Research Article

Global Dynamics and Applications of an Epidemiological Model for Hepatitis C Virus Transmission in China

Mingwang Shen, Yanni Xiao, Weike Zhou, and Zhen Li

School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an 710049, China

Correspondence should be addressed to Yanni Xiao; yxiao@mail.xjtu.edu.cn

An epidemiological model is proposed and studied to understand the transmission dynamics and prevalence of HCV infection in China. Theoretical analysis indicates that the basic reproduction number R_0 provides a threshold value determining whether the disease dies out or not. Two Lyapunov functions are constructed to prove the global asymptotic stability of the disease-free and the endemic equilibria, respectively. Based on data reported by the National Health and Family Planning Commission of China, the basic reproduction number is estimated as approximately $R_0 = 1.9897$, which is much less than that for the model when a treatment strategy is not considered. An ever-increasing HCV infection is predicted in the near future. Numerical simulations, performed to investigate the potential effect of antiviral treatment, show that increasing the treatment cure rate and enlarging the treatment rate for patients at the chronic stage remain effective in reducing the number of new infections and the equilibrium prevalence. The finding suggests that treatment measures are significantly beneficial for disease control in terms of reducing new infections and, in particular, more attention should be paid to treatment for patients at the chronic stage.

1. Introduction

Hepatitis C virus (HCV) has been considered as a leading cause of liver cirrhosis and hepatocellular carcinoma and is becoming a major and growing global health problem [1, 2]. HCV is an enveloped single-stranded RNA virus in the Flaviviridae family and mutates so rapidly that no vaccine is currently available [3]. The spread of HCV mainly results from blood-to-blood contact through blood transfusions, intravenous drug use (IDU), and the use of inadequately sterilized or unsterilized medical equipment. According to the World Health Organization (WHO) estimates [4], nearly 3% of the world's population (more than 170 million) has been infected with HCV. In a recent cross-sectional study [5], for which 8,762 Chinese subjects from six areas of China were randomly selected, the overall average prevalence of anti-HCV was estimated to be 0.58% in China, which is much lower than the WHO estimates. Surveillance data show that the annual numbers of newly reported HCV cases increased sharply from 21,145 in 2003 to 223,094 in 2013 [6], which

indicates that HCV infection is becoming a serious threat to public health in China. Therefore, it is urgently necessary to understand the present epidemic situation and to provide suggestions on how to control HCV infections.

Mathematical models have been used to analyze the spread and control of HCV infection in [7–17] and provide some insights into the disease's transmission. Martcheva and Castillo-Chavez [7] considered an epidemiological model of hepatitis C in a varying population, divided into susceptible and infected individuals with acute and chronic hepatitis C, and studied the role of the chronic infectious stage on the long-term dynamics of HCV. This model was extended by Das et al. [8] by incorporating the immune class and was also extended by Yuan and Yang [9] by incorporating the latent period. The impacts of HCV treatment on prevalence among active injecting drug users (IDUs) have been studied in [10–12] where the treated populations are assumed not to infect the susceptible populations. Imran et al. [14] and Khan et al. [17] formulated epidemic models of HCV containing an isolation class and analyzed the effects of the isolation class on

the transmission dynamics of the disease. Few models have been proposed to understand the transmission dynamics of HCV in mainland China. In [18], Zhang and Zhou extended the model in [9] by considering recovery from the acute infected stage and simulated HCV transmission in the near future based on the available HCV epidemic data from 2003 to 2010 in China. Note that their model does not involve the treatment class although a treatment strategy has been available in mainland China for several years [19]. Antiviral treatment, especially at the early stages of HCV recurrence, is an extremely effective strategy. How effective antiviral treatment remains is therefore an issue of great importance for HCV control, and quantifying this impact through a mathematical modeling framework falls within the scope of this study.

The purpose of this study is to formulate a mathematical model which involves almost all possible stages during HCV infection with the aim of accessing the potential impact of antiviral treatment on HCV prevalence of China and then providing reliable quantitative information on controlling the HCV epidemic in China. On the basis of the model in [18] we incorporate the treated and recovered classes with partial immunity. Note that we consider that the treated individuals can also infect the susceptible individuals [16], which adds to the complexity of our model and makes it considerably more insightful from an epidemiological perspective than previous models. We analyze the global dynamical behavior of the proposed system by developing suitable Lyapunov functions [20] and suggest some measures to control HCV infection in China.

The paper is organized as follows. In Section 2, we introduce the model and derive the basic reproduction number. The global stability of the disease-free equilibrium and the endemic equilibrium are studied in Sections 3 and 4, respectively. In Section 5, we apply the model to simulate the HCV data in China and investigate various control strategies with numerical simulations. Finally, we conclude the paper by a discussion in Section 6.

2. Model Formulation

We propose a mathematical model to understand the transmission dynamics and prevalence of HCV in mainland China using a system of ordinary differential equations. The population are divided into six classes: S (susceptible), E (exposed), A (infected with acute hepatitis C), C (infected with chronic hepatitis C), T (treated population), and R (recovered population with partial immunity). Let N denote the total population; that is, $N = S + E + A + C + T + R$. New susceptible individuals enter into the S class at a fixed rate Λ. Let m be the natural death rate of the population. Susceptible individuals are infected by patients in the A, C, and T classes at rates of β_1, β_2, and β_3, respectively. It is generally thought that the acute phase is more infectious than the the chronic one and that the treated individuals have the lowest infectiousness [15, 18], so it is reasonable to assume that $\beta_1 > \beta_2 > \beta_3$. Once infected, the individuals move into the exposed class E and then progress to the acute

stage at a rate of ϵ. An individual at the acute stage who can spontaneously clear the virus recovers at rate ξ; otherwise he/she will progress to the chronic stage at rate σ. Acutely and chronically infected individuals are treated at rates δ and μ, respectively. After the treatment, some patients succeed in clearing HCV and move to the class R at rate η, while the others who have not responded to the treatment move back to the chronic state C at rate θ. The disease-induced death rate in the C class is denoted as α. Individuals in the class R lose their immunity and eventually return to the susceptible class S at rate γ. A flow diagram for the model is shown in Figure 1 and the variables and parameters are described in Table 1. The complete dynamical model is as follows:

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - (\beta_1 A + \beta_2 C + \beta_3 T) S - mS + \gamma R, \\
\frac{dE}{dt} &= (\beta_1 A + \beta_2 C + \beta_3 T) S - (m + \epsilon) E, \\
\frac{dA}{dt} &= \epsilon E - (m + \sigma + \delta + \xi) A, \\
\frac{dC}{dt} &= \sigma A + \theta T - (m + \alpha + \mu) C, \\
\frac{dT}{dt} &= \delta A + \mu C - (m + \theta + \eta) T, \\
\frac{dR}{dt} &= \xi A + \eta T - (m + \gamma) R.
\end{aligned}
\tag{1}
$$

Since $dN/dt = \Lambda - mN - \alpha C \le \Lambda - mN$, we can study the dynamical behavior of system (1) in the positively invariant set:

$$
\begin{aligned}
\mathscr{D} = \Big\{ &(S, E, A, C, T, R) \in \mathbb{R}_+^6 : \\
&S + E + A + C + T + R \le \frac{\Lambda}{m} \Big\}.
\end{aligned}
\tag{2}
$$

By using the next generation matrix approach given in [21], we obtain the basic reproduction number:

$$
\begin{aligned}
R_0 = \frac{\Lambda \epsilon}{m(m+\epsilon)(m+\sigma+\delta+\xi)} \\
\cdot \Big(\beta_1 + \big((\beta_2(\delta\theta + \sigma(m+\theta+\eta)) \\
+ \beta_3(\mu\sigma + \delta(m+\alpha+\mu))) \\
\cdot ((m+\alpha+\mu)(m+\eta) + (m+\alpha)\theta)^{-1} \big) \Big),
\end{aligned}
\tag{3}
$$

which can be interpreted as the average number of new infections generated by a single infectious individual in the acute (A), chronic (C), and treated (T) classes.

To investigate the effect of therapy, we study variation in the basic reproduction number R_0 with treatment rates δ,

TABLE 1: Parameters and initial data chosen for the simulation.

| Variable and parameter	Description	Initial or default values	Source
Variables			
$S(t)$	Susceptible population	1.287×10^9	LS
$E(t)$	Exposed population	4187	LS
$A(t)$	Acutely infected population	151360	LS
$C(t)$	Chronically infected population	1.04×10^6	LS
$T(t)$	Treated population	50000	LS
$R(t)$	Recovered population with partial immunity	2×10^5	LS
Parameters			
Λ	Recruitment rate	1.573×10^7 year^{-1}	See text
m	Natural death rate	0.007 year^{-1}	[18, 24]
β_1	Transmission rate of acutely infected population	3.0769×10^{-11}	LS
β_2	Transmission rate of chronically infected population	2.5846×10^{-11}	LS
β_3	Transmission rate of treated population	2.0846×10^{-11}	LS
ϵ	Rate of progression to acute stage from the exposed	6 year^{-1}	[18]
ξ	Recovery rate for the acute state	0.5 year^{-1}	[15]
σ	Rate of moving from acute stage to chronic stage	4 year^{-1}	[18]
δ	Treatment rate of acutely infected population	0.1545 year^{-1}	see text
μ	Treatment rate of chronically infected population	0.04 year^{-1}	[15]
η	Treatment cure rate	0.67 year^{-1}	[15]
θ	Treatment failure rate	0.82 year^{-1}	[15]
α	HCV induced death rate at the chronic stage	0.001 year^{-1}	[18]
γ	Rate of waning immunity	0.025 year^{-1}	[15]

LS, least square.
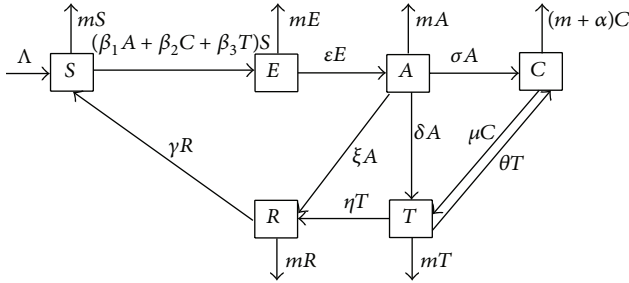
FIGURE 1: A schematic flow diagram illustrating the transmission dynamics of the HCV infection with treatment.

μ, treatment failure rate θ, and cure rate η. Calculating the derivative of R_0 with respect to μ gives

$$\frac{\partial R_0}{\partial \mu} = \frac{-\Lambda \epsilon}{m(m+\epsilon)(m+\sigma+\delta+\xi)}$$
$$\cdot \frac{[\delta\theta + \sigma(m+\theta+\eta)][(\beta_2-\beta_3)m + (\beta_2\eta - \beta_3\alpha)]}{[(m+\alpha+\mu)(m+\eta)+(m+\alpha)\theta]^2}. \tag{4}$$

Note that $\beta_1 > \beta_2 > \beta_3$; then $\partial R_0/\partial \mu < 0$ if the condition $\beta_2\eta - \beta_3\alpha > 0$ holds. This condition is likely to be true because the disease-induced death rate α is always

relatively low [7] (i.e., $\eta > \alpha$). Thus, R_0 decreases with increasing treatment uptake for the patients at the chronic stage. Similarly, by finding the derivative of R_0 with respect to θ,

$$\frac{\partial R_0}{\partial \theta} = \frac{\Lambda \epsilon}{m(m+\epsilon)(m+\sigma+\delta+\xi)}$$
$$\cdot \frac{[\mu\sigma + \delta(m+\alpha+\mu)][(\beta_2-\beta_3)m + (\beta_2\eta - \beta_3\alpha)]}{[(m+\alpha+\mu)(m+\eta)+(m+\alpha)\theta]^2}, \tag{5}$$

we obtain $\partial R_0/\partial \theta > 0$ provided $\beta_2\eta - \beta_3\alpha > 0$, which implies that decreasing the treatment failure rate θ results in R_0 declining and thus is beneficial to disease control.

Regardless, R_0 is inversely related to η:

$$\frac{\partial R_0}{\partial \eta} = \frac{-\Lambda \epsilon}{m(m+\epsilon)(m+\sigma+\delta+\xi)}$$
$$\cdot \frac{[\mu\sigma + \delta(m+\alpha+\mu)][\beta_2\theta + \beta_3(m+\alpha+\mu)]}{[(m+\alpha+\mu)(m+\eta)+(m+\alpha)\theta]^2} < 0. \tag{6}$$

Therefore, a higher cure rate leads to lower R_0 and a lower intensity of the epidemic. Differentiating R_0 with respect to δ yields

$$
\begin{aligned}
\frac{\partial R_0}{\partial \delta} = & -\Lambda \epsilon \left(m \left(m + \epsilon\right) \left[\left(m + \alpha + \mu\right) \left(m + \eta\right) + \left(m + \alpha\right) \theta \right] \right. \\
& \left. \cdot \left[\left(m + \sigma + \delta + \xi\right) \right]^2 \right)^{-1} \\
& \times \left[\left(\beta_1 - \beta_3\right) m \left(m + \alpha + \mu\right) \right. \\
& + \left(\beta_1 - \beta_2\right) m\theta + \left(\beta_2 - \beta_3\right) m\sigma \\
& + \left(m + \alpha + \mu\right) \left(\beta_1 \eta - \beta_3 \xi\right) \\
& \left. + \beta_2 \left(\sigma \eta - \theta \xi\right) + \alpha \left(\beta_1 \theta - \beta_3 \sigma\right) \right].
\end{aligned}
\tag{7}
$$

If $(\beta_3/\beta_1)\sigma < \theta < (\eta/\xi)\sigma$, then $\partial R_0/\partial \delta < 0$. Thus, we get a sufficient condition to make sure that R_0 is inversely related to δ, which means that increasing treatment uptake for the patients at the acute stage is beneficial to control the disease for certain conditions of the treatment failure rate.

Model (1) always has a disease-free equilibrium $\overline{P} = (\Lambda/m, 0, 0, 0, 0, 0)$. There is an endemic equilibrium $P^* = (S^*, E^*, A^*, C^*, T^*, R^*)$ if $R_0 > 1$, where

$$
S^* = \frac{\Lambda}{mR_0}, \qquad E^* = \frac{(m + \sigma + \delta + \xi)}{\epsilon} A^*,
$$

$$
A^* = \frac{\Lambda (R_0 - 1)}{\widetilde{A} R_0},
$$

$$
C^* = \frac{\delta\theta + \sigma (m + \theta + \eta)}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta} A^*,
$$

$$
T^* = \frac{\mu\sigma + \delta (m + \alpha + \mu)}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta} A^*,
$$

$$
R^* = \frac{1}{m + \gamma} \left(\xi + \eta \frac{\mu\sigma + \delta (m + \alpha + \mu)}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta} \right) A^*,
\tag{8}
$$

with

$$
\begin{aligned}
\widetilde{A} = & \frac{m + \epsilon}{\epsilon} (m + \sigma + \delta + \xi) \\
& - \frac{\gamma}{m + \gamma} \left(\xi + \eta \frac{\mu\sigma + \delta (m + \alpha + \mu)}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta} \right) > 0.
\end{aligned}
\tag{9}
$$

3. Global Stability of the Disease-Free Equilibrium

Theorem 1. *(i) If $R_0 \leq 1$, then the unique disease-free equilibrium $\overline{P}$ of system (1) is globally asymptotically stable in $\mathscr{D}$.*

(ii) If $R_0 > 1$, then $\overline{P}$ is unstable and system (1) is uniformly persistent; that is, there exists a constant $\epsilon_0 > 0$ such that, for

all initial values $(S(0), E(0), A(0), C(0), T(0), R(0)) \in \mathbb{R}_+ \times$ Int $(\mathbb{R}_+^5)$, the solutions of system (1) satisfy $\liminf_{t \to \infty} S(t) > \epsilon_0$, $\liminf_{t \to \infty} E(t) > \epsilon_0$, $\liminf_{t \to \infty} A(t) > \epsilon_0$, $\liminf_{t \to \infty} C(t) > \epsilon_0$, $\liminf_{t \to \infty} T(t) > \epsilon_0$, and $\liminf_{t \to \infty} R(t) > \epsilon_0$.

Proof. (i) Construct a continuously differentiable and positive definite Lyapunov function

$$
\begin{aligned}
L = & \frac{m}{\Lambda} E + \frac{m (m + \epsilon)}{\Lambda \epsilon} A + H \left(\beta_3 \mu + \beta_2 (m + \theta + \eta)\right) C \\
& + H \left(\beta_2 \theta + \beta_3 (m + \alpha + \mu)\right) T,
\end{aligned}
\tag{10}
$$

where H is

$$
H = \frac{1}{R_0 \left((m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta\right)}.
\tag{11}
$$

Calculating the derivative of L along (1), we obtain

$$
\begin{aligned}
\frac{dL}{dt} = & \frac{m}{\Lambda} \frac{dE}{dt} + \frac{m (m + \epsilon)}{\Lambda \epsilon} \frac{dA}{dt} \\
& + H \left(\beta_3 \mu + \beta_2 (m + \theta + \eta)\right) \frac{dC}{dt} \\
& + H \left(\beta_2 \theta + \beta_3 (m + \alpha + \mu)\right) \frac{dT}{dt} \\
= & \frac{m}{\Lambda} \left(\left(\beta_1 A + \beta_2 C + \beta_3 T\right) S - (m + \epsilon) E \right) \\
& + \frac{m (m + \epsilon)}{\Lambda \epsilon} \left(\epsilon E - (m + \sigma + \delta + \xi) A\right) \\
& + H \left(\beta_3 \mu + \beta_2 (m + \theta + \eta)\right) \\
& \cdot \left(\sigma A + \theta T - (m + \alpha + \mu) C\right) \\
& + H \left(\beta_2 \theta + \beta_3 (m + \alpha + \mu)\right) \\
& \cdot \left(\delta A + \mu C - (m + \theta + \eta) T\right) \\
= & \frac{m}{\Lambda} \left(\beta_1 A + \beta_2 C + \beta_3 T\right) S - \frac{1}{R_0} \left(\beta_1 A + \beta_2 C + \beta_3 T\right) \\
= & \frac{1}{R_0} \left(\beta_1 A + \beta_2 C + \beta_3 T\right) \left(R_0 \frac{m}{\Lambda} S - 1\right).
\end{aligned}
\tag{12}
$$

In the domain $\mathscr{D}$, it is easy to see that $S \leq \Lambda/m$, which gives $(m/\Lambda)S \leq 1$. Thus, if $R_0 \leq 1$, then we have $dL/dt \leq 0$ for all $S, A, C, T > 0$. Every solution of system (1) converges to $\mathscr{M}$, where $\mathscr{M}$ is the largest invariant set in $\{(S, E, A, C, T, R) \in \mathscr{D} : dL/dt = 0\}$. When $R_0 < 1$, the equality $dL/dt = 0$ holds if and only if $A = C = T = 0$, which implies that $E = R = 0$ and $S = \Lambda/m$ from (1). When $R_0 = 1$, the equality $dL/dt = 0$ holds if and only if $A = C = T = 0$ or $S = \Lambda/m$. Both of these cases indicate that $\mathscr{M} = \overline{P}$. By the LaSalle largest invariant set theorem, the disease-free equilibrium $\overline{P}$ is globally asymptotically stable if $R_0 \leq 1$.

(ii) The Jacobian matrix of system (1) at $\overline{P}$ is

$$J\left(\overline{P}\right) = \begin{pmatrix} -m & 0 & -\beta_1\dfrac{\Lambda}{m} & -\beta_2\dfrac{\Lambda}{m} & -\beta_3\dfrac{\Lambda}{m} & \gamma \\ 0 & -(m+\epsilon) & \beta_1\dfrac{\Lambda}{m} & \beta_2\dfrac{\Lambda}{m} & \beta_3\dfrac{\Lambda}{m} & 0 \\ 0 & \epsilon & -(m+\sigma+\delta+\xi) & 0 & 0 & 0 \\ 0 & 0 & \sigma & -(m+\alpha+\mu) & \theta & 0 \\ 0 & 0 & \delta & \mu & -(m+\theta+\eta) & 0 \\ 0 & 0 & \xi & 0 & \eta & -(m+\gamma) \end{pmatrix}. \tag{13}$$

For convenience of denotation, let $h_1 = m + \epsilon$, $h_2 = m + \sigma + \delta + \xi$, $h_3 = m + \alpha + \mu$, and $h_4 = m + \theta + \eta$. Then we obtain the characteristic equation at $\overline{P}$ as follows:

$$(\lambda + m)(\lambda + m + \gamma)$$

$$\cdot \left[(\lambda + h_1)(\lambda + h_2)(\lambda + h_3)(\lambda + h_4) \right.$$

$$- \mu\theta(\lambda + h_1)(\lambda + h_2)$$

$$- \beta_1\frac{\Lambda}{m}\epsilon(\lambda + h_3)(\lambda + h_4) + \beta_1\frac{\Lambda}{m}\epsilon\mu\theta$$

$$- \beta_2\frac{\Lambda}{m}\epsilon\sigma(\lambda + h_4) - \beta_2\frac{\Lambda}{m}\epsilon\delta\theta - \beta_3\frac{\Lambda}{m}\epsilon\mu\sigma$$

$$\left. - \beta_3\frac{\Lambda}{m}\epsilon\delta(\lambda + h_3) \right]$$

$$= (\lambda + m)(\lambda + m + \gamma)\left(\lambda^4 + k_1\lambda^3 + k_2\lambda^2 + k_3\lambda + k_4\right) = 0, \tag{14}$$

where

$$k_1 = h_1 + h_2 + h_3 + h_4,$$

$$k_2 = h_1 h_2 + h_1 h_3 + h_1 h_4 + h_2 h_3$$

$$\quad + h_2 h_4 + h_3 h_4 - \mu\theta - \beta_1\frac{\Lambda}{m}\epsilon,$$

$$k_3 = h_1 h_2 h_3 + h_1 h_2 h_4 + h_1 h_3 h_4 + h_2 h_3 h_4 - \mu\theta(h_1 + h_2)$$

$$\quad - \beta_1\frac{\Lambda}{m}\epsilon(h_3 + h_4) - \beta_2\frac{\Lambda}{m}\epsilon\sigma - \beta_3\frac{\Lambda}{m}\epsilon\delta,$$

$$k_4 = h_1 h_2 h_3 h_4 - \mu\theta h_1 h_2 - \beta_1\frac{\Lambda}{m}\epsilon h_3 h_4 + \beta_1\frac{\Lambda}{m}\epsilon\mu\theta$$

$$\quad - \beta_2\frac{\Lambda}{m}\epsilon\sigma h_4 - \beta_2\frac{\Lambda}{m}\epsilon\delta\theta - \beta_3\frac{\Lambda}{m}\epsilon\mu\sigma - \beta_3\frac{\Lambda}{m}\epsilon\delta h_3. \tag{15}$$

Denote the eigenvalues of the characteristic equation (14) as $\lambda_i, i = 1, 2, \ldots, 6$. Obviously, $\lambda_1 = -m < 0$, $\lambda_2 = -(m+\gamma) < 0$,

and $\lambda_3, \lambda_4, \lambda_5, \lambda_6$ satisfy the equation $(\lambda^4 + k_1\lambda^3 + k_2\lambda^2 + k_3\lambda + k_4) = 0$. When $R_0 > 1$, we get

$$k_4 = h_1 h_2 (h_3 h_4 - \mu\theta) - \beta_1\frac{\Lambda}{m}\epsilon(h_3 h_4 - \mu\theta)$$

$$\quad - \beta_2\frac{\Lambda}{m}\epsilon(\sigma h_4 + \delta\theta) - \beta_3\frac{\Lambda}{m}\epsilon(\delta h_3 + \mu\sigma)$$

$$= h_1 h_2 (h_3 h_4 - \mu\theta)$$

$$\quad \cdot \left[1 - \frac{\Lambda\epsilon}{m h_1 h_2}\left(\beta_1 + \frac{\beta_2(\delta\theta + \sigma h_4) + \beta_3(\mu\sigma + \delta h_3)}{h_3 h_4 - \mu\theta}\right) \right]$$

$$= (m+\epsilon)(m+\sigma+\delta+\xi)$$

$$\quad \cdot [(m+\alpha+\mu)(m+\eta) + (m+\alpha)\theta]$$

$$\quad \times \left[1 - \frac{\Lambda\epsilon}{m(m+\epsilon)(m+\sigma+\delta+\xi)} \right.$$

$$\quad \cdot \left(\beta_1 + \left((\beta_2(\delta\theta + \sigma(m+\theta+\eta))\right.\right.$$

$$\quad + \beta_3(\mu\sigma + \delta(m+\alpha+\mu)))$$

$$\quad \cdot \left((m+\alpha+\mu)(m+\eta) + (m+\alpha)\theta)^{-1}\right)\bigg] $$

$$= (m+\epsilon)(m+\sigma+\delta+\xi)$$

$$\quad \cdot [(m+\alpha+\mu)(m+\eta) + (m+\alpha)\theta](1 - R_0)$$

$$< 0, \tag{16}$$

which means that $\lambda_3\lambda_4\lambda_5\lambda_6 = k_4 < 0$. This indicates that at least one of $\lambda_3, \lambda_4, \lambda_5, \lambda_6$ has positive real part. Thus, $\overline{P}$ is unstable if $R_0 > 1$.

Define

$$X = \{(S, E, A, C, T, R) \mid$$

$$\quad S \geq 0, E \geq 0, A \geq 0, C \geq 0, T \geq 0, R \geq 0\},$$

$$X_0 = \{(S, E, A, C, T, R) \mid$$

$$\quad S \geq 0, E > 0, A > 0, C > 0, T > 0, R > 0\},$$

$$\partial X_0 = X \setminus X_0,$$
$$M_\partial = \{(S(0), E(0), A(0), C(0), T(0), R(0)) \mid$$
$$(S(t), E(t), A(t), C(t), T(t), R(T))$$
$$\text{satisfies } (1),$$
$$(S(t), E(t), A(t), C(t), T(t), R(T)) \in \partial X_0,$$
$$\forall t \geq 0\}.$$

(17)

It then suffices to show that system (1) is uniformly persistent with respect to $(X_0, \partial X_0)$. First, it is easy to see that both X and X_0 are positively invariant. Obviously, ∂X_0 is relatively closed in X. Furthermore, it follows from (2) that system (1) is point dissipative. Next we prove that $M_\partial = \{(S, 0, 0, 0, 0, 0) \mid S \geq 0\}$. Assume, by contradiction, that $\varphi_0 = (S(0), E(0), A(0), C(0), T(0), R(0)) \in M_\partial$ and there exists a $t_0 \geq 0$ such that at least one of $E(t), A(t), C(t), T(t), R(t)$ is greater than zero at $t = t_0$; for example, $A(t_0) > 0$ and $E(t_0) = C(t_0) = T(t_0) = R(t_0) = 0$. Then we get $C'(t_0) = \sigma A(t_0) > 0$, $T'(t_0) = \delta A(t_0) > 0$, $R'(t_0) = \xi A(t_0) > 0$. This indicates that there exists a $t_1 > 0$ such that $C(t) > 0$, $T(t) > 0$, $R(t) > 0$, and $E(t) > 0$, $A(t) > 0$, for $t_0 < t < t_0 + t_1$, which means that $(S(t), E(t), A(t), C(t), T(t), R(t)) \notin \partial X_0$ for $t_0 < t < t_0 + t_1$, contradicting the assumption that $\varphi_0 \in M_\partial$. Other cases can be proved in the same way. Thus we have $M_\partial = \{(S, 0, 0, 0, 0, 0) \mid S \geq 0\}$. Let φ_0 be an initial value. There is only one equilibrium $\overline{P}$ in M_∂, so $\cup_{\varphi_0 \in M_\partial} \omega(\varphi_0) = \overline{P}$. Therefore, $\overline{P}$ is a compact and isolated invariant set for φ_0 in ∂X_0.

Next we claim that there exists a positive constant δ_0 such that any solution $u(t, \varphi_0), \varphi_0 \in X_0$, satisfies

$$\lim_{t \to \infty} \sup \left\| u(t, \varphi_0) - \overline{P} \right\| \geq \delta_0, \quad \text{i.e., } W^s(\overline{P}) \cap X_0 = \emptyset. \quad (18)$$

Suppose the claim is not true. Then $\lim_{t \to \infty} \sup \|u(t, \varphi_0) - \overline{P}\| < \delta_0$, for any $\delta_0 > 0$; namely, there exists a positive constant η_0 such that $\Lambda/m - \delta_0 < S(t) < \Lambda/m + \delta_0$, $E(t) < \delta_0$, $A(t) < \delta_0$, $C(t) < \delta_0$, $T(t) < \delta_0$, and $R(t) < \delta_0$, for any $t > \eta_0$. While $t > \eta_0$, we have

$$\frac{dE}{dt} > (\beta_1 A + \beta_2 C + \beta_3 T)\left(\frac{\Lambda}{m} - \delta_0\right) - (m + \epsilon) E. \quad (19)$$

Consider the auxiliary system

$$\frac{dx_1}{dt} = (\beta_1 x_2 + \beta_2 x_3 + \beta_3 x_4)\left(\frac{\Lambda}{m} - \delta_0\right) - (m + \epsilon) x_1,$$
$$\frac{dx_2}{dt} = \epsilon x_1 - (m + \sigma + \delta + \xi) x_2,$$
$$\frac{dx_3}{dt} = \sigma x_2 + \theta x_4 - (m + \alpha + \mu) x_3, \quad (20)$$
$$\frac{dx_4}{dt} = \delta x_2 + \mu x_3 - (m + \theta + \eta) x_4,$$
$$\frac{dx_5}{dt} = \xi x_2 + \eta x_4 - (m + \gamma) x_5.$$

Define

$$M_1(\delta_0) = \begin{pmatrix} -(m+\epsilon) & \beta_1\left(\dfrac{\Lambda}{m} - \delta_0\right) & \beta_2\left(\dfrac{\Lambda}{m} - \delta_0\right) & \beta_3\left(\dfrac{\Lambda}{m} - \delta_0\right) & 0 \\ \epsilon & -(m+\sigma+\delta+\xi) & 0 & 0 & 0 \\ 0 & \sigma & -(m+\alpha+\mu) & \theta & 0 \\ 0 & \delta & \mu & -(m+\theta+\eta) & 0 \\ 0 & \xi & 0 & \eta & -(m+\gamma) \end{pmatrix}. \quad (21)$$

Let $s(M_1(\delta_0))$ be the maximum real part of the eigenvalues of $M_1(\delta_0)$. Since $M_1(\delta_0)$ is irreducible and has nonnegative off-diagonal elements, $s(M_1(\delta_0))$ is a simple eigenvalue of $M_1(\delta_0)$ with a positive eigenvector. It follows from Lemma 2.1 in [22] that $s(M_1(0)) > 0$ when $R_0 > 1$. Since $s(M_1(\delta_0))$ is continuous for small δ_0, there exists a positive constant δ_0 small enough such that $s(M_1(\delta_0)) > 0$. Therefore, there is a positive eigenvalue of $M_1(\delta_0)$ with a positive eigenvector. It is easy to see $x_i \to \infty$ as $t \to \infty$, $i = 1, 2, \ldots, 5$. Then according to the comparison principle we have

$$\lim_{t \to \infty} E(t) = \infty, \qquad \lim_{t \to \infty} A(t) = \infty, \qquad \lim_{t \to \infty} C(t) = \infty,$$
$$\lim_{t \to \infty} T(t) = \infty, \qquad \lim_{t \to \infty} R(t) = \infty,$$

(22)

which contradicts our assumption. This completes the proof of the claim, which implies that $\overline{P}$ is an isolated invariant set in X and $W^s(\overline{P}) \cap X_0 = \emptyset$. Using the uniform persistence theory (Theorem 4.2) in [23], we obtain that system (1) is uniformly persistent if $R_0 > 1$. This completes the proof. □

4. Global Stability of the Endemic Equilibrium

The global stability of the endemic equilibrium is studied under the simplified assumption that the immune loss rate is zero (i.e., $\gamma = 0$). Thus, we can omit the decoupled equation for dR/dt and the following theorem holds.

Theorem 2. When $R_0 > 1$, if $\gamma = 0$, then the unique endemic equilibrium P^* is globally asymptotically stable in $\mathcal{D}$.

Proof. Construct a continuously differentiable and nonnegative Lyapunov function:

$$V = S - S^* - S^* \ln \frac{S}{S^*} + E - E^*$$

$$- E^* \ln \frac{E}{E^*} + a_1 \left(A - A^* - A^* \ln \frac{A}{A^*} \right)$$

$$+ a_2 \left(C - C^* - C^* \ln \frac{C}{C^*} \right) + a_3 \left(T - T^* - T^* \ln \frac{T}{T^*} \right),$$

$$(23)$$

where

$$a_1 = \frac{m + \epsilon}{\epsilon}, \qquad a_2 = \frac{(\beta_3 \mu + \beta_2 (m + \theta + \eta)) S^*}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta},$$

$$a_3 = \frac{(\beta_2 \theta + \beta_3 (m + \alpha + \mu)) S^*}{(m + \alpha + \mu)(m + \eta) + (m + \alpha)\theta}.$$

$$(24)$$

It can be verified that the global minimum of V occurs at the endemic equilibrium P^*, and the function V takes the value $V = 0$ at the endemic equilibrium P^*.

Differentiating V along the solutions of system (1) and using the equilibrium relations, we obtain

$$\frac{dV}{dt} = \left(1 - \frac{S^*}{S} \right) (\Lambda - \beta_1 SA - \beta_2 SC - \beta_3 ST - mS)$$

$$+ \left(1 - \frac{E^*}{E} \right) (\beta_1 SA + \beta_2 SC + \beta_3 ST - (m + \epsilon) E)$$

$$+ a_1 \left(1 - \frac{A^*}{A} \right) (\epsilon E - (m + \sigma + \delta + \xi) A)$$

$$+ a_2 \left(1 - \frac{C^*}{C} \right) (\sigma A + \theta T - (m + \alpha + \mu) C)$$

$$+ a_3 \left(1 - \frac{T^*}{T} \right) (\delta A + \mu C - (m + \theta + \eta) T)$$

$$= M - mS - \beta_1 E^* \frac{SA}{E} - \beta_2 E^* \frac{SC}{E}$$

$$- \beta_3 E^* \frac{ST}{E} - \Lambda \frac{S^*}{S} - a_1 \epsilon A^* \frac{E}{A}$$

$$- a_2 \sigma C^* \frac{A}{C} - a_2 \theta C^* \frac{T}{C} - a_3 \delta T^* \frac{A}{T} - a_3 \mu T^* \frac{C}{T}$$

$$= b_1 \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + b_2 \left(3 - \frac{S^*}{S} - \frac{E^*}{S^* A^*} \frac{SA}{E} - \frac{A^* E}{E^* A} \right)$$

$$+ b_3 \left(4 - \frac{S^*}{S} - \frac{E^*}{S^* C^*} \frac{SC}{E} - \frac{A^* E}{E^* A} - \frac{C^* A}{A^* C} \right)$$

$$+ b_4 \left(5 - \frac{S^*}{S} - \frac{E^*}{S^* C^*} \frac{SC}{E} - \frac{A^* E}{E^* A} - \frac{C^* T}{T^* C} - \frac{T^* A}{A^* T} \right)$$

$$+ b_5 \left(5 - \frac{S^*}{S} - \frac{E^*}{S^* T^*} \frac{ST}{E} - \frac{A^* E}{E^* A} - \frac{C^* A}{A^* C} - \frac{T^* C}{C^* T} \right)$$

$$+ b_6 \left(4 - \frac{S^*}{S} - \frac{E^*}{S^* T^*} \frac{ST}{E} - \frac{A^* E}{E^* A} - \frac{T^* A}{A^* T} \right)$$

$$+ b_7 \left(2 - \frac{C^* T}{T^* C} - \frac{T^* C}{C^* T} \right),$$

$$(25)$$

where $M = \Lambda + mS^* + (m + \epsilon)E^* + a_1(m + \sigma + \delta + \xi)A^* + a_2(m + \alpha + \mu)C^* + a_3(m + \theta + \eta)T^*$ and b_i $(i = 1, \ldots, 7)$ satisfy the following equations:

$$2b_1 + 3b_2 + 4b_3 + 5b_4 + 5b_5 + 4b_6 + 2b_7 = M,$$

$$b_1 = mS^*,$$

$$b_1 + b_2 + b_3 + b_4 + b_5 + b_6 = \Lambda,$$

$$b_2 + b_3 + b_4 + b_5 + b_6 = a_1 \epsilon E^*,$$

$$b_3 + b_5 = a_2 \sigma A^*,$$

$$b_4 + b_7 = a_2 \theta T^*, \qquad (26)$$

$$b_4 + b_6 = a_3 \delta A^*,$$

$$b_5 + b_7 = a_3 \mu C^*,$$

$$b_2 = \beta_1 S^* A^*,$$

$$b_3 + b_4 = \beta_2 S^* C^*,$$

$$b_5 + b_6 = \beta_3 S^* T^*.$$

Obviously, $b_1 > 0$ and $b_2 > 0$. Next we will show that $b_i \geq 0$ $(i = 3, \ldots, 7)$. From the equations above, we have

$$b_3 = a_2 \sigma A^* - a_3 \mu C^* + b_7 = \beta_2 S^* C^* - a_2 \theta T^* + b_7,$$

$$b_4 = a_2 \theta T^* - b_7,$$

$$b_5 = a_3 \mu C^* - b_7, \qquad (27)$$

$$b_6 = a_3 \delta A^* - a_2 \theta T^* + b_7 = \beta_3 S^* T^* - a_3 \mu C^* + b_7.$$

At the equilibrium, the equalities $\sigma A^* + \theta T^* = (m + \alpha + \mu)C^*$, $\delta A^* + \mu C^* = (m + \theta + \eta)T^*$ hold. Then by substituting the values of a_2 and a_3, it is easy to obtain that

$$a_2 \sigma A^* - a_3 \mu C^* = \beta_2 S^* C^* - a_2 \theta T^*,$$

$$a_3 \delta A^* - a_2 \theta T^* = \beta_3 S^* T^* - a_3 \mu C^*. \qquad (28)$$

In order to assure $b_i \geq 0$ $(i = 3, 4, 5, 6)$, from (27) we know that b_7 must satisfy the inequalities:

$$\max \{0, a_3 \mu C^* - a_2 \sigma A^*, a_3 \mu C^* - \beta_3 S^* T^*\}$$

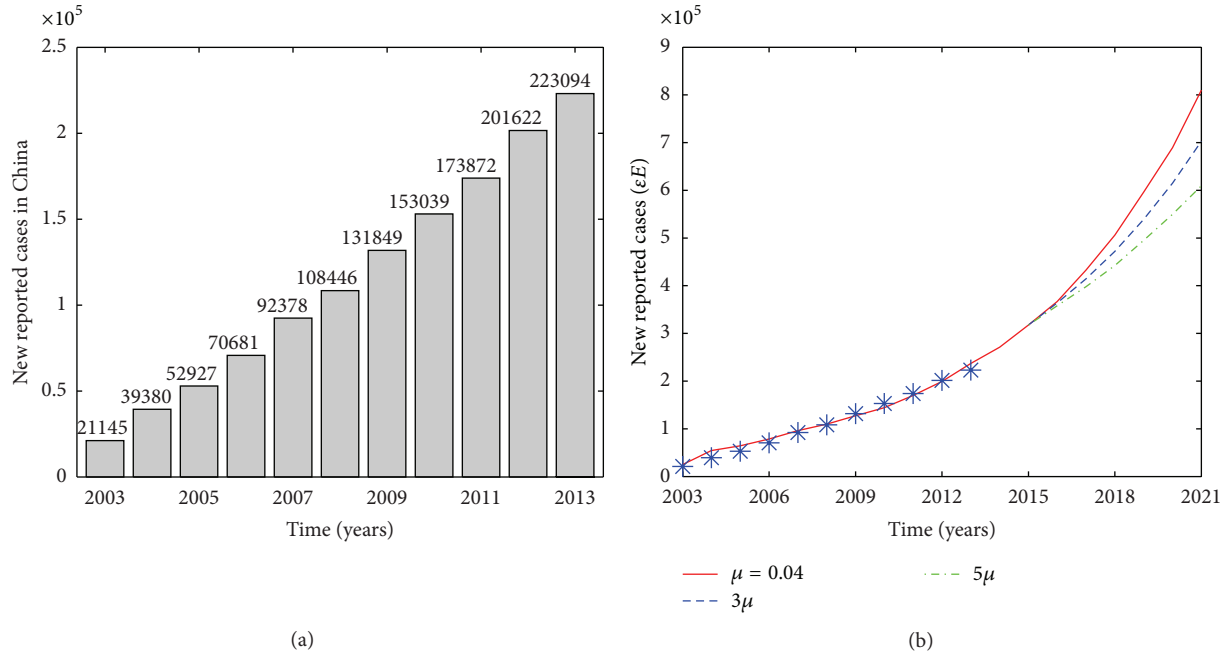$$\leq b_7 \leq \min \{a_2 \theta T^*, a_3 \mu C^*\}. \qquad (29)$$

(a)

(b)

FIGURE 2: (a) Annual newly reported HCV cases for mainland China; (b) goodness of fit and prediction of HCV trends until 2021. Stars represent the reported number of people with HCV by year. The solid line shows the fit based on the current circumstances ($\mu = 0.04$). The dashed and dash dot lines show the prediction at higher treatment rates $\mu = 0.12$ and $\mu = 0.2$ for patients at the chronic stage from 2015, respectively. All the other parameters are as shown in Table 1.

Using (28) yields

$$a_3\mu C^* > 0, \qquad a_3\mu C^* > a_3\mu C^* - a_2\sigma A^*,$$

$$a_3\mu C^* > a_3\mu C^* - \beta_3 S^* T^*,$$

$$a_2\theta T^* > 0, \tag{30}$$

$$a_2\theta T^* > a_2\theta T^* - \beta_2 S^* C^* = a_3\mu C^* - a_2\sigma A^*,$$

$$a_2\theta T^* > a_2\theta T^* - a_3\delta A^* = a_3\mu C^* - \beta_3 S^* T^*,$$

and then inequalities (29) must have a nonnegative solution, and so has (27). This indicates that $b_i \geq 0$ ($i = 3, \ldots, 7$). Because the geometric mean is always less than or equal to the arithmetic mean, we have $dV/dt \leq 0$ and the equality holds if and only if (S, E, A, C, T) take the equilibrium values (S^*, E^*, A^*, C^*, T^*). Therefore, by LaSalle's Invariance Principle, it follows that the endemic equilibrium P^* is globally asymptotically stable in the feasible region $\mathscr{D}$. □

5. Numerical Results

The annual reported HCV case numbers have been released by the National Health and Family Planning Commission of China [6], shown in Figure 2(a). The birth rate is fixed as 0.0121 in [24] and the total population of China is about 1.3×10^9, so we obtain that the recruitment rate is $\Lambda = 0.0121 \times 1.3 \times 10^9 = 1.573 \times 10^7$ per year. Okosun [16] chose the rate of progression for treatment from acute infected individuals as in the interval (0.12, 0.189); thus, we choose

the mean treatment rate for the patients at the acute stage as $\delta = 0.1545$ per year. By fitting (1) to the annual reported HCV data (Figure 2(a)) we obtain estimates for the transmission rates and the initial population size, which are listed in Table 1 and the goodness of fit is shown in Figure 2(b). Figure 2(b) shows that the estimated reported case numbers will reach 809,970 in 2021 in mainland China if the current surveillance, testing, and interventions are unchanged.

Using the estimated parameter values we calculated the basic reproduction number R_0 as 1.9897, which is similar to other estimates in the literature [25, 26] but is smaller than the value of 4.0636 estimated in [18]. This is because the treated individuals included in our model have relatively low infectiousness, which results in a smaller basic reproduction number. Moreover, it is interesting to note that the prevalence of HCV infection in China (Figure 3) is estimated as 0.51% in 2013 and 0.58% in 2014, which is in good agreement with the cross-sectional study [5]. Note that this estimated HCV prevalence is much lower than the WHO estimation. This is partial because strict HCV screening in blood began in the 1990s in China, which reduced the transmission rate of HCV by blood transfusion and other sources of iatrogenic infection.

To examine the impact of treatment on HCV transmission dynamics and prevalence and identify the most effective measures to control the transmission of HCV in mainland China we investigated variation in the basic reproduction number and prevalence (i.e., ($E(t) + A(t) + C(t) + T(t))/N(t)$) with parameters associated with treatment. If the treatment rate μ for the infected people at the chronic stage increases threefold, then
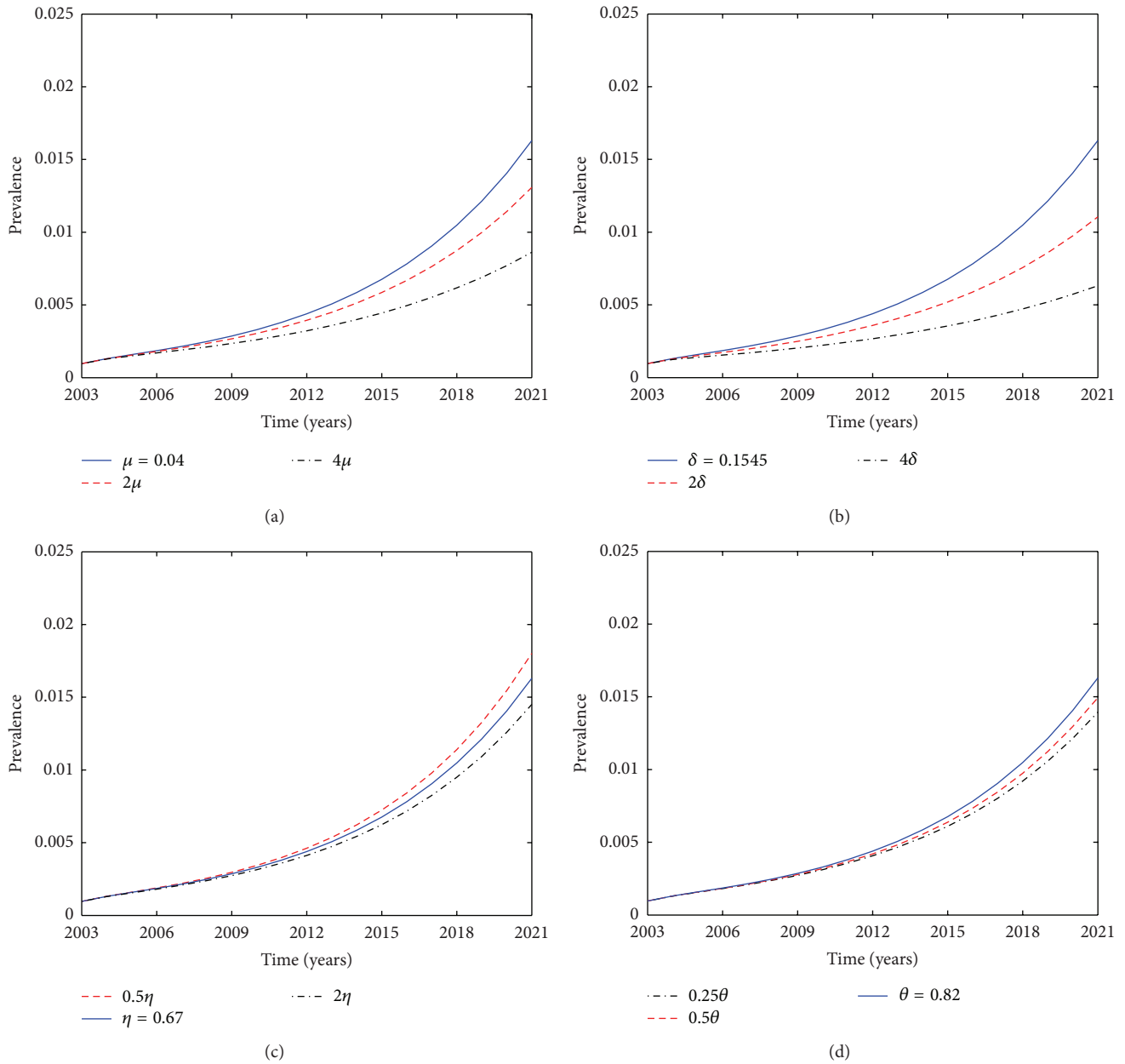
FIGURE 3: Plots of the prevalence against time at varying parameter values: (a) the treatment rate μ for patients at the acutely infected stage; (b) the treatment rate δ for patients at the chronic stage; (c) the treatment cure rate η; (d) the treatment failure rate θ. All the other parameters are as shown in Table 1.

the predicted reported case number will decrease by 13.21% to 702,960 in 2021, while if μ increases fivefold, then the predicted number will decrease by 24.74% to 609,580 in 2021, as shown in Figure 2(b). It follows from Figure 3 that the HCV prevalence in China will continue to rise and reach 1.63% in year 2021 under the current circumstances. Figure 3(a) shows that increasing the treatment rate μ for the patients at the chronic stage by 200% and 400% from the baseline value can decrease the prevalence in 2021 by 19.75% and 47.15%, respectively. Figure 3(b) shows that increasing the treatment rate δ for the patients at the acute stage by 200% and 400% from the baseline value can decrease the prevalence

in 2021 by 32.16% and 61.28%, respectively. Figure 3(c) shows that increasing the cure rate η by 200% from $\eta = 0.67$ can decrease the prevalence in 2021 by 11.01%. It follows from Figure 3(d) that reducing the treatment failure rate θ by 50% and 25% from the baseline value can decrease the prevalence in 2021 by 8.37% and 14.44%, respectively. These results indicate that, to decrease the prevalence effectively, it will be better to enlarge the treatment rate for the patients at the acute and chronic stage and cure rate and decrease the treatment failure rate in the short term.

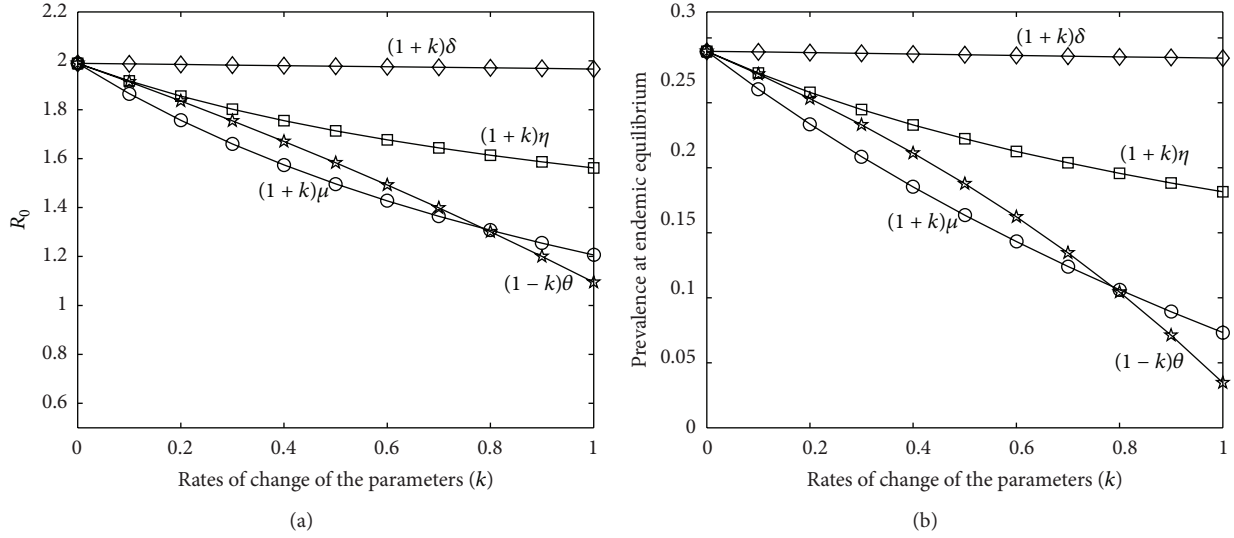To access the effectiveness of treatment interventions in the long term, we examine the effects of the corresponding

FIGURE 4: (a) Plots of the basic reproduction number R_0 by varying k (the rates of change of μ; δ; η; and θ); (b) plots of the prevalence at the steady state by varying k (the rates of change of μ; δ; η; and θ). Each column of markers denote that k increases 10% per time. All the other parameters are as shown in Table 1.

TABLE 2: PRCC values for R_0 and prevalence at endemic equilibrium.

Input parameters	Distributions	R_0		Prevalence	
		PRCC	P value	PRCC	P value
β_1	$U(7.6923 \times 10^{-12}, 7.6923 \times 10^{-10})$	0.0395	0.0781	0.0337	0.1328
β_2	$U(7.6923 \times 10^{-12}, 7.6923 \times 10^{-10})$	0.7609	0	0.4823	0
β_3	$U(7.6923 \times 10^{-12}, 7.6923 \times 10^{-10})$	0.4123	0	0.2284	0
η	$U(0.01, 1)$	−0.8065	0	−0.7549	0
δ	$U(0.01, 1)$	−0.0311	0.1645	−0.0380	0.0902
μ	$U(0.01, 1)$	−0.7644	0	−0.7151	0
θ	$U(0.01, 1)$	0.0386	0.0845	0.2219	0
γ	$U(0.01, 1)$	—	—	0.6550	0

treatment parameters μ, δ, η, and θ on the basic reproduction number and prevalence at the endemic equilibrium (i.e., $(E^* + A^* + C^* + T^*)/N^*$). Let k $(0 \le k \le 1)$ be the rate of change of each parameter; then we could increase the treatment rate for the patients at the chronic (or acute) stage (represented by $(1 + k)\mu$ or $((1 + k)\delta)$), the cure rate $((1 + k)\eta)$, and decrease the treatment failure rate $((1 - k)\theta)$ by increasing parameter k. In particular, increasing μ by 30% or decreasing θ by 30% from baseline values (while keeping other parameters fixed) can reduce R_0 by 16.56% or 11.83% and can reduce the equilibrium prevalence by 27.98% or 19.54%, respectively. However, increasing δ or η by 30% from baseline values can only reduce R_0 by 0.36% or 9.42% and reduce the equilibrium prevalence by 0.56% or 15.47%, respectively. It follows from Figure 4 that increasing the treatment rate μ for the patients at the chronic stage and the cure rate η and decreasing the treatment failure rate θ are more effective than increasing the treatment rate δ for the patients at the acute stage in terms of reducing both the basic reproduction number and the equilibrium prevalence in the long run.

To examine the sensitivity of our results to parameter variation, we used Latin hypercube sampling (LHS) and partial rank correlation coefficients (PRCCs) [27, 28] to examine the dependence of R_0 and the equilibrium prevalence on each parameter. Because of limited information on the distributions of each parameter, we chose a uniform distribution as in [28] for all input parameters with ranges listed in Table 2. To know whether the significance of any parameter varies over an entire time interval during model dynamics, PRCC values were calculated for numerous times and plotted versus time. This enables us to assess whether the significance of one parameter changes over an entire time interval during the progression of the model dynamics. Figure 5(a) shows PRCC values plotted from 2003 to 2021 and it indicates that there are five PRCC values that are significantly different from zero and that the PRCC values of the eight examined parameters vary little with time and stabilize at fixed values in about 2006. It follows from Figure 5(b) that the first four parameters with the most significant impact on R_0 are the transmission rate for the chronically infected individuals β_2 and the transmission rate for the treated
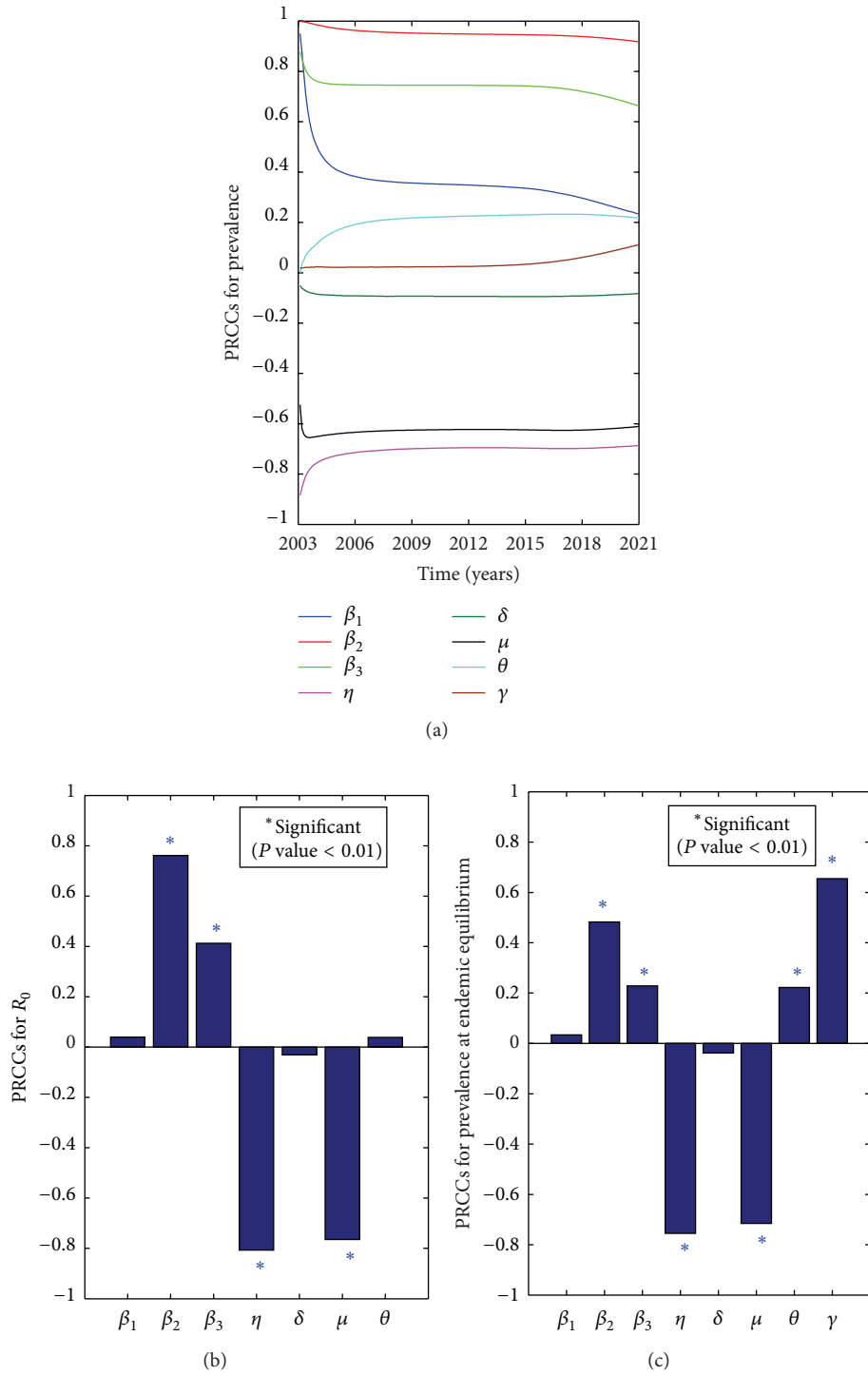
FIGURE 5: (a) PRCCs of the eight parameters for prevalence from 2003 to 2021. (b) PRCCs for R_0. (c) PRCCs for the equilibrium prevalence. Sample size is set to 2000. ∗ denotes PRCCs are significant (P value < 0.01). Parameter values and ranges are as shown in Tables 1 and 2.

population β_3, the cure rate η, and the treatment rate μ for the population with chronic infection. This implies that a greater efficacy of treatment, a larger treatment uptake for the population with chronic infection, and lower transmission rates at the chronic stage definitely result in lower new HCV infections. Moreover, these four parameters $\eta, \mu, \beta_2, \beta_3$

also have significant impact on equilibrium prevalence, as shown in (Figure 5(c)). It is worth mentioning that the rate of waning immunity γ, although it has no effect on R_0, greatly affects the equilibrium prevalence because quick waning of immunity significantly increases the number of the susceptible individuals and hence the prevalence. It should be

noted that the transmission rate β_1 and the treatment rate δ for the population with acute infection have little effect on both the basic reproduction number R_0 and the prevalence at the endemic equilibrium because of the relative short duration of the acute stage.

6. Discussion

In order to understand the prevalence of HCV infection in China based on the reported data [6] and examine the role that treatment plays in the transmission dynamics, we proposed a mathematical model which includes realistic features of HCV transmission such as treatment and partial immunity. Theoretically, the global dynamics of our model are determined by the basic reproduction number R_0. The disease-free equilibrium is globally asymptotically stable if $R_0 \leq 1$, which means that hepatitis C can be entirely eliminated from the population. When $R_0 > 1$, hepatitis C will persist in the population and the endemic equilibrium is globally asymptotically stable for a special case. It is worth mentioning that although the constructed Lyapunov function $V(t)$ is deterministic when proving the global stability of the positive steady state, the coefficients b_k ($k = 3, 4, \ldots, 7$) of function dV/dt which appeared in (25) were chosen to be a positive solution of (27) and are nonunique, which is more general than the proof of Theorem 3.3 in [15].

When the model was applied to HCV transmission in China, we estimated the basic reproduction number R_0 as 1.9897, which is similar to other estimates in the literature [25, 26] but is smaller than the value 4.0636 estimated in [18]. This is because the treated population has relatively low infectiousness which is included in our model, resulting in a smaller basic reproduction number. Goodness of fit and prediction of HCV trends (Figure 2(b)) show a more accurate result than the overestimated simulation in [18] and the prediction indicates that newly reported cases will continue to rise rapidly in the near future. Moreover, we estimate that the prevalence of HCV infection in China (Figure 3) was 0.51% in 2013 and 0.58% in 2014, in good agreement with the cross-sectional study [5], and will reach 1.63% in 2021. These findings lead us to believe that the exact HCV prevalence is much lower than what the WHO estimation indicates. Also, HCV screening in blood, a practice that may significantly reduce the transmission rate of HCV by blood transfusion and other sources of iatrogenic infection, began in the 1990s in China, and thus it is reasonable to believe that strict blood screening and other procedural measures are preventing the spread of HCV and are leading to a lower prevalence.

It follows from sensitivity analysis (Figure 5) that the transmission rate β_3 of the treated population contributes greatly to the transmission of HCV throughout the period of the disease spread. So the prevalence of HCV may be underestimated in [10–12] because in their models the treated population are assumed not to infect the susceptible populations. Figures 4 and 5 show that the basic reproduction number R_0 and equilibrium prevalence are not sensitive to the transmission rate β_1 and the treatment rate δ for population with acute infection, indicating that the acute

stage does not substantially affect the transmission of HCV in the long run due to its relatively short duration, but it may affect the prevalence at the beginning of the epidemic (Figure 3(b)).

It should be acknowledged that one limitation of our results is that the reported national data may not be completely composed of exposed people who enter into the acute stage. The data may contain some cases diagnosed at the acute or chronic stage; though the number of these cases is low, it may still result in a slight overestimate of the prevalence of HCV in China. However, the slightly overestimated results were not caused by our model, but rather by the deficiency of data which did not distinguish which stage the reported cases came from. More realistic models about HCV infection on complex networks [29–31] will be studied in the future work.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Acknowledgments

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