

The effects of an imperfect vaccine on cholera control

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ABSTRACT

In this paper, we consider a SVIR-B cholera model with imperfect vaccination. By analyzing the corresponding characteristic equations, the local asymptotically stability of a disease-free equilibrium and an endemic equilibrium is established. We calculate the certain threshold known as the basic reproduction number R_v . If $R_v < 1$, we obtain sufficient conditions for the global asymptotically stability of the disease-free equilibrium, the diseases will be eliminated from the community. By comparison arguments, it is proved that if $R_v > 1$, the unique endemic equilibrium is local asymptotically stable. We perform sensitivity analysis of R_v on the parameters in order to determine their relative importance to disease control and show that an imperfect vaccine is always beneficial in reducing disease spread within the community.

Keywords: Cholera Model; Stability; The Basic Reproduction Number; Sensitivity Analysis

1. INTRODUCTION

Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacterium vibrio cholera. Since Koch found vibrio cholera in 1883, the research for cholera vaccine has more than one hundred years. People have developed a variety of vaccines. However, these vaccines were parenteral, which have short effective protection and big side effects. In 1973, the World Health Organization canceled the vaccine inoculation which attracted a major concern to oral vaccines. At present, there are three kinds of oral vaccine (*i.e.*, WC/BS vaccine, WC/rBS vaccine and CVD₁₀₃-HgR vaccine) have been proved to be safe, effective and immunogenic, which were approved to apply in some countries [1].

In this paper, according to the natural history of cholera, we improve the model of [2] in the following two aspects. Firstly, if the cholera persists for a long time, it will cause the death [3], especially in the area where water and sanitation resources are not adequate [4], a pa-

rameter d is added to describe the rate of disease-related death. Secondly, we propose a proportion of the vaccination in susceptible individuals. As is shown in the following differential equations:

$$\begin{cases} \frac{dS(t)}{dt} = \mu_1 - \beta_1 S(t) B(t) - \beta_2 S(t) I(t) - \phi S(t) \\ \quad - \mu_1 S(t) + \theta V(t), \\ \frac{dV}{dt} = \phi S(t) - \theta V(t) - \mu_1 V(t), \\ \frac{dI(t)}{dt} = \beta_1 S(t) B(t) + \beta_2 S(t) I(t) - (d + \alpha + \mu_1) I(t) \\ \frac{dR}{dt} = \alpha I(t) - \mu_1 R(t), \\ \frac{dB(t)}{dt} = \eta I(t) - \mu_2 B(t). \end{cases} \quad (1.1)$$

The flow diagram of the model is depicted in **Figure 1**. Since the first three and last equations in (1.1) are independent of the variable R , it suffices to consider the following reduced model:

$$\begin{cases} \frac{dS(t)}{dt} = \mu_1 - \beta_1 S(t) B(t) - \beta_2 S(t) I(t) - \phi S(t) \\ \quad - \mu_1 S(t) + \theta V(t), \\ \frac{dV}{dt} = \phi S(t) - \theta V(t) - \mu_1 V(t), \\ \frac{dI(t)}{dt} = \beta_1 S(t) B(t) + \beta_2 S(t) I(t) - (d + \alpha + \mu_1) I(t) \\ \frac{dB(t)}{dt} = \eta I(t) - \mu_2 B(t). \end{cases} \quad (1.2)$$

Here, S , V , I and R refer to the susceptible individuals, vaccinated individuals, infected individuals, and recovered individuals, respectively.

The pathogen population at time t , is given by $B(t)$. The parameter μ_1 denotes the natural human birth and

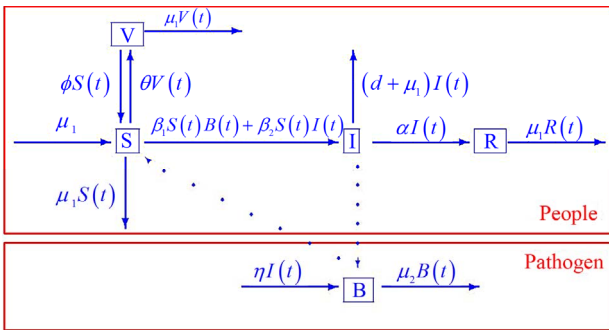


Figure 1. Progression of infection from susceptible (*S*) and vaccinated (*V*) individuals through the infected (*I*) and recovered (*R*) compartments for the combined human-environment epidemiological model with an environmental component.

death rate, α denotes the rate of recovery from the disease, η represents the rate of human contribution to the growth of the pathogen, and μ_2 represents the death rate of the pathogen in the environment. The coefficients β_1 and β_2 represent the contact rates for the human-environment and human-human interactions, respectively. The rate at which the susceptible population is vaccinated is ϕ , and the rate at which the vaccine wears off is θ .

All parameters are assumed non-negative, and the initial conditions of the system (1.2) are assumed as following

$$S(0) > 0, V(0) > 0, I(0) > 0, B(0) > 0. \quad (1.3)$$

The organization of this paper is as follows: the positivity and boundedness of solutions are obtained in Section 2. In Section 3, we firstly calculate the basic reproduction number and obtain the existence of the endemic equilibrium. We get the local and global asymptotically stability of the disease-free equilibrium in Section 4. In Section 5, we show that the local asymptotically stability of the endemic equilibrium. We analyze the sensitivity of R_v on the parameters, and we present the numerical simulation in Section 6. The paper ends with a conclusion in Section 7.

2. POSITIVITY AND BOUNDEDNESS OF SOLUTIONS

In the following, we show that the solutions of the system (1.2) are positive with the non-negative initial conditions (1.3).

Theorem 2.1. The solutions ($S(t), V(t), I(t), B(t)$) of the model (1.2) are non-negative for all $t > 0$ with initial conditions (1.3).

Proof. The system (1.2) can be put into the matrix form

$$X' = M(X),$$

where $X = (S, V, I, B)^T \in R^4$ and $M(X)$ is given by

$$M(X) = \begin{pmatrix} M_1(X) \\ M_2(X) \\ M_3(X) \\ M_4(X) \end{pmatrix} = \begin{pmatrix} \mu_1 - \beta_1 S(t)B(t) - \beta_2 S(t)I(t) - \phi S(t) \\ -\mu_1 S(t) + \theta V(t) \\ \phi S(t) - \theta V(t) - \mu_1 V(t) \\ \beta_1 S(t)B(t) + \beta_2 S(t)I(t) - (d + \alpha + \mu_1)I(t) \\ \eta I(t) - \mu_2 B(t) \end{pmatrix}$$

We have

$$\left. \frac{dS}{dt} \right|_{S=0} = \mu_1 + \theta V > 0, \quad \left. \frac{dV}{dt} \right|_{V=0} = \phi S > 0,$$

$$\left. \frac{dI}{dt} \right|_{I=0} = \beta_1 S B \geq 0, \quad \left. \frac{dB}{dt} \right|_{B=0} = \eta I \geq 0.$$

Therefore,

$$M_i \Big|_{X_i=0, X_j \in C^+} \geq 0, i = 1, 2, 3, 4.$$

Due to Lemma 2 in [5], any solution of the system (1.2) is such that $X(T) \in R^4_+$ for all $t \geq 0$. This completes the proof of Theorem 2.1.

Theorem 2.2. All solutions ($S(t), V(t), I(t), B(t)$) of the model (1.2) are bounded.

Proof. The system (1.2) is split into two parts, the human population (*i.e.*, $S(t), V(t)$, and $I(t)$) and pathogen population (*i.e.*, $B(t)$). It follows from the first three equations of the system (1.2) that

$$\begin{aligned} \frac{d(S+V+I)}{dt} &= \mu_1(1-S-V-I) - dI - \alpha I \\ &\leq \mu_1(1-S-V-I), \end{aligned}$$

then it follows that $\limsup_{t \rightarrow +\infty} (S+V+I) \leq 1$. From the first equation, we can get

$$\frac{dS}{dt} \leq \mu_1 - \mu_1 S - \phi S + \theta V \leq \mu_1 + \theta - (\mu_1 + \theta + \phi)S.$$

Thus $\frac{dS}{dt} \leq 0$, as $S(t) \geq \frac{\mu_1 + \theta}{\mu_1 + \theta + \phi}$. It is easy obtain

$$\frac{dV}{dt} \leq \phi(1-V) - (\mu_1 + \theta)V = \phi - (\mu_1 + \theta + \phi)V.$$

$\frac{dV}{dt} \leq 0$, as $V(t) \geq \frac{\phi}{\mu_1 + \theta + \phi}$. From the last equation,

we can obtain

$$\frac{dB}{dt} \leq \eta - \mu_2 B.$$

Hence, $\frac{dB}{dt} \leq 0$, when $B \geq \frac{\eta}{\mu_2}$. Therefore, all solutions $(S(t), V(t), I(t), B(t))$ of the model (1.2) are bounded.

From above discussion, we can see that the feasible region of human population for system (1.2) is

$$\Omega_H = \left\{ (S, V, I) \mid S + V + I \leq 1, 0 \leq S \leq \frac{\mu_1 + \theta}{\mu_1 + \theta + \phi}, 0 \leq V \leq \frac{\phi}{\mu_1 + \theta + \phi}, I \geq 0 \right\}$$

and the feasible region of pathogen population for system (1.2) is

$$\Omega_B = \left\{ B \mid 0 \leq B \leq \frac{\eta}{\mu_2} \right\}.$$

Define $\Omega = \Omega_H \times \Omega_B$. Let $\text{int}\Omega$ denote the interior of Ω . It is easy to verify that the region Ω is a positively invariant region (*i.e.*, the solutions with initial conditions in Ω remain in Ω) with respect to the system (1.2). Hence, we will consider the global asymptotically stability of (1.2) in region Ω .

3. THE EXISTENCE OF EQUILIBRIA

In this section, we investigate the existence of equilibria of system (1.2). Solving the right hand side of the model system (1.2) by equating it to zero, we obtain the following biologically relevant equilibria.

It is easy to see that model (1.2) always has a disease-free equilibrium (the absence of infection, that is, $I = B = 0$, $E_0(S_0, V_0, 0, 0)$, where $S_0 = \frac{\mu_1 + \theta}{\mu_1 + \theta + \phi}$ and $V_0 = \frac{\phi}{\mu_1 + \theta + \phi}$. Let $X = (I, B, S, V)^T$. Then model (1.2) can be written as

$$\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x),$$

where

$$\mathcal{F}(x) = \begin{pmatrix} \beta_1 SB + \beta_2 SI \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$\mathcal{V}(x) = \begin{pmatrix} (d + \alpha + \mu_1)I \\ -\eta I(t) + \mu_2 B \\ -\mu_1 + \beta_1 SB + \beta_2 SI + \phi S + \mu_1 S - \theta V \\ -\phi S + \theta V + \mu_1 V \end{pmatrix}.$$

We can get

$$F = \begin{pmatrix} \beta_2 S_0 & \beta_1 S_0 \\ 0 & 0 \end{pmatrix}, V = \begin{pmatrix} d + \alpha + \mu_1 & 0 \\ -\eta & \mu_2 \end{pmatrix},$$

giving

$$V^{-1} = \begin{pmatrix} \frac{1}{d + \alpha + \mu_1} & 0 \\ \frac{\eta}{\mu_2(d + \alpha + \mu_1)} & \frac{1}{\mu_2} \end{pmatrix}.$$

FV^{-1} is the next generation matrix for model (1.2). It then follows that the spectral radius of matrix FV^{-1} is

$$\rho(FV^{-1}) = \frac{S_0(\beta_2 \mu_2 + \beta_1 \eta)}{\mu_2(d + \alpha + \mu_1)}.$$

According to Theorem 2 in [6], the basic reproduction number of model (1.2) is

$$R_v = \frac{(\mu_1 + \theta)(\beta_2 \mu_2 + \beta_1 \eta)}{\mu_2(\mu_1 + \theta + \phi)(d + \alpha + \mu_1)}.$$

In the following, we will discuss the case with $R_v > 1$. The existence and uniqueness of the endemic equilibrium is established as follows.

The endemic equilibrium $E^*(S^*, V^*, I^*, B^*)$ can be deduced by the following system:

$$\begin{cases} \mu_1 - \beta_1 S^* B^* - \beta_2 S^* I^* - \phi S^* - \mu_1 S^* + \theta V^* = 0, & (3.1) \\ \phi S^* - \theta V^* - \mu_1 V^* = 0, & (3.2) \end{cases}$$

$$\begin{cases} \beta_1 S^* B^* + \beta_2 S^* I^* - (d + \alpha + \mu_1) I^* = 0, & (3.3) \end{cases}$$

$$\begin{cases} \eta I^* - \mu_2 B^* = 0. & (3.4) \end{cases}$$

which gives,

$$S^* = \frac{\mu_1 + \theta}{\mu_1 + \theta + \phi R_v},$$

$$V^* = \frac{\phi}{\mu_1 + \theta + \phi R_v},$$

$$I^* = \frac{\mu_1}{d + \alpha + \mu_1} \left(1 - \frac{1}{R_v} \right),$$

$$B^* = \frac{\eta \mu_1}{\mu_2(d + \alpha + \mu_1)} \left(1 - \frac{1}{R_v} \right).$$

Obviously, when $R_v > 1$, $I^* > 0$, $B^* > 0$.

Theorem 3.1. The system (1.2) has a unique endemic equilibrium when $R_v > 1$ and no positive endemic equilibrium when $R_v < 1$.

4. STABILITY OF DISEASE-FREE EQUILIBRIUM

Now, we will discuss the local and global asymptotically stability of the disease-free equilibrium. From above and [6], we can obtain the following theorem.

Theorem 4.1. The disease-free equilibrium E_0 is locally asymptotically stable for $R_v < 1$ and unstable for R_v

> 1.

Proof. The Jacobian matrix of the system (1.2) at $X = E_0$ is

$$J(E_0) = \begin{pmatrix} -\mu_1 - \phi & \theta & -\beta_2 S_0 & -\beta_1 S_0 \\ \phi & -\theta - \mu_1 & 0 & 0 \\ 0 & 0 & \beta_2 S_0 - (d + \alpha + \mu_1) & \beta_1 S_0 \\ 0 & 0 & \eta & -\mu_2 \end{pmatrix}$$

The characteristic polynomial of the matrix $J(E_0)$ is given by

$$\det(\lambda I - J(E_0)) = a_0 \lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4,$$

where

$$\begin{aligned} a_0 &= 1, \\ a_1 &= 2\mu_1 + \mu_2 + \theta + \phi + (d + \alpha + \mu_1 - \beta_2 S_0), \\ a_2 &= (\theta + 2\mu_1 + \phi)(d + \alpha + \mu_1 - \beta_2 S_0) \\ &\quad + [\mu_2(d + \alpha + \mu_1) - (\beta_1 S_0 \eta + \beta_2 S_0 \mu_2)] \\ &\quad + \mu_1^2 + 2\mu_1 \mu_2 + \theta \mu_2 + \phi \mu_2 + \phi \mu_1 + \theta \mu_1 \\ a_3 &= (2\mu_1 + \phi + \theta) \\ &\quad \times [\mu_2(d + \alpha + \mu_1) - (\beta_1 S_0 \eta + \beta_2 \cdot S_0 \mu_2)] \\ &\quad + (\mu_1 \theta + \mu_1^2 + \phi \mu_1)(d + \alpha + \mu_1 - \beta_2 \cdot S_0) \\ &\quad + \mu_1^2 \mu_2 + (\theta + \phi) \mu_1 \mu_2 \\ a_4 &= \mu_1 \mu_2 (\theta + \phi + \mu_1)(d + \alpha + \mu_1)(1 - R_v), \\ a_1 a_2 - a_3 &= (d + \alpha + \mu_1 - \beta_2 S_0) \\ &\quad \times (4\mu_1 \theta + 4\phi \mu_1 + 4 \cdot \mu_1^2 + 4\mu_1 \mu_2 + \phi^2 + \theta^2 \\ &\quad + 2\mu_2 \phi + 2\mu_2 \theta + 2\theta \phi) \\ &\quad + [\mu_2(d + \alpha + \mu_1) - (\beta_1 S_0 \eta + \beta_2 S_0 \mu_2)] \\ &\quad \times \mu_2(d + \alpha + \mu_1 - \beta_2 S_0)^2 (\theta + \phi + 2\mu_1) \\ &\quad + 4(\theta + \phi + \mu_1) \mu_1 \mu_2 + 2\mu_1 \mu_2^2 + \theta \mu_2^2 \\ &\quad + 3(\phi + \theta) \mu_1^2 + (\phi^2 + \theta^2) \mu_2 + \theta^2 \mu_1^2 \\ &\quad + 2\theta \phi (\mu_2 + \mu_1) + 2\mu_1^3. \end{aligned}$$

If $R_v < 1$, then

$$\mu_2(d + \alpha + \mu_1) > \beta_2 S_0 \mu_2 + \beta_1 S_0 \eta,$$

further

$$d + \alpha + \mu_1 > \beta_2 S_0$$

After some calculations, if $R_v < 1$ we have $a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0, a_1 a_2 - a_3 > 0, a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$ (see Appendix A). Thus, using the Routh-Hurwitz criterion,

all eigenvalues of $J(E_0)$ have negative real part, E_0 is local asymptotically stable for the system (1.2). If $R_v \geq 1$, then $a_4 \leq 0$ and we show that $J(E_0)$ has at least one eigenvalues with non-negative real part. Consequently, E_0 is not stable.

Theorem 4.2. When $R_v < 1$ the disease-free equilibrium is globally asymptotically stable.

We will prove the global asymptotically stability of the disease-free equilibrium using Lemma 4.1.

Lemma 4.1. [7] If a model system can be written in the form

$$\begin{cases} \frac{d\mathcal{X}}{dt} = P(\mathcal{X}, \mathcal{Z}), \\ \frac{d\mathcal{Z}}{dt} = G(\mathcal{X}, \mathcal{Z}), G(\mathcal{Z}, 0) = 0, \end{cases}$$

where $\mathcal{X} \in R^m$ denotes (its components) the number of uninfected individuals and $\mathcal{Z} \in R^n$ denotes (its components) the number of infected individuals including latent, etc. $U_0 = (\mathcal{X}^*, 0)$ denotes the disease-free equilibrium of the system.

And assume that

$$(H1) \quad \frac{d\mathcal{X}}{dt} = P(\mathcal{X}, 0), \quad \mathcal{X}^* \text{ is globally asymptotically}$$

stable;

$$(H2) \quad G(\mathcal{X}, \mathcal{Z}) = \mathcal{A}\mathcal{Z} - \hat{G}(\mathcal{X}, \mathcal{Z}), \hat{G}(\mathcal{X}, \mathcal{Z}) \geq 0, \text{ for}$$

$$(\mathcal{X}, \mathcal{Z}) \in \Omega, \text{ where the Jacobian matrix } \mathcal{A} = \frac{\partial G}{\partial \mathcal{Z}}(\mathcal{X}^*, 0)$$

is an Metzler matrix (the off-diagonal elements of \mathcal{A} are non-negative) and Ω is the region where the model makes biological sense. Then the fixed point $U_0 = (\mathcal{X}^*, 0)$ is a globally asymptotically stable equilibrium of cholera model system (1.2) provided that $R_v < 1$.

We begin by showing condition (H1) as

$$P(\mathcal{X}, 0) = \begin{pmatrix} \mu_1 - \mu_1 S - \phi \mu_1 + \theta V \\ \phi S - \theta V - \mu_1 V \end{pmatrix}.$$

For the equilibrium $U_0 = (\mathcal{X}^*, 0)$, the system reduces to

$$\begin{cases} \frac{dS(t)}{dt} = \mu_1 - \phi S(t) - \mu_1 S(t) + \theta V(t), \\ \frac{dV(t)}{dt} = \phi S(t) - \theta V(t) - \mu_1 V(t). \end{cases}$$

The characteristic polynomial of the system is given by

$$(\lambda + \mu_1)(\lambda + \theta + \phi + \mu_1) = 0.$$

There are two negative characteristic roots are $\lambda = -\mu_1, \lambda = -\theta - \phi - \mu_1$. Hence, \mathcal{X}^* is always globally asymptotically stable.

Next, applying Lemma 4.1 to the cholera model system (1.2) gives

$$G(\mathcal{X}, \mathcal{Z}) = A\mathcal{Z} - G(\mathcal{X}, \mathcal{Z}) = \begin{pmatrix} \beta_2 S_0 - (d + \alpha + \mu_1) & \beta_1 S_0 \\ \eta & -\mu_2 \end{pmatrix} \begin{pmatrix} I \\ B \end{pmatrix} - \begin{pmatrix} 0 \\ 0 \end{pmatrix},$$

which is clearly an Metzler matrix. Meanwhile, we find $\hat{G}(\mathcal{X}, \mathcal{Z}) = 0$. Hence, the disease-free equilibrium is globally asymptotically stable.

5. STABILITY OF THE ENDEMIC EQUILIBRIUM

Now we consider the case with $R_v > 1$. The stability of the endemic equilibrium is established as follows:

Theorem 5.1. If $R_v > 1$, $E^*(S^*, V^*, I^*, B^*)$ is locally asymptotically stable.

Proof. Let

$$J_1 = \beta_1 B^* + \beta_2 I^*, \quad J_2 = \beta_2 S^*, \quad J_3 = \beta_1 S^*.$$

The Jacobian matrix at $E^*(S^*, V^*, I^*, B^*)$ is

$$J(E^*) = \begin{pmatrix} -J_1 - \mu_1 - \phi & \theta & -J_2 & -J_3 \\ \phi & -\theta - \mu_1 & 0 & 0 \\ 0 & 0 & J_2 - (d + \alpha + \mu_1) & J_3 \\ 0 & 0 & \eta & -\mu_2 \end{pmatrix}$$

The characteristic polynomial of the matrix $J(E^*)$ is given by

$$\det(\lambda I - J(E^*)) = b_0 \lambda^4 + b_1 \lambda^3 + b_2 \lambda^2 + b_3 \lambda + b_4,$$

where

$$b_0 = 1,$$

$$b_1 = J_1 + 2\mu_1 + \mu_2 + \theta + \phi + (d + \alpha + \mu_1 - J_2),$$

$$b_2 = (d + \alpha + \mu_1 - J_2)(\theta + 2\mu_1 + \phi) + [\mu_2(d + \alpha + \mu_1) - (J_2\mu_2 + J_3\eta)] + J_3\mu_1^2 + 2\mu_1\mu_2 + \theta\mu_2 + \phi\mu_1 + \phi\mu_2 + \theta\mu_1 + \alpha J_1 + 2\mu_1 J_1 + \mu_2 J_2 + dJ_1,$$

$$b_3 = (d + \alpha + \mu_1 - J_2)(\mu_1\theta + \mu_1^2 + \mu_1\phi) + [\mu_2(d + \alpha + \mu_1) - (J_2\mu_2 + J_3\eta)](2\mu_1 + \phi + \theta) + J_3 \cdot \mu_1^2 + \mu_1^2 \mu_2 + \theta\mu_1\mu_2 + \phi\mu_1\mu_2 + \theta\alpha J_1 + \alpha\mu_1 J_1 + J_1\mu_1^2 + d\mu_1 J_1 + 2\mu_1\mu_2 J_1 + (d + \alpha + \theta)\mu_2 \cdot J_1 + d\theta J_1 + \theta\mu_1 J_1,$$

$$b_4 = [\mu_2(d + \alpha + \mu_1) - (J_2\mu_2 + J_3\eta)](\phi + \mu_1 + \theta) \cdot \mu_1 + \theta\alpha\mu_2 J_1 + (d + \alpha + \mu_1 + \theta)\mu_1\mu_2 J_1 + d\theta \cdot \mu_2 J_1,$$

$$b_1 b_2 - b_3$$

$$= (d + \alpha + \mu_1 - J_2) \times (4\mu_1\theta + 4\mu_1^2 + 4\mu_1\phi + \theta^2 + \phi^2 + 2\mu_2\phi + 4\mu_1\mu_2 + \alpha J_1 + 2\theta\mu_2 + \theta J_1 + \phi J_1 + 2\theta\phi + 4\mu_1 J_1 + \mu_2 J_1 + dJ_1) + [\mu_2(d + \alpha + \mu_1) - (J_2\mu_2 + J_3\eta)](\mu_2 + J_1) + (d + \alpha + \mu_1 - J_2)^2(\theta + \phi + 2\mu_1) + (d + \alpha)\mu_1 J_1 + \theta\mu_2 J_1 + 4(\theta + \phi + J_1)\mu_1\mu_2\phi + (\alpha + 2\mu_1 + \mu_2 + d)J_1^2 + 3(\phi + \theta)\mu_1^2 + \phi^2(\mu_1 + \mu_2) + \theta^2(\mu_1 + \mu_2) + 3\phi\mu_1 J_1 + 2\theta\phi\mu_2 + \alpha\phi J_1 + 2\phi\mu_2 J_1 + d\phi J_1 + 2\theta \cdot \phi\mu_1 + 2\mu_1^3.$$

Based on **Eq.3.3** and **Eq.3.4**, we have

$\mu_2(d + \alpha + \mu_1) = \mu_2\beta_2 S^* + \eta\beta_1 S^*$. It is then easy to observe that

$$\mu_2(d + \alpha + \mu_1) = \mu_2 J_2 + \eta J_3,$$

further,

$$d + \alpha + \mu_1 > J_2.$$

After some calculations, we have $b_1 > 0, b_2 > 0,$

$$b_3 > 0, b_4 > 0, b_1 b_2 - b_3 > 0, b_1 b_2 b_3 > b_3^2 + b_1^2 b_4,$$

(see Appendix B). Using the well-known Routh-Hurwitz criterion, the proof is thus complete.

6. SENSITIVITY ANALYSIS OF R_v

To facilitate the interpretation of the sensitivity of R_v , we now present some numerical simulations by using the set of parameters values in **Table 1**.

Now, we regard the vaccinated rate ϕ and the wanning rate θ as the control parameter, while the other parameters are fixed. From **Figures 2** and **3**, the effects of various parameters, *i.e.*, ϕ and θ on the basic reproduction number R_v have been shown. It is noted that as the parameter ϕ increases, R_v decreases; as θ decreases, R_v decreases. In fact, we can obtain the critical values of ϕ and θ that reduce R_v to 1,

$$\phi = -\frac{-\mu_1\mu_2\beta_2 - \mu_1\beta_1\eta - \theta\mu_2\beta_2 - \theta\eta\beta_1}{\mu_2(d + \alpha + \mu_1)} + \frac{(d + \alpha + \theta + \mu_1)\mu_1\mu_2 + d\theta\mu_2 + \alpha\theta\mu_2}{\mu_2(d + \alpha + \mu_1)},$$

and

$$\theta = -\frac{-\mu_1\mu_2\beta_2 - \mu_1\beta_1\eta +}{-\mu_2\beta_2 - \beta_1\eta + \mu_2(d + \alpha + \mu_1)} + \frac{(d + \alpha + \phi + \mu_1)\mu_1\mu_2 + d\phi\mu_2 + \alpha\phi\mu_2}{-\mu_2\beta_2 - \beta_1\eta + \mu_2(d + \alpha + \mu_1)},$$

Table 1. Estimation of parameters.

Parameters	Meaning	Values	Reference
μ_1	Natural human birth and death rate	9.13×10^{-5} /day	[8]
β_1	Contact rates for the human-environment interaction	0.214/day	[8]
β_2	Contact rates for the human-human interaction	0.02/day	[8]
d	Disease-induced death rate	0.013/day	[4]
α	Recovery Rate at which people recover from environment	0.2/day	[8]
η	Contribution of infected individuals to the population of vibrio cholera	10	[9]
μ_2	Net death rate of vibrio cholera	0.33/day	[9]

In **Figure 2**, we select $\theta = 0.07, 0.03, 0.007, 0.0001$, corresponding $\phi_v = 2.07, 0.89, 0.21, 0.01$, respectively. We can see that when the wanning rate θ has a greater value, ϕ_v has not reasonable value so that when $\phi > \phi_v, R_v < 1$. Similarly, in **Figure 3**, we select $\phi = 0.01, 0.1, 0.3, 0.6, 0.99$, corresponding $\theta_v = 0.0002, 0.003, 0.01, 0.02, 0.03$, respectively. We can see that when ϕ is smaller, θ_v has not reasonable value so that when $\theta < \theta_v, R_v < 1$. Thus, the basic reproduction number can not reduces below unity only by increasing θ or decreasing ϕ . The critical values ϕ_v and θ_v play a key role in regulation the infection magnitude. In order to reduce R_v to 1, a greater vaccinated rate than ϕ_v and a smaller wanning rate than θ_v have to be achieved simultaneously. We will deduce R_v below 1 by using both ϕ and θ at the same time, which can control cholera (see **Figure 4**).

7. CONCLUSION

In this paper, we have conducted stability analysis of a SVIR-B cholera model. The mathematical analysis results show that the basic reproduction number R_v satisfies a threshold property with threshold value 1. R_v in our model include the parameters ϕ and θ which reflect the effect of vaccination. Numerical simulation show also that the vaccination is always beneficial to the eradication of cholera.

However, there are inherent disadvantages towards the vaccination modeling. For cholera with incubation period, it is hard to rapidly identify those with ambiguous symptoms [4]. Moreover, the vaccination does not always work well due to the limitations of medical development level and financial budget (some vaccine is very expensive and some portion of people cannot be covered) [10].

Hence, incorporating some other control strategies, for example, public health improvement, isolation etc, we may consider the more realistic ordinary differential equation model. The theoretical study of cholera models has been in progress, and is an exciting area of future research.

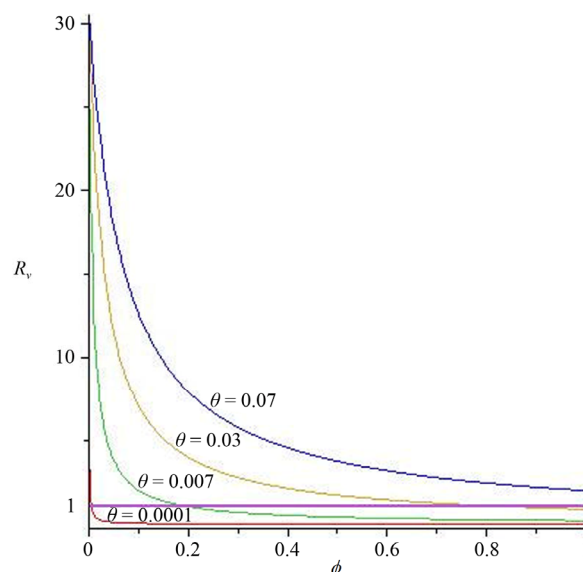


Figure 2. The contour diagram of the basic reproduction number R_v with ϕ, θ has some fixed value.

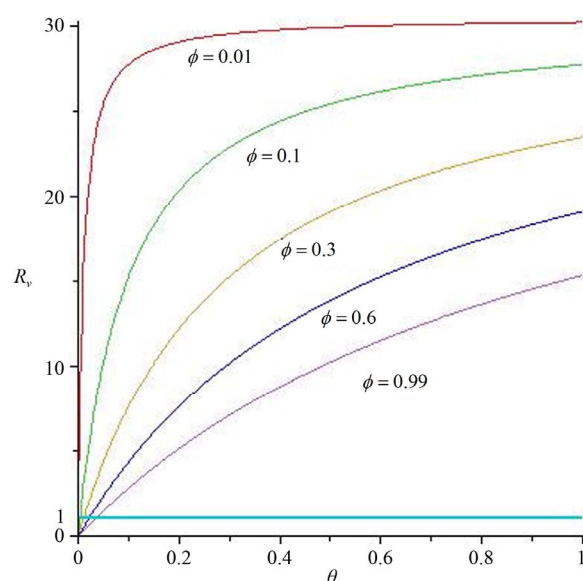


Figure 3. The contour diagram of the basic reproduction number R_v with ϕ, θ has some fixed value.

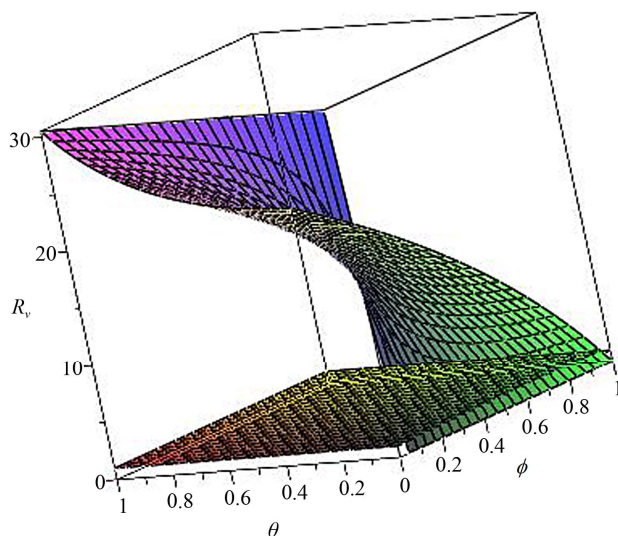


Figure 4. The contour diagram of the basic reproduction number R_v with ϕ , θ variables. all the other parameter value are the same as those in **Figure 2**.

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APPENDIX A

$$a_1 a_2 a_3 - a_3^2 - a_1^2 a_4$$

$$\begin{aligned}
 &= (d + \alpha + \mu_1 - \beta_2 S_0)^3 (\theta^2 \mu_1 + \phi^2 \mu_1 + 3\theta \mu_1^2 + 2\mu_1^3 + 2\theta \phi \mu_1 + 3\phi \mu_1^2) \\
 &+ (d + \alpha + \mu_1 - \beta_2 S_0)^2 \{ \phi^3 \mu_1 + 4\theta \mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 4\mu_1^2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 3\phi^2 \mu_1 \mu_2 + 9\phi \mu_1^2 \mu_2 + 4\mu_1^4 + 10\theta \phi \mu_1^2 \\
 &+ \theta^2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 8\phi \mu_1^3 + 6\theta \phi \mu_1 \mu_2 + 5\phi^2 \mu_1^2 \\
 &+ \phi^2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 9\theta \mu_1^2 \mu_2 + 3\theta \phi^2 \mu_1 + 8\theta \mu_1^3 \\
 &+ 4\phi \mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 5\theta^2 \mu_1^2 + 2\theta \cdot \phi [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 3\theta^2 \phi \mu_1 + 6\mu_1^3 \mu_2 + \theta^3 \mu_1 + 3\theta^2 \mu_1 \mu_2 \} + (d + \alpha + \mu_1 - \beta_2 S_0) \{ 4\phi^2 \mu_1^3 + 7d\theta \phi \mu_1 + 3\phi \theta^2 \mu_1^2 + 10\phi^2 \mu_1^2 \mu_2 + 2\theta^3 \mu_1 \cdot \mu_2 \\
 &+ 8\theta \phi \mu_1^3 + 9\theta \mu_1^2 \mu_2^2 + 6\mu_1^3 \mu_1^2 + 16\phi \mu_1^3 \mu_2 + 4 \cdot \mu_1^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 6\phi \theta^2 \mu_1 \cdot \mu_2 + 2\mu_1^5 \\
 &+ 8\phi \mu_1 \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 4\theta^2 \mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 \cdot S_0 \eta)] \\
 &+ \phi [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)]^2 + 4\phi^2 \mu_1 \cdot [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 20 \cdot \theta \phi \mu_1^2 \mu_2 \\
 &+ 8\theta \mu_1 \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 \cdot S_0 \eta)] + 3 \cdot \theta^2 \mu_1 \mu_2^2 + 9\phi \mu_1^2 \mu_2^2 + 16\theta \mu_1^3 \mu_2 + 5\phi \mu_1^4 + 5\theta \mu_1^4 + 2\phi^3 \mu_1 \mu_2 \\
 &+ 3\phi^2 \mu_1 \mu_2^2 + 5d\phi \mu_1 \mu_2 + 6\theta \mu_1^2 \cdot [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 2\phi^2 \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ \phi^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + \phi \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \cdot \eta)] \\
 &+ 2\theta^2 \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 \cdot S_0 \mu_2 + \beta_1 S_0 \eta)] + 6\phi \mu_1^2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 4\theta \phi \mu_2 \cdot [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 4\theta^2 \mu_2^3 + 4 \cdot \theta^2 \mu_2^2 + \phi^3 \mu_1^2 + 3\theta \phi^2 \mu_1^2 + \theta^3 \mu_1^2 + 8\mu_1^4 \mu_2 \\
 &+ 2\mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 3\theta \phi^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 10\theta^2 \mu_1^2 \mu_2 \\
 &+ 3\theta^2 \phi [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 \cdot S_0 \eta)] + 8\theta \phi \mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] 6\theta \phi \mu_1 \mu_2^2 \\
 &+ \theta^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + \theta [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 8\mu_1^2 \mu_2 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \} + [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)]^2 \{ \phi \mu_2 + 2\mu_1 \mu_2 + \theta \mu_2 \} \\
 &+ [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \{ 8\theta \phi \mu_1 \mu_2 + 4\phi \cdot \mu_1 \mu_2^2 + \phi^2 \mu_2^2 + 4\theta^2 \mu_1 \mu_2 + 4\mu_1^3 \mu_2 + 6\theta \mu_1^2 \mu_2 + 4\mu_1^2 \cdot \mu_2^2 \\
 &+ \phi^3 \mu_2 + 3\theta \phi^2 \mu_2 + 2\theta \phi \mu_2^2 + 4\phi^2 \mu_1 \mu_2 + 4\theta \mu_1 \mu_2^2 + \theta^3 \mu_2 + 6\phi \mu_1^2 \mu_2 + 3\theta^2 \phi \mu_2 + \theta^2 \mu_2^2 + \theta^3 \mu_1 \mu_2^2 + \theta^3 \cdot \mu_1^2 \mu_2 \} \\
 &+ 3\theta \phi^2 \mu_1 \mu_2^2 + 4\theta^2 \mu_1^3 \mu_2 + \phi^3 \mu_1^2 \mu_2 + \phi^3 \mu_1 \cdot \mu_2^2 + 8\theta \phi \mu_1^3 \mu_2 + 3\phi \theta^2 \mu_1^2 \mu_2 + 5\phi \mu_1^4 \mu_2 + 2\mu_1^3 \mu_2^3 + 5\theta \mu_1^4 \mu_2 + 4\mu_1^4 \mu_2^2 + \theta^2 \mu_1 \mu_2^3 \\
 &+ 10\theta \phi \mu_1^2 \mu_2^2 + 3\theta \phi^2 \cdot \mu_1^2 \mu_2 + 3\phi \theta^2 \mu_1 \mu_2^2 + 2\theta \phi \mu_1 \mu_2^3 + 8\mu_1^3 \mu_2^2 (\theta + \phi) + 5\mu_1^2 \mu_2^2 (\theta^2 + \phi^2) \\
 &+ 4\phi^2 \mu_1^3 \mu_2 + 3\mu_1^2 \mu_2^3 (\theta + \phi) + \phi^2 \mu_1 \mu_2^3
 \end{aligned}$$

From Section 4, we know that $R_v < 1$,

$$\mu_2 (d + \alpha + \mu_1) > \beta_2 S_0 \mu_2 + \beta_1 S_0 \eta$$

and

$$d + \alpha + \mu_1 > \beta_2 S_0 .$$

After some algebraic manipulations, we have $a_1 a_2 a_3 - a_3^2 - a_1^2 a_4 > 0$, Thus, $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$, when $R_v < 1$.

APPENDIX B

$$\begin{aligned}
 & b_1 b_2 b_3 - b_3^2 - b_1^2 b_4 \\
 & = (d + \alpha + \mu_1 - J_2)^3 \left(\theta^2 \mu_1 + \phi^2 \mu_1 + 3\theta \mu_1^2 + 2\mu_1^3 + 2\theta \phi \mu_1 + 3\phi \mu_1^2 \right) \\
 & \quad + (d + \alpha + \mu_1 - J_2)^2 \left\{ \mu_1 \mu_2 \alpha J_1 + 4\alpha \mu_1^2 J_1 + \phi^3 \mu_1 + 4\mu_1^2 \mu_2 J_1 + 4\theta \mu_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \right. \\
 & \quad + 4\alpha \theta \mu_1 J_1 + 4\mu_1^2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 2\alpha \phi \mu_1 J_1 + \alpha \phi \mu_2 J_1 + \alpha \theta^2 J_1 + \theta^2 \mu_2 J_1 + 3\phi^2 \mu_1 \mu_2 \\
 & \quad + \phi^2 \mu_1 J_1 + 9\phi \mu_1^2 \mu_2 + 4\mu_1^4 + 10\theta \phi \mu_1^2 + \theta^2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 8\phi \mu_1^3 + 6\theta \phi \mu_1 \mu_2 \\
 & \quad + 5\phi^2 \mu_1^2 + \phi^2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 9\theta \mu_1^2 \mu_2 + 4\theta \mu_1 \mu_2 J_1 + 3\theta \phi^2 \mu_1 + 8\theta \mu_1^3 \\
 & \quad + 4\phi \mu_1 \left[\mu_2 \cdot (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 5\theta^2 \mu_1^2 + 3\phi \mu_1 \cdot \mu_2 J_1 + 6 \cdot \phi \mu_1^2 J_1 + 3d \mu_1^2 J_1 + 2d \phi \mu_1 J_1 \\
 & \quad + 2\theta \phi \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 8\theta \mu_1^2 J_1 + 3\theta^2 \phi \mu_1 \\
 & \quad + \theta \phi \mu_2 J_1 + \theta \phi \mu_2 J_1 + 4d \theta \mu_1 J_1 + \theta \phi \alpha J_1 + 6\mu_1^3 \mu_2 + 2\theta^2 \mu_1 J_1 + d \mu_1 \mu_2 J_1 + \theta^3 \mu_1 + 3\theta \phi \mu_1 J_1 + d \phi \mu_2 J_1 + 6\mu_1^3 J_1 + d \theta^2 J_1 \\
 & \quad + 3\theta^2 \mu_1 \mu_2 \left. \right\} + (d + \alpha + \mu_1 - J_2) \left\{ 4 \cdot \phi^2 \mu_1^3 + 7d \theta \phi \mu_1 + d^2 \mu_2 J_1^2 + \theta d^2 J_1^2 + 3\phi \mu_1 \mu_2 J_1^2 + 3\phi \theta^2 \mu_1^2 + 10\phi^2 \mu_1^2 \mu_2 + 2\alpha \theta d J_1^2 \right. \\
 & \quad + 2\theta^3 \mu_1 \mu_2 + d^2 \mu_1 J_1^2 + d \phi \mu_2 J_1^2 + 8\theta \phi \mu_1^3 + \theta \alpha^2 J_1^2 + 8\mu_1^2 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 2d \alpha \mu_1 J_1^2 + 9\theta \mu_1^2 \mu_2^2 \\
 & \quad + 5d \theta \mu_1 \mu_2 J_1 + 2d \theta J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 6\mu_1^3 \mu_2^2 + 16\phi \mu_1^3 \mu_2 + \alpha \theta^2 \cdot J_1^2 \\
 & \quad + 4\mu_1^3 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 6\phi \theta^2 \mu_1 \mu_2 + \theta^2 \mu_2 J_1^2 + 2\mu_1^5 + \theta^2 \mu_1 J_1^2 + 6\mu_1^3 J_1^2 \\
 & \quad + 8 \cdot \phi \mu_1 \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 4 \cdot \theta^2 \mu_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + \phi \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right]^2 + 2\alpha \phi \mu_2^2 J_1 + \phi^2 \cdot J_1 \cdot \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 5\theta \alpha \mu_1 \cdot \mu_2 J_1 + 5d \mu_1^3 J_1 + 2\alpha \phi \mu_1 J_1^2 + 2d \phi \mu_1 J_1^2 + 2\mu_1 \mu_2^2 J_1^2 + 8\mu_1^2 \mu_2^2 J_1 + \theta \phi \mu_2 J_1^2 \\
 & \quad + 4\phi^2 \mu_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \alpha \phi^2 \mu_2 J_1 + \theta \phi^2 \mu_1 J_1 + 14\theta \mu_1^3 \cdot J_1 + 8\mu_1^2 \mu_2 J_1^2 + 5\alpha \theta^2 \mu_1 J_1 \\
 & \quad + 2\theta \mu_2 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \theta \alpha \phi J_1^2 + 20\theta \phi \mu_1^2 \mu_2 \\
 & \quad + \theta^2 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 6 \cdot \alpha \phi \mu_1^2 J_1 + 8\theta \mu_1 \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 \cdot S_0 \eta) \right] \\
 & \quad + 2\alpha \phi^2 \mu_1 J_1 + d \phi^2 \mu_2 J_1 + d \theta \phi J_1^2 + \alpha \mu_2^2 J_1^2 + 3\theta^2 \mu_1 \mu_2^2 + 7\alpha \theta \mu_1 J_1^2 + d \theta \phi^2 J_1 + 9\phi \mu_1^2 \mu_2^2 + 6\theta \mu_1 \cdot \mu_2 J_1^2 + 16\theta \mu_1^3 \mu_2 \\
 & \quad + 6d \mu_1^2 J_1^2 + 5\phi \mu_1^4 + 9d \theta \mu_1^2 J_1 + d \theta^2 J_1^2 + 5\alpha \phi \mu_1 \mu_2 J_1 + 2\theta \phi J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 \cdot S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 5\phi \mu_1 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 5\theta \mu_1^4 + 4\phi^2 \mu_1^2 J_1 + d \theta^3 J_1 + 2\phi^3 \mu_1 \mu_2 + 7\alpha \theta \phi \mu_1 J_1 + 3\phi^2 \mu_1 \mu_2^2 \\
 & \quad + 5d \phi \mu_1 \mu_2 + 13\theta \phi \mu_1 \mu_2 J_1 + \theta^3 \mu_2 J_1 + \theta^3 \mu_1 J_1 + 2d \theta \phi \mu_2 J_1 + \alpha \phi \mu_2 J_1^2 + \alpha \phi J_1 \left[\mu_2 \cdot (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 6\theta \mu_1^2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \theta \phi \mu_1 J_1^2 + 5\alpha \mu_1 \mu_2 J_1^2 + 2\phi^2 \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + \phi^3 \left[\mu_2 \cdot (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \phi \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 22\theta \mu_1^2 \mu_2 J_1 + 5\phi^2 \mu_1 \mu_2 J_1 \\
 & \quad + 2\theta^2 \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 5\alpha \cdot \mu_1^2 \mu_2 J_1 + 8\theta^2 \mu_1^2 \mu_2 J_1 + 8\theta^2 \mu_1^2 J_1 + 5d \theta^2 \mu_1 J_1 \\
 & \quad + 6 \cdot \phi \mu_1^2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \alpha \theta \phi^2 J_1 + 2\alpha \theta \phi \mu_2 J_1 + d \theta \mu_2 J_1^2 + 9\alpha \theta \mu_1^2 J_1 + \alpha \theta \mu_2 J_1^2 \\
 & \quad + 2d \cdot \mu_1 \mu_2^2 J_1 + 8\mu_1^4 J_1 + 6\alpha \mu_1^2 J_1^2 + 19\phi \mu_1^2 \mu_2 J_1 + \alpha \mu_2 J_1 \cdot \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 6d \phi \mu_1^2 J_1 + 8\theta \mu_1 \mu_2^2 J_1 + 2d \theta^2 \phi J_1 + 4\theta \phi \mu_2 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 6\theta \mu_1 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \cdot \mu_2 + \beta_1 S_0 \eta) \right] + 4\theta^2 \mu_2^3 + 5d \mu_1 \mu_2 J_1^2 \\
 & \quad + 4\mu_1 \mu_2 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 6\theta \mu_1 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 4\theta^2 \mu_2^2 + 5d \mu_1 \mu_2 J_1^2 + 4 \cdot \mu_1 \mu_2 J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] \\
 & \quad + 3d \mu_1 \cdot J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + 2\alpha \mu_1 \mu_2^2 J_1 + 7\theta \mu_1^2 J_1^2 + \alpha^2 \mu_2 J_1^2 + \alpha \theta^3 J_1 + \phi^3 \mu_1^2 + 2\theta^2 \phi \mu_1 J_1 \\
 & \quad + 3\phi \mu_1^2 J_1^2 + 3\theta \phi^2 \mu_1^2 + \theta^3 \mu_1^2 + 2\alpha \theta J_1 \left[\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta) \right] + \theta \phi^2 \mu_2 J_1 + 8\mu_1^4 \mu_2 + 16\mu_1^3 \mu_2 \cdot J_1 + 7\theta^2 \mu_1^2 J_1
 \end{aligned}$$

$$\begin{aligned}
 &+ d\phi J_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 7d\theta \mu_1 J_1^2 + 2\alpha \phi \theta^2 J_1 + d\mu_2 J_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 3\alpha \mu_1 J_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + \alpha \theta^2 \mu_2 J_1 + 5d\mu_1^2 \mu_2 J_1 + 5 \cdot \alpha \mu_1^3 J_1 + 6\phi \mu_1 \mu_2^3 J_1 \\
 &+ 2\mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 \cdot S_0 \mu_2 + \beta_1 S_0 \eta)] + 2d\phi^2 \mu_1 J_1 + 11\theta \phi \mu_1^2 J_1 + \alpha^2 \mu_1 J_1^2 + 2\theta^2 \mu_2^2 J_1 + d\theta^2 \mu_2 J_1 \\
 &+ 3\theta \phi^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 10\theta^2 \mu_1^2 \mu_2 + 3\theta^2 \phi [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ 8\theta \phi \mu_1 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 11\phi \mu_1^3 J_1 + \theta \mu_2^2 J_1^2 + d\mu_2^2 \cdot J_1^2 + 6\theta \phi \mu_1 \mu_2^2 \\
 &+ \theta^3 [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 2\theta \phi \mu_2^2 J_1 + 2d\alpha \mu_2 J_1^2 + 2\theta^2 \phi \mu_2 J_1 \\
 &+ \theta \cdot [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] + 8\mu_1^2 \mu_2 [\mu_2 \cdot (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)] \\
 &+ [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 S_0 \eta)]^2 \{ \phi \mu_2 + 2\mu_1 \mu_2 + \theta J_1 + \phi J_1 + \theta \mu_2 + 2\mu_1 J_1 \} \\
 &+ [\mu_2 (d + \alpha + \mu_1) - (\beta_2 S_0 \mu_2 + \beta_1 \cdot S_0 \eta)] \{ 8\theta \phi \mu_1 \mu_2 + 3\theta \phi \mu_2 J_1 + 3d\mu_1 J_1^2 + 4\phi \mu_1 \mu_2^2 + 2\theta \mu_1^2 J_1 + \phi^2 \mu_2^2 \\
 &+ 4\theta^2 \mu_1 \mu_2 + \alpha \theta \phi J_1 + \alpha \theta \mu_1 J_1 + \alpha \cdot \mu_2^2 J_1 + 4\mu_1^3 \mu_2 + 8\mu_1^2 \mu_2 J_1 + \phi \mu_2 J_1^2 + 6\theta \mu_1^2 \mu_2 + \alpha \mu_2 J_1^2 + 3\alpha \phi \mu_1 J_1 \\
 &+ 6\theta \mu_1 \mu_2 J_1 + d\mu_2 J_1^2 + \theta^2 \mu_2 J_1 + 4\mu_1^2 \mu_2^2 + d\mu_2^2 J_1 + 4\mu_1^2 J_1^2 + d\theta \phi J_1 + \phi^3 \mu_2 + \alpha \cdot \phi^2 J_1 + 3\theta \phi^2 \mu_2 + 2\alpha \theta J_1^2 \\
 &+ 2\theta \mu_2 J_1^2 + \phi^2 \mu_1 J_1 + \alpha \mu_1 \cdot \mu_2 J_1 + \phi \mu_1 J_1^2 + 2\theta \phi \mu_2^2 + d\phi J_1^2 + 4\phi^2 \mu_1 \mu_2 + 4\theta \mu_1 \cdot \mu_2^2 + d\theta \mu_1 J_1 + d\mu_1 \mu_2 J_1 + \theta^3 \mu_2 \\
 &+ \alpha \phi J_1^2 + \phi \mu_2^2 J_1 + 4\mu_1 \mu_2^2 J_1 + 4\mu_1 \mu_2 J_1^2 + 2\alpha \mu_1^2 J_1 + 6\phi \mu_1^2 \mu_2 + 3\theta^2 \phi \mu_2 + 4\phi \mu_1^2 J_1 + 3\alpha \mu_1 J_1^2 + d\phi^2 J_1 + 2d\theta J_1^2 \\
 &+ 2d\mu_1^3 J_1^2 + 2\phi \theta^2 \mu_2^2 J_1 + 13\phi \mu_1^3 \mu_2 J_1 + \theta \mu_2^2 J_1^3 + 5\alpha \theta \phi \mu_1^2 J_1 + 3 \cdot d\phi \mu_1^3 J_1 + 2\theta^2 \phi \mu_1 \mu_2 J_1 + 4\alpha \theta^2 \mu_1^2 J_1 + 5\theta \phi \mu_1^3 J_1 \\
 &+ 10 \cdot \theta \phi \mu_1 \mu_2^2 J_1 + 3\alpha \mu_1^3 \mu_2 J_1 + 4\phi^2 \mu_1 \mu_2^2 J_1 + \alpha \theta \mu_1 \mu_2^2 J_1 + 2\theta \phi \mu_2^2 J_1^2 + 2d\alpha \theta \phi J_1^2 + \alpha \theta \phi^2 \mu_1 J_1 + \theta^3 \mu_2^2 J_1 \\
 &+ 4 \cdot \alpha \theta \phi \mu_1 \mu_2^2 J_1 + \theta \phi \mu_2^3 J_1 + 3d\theta \phi \mu_1 \mu_2 J_1 + 12\theta \phi \mu_1^2 \mu_2 J_1 + 14\theta \mu_1^2 \mu_2^2 J_1^2 + \theta^3 \mu_1 \mu_2 J_1 + \alpha \theta^3 \mu_1 J_1 + d\theta^3 \mu_1 J_1 \\
 &+ \theta^3 \cdot \mu_2^2 J_1 + 2d\alpha \mu_2^2 J_1 + 2d\alpha \mu_1 \mu_2 J_1^2 + d\alpha \mu_1 \mu_2^3 J_1 + 3d\phi \mu_1 \mu_2^3 J_1 + \theta \phi^2 \mu_1 \mu_2 J_1 + 3\alpha \phi \mu_1^3 J_1 + d\phi \mu_2^3 J_1 \\
 &+ 2d\mu_1^2 \cdot \mu_2^2 J_1 + 3d\theta \mu_1 J_1^3 + 5d\phi \mu_1^2 \mu_2 J_1 + d\theta \phi \mu_2^2 J_1 + 8\mu_1^2 \cdot \mu_2^2 J_1^2 + 5\alpha \theta \mu_1^3 J_1 + 7\theta^2 \mu_1 \mu_2 J_1 + \theta^3 \mu_1 \mu_2^2 \\
 &+ 4\mu_1^2 \cdot \mu_2 J_1^2 + 4\theta \mu_1 \mu_2^3 J_1 + 5\alpha \mu_1^3 J_1^2 + d^2 \phi \mu_2 J_1^2 + 3d\mu_1 \mu_2^2 \cdot J_1^2 + 3\phi \mu_1 \cdot \mu_2^3 J_1 + 3\alpha \theta \phi \mu_1 \mu_2 J_1 + 4\mu_1^4 J_1^2 \\
 &+ \theta^3 \mu_1^2 \cdot \mu_2 + \theta \mu_2^2 J_1 + d \cdot \theta \mu_2 J_1 + 3d\phi \mu_1 J_1 + 2\phi^2 \mu_2 J_1 + \alpha \theta \cdot \mu_2 J_1 + 2d\mu_1^2 J_1 + 2\theta \mu_1 \cdot J_1^2 + 4\mu_1^3 J_1 \\
 &+ \theta \phi \mu_1 J_1 + 7\phi \cdot \mu_1 \mu_2 J_1 \} + (1-d)\theta^2 J_1^2 \mu_2 + (\mu_2^2 - \alpha \theta^2) \alpha J_1^2 \mu_2 + 2d \cdot \theta^2 J_1^2 \mu_1 + 2\alpha \theta^2 J_1^2 \mu_1 + \alpha \theta \phi \mu_2^2 J_1 \\
 &+ \phi \alpha^2 J_1^2 \mu_1 + 3d \cdot \mu_1^3 \mu_2 J_1 + \phi^2 \mu_1^3 J_1 + 8\phi \mu_1^2 \mu_2 J_1^2 + \theta^3 \mu_1^2 J_1 + 3d\mu_1^2 \cdot J_1^3 + \alpha \theta \mu_2 J_1^2 + d\theta \mu_2 J_1^3 + 5d\theta \phi \mu_1^2 J_1 \\
 &+ \alpha^2 \theta \phi J_1^2 + \phi \mu_1 \mu_2^2 J_1^2 + 2d\phi \mu_2^2 J_1^2 + 2d\alpha \theta \mu_1 J_1^2 + 3d\theta \mu_1 \mu_2 J_1^2 + 4d\phi \mu_1^2 J_1^2 + d^2 \phi \mu_1 J_1^2 + 2\theta \phi \mu_1 \mu_2^3 \\
 &+ 6\theta \mu_1^3 J_1^2 + 8 \cdot \mu_1^3 \mu_2^2 (\theta + \phi) + 2d\phi^2 \mu_1 \mu_2 J_1 + 5\mu_1^2 (\theta^2 + \phi^2) + 2\theta^2 \cdot \mu_1^2 J_1^2 + 4\phi^2 \mu_1^3 \mu_2 + 2\mu_1^5 \mu_2 + 3\phi \mu_1^3 J_1^2 \\
 &+ 4\alpha \phi \mu_1^2 J_1^2 + 13\phi \mu_1^2 \mu_2^2 J_1 + \alpha \phi^2 \mu_1^2 J_1 + d^2 \theta \phi J_1^2 + \theta \alpha^2 \mu_1 J_1^2 + 3\mu_1^2 \mu_2^3 (\theta + \phi) + 7d\mu_1^2 \mu_2 J_1^2 + 4d\theta^2 \mu_1^2 J_1 \\
 &+ d\theta \mu_1 \mu_2^2 J_1 + d^2 \mu_1^2 J_1^2 + \phi^2 \mu_1 \mu_2^3 + 2\alpha \mu_1^2 \mu_2^2 J_1 + 6\theta^2 \mu_1 \mu_2^2 J_1 + 2d\alpha \phi \mu_1 J_1^2.
 \end{aligned}$$

From Section 5, we know that

$$\mu_2 (d + \alpha + \mu_1) = \mu_2 J_2 + \eta J_3,$$

and

$$d + \alpha + \mu_1 > J_2.$$

After some algebraic manipulations, we have $b_1 b_2 b_3 - b_3^2 - b_1^2 b_4 > 0$, Thus, $b_1 b_2 b_3 > b_3^2 + b_1^2 b_4$, when $R_v > 1$.