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Research paper

Transmission dynamics of cholera: Mathematical modeling and control strategies

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ABSTRACT

Cholera, as an endemic disease around the world, has generated great threat to human society and caused enormous morbidity and mortality with weak surveillance system. In this paper, we propose a mathematical model to describe the transmission of Cholera. Moreover, basic reproduction number and the global dynamics of the dynamical model are obtained. Then we apply our model to characterize the transmission process of Cholera in China. It was found that, in order to avoid its outbreak in China, it may be better to increase immunization coverage rate and make effort to improve environmental management especially for drinking water. Our results may provide some new insights for elimination of Cholera.

1. Introduction

Historically, Cholera, as a kind of acute diarrheal disease, could fast spread through the direct contact of human beings and imposed a considerable burden on human populations, such as severe dehydration and even death. Thus, how to control propagation of Cholera, mainly caused by the bacteria *Vibrio Cholerae*, has become one open question around the world [1]. While with respect to infection reasons, the most well-known one is that it is usually caused by faecally contaminated water or food [2].

Although there has been a long history since the discovery of Cholera, it is still distributed worldwide. According to the official statistics, global Cholera incidence rate steadily increases since 2000. For example, in 2008–2009, 98,585 agents were infected by Cholera in Zimbabwe [3–5]; the outbreak of Cholera in Haiti caused hundreds of people to die in 2010 [6–8]. Moreover, the World Health Assembly (WHA) deemed that emergent Cholera was an important public health issue and appealed to adopt WHA64.15 resolution to control Cholera in 2011. In this sense, the study about infection features and control of Cholera becomes of utmost importance. Various epidemiology models and frameworks have been intensively explored [9–11]. Among these identified scenarios, we have heterogeneous infectivity [12,13], the impact of human mobility [14], potential control interventions [15]. More specially, in a recent research work [7], where Andrews et al. studied the case of Cholera in Haiti, the comparative estimation of effects of various interventions was shown. In [16], Bertuzzo et al.

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Table 1
Summary of the parameters used in the model.

Parameter	Value	Comments	Unit
μ	0.0066	Natural birth or death rate	$year^{-1}$
k	500	Concentration of Vibrio Cholerae in environment	$cells/mL$
N	1.36×10^9	Human number in China	None
β_e	Estimated	Environment-to-human transmission rate	$year^{-1}$
β_h	Estimated	Human-to-human transmission rate	$year^{-1}$
v	Estimated	Vaccination rate	$year^{-1}$
γ	0.2	Recovery rate	day^{-1}
ξ	10	Rate of human contribution to Vibrio Cholerae	$cells \cdot mL^{-1} \cdot day^{-1}$
δ	1/30	Decay rate of vibrios	day^{-1}
c	4	Disinfection rate	$year^{-1}$

proposed spatial populations and obtained travelling cholera waves. Motivated by these successful achievements, an interesting question naturally poses itself, namely, what is the existing situation of Cholera in China? To guarantee public health, could we propose more effective intervention measures?

During the past two decades, China has suffered a great number of attacks from Cholera [17]. Besides, some novel characters of Cholera recently arise. The first feature is that though less and less people are infected, the outbreak seems more divergent [18], which makes the constitution of uniform intervention measures more difficult. In addition, its outbreak is usually sudden and persists for several weeks or even months, which would lead to huge economic loss [19]. Last, the circumstance of neighboring countries, such as Vietnam, Burma and so on, is very serious, which easily causes imported infections [20]. Thus, proposing a suitable estimation system of Cholera in China is very nontrivial.

The paper is organized as follows. Firstly, we propose a dynamical model for Cholera transmission in a compartmental form. Then we obtain the basic reproduction number and the global dynamics. Furthermore, we apply our model to estimate the degree of Cholera transmission in China. Finally, we give some conclusions and discussions.

2. A dynamical model of Cholera transmission

In the present work, we propose a compartmental model, considering disinfection and vaccination as the basic control strategies, to describe the transmission of Cholera. As previous setup [3], the whole population is divided into three classes: susceptible individual (S) who is health but can catch the disease with transmission rate β if exposed to infected individuals; infected individual (I), who usually passes on disease but can obtain immunity with recovery rate γ; recovered individual (R) who either acquires immunity to the disease or dies due to severe infection [10]. Besides these common classifications, it is worth mentioning that we consider the potential impact of disinfection on Cholera control in China, which is closely related with the concentration of vibrios in contaminated water (denoted by the state B). With regard to protection measures, we use v and c to denote the ratio of vaccination and disinfection in population, respectively.

As is well-known, there mainly exist two transmission paths for Cholera: environment-to-human transmission and human-to-human transmission, which thus compels us to split transmission rate into two components. One is environment-to-human transmission rate β_e; and the other is human-to-human transmission rate β_h. If the number of susceptible, infected, and recovered individuals is S, I, and R, respectively, we can express the time evolution of the population states in the following deterministic ordinary differential equations:

$$\begin{cases} \dfrac{dS}{dt} = \mu N - (\beta_e S \dfrac{B}{k+B} + \beta_h SI) - \mu S - vS, \\ \dfrac{dI}{dt} = \beta_e S \dfrac{B}{k+B} + \beta_h SI - (\gamma + \mu)I, \\ \dfrac{dR}{dt} = \gamma I - \mu R + vS, \\ \dfrac{dB}{dt} = \xi I - \delta B - cB, \end{cases} \tag{1}$$

where μ represents natural birth or death rate, N ($S+I+R=N$) denotes the total human number in China, k corresponds to the concentration of vibrios in contaminated water, ξ is the rate of human contribution to vibrio Cholera, δ is the decay rate of vibrios. Moreover, We provide more details about parameters in Table 1. Based on the aforementioned dynamics, the transmission process of Cholera can also be schematically demonstrated in a flowchart (see Fig. 1).

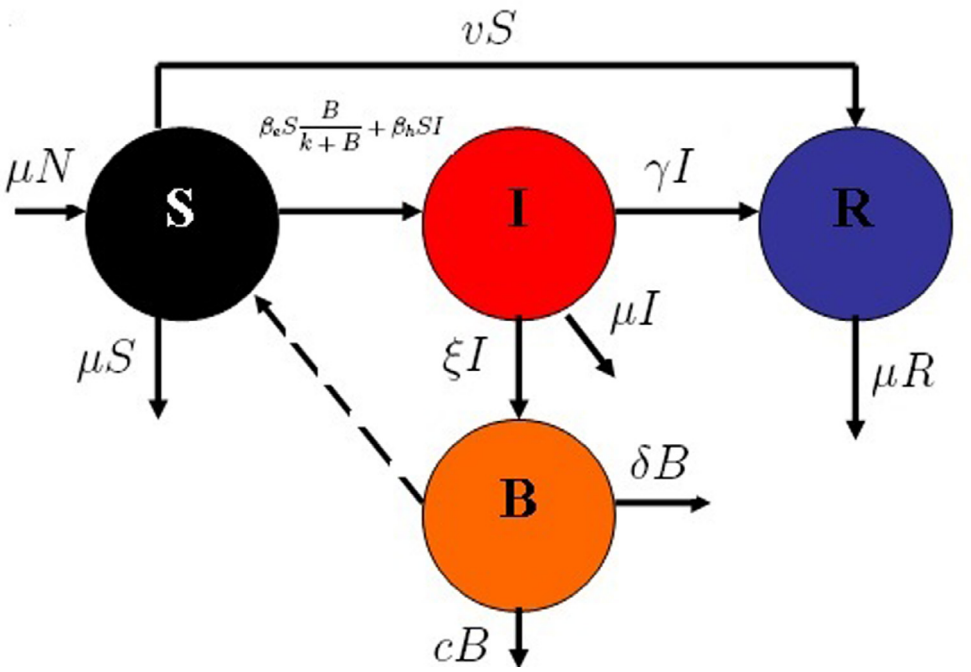

Fig. 1. Transmission model of Cholera in China. *S, I, R* and *B* represent susceptible human, infectious human, recovered human and concentration of vibrios in contaminated water, respectively.

3. Basic reproduction number and global dynamics of system (1)

Because of $d(S+I+R)/dt=0$, we can adjust the above equations into the following expression:

$$\begin{cases} \dfrac{dS}{dt} = \mu N - \beta_e S\dfrac{B}{k+B} - \beta_h SI - \mu S - \upsilon S, \\ \dfrac{dI}{dt} = \beta_e S\dfrac{B}{k+B} + \beta_h SI - (\gamma+\mu)I, \\ \dfrac{dB}{dt} = \xi I - \delta B - cB. \end{cases} \tag{2}$$

By resolving these equations, we can correspondingly acquire the equilibrium solutions of different states: disease-free equilibrium $E_0=(\mu N/(\mu+\upsilon),0,0)$, and endemic equilibrium $E^*=(S^*,I^*,B^*)$, where $I^*=\frac{(\delta+c)B^*}{\xi}$ and $S^*=\frac{\mu N\xi-(\gamma+\mu)(\delta+c)B^*}{(\mu+\upsilon)\xi}$.

In the epidemiology research, there exists a critical estimation parameter: basic reproduction number R_0, which is the average number of secondary infections caused by a single infected agent, during his/her entire infectious period, in a completely susceptible population [10]. According to the methods in Refs. [21–23], we can first order the infected variables (based on disease state) by rewriting the vector on the right hand side of Eq. (2) into $y=(I,B,S)$. Then, combine the following consideration

$$\begin{cases} \dfrac{dI}{dt} = \beta_e S\dfrac{B}{k+B} + \beta_h SI - (\gamma+\mu)I, \\ \dfrac{dB}{dt} = \xi I - \delta B - cB, \end{cases} \tag{3}$$

we can obtain

$$\mathbf{F}=\begin{pmatrix} \beta_e S\frac{B}{k+B}+\beta_h SI \\ 0 \end{pmatrix}, \qquad \mathbf{V}=\begin{pmatrix} (\gamma+\mu)I \\ (\delta+c)B-\xi I \end{pmatrix}.$$

where **F** represents the rate of appearance of new infection and **V** denotes the rate of transfer of individuals. Calculating the derivatives of **F** and **V** about $x=(I,B)$, and substituting disease-free equilibrium $E_0=(S_0,0,0)$ into the states *S, I* and *B*, we can obtain

$$F=\begin{pmatrix} \beta_h S_0 & \frac{\beta_e S_0}{k} \\ 0 & 0 \end{pmatrix}, V=\begin{pmatrix} \gamma+\mu & 0 \\ -\xi & \delta+c \end{pmatrix}.$$

Finally, the basic reproduction number of system is as

$$R_0 = \rho(FV^{-1}) = \beta_h \frac{\mu N}{(\mu+\nu)(\gamma+\mu)} + \beta_e \frac{\mu N \xi}{(\mu+\nu)(\gamma+\mu)(\delta+c)k} \triangleq R_h + R_e, \tag{4}$$

where R_h and R_e are partial basic reproduction number induced by human-to-human transmission and environment-to-human transmission, respectively.

Theorem 1. *If $R_0 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable.*

Proof. Define a Lyapunov function:

$$V = \int_N^S \left(1 - \frac{\mu N}{(\mu+\nu)x}\right)dx + R_0 I + \frac{\mu N \beta_e}{k(\mu+\nu)(\delta+c)} B.$$

Then, the derivative of V along solutions of system (2) is:

$$\begin{aligned}
\frac{dV}{dt} &= \left[1 - \frac{\mu N}{(\mu+\nu)S}\right]\dot{S} + R_0\dot{I} + \frac{\mu N\beta_e}{k(\mu+\nu)(\delta+c)}\dot{B} \\
&= \left[1 - \frac{\mu N}{(\mu+\nu)S}\right]\left(\mu N - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S - \nu S\right) + R_0[\beta_e S\frac{B}{k+B} \\
&\quad + \beta_h SI - (\gamma+\mu)I] + \frac{\mu N\beta_e}{k(\mu+\nu)(\delta+c)}(\xi I - \delta B - cB) \\
&= (R_0 - 1)\left(\beta_e S\frac{B}{k+B} + \beta_h SI\right) + \left[2\mu N - (\mu+\nu)S - \frac{(\mu N)^2}{(\mu+\nu)S}\right] \\
&\quad + \frac{\beta_e B\mu N}{(k+B)(\mu+\nu)} + \frac{\beta_h I\mu N}{(\mu+\nu)} - R_0(\gamma+\mu)I + \frac{\mu N\beta_e}{k(\mu+\nu)(\delta+c)}(\xi I - \delta B - cB) \\
&= (R_0 - 1)\left(\beta_e S\frac{B}{k+B} + \beta_h SI\right) + \left[2\mu N - (\mu+\nu)S - \frac{(\mu N)^2}{(\mu+\nu)S}\right] + \frac{\beta_e \mu N B}{\mu+\nu}\left[\frac{1}{k+B} - \frac{1}{k}\right] \\
&\le (R_0 - 1)\left(\beta_e S\frac{B}{k+B} + \beta_h SI\right).
\end{aligned}$$

If $R_0 < 1$, we get $\frac{dV}{dt} < 0$ which implies that the disease-free equilibrium E_0 of system (2) is globally asymptotically stable. □

Theorem 2. *If $R_0 > 1$, the endemic equilibrium E^* is globally asymptotically stable.*

Proof. Define a Lyapunov function:

$$V = \int_{S^*}^S \left(1 - \frac{S^*}{x}\right)dx + \int_{I^*}^I \left(1 - \frac{I^*}{x}\right)dx + \frac{\beta_e S^* B^*}{\xi I^*(k+B^*)}\int_{B^*}^B \left(1 - \frac{B^*}{x}\right)dx.$$

Then the derivative of V along solutions of system (2) is:

$$\dot{V} = \left(1 - \frac{S^*}{S}\right)\dot{S} + \left(1 - \frac{I^*}{I}\right)\dot{I} + \frac{\beta_e S^* B^*}{\xi I^*(k+B^*)}\left(1 - \frac{B^*}{B}\right)\dot{B}.$$

By direct calculations, we have that:

$$\begin{aligned}
\left(1 - \frac{S^*}{S}\right)\dot{S} &= \left(1 - \frac{S^*}{S}\right)\left(\mu N - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S - \nu S\right) \\
&= \left(1 - \frac{S^*}{S}\right)\left(\beta_e S^*\frac{B^*}{k+B^*} + \beta_h S^* I^* + \mu S^* + \nu S^* - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S - \nu S\right) \\
&= \left(1 - \frac{S^*}{S}\right)\left(\beta_e S^*\frac{B^*}{k+B^*} - \beta_e S\frac{B}{k+B}\right) + \left(1 - \frac{S^*}{S}\right)(\beta_h S^* I^* - \beta_h SI) \\
&\quad + \left(1 - \frac{S^*}{S}\right)(\mu S^* - \mu S) + \left(1 - \frac{S^*}{S}\right)(\nu S^* - \nu S) \\
&= \beta_e S^*\frac{B^*}{k+B^*}\left(1 - \frac{S^*}{S}\right)\left[1 - \frac{SB(k+B^*)}{S^*B^*(k+B)}\right] + \beta_h S^* I^*\left(1 - \frac{S^*}{S}\right)\left(1 - \frac{SI}{S^*I^*}\right) - \frac{\mu+\nu}{S}(S^* - S)^2 \\
&\le \beta_e S^*\frac{B^*}{k+B^*}\left(1 - \frac{S^*}{S}\right)\left[1 - \frac{SB(k+B^*)}{S^*B^*(k+B)}\right] + \beta_h S^* I^*\left(1 - \frac{S^*}{S}\right)\left(1 - \frac{SI}{S^*I^*}\right),
\end{aligned}$$

$$\begin{aligned}\left(1-\frac{I^*}{I}\right)\dot{I} &= \left(1-\frac{I^*}{I}\right)\left[\beta_e S\frac{B}{k+B}+\beta_h SI-(\gamma+\mu)I\right]\\ &= \left(1-\frac{I^*}{I}\right)\left(\beta_e S\frac{B}{k+B}+\beta_h SI-(\beta_e S^*\frac{B^*}{k+B^*}+\beta_h S^*I^*)\frac{I}{I^*}\right)\\ &= \left(1-\frac{I^*}{I}\right)\left(\beta_e S\frac{B}{k+B}-\beta_e S^*\frac{B^*}{k+B^*}\frac{I}{I^*}\right)+\left(1-\frac{I^*}{I}\right)\left(\beta_h SI-\beta_h S^*I^*\frac{I}{I^*}\right)\\ &= \beta_e S^*\frac{B^*}{k+B^*}\left(1-\frac{I^*}{I}\right)\left(\frac{S\frac{B}{k+B}}{S^*\frac{B^*}{k+B^*}}-\frac{I}{I^*}\right)+\beta_h S^*I^*\left(1-\frac{I^*}{I}\right)\left(\frac{SI}{S^*I^*}-\frac{I}{I^*}\right),\end{aligned}$$

and

$$\begin{aligned}\frac{\beta_e S^*B^*}{\xi I^*(k+B^*)}\left(1-\frac{B^*}{B}\right)\dot{B} &= \frac{\beta_e S^*B^*}{\xi I^*(k+B^*)}\left(1-\frac{B^*}{B}\right)(\xi I-\delta B-cB)\\ &= \frac{\beta_e S^*B^*}{\xi I^*(k+B^*)}\left(1-\frac{B^*}{B}\right)\left(\xi I-\frac{\xi I^*B}{B^*}\right)\\ &= \frac{\beta_e S^*B^*}{k+B^*}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right).\end{aligned}$$

As a result, we get

$$\begin{aligned}\dot{V} \le\ & \beta_e S^*\frac{B^*}{k+B^*}(1-\frac{S^*}{S})[1-\frac{SB(k+B^*)}{S^*B^*(k+B)}]+\beta_h S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{SI}{S^*I^*}\right)\\ &+\beta_e S^*\frac{B^*}{k+B^*}\left(1-\frac{I^*}{I}\right)\left(\frac{S\frac{B}{k+B}}{S^*\frac{B^*}{k+B^*}}-\frac{I}{I^*}\right)+\beta_h S^*I^*\left(1-\frac{I^*}{I}\right)\left(\frac{SI}{S^*I^*}-\frac{I}{I^*}\right)\\ &+\frac{\beta_e S^*B^*}{k+B^*}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right).\end{aligned}$$

For the function $\nu(x)=1-x+\ln x$, we know that $x>0$ leads to $\nu(x)\le 0$. And if $x=1$, then $\nu(x)=0$. Note that

$\beta_e S^*\frac{B^*}{k+B^*}(1-\frac{S^*}{S})(1-\frac{SB(k+B^*)}{S^*B^*(k+B)})+\beta_e S^*\frac{B^*}{k+B^*}(1-\frac{I^*}{I})(\frac{S\frac{B}{k+B}}{S^*\frac{B^*}{k+B^*}}-\frac{I}{I^*})$

$$\begin{aligned}&= \beta_e S^*\frac{B^*}{k+B^*}\{1-\frac{S^*}{S}-\frac{SB(k+B^*)}{S^*B^*(k+B)}+\frac{S^*SB(k+B^*)}{SS^*B^*(k+B)}+\frac{SB(k+B^*)}{S^*B^*(k+B)}-\frac{I}{I^*}-\frac{I^*SB(k+B^*)}{IS^*B^*(k+B)}+1\}\\ &= \beta_e S^*\frac{B^*}{k+B^*}\{2-\frac{S^*}{S}-\frac{I}{I^*}+\frac{B(k+B^*)}{B^*(k+B)}-\frac{I^*SB(k+B^*)}{IS^*B^*(k+B)}\}\\ &= \beta_e S^*\frac{B^*}{k+B^*}\{[\frac{B(k+B^*)}{B^*(k+B)}-1](1-\frac{k+B}{k+B^*})+\nu(\frac{S^*}{S})+\nu(\frac{I^*SB(k+B^*)}{IS^*B^*(k+B)})+\nu(\frac{k+B}{k+B^*})\\ &\quad+\frac{B}{B^*}-\ln(\frac{B}{B^*})-\frac{I}{I^*}+\ln(\frac{I}{I^*})\}\\ &\le \beta_e S^*\frac{B^*}{k+B^*}\{\frac{B}{B^*}-\ln(\frac{B}{B^*})-\frac{I}{I^*}+\ln(\frac{I}{I^*})\}.\end{aligned}$$

Moreover, we can obtain

$\beta_h S^*I^*(1-\frac{S^*}{S})(1-\frac{SI}{S^*I^*})+\beta_h S^*I^*(1-\frac{I^*}{I})(\frac{SI}{S^*I^*}-\frac{I}{I^*})$

$$\begin{aligned}&= \beta_h S^*I^*\left(1-\frac{SI}{S^*I^*}-\frac{S^*}{S}+\frac{S^*SI}{SS^*I^*}+\frac{SI}{S^*I^*}-\frac{I}{I^*}-\frac{I^*SI}{IS^*I^*}+1\right)\\ &= \beta_h S^*I^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right)\le 0.\end{aligned}$$

and

$$\begin{aligned}\frac{\beta_e S^*B^*}{k+B^*}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right) &= \frac{\beta_e S^*B^*}{k+B^*}\left(\frac{I}{I^*}-\frac{B^*I}{BI^*}-\frac{B}{B^*}+1\right)\\ &= \frac{\beta_e S^*B^*}{k+B^*}\left[\nu\left(\frac{B^*I}{BI^*}\right)+\frac{I}{I^*}-\ln\left(\frac{I}{I^*}\right)-\frac{B}{B^*}+\ln\left(\frac{B}{B^*}\right)\right]\\ &\le \frac{\beta_e S^*B^*}{k+B^*}\left[\frac{I}{I^*}-\ln(\frac{I}{I^*})-\frac{B}{B^*}+\ln\left(\frac{B}{B^*}\right)\right].\end{aligned}$$

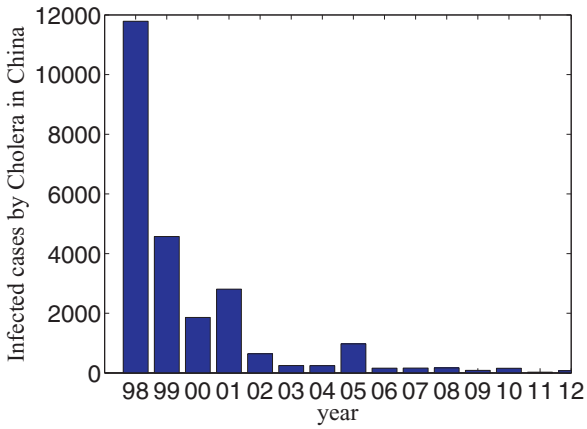

Fig. 2. The empirical infection cases of Cholera in China from 1998 to 2012 [17].

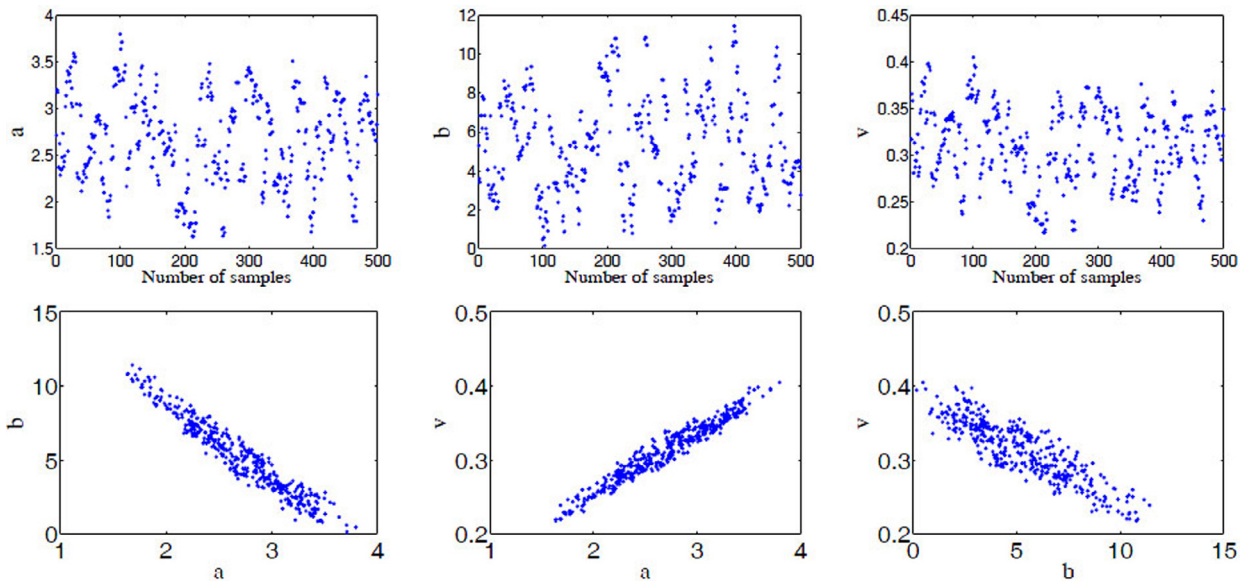

Fig. 3. Simulation results for parameters *a, b* and *v* with 1D parameter MCMC chain with 500 sample realizations (top panel), computed 2D MCMC chain (bottom panel).

Consequently, we gain

$$\dot{V} \le \frac{\beta_e S^* B^*}{k + B^*}\left[\frac{B}{B^*} - \ln\left(\frac{B}{B^*}\right) - \frac{I}{I^*} + \ln\left(\frac{I}{I^*}\right)\right] + \frac{\beta_e S^* B^*}{k + B^*}\left[\frac{I}{I^*} - \ln\left(\frac{I}{I^*}\right) - \frac{B}{B^*} + \ln\left(\frac{B}{B^*}\right)\right] = 0.$$

One can see that the largest invariant subset, where $\dot{V} = 0$, is E^*. By LaSalle's Invariance Principle [24], E^* is globally asymptotically stable when $R_0 > 1$. □

4. An application: Cholera transmission in China

In the past twenty years, there are many people infected by Cholera (for more accurate statistics results see Fig. 2). Aiming to calculate the basic reproduction number R_0 in China, it seems necessary to first estimate other related model parameters. Since vast majority of parameters have been endowed with values according to existing empirical works (see Table 1), we just need to make estimation for three remaining ones: environment-to-human transmission rate $\beta_e = a \times 10^{-6}$, human-to-human transmission rate $\beta_h = b \times 10^{-9}$ and the vaccination rate v. Subsequently, we implement extensive Markov-chain Monte-Carlo (MCMC) simulations based on the adaptive combination Delayed rejection and Adaptive Metropolis (DRAM) algorithm [25]. Using 500 sample realizations, we can acquire the parameter values for *a, b* and *v* with 1D parameter MCMC chain and the computed 2D MCMC chain in Fig. 3. Then we further get the mean value, the standard deviation, MCMC error and Geweke for these parameters, which are shown in Table 2.

Table 2
Parameter estimation for three key parameters a, b and v with the method of MCMC.

Parameter	Mean	Standard	MCMC error	Geweke
a	2.6699	0.47607	0.055218	0.95468
b	5.3508	2.4914	0.30616	0.99076
v	0.31017	0.040146	0.0047384	0.94347

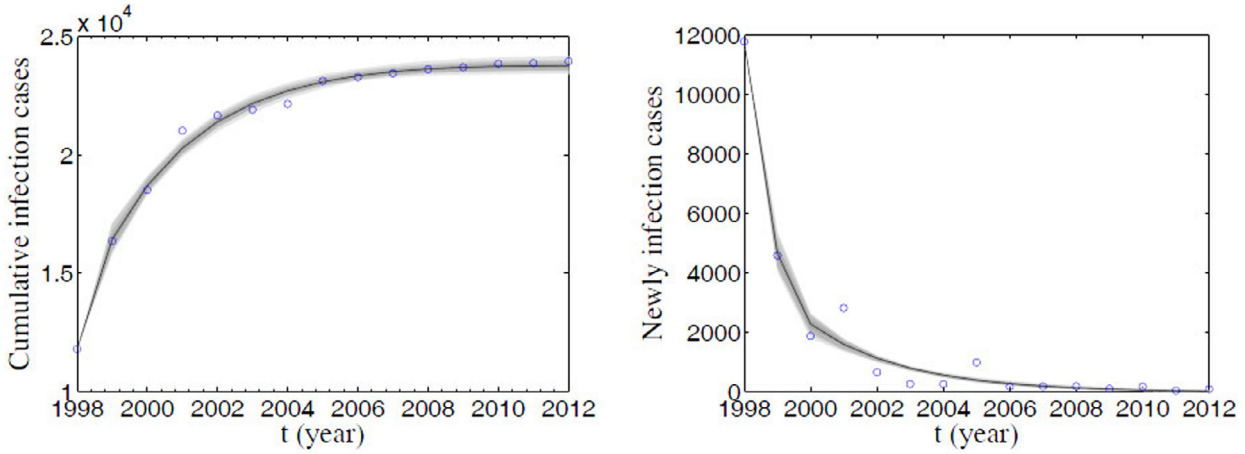

Fig. 4. The comparison of cumulative infection cases (left panel), newly infection cases of each year (right panel) between simulation results and empirical data (from 1998 to 2012) in China. Circles (○) present the realistic record, the solid lines show the median fits and darker areas correspond to 95% posterior limits of the model uncertainty.

Substituting the above parameter values into the proposed transmission dynamics, we can now simulate theoretical infection cases in China and then compare with empirical data provided by Fig.1 to validate the accuracy of our model. For this purpose, we mainly focus on the cumulative infection cases and newly infection cases of each year in China. The former can be calculated according to the following equation,

$$\frac{dX(t)}{dt} = \beta_e S\frac{B}{k+B} + \beta_h SI, \tag{5}$$

where $X(t)$ is the so-called accumulative infection cases. The right hand side of this equation is composed of two parts, which correspond to two types of transmission paths. The first term in right hand side denotes the newly increased infection cases caused by virus in environment; while the second term represents the newly increased infection cases by direct contact.

As for newly infected cases, it is expressed as follows,

$$Z(t) = X(t) - X(t-1), \tag{6}$$

where t is regarded as year in the simulations.

Fig. 4 unveils the time evolution of both infection cases and comparison with empirical record of Cholera in China. It is clear that the theoretical prediction is nearly full agreement with real data, which well validates the accuracy of proposed model. Due to ensuring enough accuracy, we can now calculate the basic reproduction number $R_0 \approx 0.4749$ for Cholera in China. According to equilibrium analysis in theoretical analysis of R_0, this indicates that Cholera can get effective control with the current prevention measures in China, which is consistent with real situation as well.

An important remaining question concerns how existing control measures affect Cholera transmission (or which strategy is better for the eradication of Cholera) [26–29]. While in China, there are mainly two kinds of prevention strategies: disinfection and vaccination. To get a clear comparison, we need to examine their efficiency separately. Fig. 5 features the time evolution of infection cases with the disinfection scenario, where vaccination is not involved. It is explicit that infection fast reaches a plateau and then keeps such a high level, which means that disinfection could not provide sufficient protection and Cholera becomes an endemic epidemic in the population. However, if vaccination is considered as the only control measure, we are able to acquire completely different observation (see Fig. 6): in the most early stages of the evolutionary process infection can effectively expand, but subsequently it will have a fast decline towards the extinction. Combining with these two scenarios, it is clear that vaccination is the more effective approach in preventing Cholera than disinfection, which is consistent with the analysis of PRCC (see Table 3).

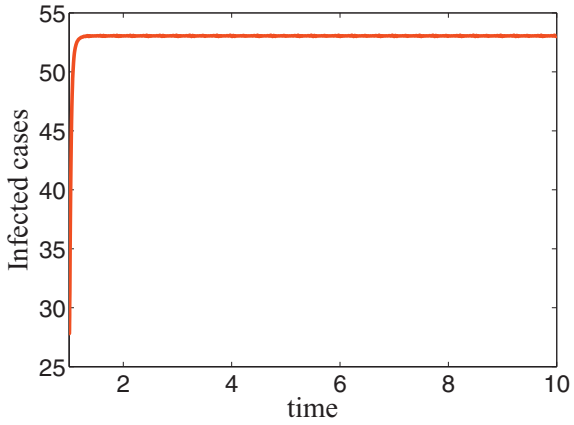

Fig. 5. Time evolution of infected human cases with disinfection. All the parameters have identical values with Table 1 except for $\upsilon = 0$.

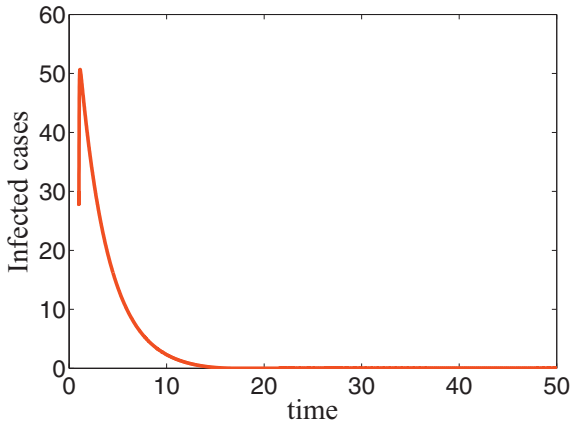

Fig. 6. Time evolution of infected human cases with vaccination. All the parameters have identical values with Table 1 except for $c = 0$.

Table 3
Partial rank correlation coefficient (PRCC) for the aggregate basic reproduction number R_0 and each input parameter variable.

Input parameter	$\mathcal{R}_0$	
	PRCC	p value
υ	−0.9121	0.00
β_e	0.9851	0.00
c	−0.3242	0.00
k	−0.2361	0.00
β_h	0.0316	0.0193

5. Conclusion and discussion

Cholera, as a typical endemic disease around the world, brings huge physical and psychological harm to human beings. Though there have existed many potential prevention measures, it still causes lots of infection in some countries and even triggers the scare in the whole world [30]. In this work, our purpose is to pose a dynamical model of Cholera transmission and investigate its global dynamics. In the aspect of applications, we take China as a studied country to estimate the transmission degree of Cholera and put forward possible control measures.

It should be noted that the model investigated in our paper is a deterministic form without spatial effects and thus there may exist a certain distance between the current framework and realistic cases. Cholera usually takes the seasonal outbreak around monsoon rains [31]. In this sense, we need to find out the detailed mechanisms about seasonal outbreak of Cholera based on a dynamical model with periodic forces. Meanwhile, the incidences are different with diverse age groups (children possess highest ones) [32,33]. It is thus reasonable that age structure should be incorporated into transmission dynamics of Cholera in future. What is more, we live in a spatial world and consequently spatial models need to be used to model the

transmission of Cholera, estimate the transmission velocity of diseases, and in turn suggest policy decisions [34–36]. For the application in China, China is a big country and the conditions of Cholera transmission are different in different cities. As a result, multi-patch models or models on complex networks may be more suitable to describe the transmission process of Cholera in China [10].

Though the basic reproduction number of Cholera in China is about 0.4749, the situation is still not optimistic due to limited environment protection and poor medical condition. While for the control of Cholera, it is instructive to increase immunization coverage rate. As mentioned in the review [37], the total number of Cholera cases reported by WHO is less than realistic infected cases. Therefore, we may also underestimate the empirical situation in China based on the reported data from 1998 to 2012. Meanwhile, the data of Cholera in China in our paper is not enough and precise. To obtain the data with more useful information, we may need more economic investment and sophisticated statistical methods, which indicates that the revealing of Cholera transmission rule requires collaborative efforts from different disciplines.

It is worth pointing that we just consider vaccination and disinfection as the control measures of Cholera. However, immigration is a potential factor for the spread of Cholera [37,38]. In this sense, we need to re-construct the dynamics equation (namely, Eq. (1)) by incorporating the immigration term

$$\begin{cases} \dfrac{dS}{dt} = c_1 A + \mu N - (\beta_e S \dfrac{B}{k+B} + \beta_h SI) - \mu S - \upsilon S, \\ \dfrac{dI}{dt} = c_2 A + \beta_e S \dfrac{B}{k+B} + \beta_h SI - (\gamma + \mu) I, \\ \dfrac{dR}{dt} = (1 - c_1 - c_2) A + \gamma I - \mu R + \upsilon S, \\ \dfrac{dB}{dt} = \xi I - \delta B - cB, \end{cases} \tag{7}$$

where A represents the number of immigration, c_1 and c_2 denote the transmission rate from immigration population to susceptible and infected population. At the same time, emigration may also have a negligible effect on the Cholera spread. Accordingly, these issues need further investigations in the future study.

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