty e^{-a_\lambda \xi(a)\rho_1(a)} \, da \int_0^\infty e^{-b_\lambda \beta_2(b)\rho_2(b)} \, db \right) \right| \\
\leq \frac{\mu + \sigma \phi}{\mu + \phi} \left( \frac{A}{\mu} \int_0^\infty \beta_1(a)\rho_1(a) \, da + \frac{cA}{k\mu} \int_0^\infty \beta_2(b)\rho_2(b) \, db \right) = \mathcal{R}_0 < 1,
\] (34)
which contradicts to (33). Thus, if $\mathcal{R}_0 < 1$, $E_0$ is locally asymptotically stable. If $\mathcal{R}_0 > 1$, denote the left side of (31) as $H(\lambda)$, it is easy to show that

$$H(0) = -\mu + \frac{\mu + \sigma \phi}{\mu + \phi} (\mu + \frac{A}{\mu} \int_0^{\infty} \beta_1(a) \rho_1(a) \, da + \frac{cA}{k\mu} \int_0^{\infty} \beta_2(b) \rho_2(b) \, db)$$

$$= \mu (1 - \mathcal{R}_0) < 0.$$  

If $\mathcal{R}_0 > 1$, due to $H'(\lambda) > 0$ and $H(0) < 0$, Equation (31) has a positive root, then $E_0$ is unstable.  

**Theorem 5.2:** If $\mathcal{R}_0 > 1$, the endemic steady state $E^*$ is locally asymptotically stable.

**Proof:** First, letting $x_1(t) = S(t) - S^*, x_2(t) = V(t) - V^*, x_3(a, t) = i(a, t) - i^*(a)$, $x_4(t) = R(t) - R^*, x_5(b, t) = p(b, t) - p^*(b)$ and linearizing system (3) at $E^*$, we obtain

$$\frac{dx_1(t)}{dt} = - (\mu + \phi) x_1(t) - x_1(t) \left( \int_0^{\infty} \beta_1(a) i^*(a) \, da + \int_0^{\infty} \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right)$$

$$- S^* \left( \int_0^{\infty} \frac{\beta_1(a) x_3(a, t)}{(1 + \alpha i^*(a))^2} \, da + \int_0^{\infty} \frac{\beta_2(b) k x_5(b, t)}{(k + p^*(b))^2} \, db \right),$$

$$\frac{dx_2(t)}{dt} = \phi x_1(t) - \mu x_2(t) - \sigma x_2(t) \left( \int_0^{\infty} \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^{\infty} \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right)$$

$$- \sigma V^* \left( \int_0^{\infty} \frac{\beta_1(a) x_3(a, t)}{(1 + \alpha i^*(a))^2} \, da + \int_0^{\infty} \frac{\beta_2(b) k x_5(b, t)}{(k + p^*(b))^2} \, db \right),$$

$$\frac{\partial x_3(a, t)}{\partial a} + \frac{\partial x_3(a, t)}{\partial a} = -\theta(a) x_3(a, t),$$

$$\frac{dx_4(t)}{dt} = \int_0^{\infty} \gamma(a) x_3(a, t) \, da - \mu x_4(t),$$

$$\frac{\partial x_5(b, t)}{\partial t} + \frac{\partial x_5(b, t)}{\partial b} = -\delta_p(b) x_5(b, t),$$

$$x_3(0, t) = (x_1(t) + \sigma x_2(t)) \left( \int_0^{\infty} \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^{\infty} \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right)$$

$$+ (S^* + \sigma V^*) \left( \int_0^{\infty} \frac{\beta_1(a) x_3(a, t)}{(1 + \alpha i^*(a))^2} \, da + \int_0^{\infty} \frac{\beta_2(b) k x_5(b, t)}{(k + p^*(b))^2} \, db \right),$$

$$x_5(0, t) = \int_0^{\infty} \xi(a) x_3(a, t) \, da.$$  

Substituting $x_1(t) = \tilde{x}_1 e^{\lambda t}, x_2(t) = \tilde{x}_2 e^{\lambda t}, x_3(a, t) = \tilde{x}_3(a) e^{\lambda t}, x_4(t) = \tilde{x}_4 e^{\lambda t}, x_5(b, t) = \tilde{x}_5(b) e^{\lambda t}$ into (36), where $\tilde{x}_1, \tilde{x}_2, \tilde{x}_3(a), \tilde{x}_4$ and $\tilde{x}_5(b)$ will be determined later and $(\tilde{x}_1, \tilde{x}_2, \tilde{x}_3, \tilde{x}_4, \tilde{x}_5) \in X$, it follows that

$$\lambda \tilde{x}_1 = - (\mu + \phi) \tilde{x}_1 - \tilde{x}_1 \left( \int_0^{\infty} \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^{\infty} \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right)$$

$$- S^* \left( \int_0^{\infty} \frac{\beta_1(a) \tilde{x}_3(a)}{(1 + \alpha i^*(a))^2} \, da + \int_0^{\infty} \frac{\beta_2(b) \tilde{x}_5(b)}{(k + p^*(b))^2} \, db \right).$$  

(37a)
\[
\lambda \ddot{x}_2 = \phi \ddot{x}_1 - \mu \ddot{x}_2 - \sigma \ddot{x}_2 \left( \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right) \\
- \sigma V^* \left( \int_0^\infty \frac{\beta_1(a) \ddot{x}_3(a)}{(1 + \alpha i^*(a))^2} \, da + \int_0^\infty \frac{\beta_2(b) k \ddot{x}_5(b)}{(k + p^*(b))^2} \, db \right),
\]
(37b)

\[
\frac{d\ddot{x}_3(a)}{da} = - (\lambda + \theta(a)) \ddot{x}_3(a),
\]
(37c)

\[
\lambda \ddot{x}_4 = \int_0^\infty \gamma(a) \ddot{x}_3(a) \, da - \mu \ddot{x}_4,
\]
(37d)

\[
\frac{d\ddot{x}_5(b)}{db} = - (\lambda + \delta_p(b)) \ddot{x}_5(b),
\]
(37e)

\[
\ddot{x}_3(0) = (\ddot{x}_1 + \sigma \ddot{x}_2) \left( \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right) \\
+ (S^* + \sigma V^*) \left( \int_0^\infty \frac{\beta_1(a) \ddot{x}_3(a)}{(1 + \alpha i^*(a))^2} \, da + \int_0^\infty \frac{\beta_2(b) k \ddot{x}_5(b)}{(k + p^*(b))^2} \, db \right),
\]
(37f)

\[
\ddot{x}_4(0) = \int_0^\infty \xi(a) \ddot{x}_3(a) \, da.
\]
(37g)

From (37a), (37b) and (37f), we have \( \ddot{x}_3(0) = -(\lambda + \mu)(\ddot{x}_1 + \ddot{x}_2) \). Integrating (37c) from 0 to \( a \) yields

\[
\ddot{x}_3(a) = -(\lambda + \mu)(\ddot{x}_1 + \ddot{x}_2) \exp \left[ - \int_0^a (\lambda + \theta(\varepsilon)) \, d\varepsilon \right].
\]
(38)

Similarly, integrating (37e) from 0 to \( b \), we obtain

\[
\ddot{x}_5(b) = - \exp \left[ - \int_0^b (\lambda + \delta_p(\varepsilon)) \, d\varepsilon \right] \\
\times \int_0^\infty \xi(a)(\lambda + \mu) (\ddot{x}_1 + \ddot{x}_2) \exp \left[ - \int_0^a (\lambda + \theta(\varepsilon)) \, d\varepsilon \right] \, da.
\]
(39)

Substituting (38) and (39) into (37a) and (37b), we obtain the characteristic equation at \( E^* \) as follows

\[
1 + \frac{\ddot{x}_1 + \sigma \ddot{x}_2}{(\lambda + \mu)(\ddot{x}_1 + \ddot{x}_2)} \left( \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \, da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right) \\
= (S^* + \sigma V^*) \left( \int_0^\infty \frac{e^{-a\lambda} \beta_1(a) \rho_1(a)}{(1 + \alpha i^*(a))^2} \, da \right) \\
+ \int_0^\infty \frac{ke^{-b\lambda} \beta_2(b) \rho_2(b)}{(k + p^*(b))^2} \, db \int_0^\infty e^{-a\lambda} \xi(a) \rho_1(a) \, da.
\]
(40)
For the sake of contradiction, let $\lambda_2 = x_2 + iy_2$ be a root with $x_2 \geq 0$ and substitute it into (40):

$$1 + \frac{\tilde{x}_1 + \sigma \tilde{x}_2}{(\lambda_2 + \mu) (\tilde{x}_1 + \tilde{x}_2)} \left( \int_0^\infty \beta_1(a) i^*(a) \, da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right)$$

$$= (S^* + \sigma V^*) \left( \int_0^\infty \frac{e^{-a\lambda_2} \beta_1(a) \rho_1(a)}{(1 + ai^*(a))^2} \, da ight)$$

$$\quad + \int_0^\infty \frac{ke^{-b\lambda_2} \beta_2(b) \rho_2(b)}{(k + p^*(b))^2} \, db \int_0^\infty e^{-a\lambda_2} \xi(a) \rho_1(a) \, da \right) .$$

According to (26), we find that

$$\left| (S^* + \sigma V^*) \left( \int_0^\infty \frac{e^{-a\lambda_2} \beta_1(a) \rho_1(a)}{(1 + ai^*(a))^2} \, da ight)$$

$$\quad + \int_0^\infty \frac{ke^{-b\lambda_2} \beta_2(b) \rho_2(b)}{(k + p^*(b))^2} \, db \int_0^\infty e^{-a\lambda_2} \xi(a) \rho_1(a) \, da \right| \leq (S^* + \sigma V^*) \left( \int_0^\infty \frac{\beta_1(a) \rho_1(a)}{1 + ai^*(a)} \, da + \int_0^\infty \frac{c \beta_2(b) \rho_2(b)}{k + p^*(b)} \, db \right) = 1.$$

Note that

$$\left| 1 + \frac{\tilde{x}_1 + \sigma \tilde{x}_2}{(\lambda_2 + \mu) (\tilde{x}_1 + \tilde{x}_2)} \left( \int_0^\infty \beta_1(a) i^*(a) \, da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \, db \right) \right| > 1,$$

which contradicts to (41). Therefore, if $R_0 > 1$, $E^*$ is locally asymptotically stable. ■

6. Global asymptotic stability

In this section, we investigate the global stability of each of steady states to system (3) by using suitable Lyapunov functionals and LaSalle’s invariance principle. Define a function $g(x) = x - 1 - \ln x$, which is always positive except for $x = 1$ where $g(x) = 0$.

**Theorem 6.1:** If $R_0 < 1$, the disease-free steady state $E_0$ of system (3) is globally asymptotically stable in $\mathcal{X}$.

**Proof:** Let $(S(t), V(t), i(a, t), R(t), p(b, t))$ be any positive solution of system (3) with boundary conditions (4) and initial condition (5). Define

$$V_1(t) = S^0 g \left( \frac{S(t)}{S^0} \right) + V^0 g \left( \frac{V(t)}{V^0} \right) + \int_0^\infty \epsilon_1(a) i(a, t) \, da + \int_0^\infty \eta_1(b) p(b, t) \, db,$$

where $\epsilon_1(a)$ and $\eta_1(b)$ will be determined later. Calculating the derivative of $V_1(t)$ along positive solutions of system (3) yields
\[
\dot{V}_1(t) = \left(1 - \frac{S^0}{S(t)}\right) \left[A - (\mu + \phi)S(t) + S(t) \left(\int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db\right)\right]
\]
\[+ \left(1 - \frac{V^0}{V(t)}\right) [\phi S(t) - \mu V(t) - \sigma V(t) \left(\int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db\right) + \int_0^\infty \epsilon_1(a) \frac{\partial i(a,t)}{\partial t} \, da + \int_0^\infty \eta_1(b) \frac{\partial p(b,t)}{\partial b} \, db.\]

Noting that \(S^0 = A/(\mu + \phi)\) and \(V^0 = \phi A/[(\mu + \phi)]\), we have

\[
\dot{V}_1(t) = \mu S^0 \left(2 - \frac{S^0}{S(t)} - \frac{S(t)}{S^0}\right) + \phi S^0 \left(3 - \frac{S^0}{S(t)} - \frac{V(t)}{V^0} - \frac{S(t)V^0}{S^0V(t)}\right) + (S^0 + \sigma V^0) \left(\int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db\right) - (S(t) + \sigma V(t)) \left(\int_0^\infty \frac{\beta_1(a)i(a,t)}{1 + \alpha i(a,t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b,t)}{k + p(b,t)} \, db\right)
\]
\[- \int_0^\infty \epsilon_1(a)\theta(a)i(a,t) \, da - \int_0^\infty \epsilon_1(a) \frac{\partial i(a,t)}{\partial a} \, da
\]
\[- \int_0^\infty \eta_1(b)\delta_p(b)p(b,t) \, db - \int_0^\infty \eta_1(b) \frac{\partial p(b,t)}{\partial b} \, db.\]  

(43)

Using integration by parts, we obtain that

\[
\int_0^\infty \epsilon_1(a) \frac{\partial i(a,t)}{\partial a} \, da = \epsilon_1(a)i(a,t) \bigg|_{a=\infty}^{a=0} - \int_0^\infty i(a,t) \, d\epsilon_1(a)
\]
\[= \epsilon_1(a)i(a,t) \bigg|_{a=\infty}^{a=0} - \epsilon_1(0)i(0,t) - \int_0^\infty i(a,t) \, d\epsilon_1(a).\]  

(44)

Similarly, we have

\[
\int_0^\infty \eta_1(b) \frac{\partial p(b,t)}{\partial b} \, db = \eta_1(b)p(b,t) \bigg|_{b=\infty}^{b=0} - \eta_1(0)p(0,t) - \int_0^\infty p(b,t) \, d\eta_1(b).\]  

(45)

Choose

\[
\eta_1(b) = \frac{A(\mu + \phi)}{k\mu(\mu + \phi)} \int_b^\infty \beta_2(s) \exp\left(-\int_b^s \delta_p(\tau) \, d\tau\right) \, ds,
\]
\[
\epsilon_1(a) = \frac{A(\mu + \phi)}{\mu(\mu + \phi)} \int_a^\infty \beta_1(s) \exp\left(-\int_a^s \theta(\tau) \, d\tau\right) \, ds + \eta_1(0) \int_a^\infty \xi(s) \exp\left(-\int_a^s \theta(\tau) \, d\tau\right) \, ds,
\]

(46)
which have the following properties

\[
\begin{align*}
\eta_1(0) &= \frac{A (\mu + \sigma \phi)}{k \mu (\mu + \phi)} \int_0^\infty \beta_2(b) \rho_2(b) \, db, \\
\varepsilon_1(0) &= \frac{A (\mu + \sigma \phi)}{\mu (\mu + \phi)} \int_0^\infty \beta_1(a) \rho_1(a) \, da + \eta_1(0) \int_0^\infty \xi(a) \rho_1(a) \, da = R_0, \\
\frac{d\eta_1(b)}{db} &= \delta_\rho(b) \eta_1(b) - \frac{A (\mu + \sigma \phi)}{k \mu (\mu + \phi)} \beta_2(b), \\
\frac{d\varepsilon_1(a)}{da} &= \theta(a) \varepsilon_1(a) - \frac{A (\mu + \sigma \phi)}{\mu (\mu + \phi)} \beta_1(a) - \eta_1(0) \xi(a).
\end{align*}
\]

From (43)–(46), it follows that

\[
\dot{V}_1(t) = \mu S^0 \left( 2 - \frac{S^0}{S(t)} - \frac{S(t)}{S^0} \right) + \phi S^0 \left( 3 - \frac{S^0}{S(t)} - \frac{V(t)}{V^0} - \frac{S(t)V^0}{S^0 V(t)} \right) + (R_0 - 1) (S(t) + \sigma V(t)) \left( \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + \alpha_i(a, t)} \, da + \int_0^\infty \frac{\beta_2(b)p(b, t)}{k + p(b, t)} \, db \right) + (S^0 + \sigma V^0) \left( \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + \alpha_i(a, t)} \, da - \int_0^\infty \beta_1(a) i(a, t) \, da \right) + (S^0 + \sigma V^0) \left( \int_0^\infty \frac{\beta_2(b)p(b, t)}{k + p(b, t)} \, db - \frac{1}{k} \int_0^\infty \beta_2(b)p(b, t) \, db \right).
\]

It is not difficult to show that \( \dot{V}_1(t) \leq 0 \) with equality holding if and only if \( S(t) = S^0, V(t) = V^0, i(a, t) = p(b, t) = 0 \). When \( i(a, t) \) tends to 0, \( R(t) \) converges to 0 as well. It can be verified that \( M_0 = \{E_0\} \subset \Omega \) is the largest invariant subset of \( \{(S(t), V(t), i(a, t), R(t), p(b, t)) : \dot{V}_1(t) = 0\} \). Noting that if \( R_0 < 1, E_0 \) is locally asymptotically stable, thus we obtain the global asymptotic stability of \( E_0 \) directly from LaSalle’s invariance principle.

Before investigating the global stability of the endemic steady state \( E^* \) to system (3), define

\[
\tilde{a} = \inf \left\{ a : \int_a^\infty \theta(a) \, da = 0 \right\}, \quad \tilde{b} = \inf \left\{ b : \int_b^\infty \delta_\rho(b) \, db = 0 \right\}.
\]

Since \( \theta(a), \delta_\rho(b) \in L^1_+(0, \infty) \), we have \( \tilde{a}, \tilde{b} > 0 \). Furthermore, let

\[
\tilde{\mathcal{Y}} = \left\{ (\psi, z, \zeta)^T \in L^1_+(0, \infty) \times \mathbb{R}^+ \times L^1_+(0, \infty) : \int_0^{\tilde{a}} \psi(a) \, da > 0, \int_0^{\tilde{b}} \zeta(b) \, db > 0 \right\},
\]

and

\[
\mathcal{Y} = \mathbb{R}^+ \times \mathbb{R}^+ \times \tilde{\mathcal{Y}}.
\]

**Theorem 6.2:** If \( R_0 > 1 \), the endemic steady state \( E^* \) of system (3) is globally asymptotically stable in \( \mathcal{Y} \).
Proof: Let \((S(t), V(t), i(a, t), R(t), p(b, t))\) be any positive solution of system (3) with boundary conditions (4) and initial condition (5). Define

\[
V_2(t) = S^* g \left( \frac{S(t)}{S^*} \right) + V^* g \left( \frac{V(t)}{V^*} \right) + \left( S^* + \sigma V^* \right) \int_0^\infty \varepsilon_2(a) i^*(a) g \left( \frac{i(a, t)}{i^*(a)} \right) da
\]

\[
+ \left( S^* + \sigma V^* \right) \int_0^\infty \eta_2(b) p^*(b) g \left( \frac{p(b, t)}{p^*(b)} \right) db,
\]

where \(\varepsilon_2(a)\) and \(\eta_2(b)\) will be determined later. Calculating the derivative of \(V_2(t)\) along positive solutions of system (3) yields

\[
\dot{V}_2(t) = \left( 1 - \frac{S^*}{S(t)} \right) \left[ A - (\mu + \phi) S(t) \right]
\]

\[
- S(t) \left( \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + a i(a, t)} da + \int_0^\infty \frac{\beta_2(b) p(b, t)}{k + p(b, t)} db \right)
\]

\[
+ \left( 1 - \frac{V^*}{V(t)} \right) \left( \phi S(t) - \mu V(t) \right)
\]

\[- \sigma V(t) \left( 1 - \frac{V^*}{V(t)} \right) \left( \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + a i(a, t)} da + \int_0^\infty \frac{\beta_2(b) p(b, t)}{k + p(b, t)} db \right)
\]

\[
+ \left( S^* + \sigma V^* \right) \int_0^\infty \varepsilon_2(a) \left( 1 - \frac{i^*(a)}{i(a, t)} \right) \frac{\partial i(a, t)}{\partial t} da
\]

\[
+ \left( S^* + \sigma V^* \right) \int_0^\infty \eta_2(b) \left( 1 - \frac{p^*(b)}{p(b, t)} \right) \frac{\partial p(b, t)}{\partial t} db.
\]

According to (21), it follows that

\[
\dot{V}_2(t) = \mu S^* \left( 2 - \frac{S^*}{S(t)} \right) + \mu V^* \left( 3 - \frac{S^*}{S(t)} - \frac{S(t)V^*}{S^*V(t)} - \frac{V(t)}{V^*} \right)
\]

\[
+ S^* \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + a i^*(a)} \left[ 1 + \frac{i(a, t)}{i^*(a, 1 + a i(a, t))} \right] da
\]

\[- S^* \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + a i^*(a)} \left[ \frac{S^*}{S(t)} + \frac{S(t) i(a, t)}{S^* i^*(a, 1 + a i(a, t))} \right] da
\]

\[+ S^* \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \left[ 1 + \frac{p(b, t)}{p^*(b, k + p(b, t))} \right] db
\]

\[- S^* \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \left[ \frac{S^*}{S(t)} + \frac{S(t) p(b, t)}{S^* p^*(b, k + p(b, t))} \right] db
\]

\[+ \sigma V^* \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + a i^*(a)} \left( 2 + \frac{i(a, t)}{i^*(a, 1 + a i(a, t))} - \frac{S^*}{S(t)} - \frac{S(t)V^*}{S^*V(t)} \right) da
\]

\[- \sigma V^* \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + a i^*(a)} \frac{V(t) i(a, t)}{V^* i^*(a, 1 + a i(a, t))} da
\]

\[+ \sigma V^* \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} \left( 2 + \frac{p(b, t)}{p^*(b, k + p(b, t))} - \frac{S^*}{S(t)} - \frac{S(t)V^*}{S^*V(t)} \right) db.
\]
\[- \sigma V^* \int_0^\infty \beta_2(b)p^*(b) \frac{V(t)p(b,t)}{k + p^*(b)} \frac{(k + p^*(b))}{V^*p^*(b)} \frac{db}{db} + (S^* + \sigma V^*) \int_0^\infty \epsilon_2(a) \left( 1 - \frac{i^*(a)}{i(a,t)} \right) \frac{\partial i(a,t)}{\partial t} da + (S^* + \sigma V^*) \int_0^\infty \eta_2(b) \left( 1 - \frac{p^*(b)}{p(b,t)} \right) \frac{\partial p(b,t)}{\partial t} db. \]
\[ -\sigma V^* \int_0^\infty \frac{\beta_2(b)p^*(b)}{k + p^*(b)} V(t)p(b, t) \left( k + p^*(b) \right) \, db \\
+ (S^* + \sigma V^*) \varepsilon_2(0)\sigma(0)g \left( \frac{i(0, t)}{i^*(0)} \right) + (S^* + \sigma V^*) \eta_2(0)p^*(0)g \left( \frac{p(0, t)}{p^*(0)} \right) \\
- (S^* + \sigma V^*) \varepsilon_2(a)i^*(a)g \left( \frac{i(a, t)}{i^*(a)} \right) \big|_{a=\infty} \\
- (S^* + \sigma V^*) \eta_2(b)p^*(b)g \left( \frac{p(b, t)}{p^*(b)} \right) \big|_{b=\infty} \\
+ (S^* + \sigma V^*) \left[ \int_0^\infty g \left( \frac{i(0, t)}{i^*(0)} \right) \varepsilon_2(a) \frac{d\xi(a)}{da} da + \int_0^\infty g \left( \frac{p(b, t)}{p^*(b)} \right) \eta_2(a) \frac{dp^*(b)}{db} da \right] \\
+ (S^* + \sigma V^*) \left[ \int_0^\infty g \left( \frac{i(a, t)}{i^*(a)} \right) \frac{d\varepsilon_2(a)}{da} da + \int_0^\infty g \left( \frac{p(b, t)}{p^*(b)} \right) \frac{d\eta_2(b)}{db} \frac{p^*(b)db}{db} \right]. \quad (51) \]

Choose
\[ \eta_2(b) = \int_0^\infty \frac{\beta_2(s)}{k + p^*(b)} \exp \left( -\int_b^s \delta_p(\tau)d\tau \right) ds, \]
\[ \varepsilon_2(a) = \int_a^\infty \frac{\beta_1(s)}{1 + \alpha i^*(s)} \exp \left( -\int_s^a \theta(\tau)d\tau \right) ds + \eta_2(0) \int_a^\infty \xi(s) \exp \left( -\int_a^s \theta(\tau)d\tau \right) ds. \quad (52) \]

It is easy to show that
\[ \eta_2(0) = \int_0^\infty \frac{\beta_2(b)p_2(b)}{k + p^*(b)} db, \]
\[ \varepsilon_2(0) = \int_0^\infty \frac{\beta_1(a)p_1(a)}{1 + \alpha i^*(a)} da + \eta_2(0) \int_0^\infty \xi(a)p_1(a)da = \frac{1}{S^* + \sigma V^*}, \quad (53) \]
\[ \frac{d\eta_2(b)}{db} = \delta_p(b)\eta_2(b) - \frac{\beta_2(b)}{k + p^*(b)}, \]
\[ \frac{d\varepsilon_2(a)}{da} = \theta(a)\varepsilon_2(a) - \frac{\beta_1(a)}{1 + \alpha i^*(a)} - \eta_2(0)\xi(a). \]

Then Equation (51) becomes
\[ \dot{V}_2(t) = \dot{V}_{21}(t) + \dot{V}_{22}(t) + \dot{V}_{23}(t), \]
where
\[ \dot{V}_{21}(t) = \mu S^* \left( 2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*} \right) + \mu V^* \left( 3 - \frac{S^*}{S(t)} - \frac{V(t)}{V^*} - \frac{S(t)V^*}{S^*V(t)} \right) \\
- S^* \int_0^\infty \left( \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} + \frac{\beta_2(b)p^*(b)}{k + p^*(b)} \right) g \left( \frac{S^*}{S(t)} \right) da \\
- \sigma V^* \int_0^\infty \left( \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} + \frac{\beta_2(b)p^*(b)}{k + p^*(b)} \right) \left[ g \left( \frac{S^*}{S(t)} \right) + g \left( \frac{S(t)V^*}{S^*V(t)} \right) \right] da \\
+ S^* \int_0^\infty \frac{\beta_1(a)i^*(a)}{1 + \alpha i^*(a)} \ln \frac{S(t)i^*(0)i(a, t)}{S^*i(0, t)i^*(a)} \left( 1 + \alpha i^*(a) \right) \, da \\
\]
Adding Equation (56) into \( \dot{V}_{21}(t) \), it follows that

\[
\dot{V}_{21}(t) = \mu S^* \left( 2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*} \right) + \mu V^* \left( 3 - \frac{S^*}{S(t)} - \frac{V(t)}{V^*} - \frac{S(t) V^*}{S^* V^*} \right) - S^* \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} \ln \frac{S(t) i^*(0) i(a, t) (1 + \alpha i^*(a))}{S^* i(0, t) i^*(a) (1 + \alpha i(a, t))} da
\]

From (21f), we obtain that

\[
i^*(0) = \left( \frac{S^*}{S(t)} + \frac{S(t)}{S^*} \right) i^*(0) \frac{(S(t) + \sigma V(t)) i^*(0) i(a, t)}{1 + \alpha i(a, t)} + \frac{(S^* + \sigma V^*)}{(S^* + \sigma V(t))} \frac{i^*(0) i(a, t)}{i^*(a) i(0, t) p(b, t)} db,
\]

and

\[
i^*(0) = \left( \frac{S^*}{S(t)} + \frac{S(t)}{S^*} \right) \left( \int_0^\infty \frac{\beta_1(a) i^*(a)}{1 + \alpha i^*(a)} da + \int_0^\infty \frac{\beta_2(b) p^*(b)}{k + p^*(b)} db, \right)
\]
It can be verified that

\[- \eta_2(0) \left( S^* + \sigma V^* \right) \int_0^\infty \xi(a) i^*(a) \ln \frac{p(0, t)}{P^*(0)} da \]

\[+ \eta_2(0) \left( S^* + \sigma V^* \right) \int_0^\infty \xi(a) i^*(a) \ln \frac{i(a, t)}{i^*(a)} da \]

\[= - \eta_2(0) \left( S^* + \sigma V^* \right) \int_0^\infty \xi(a) i^*(a) g \left( \frac{i(a, t)p^*(0)}{i^*(a)p(0, t)} \right) da, \]  

(57)

and

\[\eta_2(0)p^*(0) \left( S^* + \sigma V^* \right) \left( \frac{p(0, t)}{P^*(0)} - 1 \right) \]

\[= \eta_2(0) \left( S^* + \sigma V^* \right) \int_0^\infty \xi(a) i^*(a) \left( \frac{i(a, t)}{i^*(a)} - 1 \right) da. \]  

(58)

It is easy to see that

\[\hat{V}_{22}(t) = - \eta_2(0) \left( S^* + \sigma V^* \right) \int_0^\infty \xi(a) i^*(a) g \left( \frac{i(a, t)p^*(0)}{i^*(a)p(0, t)} \right) da \leq 0.\]

Furthermore, it can be shown that

\[g \left( \frac{i(a, t)(1 + \alpha i^*(a))}{i^*(a)(1 + \alpha i(a,t))} \right) - g \left( \frac{i(a, t)}{i^*(a)} \right) \]

\[= \frac{i(a, t)(1 + \alpha i^*(a))}{i^*(a)(1 + \alpha i(a,t))} - 1 - \ln \frac{i(a, t)(1 + \alpha i^*(a))}{i^*(a)(1 + \alpha i(a,t))} - \frac{i(a, t)}{i^*(a)} + 1 + \ln \frac{i(a, t)}{i^*(a)} \]

\[= \left( \frac{-i(a, t)}{i^*(a)(1 + \alpha i(a,t))} + \frac{1}{1 + \alpha i^*(a)} \right) \alpha \left( i(a, t) - i^*(a) \right) \]

\[+ \ln \frac{1 + \alpha i(a,t)}{1 + \alpha i^*(a)} + 1 \frac{1 + \alpha i(a, t)}{1 + \alpha i(a,t)} \]

\[= - \frac{\alpha (i(a, t) - i^*(a))^2}{i^*(a)(1 + \alpha i(a,t))(1 + \alpha i^*(a))} - g \left( \frac{1 + \alpha i(a, t)}{1 + \alpha i^*(a)} \right) \leq 0. \]
Similarly, we obtain that
\[
\begin{align*}
    g \left( \frac{p(b, t)(k + p^*(b))}{p^*(b)(k + p(b, t))} \right) - g \left( \frac{p(b, t)}{p^*(b)} \right) &= -\frac{k(p(b, t) - p^*(b))^2}{p^*(b)(k + p(b, t))(k + p^*(b))} - g \left( \frac{k + p(b, t)}{k + p^*(b)} \right) \leq 0.
\end{align*}
\]

From (59) and (60), we obtain that \( \dot{V}_{23}(t) \leq 0 \). Therefore, it follows that \( \dot{V}_2(t) \leq 0 \) with equality holding if and only if \( S(t) = S^*, V(t) = V^*, i(a, t) = i^*(a), p(b, t) = p^*(b) \). As \( i(a, t) \) converges to \( i^*(a) \), \( R(t) \) tends to \( R^* \). It can be proved that \( M_1 = \{ E^* \} \subset \Omega \) is the largest invariant subset of \( \{ (S(t), V(t), i(a, t), R(t), p(b, t)) : \dot{V}_2(t) = 0 \} \). Noting that if \( R_0 > 1 \), \( E^* \) is locally asymptotically stable, hence the global asymptotic stability of \( E^* \) follows from Lasalle’s invariance principle.

7. Optimal control strategy

From Section 6, we know that if \( R_0 > 1 \), a cholera outbreak will take place and the disease will persist. Therefore, it is critically important to investigate how to effectively control cholera and how to achieve the disease control with typically limited resources.

Control strategies, such as quarantine, vaccination, treatment, and sanitation, can realize the control of cholera to varying degree and at different cost. Thereinto, vaccination strategy is the most efficient control strategy to prevent, control and eradicate cholera. Next, we will find a cost-effective vaccination strategy to control cholera epidemic. We rewrite system (3) as

\[
\begin{align*}
    \frac{dS(t)}{dt} &= A - (\mu + u(t))S(t) - S(t) \left( \int_0^\infty \frac{\beta_1(a)i(a, t)}{1 + \alpha i(a, t)} da + \int_0^\infty \frac{\beta_2(b)p(b, t)}{k + p(b, t)} db \right), \\
    \frac{dV(t)}{dt} &= u(t)S(t) - \mu V(t) - \sigma V(t) \left( \int_0^\infty \frac{\beta_1(a)i(a, t)}{1 + \alpha i(a, t)} da + \int_0^\infty \frac{\beta_2(b)p(b, t)}{k + p(b, t)} db \right), \\
    \frac{\partial i(a, t)}{\partial t} + \epsilon \frac{\partial i(a, t)}{\partial a} &= -\beta(a)i(a, t), \\
    \frac{\partial p(b, t)}{\partial t} + \epsilon \frac{\partial p(b, t)}{\partial b} &= -\delta(b)p(b, t),
\end{align*}
\]

where the constant \( \epsilon \) is introduced to balance the different units between time and age. We also rewrite the vaccination rate as \( u(t) \), a function depending on time. The initial and boundary conditions for system (61) are given in (4) and (5). We consider this system on a time interval \([0, t_{\text{max}}]\). The control set is defined as \( \Gamma = \{ u(t) \in L^\infty(0, t_{\text{max}}) \mid 0 \leq u(t) \leq u_{\text{max}} \} \), where \( u_{\text{max}} \) denotes the upper bound due to the practical limitation on the vaccination that can be implemented within a given population and a given time period. We aim to minimize the number of infected individuals and corresponding cost of the strategy during the course of an epidemic. Define the objective functional as

\[
\mathcal{J}(u) = \min_{u(t) \in \Gamma} \int_0^{t_{\text{max}}} \int_0^{a_{\text{max}}} \left( a_1i(a, t) + a_2u(t)S(t) + a_3u^2(t) \right) da dt,
\]
where \( a_1, a_2 \) and \( a_3 \) are the weight constants of infected individuals, vaccination strategy and side effects of vaccination strategy, respectively. The square of the control variable shows the severity of the side effects. The minimization process is subject to the state equations in (61), where \( S, V, i, p \) are the state variables, while, \( u \) is the control variable.

Following [2], [7] and [8], we construct the optimal control model through the combination of the state equations, the adjoint equations, and the optimality condition. Denote a sensitivity function \( F = (S, V, i, p) \) and a solution map \( u \rightarrow F = F(u) \). Based on results in [2], the map is differentiable and the sensitivity function \( F \) is defined by the Gateaux derivative:

\[
(Q_S, Q_V, Q_i, Q_p) = \lim_{\varepsilon \to 0} \frac{F(u + \varepsilon l) - F(u)}{\varepsilon},
\]

for \( l(t) \in L^\infty(0, t_{\text{max}}) \). Hence, the sensitivities \( (Q_S, Q_V, Q_i, Q_p) \) satisfy

\[
\frac{dQ_S(t)}{dt} = -(\mu + u(t))Q_S(t) - Q_S(t) \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + \alpha i(a, t)} da - S(t) \int_0^\infty \frac{\beta_1(a) Q_i(a, t)}{(1 + \alpha i(a, t))^2} da \\
- Q_S(t) \int_0^\infty \frac{\beta_2(b) p(b, t)}{k + p(b, t)} db - S(t) \int_0^\infty \frac{k \beta_2(b) Q_p(b, t)}{(k + p(b, t))^2} db - l(t)Q_S,
\]

\[
\frac{dQ_V(t)}{dt} = u(t)Q_S(t) - \mu Q_V(t) + l(t)Q_S \\
- \sigma Q_V(t) \int_0^\infty \frac{\beta_1(a) i(a, t)}{1 + \alpha i(a, t)} da - S(t) \int_0^\infty \frac{\beta_1(a) Q_i(a, t)}{(1 + \alpha i(a, t))^2} da \\
- \sigma Q_V(t) \int_0^\infty \frac{\beta_2(b) p(b, t)}{k + p(b, t)} db - S(t) \int_0^\infty \frac{k \beta_2(b) Q_p(b, t)}{(k + p(b, t))^2} db,
\]

\[
\frac{\partial Q_i(a, t)}{\partial t} + \epsilon \frac{\partial Q_i(a, t)}{\partial a} = -\theta(a) Q_i(a, t), \\
\frac{\partial Q_p(b, t)}{\partial t} + \epsilon \frac{\partial Q_p(b, t)}{\partial b} = -\delta_p(b) Q_p(b, t),
\]

with boundary conditions

\[
Q_i(0, t) = (Q_S(t) + \sigma Q_V(t)) \left( \int_0^\infty \frac{\beta_1(a) Q_i(a, t)}{1 + \alpha Q_i(a, t)} da + \int_0^\infty \frac{\beta_2(b) Q_p(b, t)}{k + Q_p(b, t)} db \right), \quad t > 0,
\]

\[
Q_p(0, t) = \int_0^\infty \xi(a) Q_i(a, t) da, \quad t > 0,
\]

and initial condition

\[
Q_S(0) = Q_{S0} > 0, \quad Q_V(0) = Q_{V0} > 0, \\
Q_i(a, 0) = Q_{i0}(a) \in L^1(0, \infty), \quad Q_p(b, 0) = Q_{p0}(b) \in L^1(0, \infty).
\]

Denote

\[
h_1(t) = \int_0^\infty \frac{\beta_1(a)}{(1 + \alpha i(a, t))^2} da, \quad h_2(t) = \int_0^\infty \frac{k \beta_2(b)}{(k + p(b, t))^2} db.
\]
Then, the adjoint system associated with control \( u(t) \) and state variables \( S(t), V(t), i(a, t), p(b, t) \) is

\[
\frac{d\lambda_1(t)}{dt} = \lambda_1(t) \left( \mu + u(t) + f_1(t) + f_2(t) \right) \\
- \lambda_2(t)u(t) - \lambda_3(0, t) \left( f_1(t) + f_2(t) \right) - a_2 u(t),
\]

\[
\frac{d\lambda_2(t)}{dt} = \lambda_2(t) \left( \mu + \sigma f_1(t) + \sigma f_2(t) \right) - \sigma \lambda_3(0, t) \left( f_1(t) + f_2(t) \right),
\]

\[
\frac{\partial \lambda_3(a, t)}{\partial t} + \epsilon \frac{\partial \lambda_3(a, t)}{\partial a} = \lambda_1(t)S(t)h_1(t) + \sigma \lambda_2(t)V(t)h_1(t) \\
+ \theta(a)\lambda_3(a, t) - \lambda_3(0, t) \left( S(t) + \sigma V(t) \right) h_1(t) \\
- \lambda_4(0, t) \int_0^\infty \xi(a)da - a_1,
\]

\[
\frac{\partial \lambda_4(b, t)}{\partial t} + \epsilon \frac{\partial \lambda_4(b, t)}{\partial b} = \lambda_1(t)S(t)h_2(t) + \sigma \lambda_2(t)V(t)h_2(t) \\
+ \delta_p(b)\lambda_4(b, t) - \lambda_3(0, t) \left( S(t) + \sigma V(t) \right) h_2(t).
\]

Following [8] and [3], the optimality condition is found as

\[
u^* = \max[0, \min(\tilde{u}, u_{\text{max}})], \quad \tilde{u} = \frac{(\lambda_1 - \lambda_2 - a_2) S}{2a_3}.
\]

Numerical techniques for optimal control problems can often be classified as either direct or indirect. In terms of disease control, indirect methods, such as Forward-Backward Sweep Method, approximate solutions to optimal control problems by numerically solving the boundary value problem for the differential-algebraic system generated by the Maximum Principle [13].

8. Numerical simulations

In this section, we want to illustrate the theoretical results for system (3) by numerical simulations. Furthermore, by Forward-Backward Sweep Method, we obtain the optimal control strategy and show the graph trajectories of infected individuals with optimal control and without optimal control.

8.1. Dynamical behaviour of the model

Following the works of [6,10,14–17,20,29], we choose appropriate parameter values of system (3) in Table 2.

Usually, the course of cholera is 3–7 days. After 6 days of quarantine since the symptoms disappeared, the faecal vibrios of infected individuals are negative on three consecutive checks, then one can think that the disease is cured. Hence, we set the length of infection age as 12.5 days. In the first 3 days, infected individuals become infectious gradually; in the middle 3–7 days, infected individuals are in a hyperinfectious state; in the last days, infected individuals are cured or dead due to the disease, thus the transmission coefficient
Table 2. Parameter values for the age-structured cholera model (3).

| Parameter                                      | Symbol | Case 1       | Case 2       | Source   |
|------------------------------------------------|--------|--------------|--------------|----------|
| Recruitment rate                               | $A$    | 100          | 300          | Assumed  |
| Birth and natural death rate                   | $\mu$  | 9.752%       | 1.526%       | [29]     |
| Saturation incidence coefficient               | $\alpha$ | 0.1          | 0.1          | [20]     |
| Vaccination rate                               | $\phi$ | 75%          | 5%           | Assumed  |
| Reduction rate of vaccination                  | $\sigma$ | 25%          | 25%          | [16]     |
| Concentration of $V. cholerae$ in environment   | $k$    | $10^6$ cells/ml | $10^6$ cells/ml | [6]       |
| Transmission coefficient of infected individuals | $\beta_{1m}$ | 0.00092/day | 0.00011/day | [17]     |
| Transmission coefficient of $V. cholerae$      | $\beta_{2m}$ | 0.008/day | 0.075/day | [17]     |
| Recovery rate from cholera                     | $\gamma_m$ | 0.2/day     | 0.2/day     | [15]     |
| Death rate due to the disease                  | $\delta_m$ | 0.004/day   | 0.004/day   | Assumed  |
| Net death rate of $V. cholerae$                | $\delta_{pm}$ | 0.033 cells/(ml-day) | 0.033 cells/(ml-day) | [10]     |
| Contribution rate to $V. cholerae$             | $\xi_m$ | 10 cells/(ml-day) | 10 cells/(ml-day) | [10]     |

The specific function is shown as follows:

$$
\beta_1(a) = \begin{cases} 
\frac{\beta_{1m}}{3}a, & 0d \leq a < 3d, \\
\beta_{1m}, & 3d \leq a < 7d, \\
\frac{25}{11}\beta_{1m} - \frac{2}{11}\beta_{1m}a, & 7d \leq a < 12.5d.
\end{cases}
$$

As for the contribution rate of each infected person to the concentration of $V. cholerae$, the change law is associated with $\beta_1(a)$. Since the susceptible individuals newly ingest the vibrios, they cannot produce vibrios immediately; 3 days after the onset of cholera, the contribution rate keeps in a high level; in the last days, because of the treatment or death, the contribution rate become smaller. Therefore, we set $\xi(a)$ as

$$
\xi(a) = \begin{cases} 
\frac{\xi_m}{3}a, & 0d \leq a < 3d, \\
\xi_m, & 3d \leq a < 7d, \\
\frac{25}{11}\xi_m - \frac{2}{11}\xi_m a, & 7d \leq a < 12.5d.
\end{cases}
$$

Besides, $V. cholerae$ can survive in river water, well water, or sea water for 1–3 weeks, while in fresh fish or shellfish for 1–2 weeks. Similarly, we set the length of biological age as 12.5 days. In the first 5 h, vibrios from freshly passed human stool are hyperinfectious; if vibrios have been in the environment from 5 to 18 h, they are no longer hyperinfectious [17], namely, in a hypoinfectious state; in the last hours, vibrios become non-infectious gradually. Corresponding function is shown as follows:

$$
\beta_2(b) = \begin{cases} 
\beta_{2m}, & 0d \leq b < \frac{5}{24}d, \\
\frac{258}{195}\beta_{2m} - \frac{1512}{975}\beta_{2m}b, & \frac{5}{24}d \leq b < \frac{3}{4}d, \\
\frac{12}{75}\beta_{2m}e^{-(b-\frac{3}{4})}, & \frac{3}{4}d \leq b < 12.5d.
\end{cases}
$$
From the practical situation of cholera epidemic, we consider if the infected individuals receive treatment too late, the recovery rate reduces sharply. Thus, $\gamma(a)$ is set as

$$
\gamma(a) = \begin{cases} 
\gamma_m, & 0d \leq a < 7d, \\
\gamma_m - \frac{2}{11}\gamma_m \times (t-7), & 7d \leq a < 12.5d. 
\end{cases}
$$

Note that $\theta(a)$ contains the rates of recovery, disease-induced death, birth and natural death, while, the disease-induced death often happens in the middle course of cholera. Hence, $\theta(a)$ is chosen as

$$
\theta(a) = \begin{cases} 
\mu + \gamma_m, & 0d \leq a < 3d, \\
\mu + \delta_{im} + \gamma_m, & 3d \leq a < 7d, \\
\mu + \gamma_m - \frac{2}{11}\gamma_m \times (t-7), & 7d \leq a < 12.5d. 
\end{cases}
$$

The net death rate of $V. cholerae$ increases after 5 hours due to their weak resistance in the environment, then $\delta_p(b)$ follows that

$$
\delta_p(b) = \begin{cases} 
\frac{24}{5}\delta_{pm}b, & 0d \leq b < \frac{5}{24}d, \\
\delta_{pm}e^{0.5(b-\frac{5}{24})}, & \frac{5}{24}d \leq b < 12.5d. 
\end{cases}
$$

First, select Case 1 in Table 2 as the parameter values of system (3). Through direct calculation, we find that basic reproduction number $R_0$ is near 0.9877 and less than unity. From Theorem 5.1, we obtain that the disease-free steady state is locally asymptotically stable. In Figure 2, we observe that susceptible individuals $S(t)$ and vaccinated individuals $V(t)$ converge to $S^0 = 117.58$ and $V^0 = 897.10$, respectively, while, infected individuals $i(a,t)$ and $V. cholerae p(b,t)$ converge to 0.

Then, select Case 2 in Table 2 as the parameter values of system (3). We find that basic reproduction number $R_0$ is near 2.8722 and greater than unity. The endemic steady state is approximately calculated as $S^* = 2676.25, V^* = 4984.97, i^*(0) = 183.58, p^*(0) = 7869.49$. From Theorem 5.2, we obtain that the endemic steady state is locally asymptotically stable. From Figure 3, we observe that infected individuals $i(a,t)$ and $V. cholerae p(b,t)$ converge to the endemic steady state.

### 8.2. Optimal control solution

The numerical results associated with optimal control are obtained based on Forward-Backward Sweep Method [12], which has been developed for age-structured cholera models by [3]. A rough outline of the algorithm is given below. First, break the time interval $[t_0, t_1]$ into pieces with $N+1$ points. Here, $\bar{x} = (x_1, \ldots, x_{N+1})$ and $\bar{\lambda} = (\lambda_1, \ldots, \lambda_{N+1})$ are the vector approximations for the states in system (61) and the adjoint in system (65), respectively.

1. Make an initial guess for $\bar{u}$ over the interval;
Figure 2. The graph trajectories of $S(t)$, $V(t)$, $i(a, t)$ and $p(b, t)$ of system (3) with initial values $S(0) = 8000$, $V(0) = 2000$, $l_0(0) = 10$, $p_0(0) = 100$ where $R_0 = 0.9877 < 1$.

2) Using the initial condition $x_1 = x(t_0)$ and the values for $\bar{u}$, solve $\bar{x}$ forward in time and backward in age according to system (61);

3) Using the transversality condition $\lambda_{N+1} = \lambda(t_1) = 0$ and the values for $\bar{u}$ and $\bar{x}$, solve $\bar{\lambda}$ backward in time and forward in age according to system (65);

4) Update $\bar{u}$ by entering the new $\bar{x}$ and $\bar{\lambda}$ values into the characterization of the optimal control;

5) Check convergence. If values of the variables in this iteration and the last iteration are negligibly close, output the current values as solutions. If values are not close, return to Step 2.

When all steps are complete, we obtain the optimal control strategy, which can be seen in Figure 4 (a). On account of medical technology and cost, vaccination control strategy has its limitation, thus we set $u_{\text{max}} = 80\%$. We observe that vaccination strategy could be reduced 140 days later from the beginning of the cholera outbreaks, which saves much cost of vaccination. In Figure 4 (b), we compare the graph trajectories of infected individuals with optimal vaccination strategy and original vaccination strategy (with the same parameter values to Case 1 in Table 2). It is clear that infected individuals have been reduced due to optimal vaccination control strategy, where the cost of optimal and original vaccination strategies are close. From Figure 4, we suggest that taking vaccination strategy at the very beginning of cholera outbreaks can reduce the number of infected individuals remarkably, which are also cost-effective optimal strategy.
Figure 3. The graph trajectories of $S(t)$, $V(t)$, $i(a, t)$ and $p(b, t)$ of system (3) with initial values $S(0) = 2000, V(0) = 3000, I_0(0) = 10, p_0(0) = 1000$ where $R_0 = 2.8722 > 1$.

Figure 4. Figure 4 is the graph trajectory of vaccination control strategy; Figure 4 is the graph trajectories of $i(a, t)$ with optimal vaccination strategy and original vaccination strategy.

9. Conclusion

In this paper, we have considered a cholera model including both human-to-human and environment-to-human transmissions, saturation incidence and imperfect vaccination. By
a complete mathematical analysis, the threshold dynamics of the model was established and it can be fully determined by basic reproduction number. If $R_0 < 1$, the disease-free steady state $E_0$ is locally and globally asymptotically stable; if $R_0 > 1$, the endemic steady state $E^*$ is locally and globally asymptotically stable. The study of optimal control helps us seek cost-effective solutions of time-dependent vaccination control strategy against cholera outbreaks. Numerical simulations vividly illustrate our main results of stability analysis for system (3). Furthermore, we obtain the optimal solution by Forward-Backward Sweep Method.

At the beginning of cholera epidemic, hyperinfectious vibrios freshly-shed from infected individuals play an important role on cholera transmission, due to that they are likely to come into contact with other individuals [10]. Therefore, the strategy of vaccination at the very beginning of the onset can effectively control the cholera epidemic. Besides, other control strategies, such as quarantine and sanitation, should be implemented as a supplement, which can better prevent and control cholera. It is worth mentioning that, after vaccination, the vaccine efficacy is waning as time goes by. Hence, some vaccinated individuals become susceptible again, which we leave for further investigation.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

**Funding**

This work was supported by the National Natural Science Foundation of China [grant numbers 11871316, 11801340, 11371368, the Natural Science Foundation of Shanxi Province [grant numbers 201801D121006, 201801D221007], Shanxi Scientific Data Sharing Platform for Animal Diseases [grant number 201605D121014], and the Science and Technology Innovation Team of Shanxi Province [grant number 201605D131044-06].

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