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MODELING THE EFFECTS OF VACCINATING STRATEGIES AND PERIODIC OUTBREAKS ON DENGUE IN SINGAPORE*

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Abstract Effective vaccination strategies can significantly reduce virus transmission, while periodic outbreaks require model prediction and early intervention to mitigate their impact. A novel dengue epidemic model with periodicity and vaccination is introduced in this paper. First, the positivity of solutions and the invariant set are given, and the basic reproduction number is obtained. Then, the disease-free periodic solution is globally asymptotically stable when the basic reproduction number is less than one, and periodic solution is consistent persistence when the basic reproduction number is more than one. Actual data are used to develop more scientific and reasonable prevention and control measures, reducing the transmission risk of dengue fever. Next, based on the dengue fever data in Singapore from 2014 to 2017, the best fitting parameters of such model are determined by using the Markov Chain Monte Carlo algorithm. Finally, some numerical simulations are carried out. These indicate that vaccination is of great significance to control the spread of disease.

Keywords Dengue, disease extinction, vaccination, periodicity, consistent persistence.

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1. Introduction

Dengue fever is an infectious disease caused by the dengue virus. It is a mosquito-borne disease mainly transmitted by *Aedesalbopictus* and *Aedesaegypti*. The number of dengue fever infections in the whole world has increased dramatically in recent decades, putting about half of the population at risk [33]. The main symptoms are high fever, headache, eye pain, joint pain and vomiting. Severe cases can develop into dengue haemorrhagic fever and shock syndrome [11]. Mosquito-borne transmission is influenced by many factors, such as natural environment including atmospheric temperature and humidity, and the social environment including human

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activities [20,47]. One person can become infected with dengue fever once he (she) is bitten by a mosquito infected with the virus [30]. Similarly, a mosquito can become infected with dengue fever by biting a person who carries the dengue virus [13]. Fischer and Halstead [12] first used a mathematical model to study the transmission mechanism of dengue fever. Subsequently, a large number of mathematical models have been used to analyze the transmission characteristics and epidemic trends of dengue fever. Cai et al. [3] presented a model of dengue fever with bilinear and standard incidence rates, and provided a representation of the basic reproduction number. Musa et al. [29] established a deterministic model and found consistent fitting results and equivalent goodness-of-fit when the asymptomatic infection was considered. Chang et al. [5] constructed a dengue transmission model incorporating nonlocal diffusion. Li-Martín et al. [25] proposed a dengue disease transmission model with two-stage structure in the human population.

The environment in which the mosquitoes grow is influenced by a variety of factors, such as rainfall, temperature, and humidity. Because most factors affecting the environment change periodically, dengue fever also spreads periodically. Wu et al. [40] suggested that climate affects mosquito behavior and dengue transmission. Coutinho et al. [8] studied a non-autonomous dengue model with seasonality and derived time-dependent thresholds. Andraud et al. [1] established a simple vector-host model by considering seasonal variations in mosquito density. Zha and Jiang [42] showed a degenerate dengue fever model in heterogeneous environment.

Since the dengue fever can bring great disasters to humans, various measures have bee taken to control the transmission of the dengue fever. One of the effective ways is to control the mosquito. However, large-scale mosquito control efforts, such as insecticide delivery, removal of mosquito breeding sites, and release of Wolbachian mosquitoes, are costly, and the use of a large number of chemicals damages the ecological environment [46]. Therefore, the development of an effective vaccine can overcome these problems. Efforts to develop a dengue vaccine have been underway since the 1930s. Some obtained results found that the vaccine can significantly reduce the infection rate and death rate [17,18]. However, there is no specific treatment for dengue, and prevention is limited to control the mosquito. Therefore, the development of a safe and effective vaccine is of great significance for the control of the disease. Shim [34] proposed a dengue model with age structure and vaccination to study dengue dynamics in the Philippines. Their results show that age-based vaccination is good at controlling disease transmission as long as the cost of vaccination is low enough when vaccine efficacy is relatively low. Pratchaya et al. [31] proposed an SIR transmission model with vaccination, and investigated the existence of the equilibrium and stability of the model. The role of the dengue vaccine in the model was determined. Magal and Webb [23] analyzed the relationship between reported and unreported cases, and showed that the proportion of unreported cases was very high, which is significant for taking measures to control the epidemic. Xue et al. [41] established a model of dengue fever with vaccination, and considered its optimal control. Musa et al. [29] constructed a dengue fever model including the unreported cases, and obtained the basic reproduction number, the conditions of extinction and uniform persistence of the disease. There are also many results on dengue fever (seen the references [4, 16, 19, 22, 26, 27, 32, 42, 44]).

The above authors have considered models with vaccine control or periodic outbreaks alone. However, the model with vaccination and periodic outbreaks simultaneously is rare. Based on the above work [1, 29, 41], we will take the periodic

transmission, vaccination and the unreported cases into account on the spread of dengue fever in our paper. Based on the data of dengue fever in Singapore from 2014 to 2017, we will fit our model using the Markov Chain Monte Carlo (MCMC) algorithm.

The rest of this paper is as follows. In Section 2, a new dengue model with vaccination strategies and periodic outbreaks is established. In Section 3, the basic reproduction number is analyzed. The extinction of the periodic disease-free state and the uniform persistence of the periodic disease are analyzed. In Section 4, a case study and numerical results are presented. In Section 5, the uncertainty and sensitivity analyses are presented. Some discussions and conclusions are included in the final section.

2. Mathematical model

2.1. Model

The total population is divided into six compartments: $S(t)$, $V(t)$, $E(t)$, $A(t)$, $I(t)$ and $R(t)$. $S(t)$ represents the number of susceptible individuals, $V(t)$ represents the number of vaccinated individuals, $E(t)$ represents the number of individuals exposed to the infected but unable to possess infectivity, $A(t)$ represents the number of unreported infected individuals, $I(t)$ represents the number of reported infected individuals by the Ministry of Health (Singapore), $R(t)$ represents the number of recover individuals. Hence, the total number of population at time t is given by $N(t) = S(t) + V(t) + E(t) + A(t) + I(t) + R(t)$.

The total mosquito population at time t, denoted by $H(t)$, is divided into three compartments: $M(t)$, $L(t)$ and $P(t)$. $M(t)$ denotes the number of susceptible mosquitoes, $L(t)$ denotes the number of exposed mosquitoes that can not infect the people, $P(t)$ denotes the number of infected mosquitoes that can infect the people. Hence, the total number of mosquitoes at time t is given by $H(t) = M(t) + L(t) + P(t)$.

Thus, the model structure is shown in Figure 1. The corresponding system of ordinary differential equations for such flowchart is as follows:

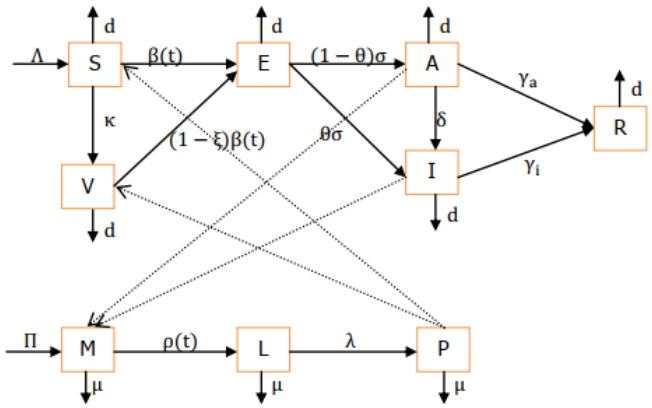


Figure 1. Flowchart of the dengue epidemic model.

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta(t)SP - \kappa S - dS, \\ \dfrac{\mathrm{d}V}{\mathrm{d}t} = \kappa S - (1-\xi)\beta(t)VP - dV, \\ \dfrac{\mathrm{d}E}{\mathrm{d}t} = \beta(t)SP + (1-\xi)\beta(t)VP - \sigma E - dE, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = (1-\theta)\sigma E - \delta A - \gamma_a A - dA, \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = \theta\sigma E + \delta A - \gamma_i I - dI, \\ \dfrac{\mathrm{d}R}{\mathrm{d}t} = \gamma_a A + \gamma_i I - dR, \\ \dfrac{\mathrm{d}M}{\mathrm{d}t} = \Pi - \rho(t)M(A+I) - \mu M, \\ \dfrac{\mathrm{d}L}{\mathrm{d}t} = \rho(t)M(A+I) - \lambda L - \mu L, \\ \dfrac{\mathrm{d}P}{\mathrm{d}t} = \lambda L - \mu P. \end{cases} \tag{2.1}$$

The initial conditions of model (2.1) are

$$\begin{aligned} &S(0) \geq 0, V(0) \geq 0, E(0) \geq 0, A(0) \geq 0, I(0) \geq 0, \\ &R(0) \geq 0, M(0) \geq 0, L(0) \geq 0, P(0) \geq 0. \end{aligned} \tag{2.2}$$

Here, $\beta(t)$ and $\rho(t)$ are two functions with periodic contagions. These parameters are described in Table 1.

Table 1. The parameters description of the dengue epidemic model.

Parameter	Description(Units)
Λ/Π	The constant recruitment rate of the humans/mosquitoes ($month^{-1}$)
d/μ	The natural mortality rate of the humans/mosquitoes ($month^{-1}$)
$\beta(t)$	Transmission probability from infectious mosquitoes to susceptible humans ($time^{-1}$)
$\rho(t)$	Transmission probability from infectious humans to susceptible mosquitoes ($time^{-1}$)
ξ	The effectiveness of a vaccine(none)
σ	Progression rate of exposed humans to infectious humans with clinical symptoms ($month^{-1}$)
θ	The proportion of infected individuals notified by MOH in Singapore (none)
δ	The rate of unreported infected to reported infected humans (none)
γ_a/γ_i	Recovery rate of infectious humans from A, I, respectively ($month^{-1}$)
λ	Progression rate of exposed mosquitoes to the infectious mosquitoes ($month^{-1}$)
κ	The rate of vaccination ($time^{-1}$)

2.2. Basic properties

To show that model (2.1) is epidemiologically, we will prove that all variables of model (2.1) are non-negative for all time $t > 0$.

2.2.1. Positivity of solutions

Lemma 2.1. *Under the initial conditions (2.2), the solutions $S(t)$, $V(t)$, $E(t)$, $A(t)$, $I(t)$, $R(t)$, $M(t)$, $L(t)$, and $P(t)$ of model (2.1) are positive for all $t > 0$.*

Proof. For the given initial conditions, it is easily proof that the solutions of model (2.1) are positive. Suppose that there exists a first time t' such that

$$S(t') = 0, S^{'}(t') < 0, \quad 0 \le t \le t'.$$

According to model (2.1), we have

$$S^{'}(t') = \Lambda > 0,$$

which is contradiction implying that $S(t) \ge 0, t \ge 0$.

Next, there exists another time t'' such that

$$V(t'') = 0, V^{'}(t'') < 0, \quad 0 \le t \le t''.$$

According to model (2.1), we have

$$V^{'}(t'') = \kappa S(t'') \ge 0,$$

which is contradiction implying that $V(t) \ge 0, t \ge 0$. By using the similar methods, it can be proven that $E(t) \ge 0, A(t) \ge 0, I(t) \ge 0, R(t) \ge 0, M(t) \ge 0, L(t) \ge 0, P(t) \ge 0$, for all $t \ge 0$. Therefore, the solutions $S(t)$, $V(t)$, $E(t)$, $A(t)$, $I(t)$, $R(t)$, $M(t)$, $L(t)$ and $P(t)$ of model (2.1) still positive for all $t > 0$. This completes the proof of Lemma 2.1. □

2.2.2. Invariant set

Define

$$\Omega = \Big\{(S, V, E, A, I, R, M, L, P) \in \mathbb{R}_+^9 : \\ 0 \le S, V, E, A, I, R \le N \le \frac{\Lambda}{d}, 0 \le H \le \frac{\Pi}{\mu}\Big\}.$$

Lemma 2.2. *The solutions of model (2.1) is bounded and the set Ω is positive invariant for model (2.1).*

Proof. Adding the former six equations of model (2.1), we have

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \frac{\mathrm{d}S}{\mathrm{d}t} + \frac{\mathrm{d}V}{\mathrm{d}t} + \frac{\mathrm{d}E}{\mathrm{d}t} + \frac{\mathrm{d}A}{\mathrm{d}t} + \frac{\mathrm{d}I}{\mathrm{d}t} + \frac{\mathrm{d}R}{\mathrm{d}t} = \Lambda - dN.$$

It follows that

$$0 \le N(t) = \frac{\Lambda}{d} + \left(N(0) - \frac{\Lambda}{d}\right) e^{-dt},$$

where $N(0)$ represents the initial value of the total population. Therefore, we can obtain $0 \leq \limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{d}$.

Next, according to the last three equations of model (2.1), we have

$$\frac{\mathrm{d}H}{\mathrm{d}t} = \frac{\mathrm{d}M}{\mathrm{d}t} + \frac{\mathrm{d}L}{\mathrm{d}t} + \frac{\mathrm{d}P}{\mathrm{d}t} = \Pi - \mu H.$$

Further, we obtain that

$$0 \leq H(t) = \frac{\Pi}{\mu} + \left(H(0) - \frac{\Pi}{\mu}\right) e^{-\mu t},$$

where $H(0)$ represents the initial value of the total mosquito. Thus, $0 \leq \limsup_{t\to\infty} H(t) \leq \frac{\Pi}{\mu}$. In the rest of our paper, we will consider the dynamics of model (2.1) in the region Ω. This completes the proof of Lemma 2.2. □

3. Mathematical analysis

3.1. The basic reproduction number

The basic reproduction number, defined as the number of expected secondary cases produced by a typically infected person throughout its infectious period in a completely susceptible population, is one of the most important threshold quantities to determine whether an epidemic will spread or die out [9, 10]. Let the right-hand sides of model (2.1) be equal to zero, we have

$$\begin{cases} \Lambda - \beta(t)SP - \kappa S - dS = 0, \\ \kappa S - (1-\xi)\beta(t)VP - dV = 0, \\ \beta(t)SP + (1-\xi)\beta(t)VP - \sigma E - dE = 0, \\ (1-\theta)\sigma E - \delta A - \gamma_a A - dA = 0, \\ \theta\sigma E + \delta A - \gamma_i I - dI = 0, \\ \gamma_a A + \gamma_i I - dR = 0, \\ \Pi - \rho(t)M(A+I) - \mu S = 0, \\ \rho(t)M(A+I) - \lambda L - \mu L = 0, \\ \lambda L - \mu P = 0. \end{cases} \tag{3.1}$$

Then, it is straightforward to see that model (2.1) has a disease-free periodic equilibrium given by

$$J_0\left(S_0, V_0, 0, 0, 0, 0, M_0, 0, 0\right) = \left(\frac{\Lambda}{\kappa + d}, \frac{\kappa\Lambda}{d(\kappa + d)}, 0, 0, 0, 0, \frac{\Pi}{\mu}, 0, 0\right).$$

Next, we can use the theorem proposed by Wang and Zhao [37] to define the basic reproduction number of model (2.1). Let $x = (E, A, I, R, L, P, S, V, M)^T$, then model (2.1) can be rewritten as

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \mathcal{F}(t, x) - \mathcal{V}(t, x),$$

where

$$\mathcal{F}(t,x)=\begin{pmatrix}\beta(t)SP+(1-\xi)\beta(t)VP\\0\\0\\0\\\rho(t)M(A+M)\\0\\0\\0\\0\end{pmatrix},$$

$$\mathcal{V}(t,x)=\begin{pmatrix}(\sigma+d)E\\-(1-\theta)\sigma E+(\delta+\gamma_a+d)A\\-\theta\sigma E-\delta A+(\gamma_i+d)I\\-\gamma_a A-\gamma_i I+dR\\(\lambda+\mu)L\\-\lambda L+\mu P\\-\Lambda+\beta(t)SP+\kappa S+dS\\-\kappa S+(1-\xi)\beta(t)VP+dV\\-\Pi+\rho(t)M(A+I)+\mu M\end{pmatrix}.$$

Obviously, the conditions $(A1)-(A5)$ of the theorem proposed by Wang and Zhao [37] are satisfied. Let

$$\begin{aligned}f(t,x(t))=&\mathcal{F}(t,x)-\mathcal{V}(t,x)\\=&(f_1(t,x(t)),f_2(t,x(t)),f_3(t,x(t)),f_4(t,x(t)),f_5(t,x(t)),\\&f_6(t,x(t)),f_7(t,x(t)),f_8(t,x(t)),f_9(t,x(t)))^T.\end{aligned}$$

Then, we define

$$U(t):=\left(\frac{\partial f_i(t,x^0(t))}{\partial x_j}\right),\ 7\le i,j\le 9,$$

where $x^0(t)=(0,0,0,0,0,0,\frac{\Lambda}{\kappa+d},\frac{\kappa\Lambda}{d(\kappa+d)},\frac{\Pi}{\mu})$ is the disease-free periodic solution.

Let $\Phi_U(t)$ be the monodromy matrix of the linear T-periodic system $\frac{\mathrm{d}z}{\mathrm{d}t}=U(t)z$. Further, we get that the spectral radius of $\Phi_U(T)$ is less than the unity. It is very obvious that the condition $(A6)$ of the theorem [37] is also satisfied.

Next, we will prove the condition $(A7)$ is satisfied according to Wang and Zhao [37]. That is, the spectral radius $\varrho(\Phi_{-V}(T))<1$. At first, we assume that

$F(t) = \left(\frac{\partial \mathcal{F}_i(t,x^0(t))}{\partial x_j}\right)_{1\le i,j\le 6}$ and $V(t) = \left(\frac{\partial \mathcal{V}_i(t,x^0(t))}{\partial x_j}\right)_{1\le i,j\le 6}$, where $\mathcal{F}_i(t,x(t))$ and $\mathcal{V}_i(t,x(t))$ denote the $i-th$ component of $\mathcal{F}(t,x(t))$ and $\mathcal{V}(t,x(t))$, respectively. After simple calculations, we can obtain

$$F(t) = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & \frac{\beta(t)\Lambda}{\kappa+d} + \frac{(1-\xi)\beta(t)\kappa\Lambda}{d(\kappa+d)} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\rho(t)\Pi}{\mu} & \frac{\rho(t)\Pi}{\mu} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$V(t) = \begin{pmatrix} \sigma+d & 0 & 0 & 0 & 0 & 0 \\ -(1-\theta)\sigma & \delta+\gamma_a+d & 0 & 0 & 0 & 0 \\ -\theta\sigma & -\delta & \gamma_i+d & 0 & 0 & 0 \\ 0 & -\gamma_a & -\gamma_i & d & 0 & 0 \\ 0 & 0 & 0 & 0 & \lambda+\mu & 0 \\ 0 & 0 & 0 & 0 & -\lambda & \mu \end{pmatrix}.$$

Clearly, $F(t)$ is nonnegative and $-V(t)$ is cooperative. Let $Y(t,s), t \ge s$ be the evolution operator of the linear T-periodic system

$$\frac{\mathrm{d}y}{\mathrm{d}t} = -V(t)y. \tag{3.2}$$

Therefor, for each $s \in \Re$, the matrix $Y(t,s)_{6\times 6}$ satisfies

$$\frac{\mathrm{d}Y(t,s)}{\mathrm{d}t} = -V(t)Y(t,s),\ \forall t \ge s,\ Y(s,s) = Z, \tag{3.3}$$

where Z is the 6×6 identity matrix.

Thus, let $\Phi_{-V}(t)$ be the monodromy matrix of the linear T-periodic system (3.2). It is proved that

$$\varrho(\Phi_{-V}(T)) = max\{e^{-(\sigma+d)T}, e^{-(\gamma_a+\delta+d)T}, e^{-(\gamma_i+d)T}, e^{-dT}, e^{-(\lambda+\mu)T}\} < 1.$$

According to the theorem in Reference [37], we assume that $\Upsilon(s)$ is the initial distribution of infectious individuals, and $\Upsilon(s)$ is T-periodic. Then, the function

$$\Psi(t) := \int_{-\infty}^{t} Y(t,s)F(s)\Upsilon(s)\mathrm{d}s$$

represents the distribution of accumulated newly infected individuals produced by all infected individuals introduced from the previous time to the time t. Let R_T

be the ordered Banach space of all T - periodic functions from $\Re$ to $\Re^6$ with the maximum norm $||\cdot||$ and the positive cone $R_T^+ := \{\Upsilon \in R_T : \Upsilon(t) \geq 0, \forall t \in \Re\}$. We can define a linear operator $L : R_T \to R_T$ as follows

$$(L\Upsilon)(t) := \int_0^\infty Y(t, t-a)F(t-a)\Upsilon(t-a)\mathrm{d}a, \ \forall t \in \Re, \ \Upsilon \in R_T. \tag{3.4}$$

L is called the next-generation infection operator and the spectral radius of L is defined as the basic reproduction number R_0. Therefore, the basic reproduction number R_0 of model (2.1) can be given as $R_0 := \varrho(L)$.

Lemma 3.1. ([37]) *The following statements are valid.*
(1) *If $\varrho(W(T,0,\eta)) = 1$ has a positive solution η_0, then η_0 is an eigenvalue of L, and hence $R_0 > 0$.*
(2) *If $R_0 > 0$, then $\eta = R_0$ is the unique solution of $\varrho(W(T,0,\eta)) = 1$.*
(3) *$R_0 = 0$ if and only if $\varrho(W(T,0,\eta)) < 1$ for all $\eta > 0$.*

Therefore, the disease-free periodic solution of model (2.1) is locally asymptotically stable if $R_0 < 1$, but unstable if $R_0 > 1$. The basic reproduction number will be calculated. We introduce the linear T-periodic system as follows.

$$\frac{\mathrm{d}w}{\mathrm{d}t} = \left[-V(t) + \frac{F(t)}{\eta}\right] w, \tag{3.5}$$

where $\eta \in (0, \infty)$. Then, let the evolution operator of system (3.5) on $\Re^6$ be $W(t,s,\eta), t \geq s, s \in \Re$. It is clear that $\Phi_{F-V}(t) = W(t,0,1), t \geq 0$ can be obtained. Hence, we derive

$$\Phi_{\frac{F}{\eta}-V}(t) = W(t,0,\eta), \ t \geq 0, \tag{3.6}$$

where

$$\frac{F(t)}{\eta} - V(t) = \begin{pmatrix} -(\sigma+d) & 0 & 0 & 0 & 0 & \frac{\beta(t)\Lambda}{\eta(\kappa+d)} + \frac{(1-\xi)\beta(t)\kappa\Lambda}{\eta d(\kappa+d)} \\ (1-\theta)\sigma & -(\delta+\gamma_a+d) & 0 & 0 & 0 & 0 \\ \theta\sigma & \delta & -(\gamma_i+d) & 0 & 0 & 0 \\ 0 & \gamma_a & \gamma_i & -d & 0 & 0 \\ 0 & \frac{\rho(t)\Pi}{\eta\mu} & \frac{\rho(t)\Pi}{\eta\mu} & 0 & -(\lambda+\mu) & 0 \\ 0 & 0 & 0 & 0 & \lambda & -\mu \end{pmatrix}.$$

Therefore, numerical algorithm is mainly used to calculate the reproduction number according to condition 2 in Lemma 3.1.

3.2. Extinction of the disease

Let $(\Re^k, \Re_+^k)$ be the standard ordered k-dimensional Euclidean space with a norm $||\cdot||$. For $u, v \in \Re^k$, if $u - v \in Int(\Re_+^k)$, then $u \gg v$; if $u - v \in \Re_+^k \backslash \{0\}$, then

$u > v$; if $u - v \in \Re_+^k$, then $u \geq v$. Assume G(t) is a continuous, irreducible and cooperative, and $w-$ periodic $k \times k$ matrix function. The linear differential system

$$\frac{\mathrm{d}z}{\mathrm{d}t} = G(t)z \tag{3.7}$$

has a fundamental solution matrix $\Phi_G(t)$. Let $\varrho(\Phi_G(w))$ be the spectral radius of $\Phi_G(w)$, where $\Phi_G(w)$ is a matrix with all entries positive for each $w > 0$ [2]. By the Perron-Frobenius theorem [36], $\varrho(\Phi_G(w))$ is the principal eigenvalue of $\Phi_G(w)$ which is simple and admits an eigenvector $v^* \gg 0$. Therefore, we can obtain the following result.

Lemma 3.2. ([43]) *Let* $q = \frac{1}{w}\ln \varrho(\Phi_G(w))$. *Then, there exists a positive,* $w-$ *periodic function* $v(t)$ *such that* $e^{qt}v(t)$ *is a solution of system (3.7).*

Theorem 3.1. *The disease-free periodic solution* J_0 *is globally asymptotically stable if* $R_0 < 1$*, but unstable if* $R_0 > 1$*.*

Proof. According to Lemma 3.2, the disease-free periodic solution J_0 is locally asymptotically stable when $R_0 < 1$. Next, we will only prove that the disease-free periodic solution J_0 is globally attractive when $R_0 < 1$.

According to Lemma 2.2, we have

$$\limsup_{t\to\infty}(S(t) + V(t) + E(t) + A(t) + I(t) + R(t)) \leq \frac{\Lambda}{d},$$
$$\limsup_{t\to\infty}(M(t) + L(t) + P(t)) \leq \frac{\Pi}{\mu}.$$

Under the initial conditions (2.2), it follows that

$$\limsup_{t\to\infty} S(t) \leq \frac{\Lambda}{\kappa + d},$$
$$\limsup_{t\to\infty} V(t) \leq \frac{\kappa\Lambda}{d(\kappa + d)},$$
$$\limsup_{t\to\infty} M(t) \leq \frac{\Pi}{\mu}.$$

Hence, for $\forall\epsilon > 0$, there exists $\bar{t} > 0$ such that $S(t) \leq \frac{\Lambda}{\kappa+d} + \epsilon$, $V(t) \leq \frac{\kappa\Lambda}{d(\kappa+d)} + \epsilon$ and $M(t) \leq \frac{\Pi}{\mu} + \epsilon$ for $t > \hat{t}$. We consider the following comparison system

$$\begin{cases} \frac{\mathrm{d}\overline{E}}{\mathrm{d}t} = \beta(t)(\frac{\Lambda}{\kappa + d} + \epsilon)\overline{P} + (1 - \xi)\beta(t)\left(\frac{\kappa\Lambda}{d(\kappa + d)} + \epsilon\right)\overline{P} - \sigma\overline{E} - d\overline{E}, \\ \frac{\mathrm{d}\overline{A}}{\mathrm{d}t} = (1 - \theta)\sigma\overline{E} - \delta\overline{A} - \gamma_a\overline{A} - d\overline{A}, \\ \frac{\mathrm{d}\overline{I}}{\mathrm{d}t} = \theta\sigma\overline{E} + \delta\overline{A} - \gamma_i\overline{I} - d\overline{I}, \\ \frac{\mathrm{d}\overline{R}}{\mathrm{d}t} = \gamma_a\overline{A} + \gamma_i\overline{I} - d\overline{R}, \\ \frac{\mathrm{d}\overline{L}}{\mathrm{d}t} = \rho(t)(\frac{\Pi}{\mu} + \epsilon)(\overline{A} + \overline{I}) - \lambda\overline{L} - \mu\overline{L}, \\ \frac{\mathrm{d}\overline{P}}{\mathrm{d}t} = \lambda\overline{L} - \mu\overline{P}. \end{cases} \tag{3.8}$$

Let $x = (\overline{E}, \overline{A}, \overline{I}, \overline{R}, \overline{L}, \overline{P})^T$, system (3.8) is equivalent to the following system

$$\dot{x} = (F(t) - V(t) + \epsilon n(t))\, x,$$

where

$$n(t) = \begin{pmatrix} 0 & 0 & 0 & 0\ 0 & (1-\xi)\beta(t) \\ 0 & 0 & 0 & 0\ 0 & 0 \\ 0 & 0 & 0 & 0\ 0 & 0 \\ 0 & 0 & 0 & 0\ 0 & 0 \\ 0 & \rho(t) & \rho(t) & 0\ 0 & 0 \\ 0 & 0 & 0 & 0\ 0 & 0 \end{pmatrix}.$$

According to Lemma 3.2, we know that there is a positive w - periodic function $v(t)$ such that $e^{qt}v(t)$ is a solution of system (3.8), where $v(t) = (v_1(t), v_2(t), v_3(t), v_4(t), v_5(t), v_6(t))$ and $q = \frac{1}{w}\ln \varrho(\Phi_{F-V+\epsilon n}(w))$. Then, we choose $\hat{t} > \bar{t}$ and a large $\tau > 0$ to make the following inequalities be true,

$$\begin{aligned} &\overline{E}(\hat{t}) \le \tau v_1(0), \quad \overline{A}(\hat{t}) \le \tau v_2(0), \quad \overline{I}(\hat{t}) \le \tau v_3(0), \\ &\overline{R}(\hat{t}) \le \tau v_4(0), \quad \overline{L}(\hat{t}) \le \tau v_5(0), \quad \overline{P}(\hat{t}) \le \tau v_6(0). \end{aligned}$$

Hence, we have

$$\begin{aligned} &\overline{E}(t) \le \tau e^{q(t-\hat{t})} v_1(t-\hat{t}),\ \overline{A}(t) \le \tau e^{q(t-\hat{t})} v_2(t-\hat{t}),\ \overline{I}(t) \le \tau e^{q(t-\hat{t})} v_3(t-\hat{t}), \\ &\overline{R}(t) \le \tau e^{q(t-\hat{t})} v_4(t-\hat{t}),\ \overline{L}(t) \le \tau e^{q(t-\hat{t})} v_5(t-\hat{t}),\ \overline{P}(t) \le \tau e^{q(t-\hat{t})} v_6(t-\hat{t}). \end{aligned}$$

According to the standard comparison principle, we obtain the inequalities as follows

$$\begin{aligned} &E(t) \le \overline{E}(t) \le \tau e^{q(t-\hat{t})} v_1(t-\hat{t}), \quad A(t) \le \overline{A}(t) \le \tau e^{q(t-\hat{t})} v_2(t-\hat{t}), \\ &I(t) \le \overline{I}(t) \le \tau e^{q(t-\hat{t})} v_3(t-\hat{t}), \quad R(t) \le \overline{R}(t) \le \tau e^{q(t-\hat{t})} v_4(t-\hat{t}), \\ &L(t) \le \overline{L}(t) \le \tau e^{q(t-\hat{t})} v_5(t-\hat{t}), \quad P(t) \le \overline{P}(t) \le \tau e^{q(t-\hat{t})} v_6(t-\hat{t}). \end{aligned}$$

We know that $R_0 < 1$ if and only if $\varrho(\Phi_{F-V}(\omega)) < 1$. Since $\varrho(\Phi_{F-V+\epsilon n}(\omega))$ is continuous for all small ϵ, we can choose all small $\epsilon > 0$ such that $\varrho(\Phi_{F-V+\epsilon n}(\omega)) < 1$. Therefore, we can obtain $q < 0$. This means that the following limits are true,

$$\begin{aligned} &\lim_{t\to\infty} E(t) = 0, \quad \lim_{t\to\infty} A(t) = 0, \quad \lim_{t\to\infty} I(t) = 0, \\ &\lim_{t\to\infty} R(t) = 0, \quad \lim_{t\to\infty} L(t) = 0, \quad \lim_{t\to\infty} P(t) = 0. \end{aligned}$$

Now, there are $\lim_{t\to\infty} S(t) = \frac{\Lambda}{\kappa+d}$, $\lim_{t\to\infty} V(t) = \frac{\kappa\Lambda}{d(\kappa+d)}$, and $\lim_{t\to\infty} M(t) = \frac{\Pi}{\mu}$. Therefore, the disease-free periodic equilibrium J_0 of system (2.1) is globally asymptotically stable. This completes the proof. □

The values of the parameters are $\Lambda = 44671$, $d = 1/(80 * 12)$, $\beta(t) = 2.1331 \times 10^{-10} + 1.468 \times 10^{-10} sin(\frac{\pi}{12}t + 1.0778)$, $\rho(t) = 1.5992 \times 10^{-10} + 4.584 \times 10^{-10} sin(\frac{\pi}{12}t + 1.0778)$, $\kappa = 0.002$, $\sigma = 30/6$, $\gamma_a = 30/7$, $\gamma_i = 30/5$, $\lambda = 30/7$, $\mu = 0.002$, $\Pi = 10000$, $\theta = 0.00462$, $\delta = 0.0109$, $\xi = 0.8$. The initial value of model (2.1) is

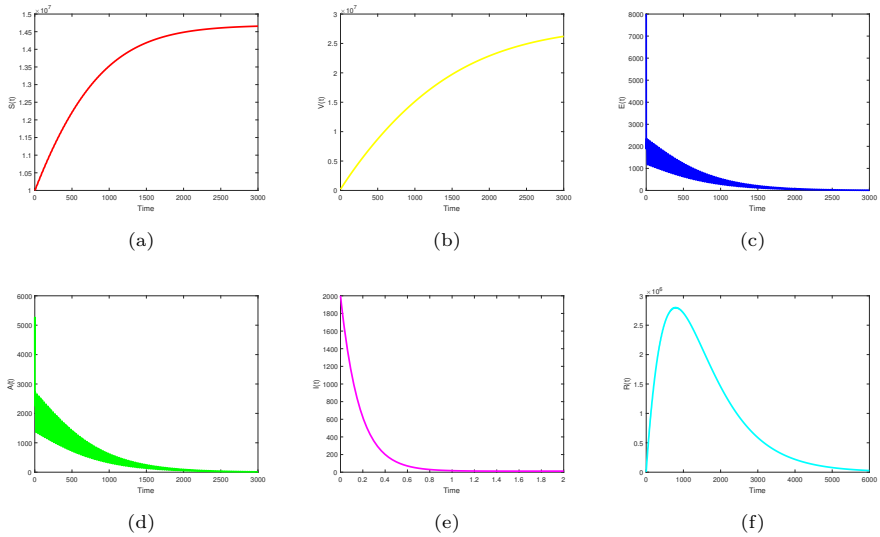


Figure 2. The global stability of the disease-free periodic solution. (a)$S(t)$, (b)$V(t)$, (c)$E(t)$, (d)$A(t)$, (e)$I(t)$, (f)$R(t)$.

$(S(0), V(0), E(0), A(0), I(0), R(0), M(0), L(0), P(0)$=$(10000000, 200000, 8000, 4000, 2000, 5000, 100000000, 1000000, 1000000))$. According to these parameters, to calculate the $R_0 = 0.0663 < 1$. We can give some numerical simulations to illustrate and extend our results in Figure 2.

From the Figure 2, it can be seen that all population in each compartment exhibit periodic fluctuation. The susceptible individuals and the vaccinated individuals tend to non-zero values, but the other individuals tend to zero values. Especially, the recover individuals increase at the beginning, then decrease, and finally approach zero.

3.3. Uniform persistence of the disease

The uniform persistence of system (2.1) is demonstrated by the theory of uniform persistence proposed by Zhao [45].

Theorem 3.2. *If $R_0 > 1$, then system (2.1) is uniformly persistent. That is, if $R_0 > 1$, then there exists a small positive constant $\eta > 0$ such that $A_\infty > 0$, $I_\infty > 0$, $P_\infty > 0$ under the initial conditions of system (2.1).*

Proof. In order to prove this result, the uniform persistence theorem in [45] is used. Define

$$X = \Big\{(S, V, E, A, I, R, M, L, P) \in \Gamma\Big\},$$
$$X_0 = \Big\{(S, V, E, A, I, R, M, L, P) \in X : E > 0, A > 0, I > 0, R > 0, L > 0, P > 0\Big\},$$
$$\partial X = X \backslash X_0.$$

Now we prove that system (2.1) is uniformly persistent with respect to (X, X_0).

First, it is easy to verify that both X and X_0 are positively invariant for system (2.1), and X_0 is relatively closed in X. Moreover, by Lemma 2.2, system (2.1) is point dissipative. Thus, there exists a global attractor of system (2.1).

Let

$$\begin{aligned}M_\partial = \{&(S(0),V(0),E(0),A(0),I(0),R(0),M(0),L(0),P(0)) \in \partial X_0 :\\ &(S(t),V(t),E(t),A(t),I(t),R(t),M(t),L(t),P(t)) \in \partial X_0, \forall t \geq 0\},\\ M'_\partial = \{&(S,V,0,0,0,0,M,0,0) \in \partial X_0 : S \geq 0, V \geq 0, M \geq 0\}.\end{aligned}$$

We will prove that

$$M_\partial = M'_\partial.$$

It is clearly that $M'_\partial \subseteq M_\partial$. We only need to show the validity of $M_\partial \subseteq M'_\partial$. Suppose not, let $\Gamma(t)$ be a solution of system (2.1) with initial condition $\Gamma(0)$. Hence, for any

$$\Gamma(t) = (S(t),V(t),E(t),A(t),I(t),R(t),M(t),L(t),P(t)) \in M_\partial$$

and $\Gamma(t) \neq M'_\partial$, for $\forall t > 0$, the following inequalities are given

$$\begin{aligned}E(t) &= e^{-(\sigma+d)}\left[E(0) + \int_0^t [S(\tau)\beta(\tau)p(\tau) + (1-\xi)\beta(\tau)V(\tau)P(\tau)]\,d\tau\right] > 0,\\ A(t) &= e^{-(\gamma_a+\delta+d)}\left[A(0) + \int_0^t [(1-\theta)\sigma E(\tau)]\,d\tau\right] > 0,\\ I(t) &= e^{-(\gamma_i+d)}\left[I(0) + \int_0^t [\theta\sigma E(\tau) + \delta A(\tau)]\,d\tau\right] > 0,\\ R(t) &= e^{-d}\left[P(0) + \int_0^t [\gamma_a A(\tau) + \gamma_i I(\tau)]d\tau\right] > 0,\\ L(t) &= e^{-(\lambda+\mu)}\left[l(0) + \int_0^t [\rho(\tau)(A(\tau)+I(\tau))M(\tau)]d\tau\right] > 0,\\ P(t) &= e^{-\mu}\left[P(0) + \int_0^t [\lambda L(\tau)]d\tau\right] > 0.\end{aligned}$$

There exists at least one of $E(t), A(t), I(t), R(t), L(t)$ and $P(t)$, which is not zero. This means that $\Gamma(t) \notin \partial X_0$ for $t > 0$, which contradicts the hypothesis that $\Gamma(t) \in M_\partial$. Therefore, we can get that $M_\partial \subseteq M'_\partial$ which indicates $M_\partial = M'_\partial$. We can obtain that M_∂ only has the $J_0(\frac{\Lambda}{\kappa+d}, \frac{\kappa\Lambda}{d(\kappa+d)}, 0, 0, 0, 0, \frac{\Pi}{\mu}, 0, 0)$ and J_0 is isolate and compact invariant.

Then we will prove that $W^s(J_0) \cap X_0 = \emptyset$, where $W^s(J_0)$ indicates the stable manifold of J_0. There exists a positive constant ϵ such that under the initial condition $\Gamma(0) \in X_0$, the follow inequality is true for any solution $\Gamma_t(\Gamma(0))$ of system

$$D(\Gamma_t(\Gamma(0)), J_0)^\infty \geq \epsilon,$$

where D is a distance function in X_0. Inverse, for $\forall \bar{\epsilon} > 0$, we assume that $D(\Gamma_t(\Gamma(0)), J_0)^\infty < \bar{\epsilon}$. For $\forall \bar{\epsilon} > 0$, there exists the period $\omega > 0$ such that $\frac{\Lambda}{\kappa+d} - \bar{\epsilon} \leq S(t) \leq \frac{\Lambda}{\kappa+d} + \bar{\epsilon}$, $\frac{\kappa\Lambda}{d(\kappa+d)} - \bar{\epsilon} \leq V(t) \leq \frac{\kappa\Lambda}{d(\kappa+d)} + \bar{\epsilon}$, $0 \leq E(t) \leq \bar{\epsilon}$, $0 \leq A(t) \leq \bar{\epsilon}$, $0 \leq I(t) \leq \bar{\epsilon}$, $0 \leq R(t) \leq \bar{\epsilon}$, $\frac{\Pi}{\mu} - \bar{\epsilon} \leq M(t) \leq \frac{\Pi}{\mu} + \bar{\epsilon}$, $0 \leq L(t) \leq \bar{\epsilon}$ and $0 \leq P(t) \leq \bar{\epsilon}$.

Further, we consider the following comparison system

$$\begin{cases} \dfrac{\mathrm{d}\tilde{E}}{\mathrm{d}t} \geq \beta(t)(\dfrac{\Lambda}{\kappa+d}-\bar{\epsilon})\tilde{P}+(1-\xi)\beta(t)\left(\dfrac{\kappa\Lambda}{d(\kappa+d)}-\bar{\epsilon}\right)\tilde{P}-\sigma\tilde{E}-d\tilde{E}, \\ \dfrac{\mathrm{d}\tilde{A}}{\mathrm{d}t} = (1-\theta)\sigma\tilde{E}-\delta\tilde{A}-\gamma_a\tilde{A}-d\tilde{A}, \\ \dfrac{\mathrm{d}\tilde{I}}{\mathrm{d}t} = \theta\sigma\tilde{E}+\delta\tilde{A}-\gamma_i\tilde{I}-d\tilde{I}, \\ \dfrac{\mathrm{d}\tilde{R}}{\mathrm{d}t} = \gamma_a\tilde{A}+\gamma_i\tilde{I}-d\tilde{R}, \\ \dfrac{\mathrm{d}\tilde{L}}{\mathrm{d}t} \geq \rho(t)(\dfrac{\Pi}{\mu}-\bar{\epsilon})(\tilde{A}+\tilde{I})-\lambda\tilde{L}-\mu\tilde{L}, \\ \dfrac{\mathrm{d}\tilde{P}}{\mathrm{d}t} = \lambda\tilde{L}-\mu\tilde{P}. \end{cases} \tag{3.9}$$

System (3.9) can be represented as

$$\dot{x} = [F(t)-V(t)-\bar{\epsilon}n(t)]\,x,$$

where $x=(\tilde{E},\tilde{A},\tilde{I},\tilde{R},\tilde{L},\tilde{P})^T$ and

$$n(t)=\begin{pmatrix} 0 & 0 & 0 & 0\,0 & (1-\xi)\beta(t) \\ 0 & 0 & 0 & 0\,0 & 0 \\ 0 & 0 & 0 & 0\,0 & 0 \\ 0 & 0 & 0 & 0\,0 & 0 \\ 0 & \rho(t) & \rho(t) & 0\,0 & 0 \\ 0 & 0 & 0 & 0\,0 & 0 \end{pmatrix}.$$

According to Lemma 3.2, we know that there is a positive w-periodic function $v^*(t)$ such that $e^{q^*t}v^*(t)$ is a solution of system (3.9), where $v^*(t)=(v_1^*(t),v_2^*(t),v_3^*(t),v_4^*(t),v_5^*(t),v_6^*(t))$ and $q^*=\frac{1}{w}\ln\varrho(\Phi_{F-V+\epsilon n}(w))$. Due to $R_0>1$, $\varrho(\Phi_{F-V+\epsilon n}(w))>1$. Therefore, according to the comparison principle, we can obtain

$$\begin{aligned} &\lim_{t\to\infty}E(t)=+\infty, \quad \lim_{t\to\infty}A(t)=+\infty, \quad \lim_{t\to\infty}I(t)=+\infty, \\ &\lim_{t\to\infty}R(t)=+\infty, \quad \lim_{t\to\infty}L(t)=+\infty, \quad \lim_{t\to\infty}P(t)=+\infty, \end{aligned}$$

which is contradictory to $0\leq E(t)\leq\bar{\epsilon}$, $0\leq A(t)\leq\bar{\epsilon}$, $0\leq I(t)\leq\bar{\epsilon}$, $0\leq R(t)\leq\bar{\epsilon}$, $0\leq L(t)\leq\bar{\epsilon}$ and $0\leq P(t)\leq\bar{\epsilon}$. Then, there exists $W^s(E_0)\cap X_0=\emptyset$. Hence, system (2.1) is uniformly persistent when $R_0>1$.

Next, we prove the existence of a positive ω - period solution of system (2.1), that is, f has a fixed point. We consider $(S^*(0),V^*(0),E^*(0),A^*(0),I^*(0),R^*(0),M^*(0),L^*(0),P^*(0))\in X_0$. We can easily obtain that $S^*(0)>0,V^*(0)>0,E^*(0)>0,A^*(0)>0,I^*(0)>0,R^*(0)>0,M^*(0)>0,L^*(0)>0,P^*(0)>0$. First, $S^*(0)>0$ is satisfied. Suppose not, assuming $S^*(0)=0$, the first equation of system (2.1)

is expressed as follows

$$\frac{\mathrm{d}S^*(t)}{\mathrm{d}t} = \Lambda - \beta(t)S^*P - \kappa S^* - dS^* = \Lambda - (\alpha(t)+d)S^*,$$

where $\alpha(t) = \beta(t)P + \kappa$. Hence, we obtain

$$\begin{aligned} S^*(t) &= e^{\int_0^t -(\alpha(\tau)+d)\mathrm{d}\tau}\left[S^*(0) + \int_0^t \Lambda e^{\int_0^{\tilde{\tau}}(\alpha(\tau)+d)\mathrm{d}\tau}\mathrm{d}\tilde{\tau}\right] \\ &= e^{\int_0^t -(\alpha(\tau)+d)\mathrm{d}\tau}\int_0^t \Lambda e^{\int_0^{\tilde{\tau}}(\alpha(\tau)+d)\mathrm{d}\tau}\mathrm{d}\tilde{\tau}, \forall t \geq 0. \end{aligned}$$

Further, the following inequality

$$S^*(n\omega) = e^{\int_0^{n\omega} -(\alpha(\tau)+d)\mathrm{d}\tau}\int_0^{n\omega} \Lambda e^{\int_0^{\tilde{\tau}}(\alpha(\tau)+d)\mathrm{d}\tau}\mathrm{d}\tilde{\tau} > 0$$

can be obtained. From the periodicity of $S^*(t)$. it is easy to see that $S^*(0) = S^*(n\omega) = 0, n = 1, 2, 3...$, which is inconsistent with $S^*(n\omega) > 0$. Therefore, we can obtain $S^*(0) > 0$.

Thus, we obtain that $u(S^*(0), V^*(0), E^*(0), A^*(0), I^*(0), R^*(0), M^*(0), L^*(0), P^*(0)) \in \Re_+^9$ and $(S^*(\omega), V^*(\omega), E^*(\omega), A^*(\omega), I^*(\omega), R^*(\omega), M^*(\omega), L^*(\omega), P^*(\omega))$ is the positive ω-period solution of system (2.1). This completes the proof. □

The values of the parameters are $\Lambda = 100000$, $d = 1/(80*12)$, $\beta(t) = 8.0\times10^{-7}(1 + sin(\frac{\pi}{12}t+4))$, $\rho(t) = 3\times10^{-7}(1++sin(\frac{\pi}{12}t+4))$, $\kappa = 0.002$, $\sigma = 30/6$, $\gamma_a = 30/7$, $\gamma_i = 30/5$, $\lambda = 30/7$, $\mu = 0.002$, $\Pi = 10000$, $\theta = 0.5$, $\delta = 0.80935$, $\xi = 0.8$. The initial value of model (2.1) is $(S(0), V(0), E(0), A(0), I(0), R(0), M(0), L(0), P(0)) = (1000000, 20000, 10000, 4000, 3000, 5000, 1000000, 10000, 10000)$. According to these parameters, we calculate that $R_0 = 8.2813 > 1$. We can give some numerical simulations to illustrate and extend our results in Figure 3.

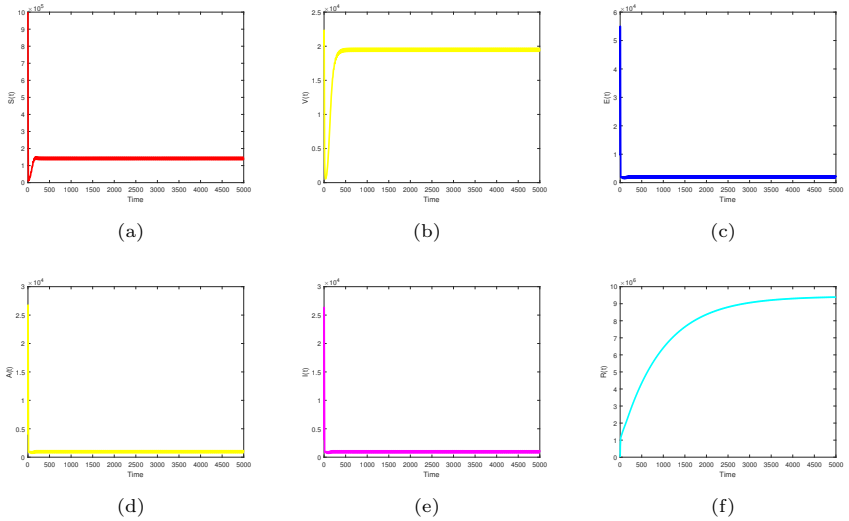


Figure 3. The global stability of the disease-free periodic solution. (a)$S(t)$, (b)$V(t)$, (c)$E(t)$, (d)$A(t)$, (e)$I(t)$, (f)$R(t)$.

From Figure 3, it can be seen that all population in each compartment exhibit periodic fluctuation and tend to non-zero values.

4. A case study

In this section, we will estimate the unknown parameters of model (2.1) on the basis of the dengue fever data in Singapore from January 2014 to June 2017 by using the MCMC algorithm. According to the estimated unknown parameters, the mean and confidence interval of the basic reproduction number R_0 is also calculated.

Since the early dengue vaccine is very flawed and the number of people vaccinated is also very small, we will ignore the number of people vaccinated and will study the significance of vaccination for controlling the disease later. Therefore, model (2.1) is transformed to

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta(t)SP - dS, \\ \dfrac{\mathrm{d}E}{\mathrm{d}t} = \beta(t)SP - \sigma E - dE, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = (1-\theta)\sigma E - \delta A - \gamma_a A - dA, \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = \theta\sigma E + \delta A - \gamma_i I - dI, \\ \dfrac{\mathrm{d}R}{\mathrm{d}t} = \gamma_a A + \gamma_i I - dR, \\ \dfrac{\mathrm{d}M}{\mathrm{d}t} = \Pi - \rho(t)M(A+I) - \mu M, \\ \dfrac{\mathrm{d}L}{\mathrm{d}t} = \rho(t)M(A+I) - \lambda L - \mu L, \\ \dfrac{\mathrm{d}P}{\mathrm{d}t} = \lambda L - \mu P. \end{cases} \tag{4.1}$$

4.1. Parameter estimation and model fitting

According to the periodic characteristics of dengue fever in Singapore, we define the periodic direct transmission rate between susceptible humans and infected mosquitoes as follows

$$\beta(t) = \beta_0 + \beta_1 \sin(\frac{\pi}{12}t + \varphi), \tag{4.2}$$

where $\frac{\pi}{12}$ means that the reporting cases period is π and the time period is 12 months. β_0 and β_1 indicate coefficients of direct transmission rate between susceptible humans and infected mosquitoes, φ indicates the phase of the T-periodic function.

Similarly, periodic indirect transmission rates between infected humans and susceptible mosquitoes are defined as follows

$$\rho(t) = \rho_0 + \rho_1 \sin(\frac{\pi}{12}t + \varphi), \tag{4.3}$$

where $\frac{\pi}{12}$ means that the reporting cases period is π and the time period is 12 months. ρ_0 and ρ_1 indicate coefficients of direct transmission rate between infected humans and susceptible mosquitoes, φ indicates the phase of the T-periodic function.

For the sake of simulating the number of new cases of dengue in Singapore, the rationality of the model is verified by the number of cases actually monitored.

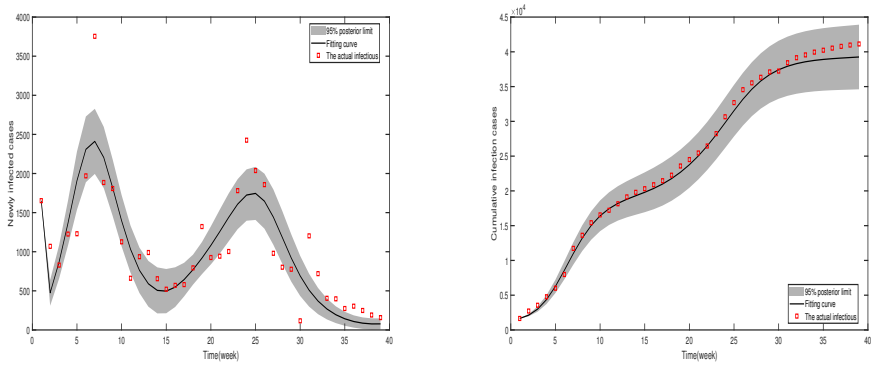
Therefore, we mainly focus on new infections and cumulative infections every month in Singapore. Cumulative infections reported cases can be expressed as follows

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \theta\sigma E + \delta A, \tag{4.4}$$

where $I(t)$ indicates the number of cumulative infections of reported infected humans. As for the newly infected cases, it can be expressed as follows

$$G_I = I(t) - I(t-1), \tag{4.5}$$

where G_I represents the number of new cases of reported infected humans, and t is regarded as month in the simulations. In what follows, we use Eq. (4.5) to fit the number of new cases of reported infected humans in Singapore. The fitting results are shown in Figure4. In Figure4, the solid black line represents the fitted data, and the red boxes represent the actual data. The areas from the darkest to the lightest is the 95% of the model uncertainty.



(a) (b)

Figure 4. The fitting results from January 2014 to April 2017. (a) The number of new cases reported, (b) The number of cumulative reported.

It can be seen from Figure 4 that our fitting is adequate. In addition, we also get that the number of reported dengue cases is much lower than the number of unreported dengue cases.

In order to compute the basic reproduction number R_0 of dengue in Singapore and effectively control the spread of disease, it is necessary to estimate the unknown parameters of model (4.1) since several parameters and initial values are assigned values based on existing data and experience. According to some relevant reports and literatures, we can determine the following initial values and some parameters of model (4.1).

(i) The recruitment rate of susceptible humans (Λ): we obtain that the birth rate in Singapore at the end of 2013 is 9.8 per thousand by the relevant data of the Department of Statistics Singapore [39], and we also get the total population of Singapore at the end of 2013 is 5.4697 million. Therefore, we can get that the monthly birth population of Singapore is about 4467.

(ii) The natural mortality rate of the humans (d): according to the statistics of the Department of Statistics Singapore [39], we conclude that the monthly

natural mortality rate of the population in Singapore in 2013 is approximately $d = 1/(80 \times 12)$, where the constant 80 represents the average life span expectancy of the population of Singapore and the constant 12 represents the month of year.

(iii) The average incubation period in humans (σ): the incubation period of dengue fever is different in different areas, such as, a few from 3 to 14 days, the most common being 3 to 7 days [35]. In this paper, we assume that the mean incubation time is 6 days. Hence, the mean incubation period σ can be determined by 30/6.

(iv) The recovery rate of reported infected individuals (γ_i) and the recovery rate of the unreported infected individuals (γ_a): the recovery rate for dengue is also different, a few from 4 to 15 days [6, 21]. We assume that the average recovery time of reported dengue patients is 5 days , then the recovery rate of monthly is 30/5. The average recovery time of unreported dengue patients is 7 days, then the recovery rate of monthly is 30/7. According to the report of Ministry of Health Singapore [28] and related mosquito control work, we assume that the birth number of mosquitoes is $\Pi = 10000$ and the mortality rate is $\mu = 0.002$.

(v) The average incubation period in mosquitoes (λ): according to reference [35], we assume that the average incubation time is 7 days, then the average incubation period λ can be determined by 30/7.

Other parameters are estimated in Table 2 based on the actual reported dengue data of Singapore [28] by using MCMC.

The unknown parameters and initial values of model (4.1) are estimated by MATLAB software. In this paper, we use an adaptive combination of delayed rejection and adaptive metropolis algorithm to carry out the Markov Chain Monte Carlo procedure [15]. The algorithm runs 10 thousands iteration and uses the Geweke convergence diagnostic method to evaluate the chain convergence [14]. We can estimate the convergence of the Markov chain by its closeness to 1. The mean, standard deviation and 95% confidence interval of the estimated parameters are shown in Table 2.

According to the parameters in Table 2, we can use the theory developed by Wang and Zhao [37] to calculate the basic reproduction number of model (4.1). The basic reproduction number R_0 can be calculated by Lemma 3.1 and R_0 is estimated to be 1.602 (95% CI:(1.248, 1.958)), as shown in Figure 5.

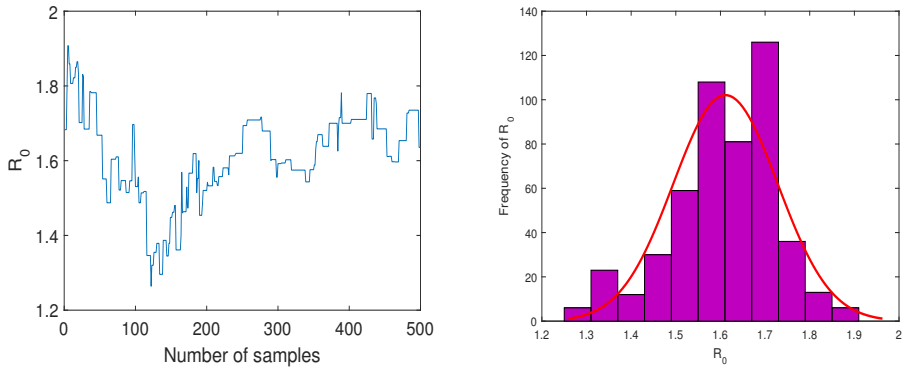
This means that dengue in Singapore is impossible to ignore. It can be seen from Figure 5 (b) that the basic reproduction number R_0 is normally distributed. Therefore, we can easily obtain the confidence interval and mean of R_0.

5. Uncertainty and sensitivity analysis

The sensitivity of numerical simulations to the variation of various parameters in model (4.1) is evaluated using Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficients (PRCC) which are significant for differential equations [24]. LHS is a stratified sampling technique where the variation of each parameter can be effectively analyzed by simultaneous uncertainty ranges. PRCC represents the relationship between parameters and results, explaining the influence of parameters on the output variables. Therefore, the positive (or negative) correlation between the input parameters and the output parameters is represented by the corresponding positive (or negative) PRCC value.

Table 2. The parameters description of the epidemic model.

Parameter	Mean value	Std	95% CI	Source
Λ	4467	–	–	(i)
d	$1/(80 \times 12)$	–	–	(ii)
σ	30/6	–	–	(iii)
γ_i	30/5	–	–	(iv)
γ_a	30/7	–	–	(iv)
Π	10000	–	–	(iv)
μ	0.002	–	–	(iv)
λ	30/7	–	–	(v)
β_0	2.4963×10^{-8}	9.4183×10^{-9}	$[6.5031 \times 10^{-9}, 4.3423 \times 10^{-8}]$	MCMC
β_1	1.5424×10^{-8}	4.4259×10^{-9}	$[6.7492 \times 10^{-9}, 2.4099 \times 10^{-8}]$	MCMC
ρ_0	2.2396×10^{-7}	7.8214×10^{-8}	$[7.0661 \times 10^{-8}, 3.7726 \times 10^{-7}]$	MCMC
ρ_1	5.9320×10^{-7}	5.6658×10^{-8}	$[4.8215 \times 10^{-7}, 7.0425 \times 10^{-7}]$	MCMC
φ	1.346	0.19287	$[0.9680, 1.7240]$	MCMC
θ	0.0063071	0.00055649	$[0.0052, 0.0074]$	MCMC
δ	0.002162	0.0014369	$[0, 0.0050]$	MCMC
$S(0)$	5465700	–	–	[39]
$E(0)$	1.0456×10^4	5.1044×10^3	$[4.5137 \times 10^2, 2.0461 \times 10^4]$	MCMC
$A(0)$	6.5768×10^3	4.1924×10^1	$[6.4946 \times 10^3, 6.6590 \times 10^3]$	MCMC
$I(0)$	1653	–	–	[28]
$R(0)$	3.2046×10^3	1.2984×10^1	$[3.1792 \times 10^3, 3.2300 \times 10^3]$	MCMC
$M(0)$	2.9559×10^7	7.2871×10^6	$[1.5276 \times 10^7, 4.3842 \times 10^8]$	MCMC
$L(0)$	2.0807×10^5	8.8522×10^4	$[3.4567 \times 10^4, 3.8157 \times 10^5]$	MCMC
$P(0)$	1.0745×10^5	6.0450×10^3	$[3.4567 \times 10^4, 1.1930 \times 10^5]$	MCMC



(a) (b)

Figure 5. The basic reproduction number of R_0. (a) The Markov chain of the last 500 samples of R_0. The purple dot represents the size of the R_0 value. (b) The frequency distribution of R_0. The red curve is the probability density function curve of R_0 (For an explanation of the reference to color in this illustration, the reader is referred to the Web version of this article).

5.1. Sensitivity of other parameters to model

The absolute value of PRCC ranges from 0.4 to 1, which indicates that there is a high correlation between input parameters and output variables. The absolute values of PRCC between 0.2 and 0.4 indicate a moderate correlation between input parameters and output variables. The absolute value of PRCC between 0 and 0.2, indicates that there is no significant correlation between input parameters and output variables. According to the above values, we can obtain some results of model (4.1), which is showed in Figure 6. Figure 6 shows 1000 sample fits of model

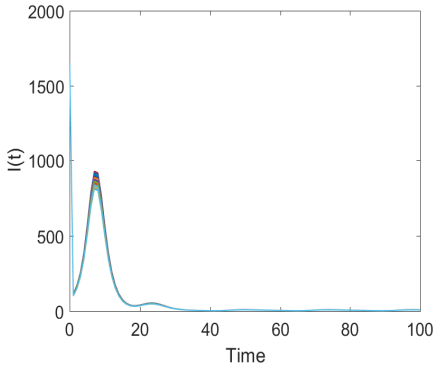


Figure 6. Plot of the output (1000 runs) of model (4.1). The ordinate represents variable I(t), and the abscissa represents time (weeks).

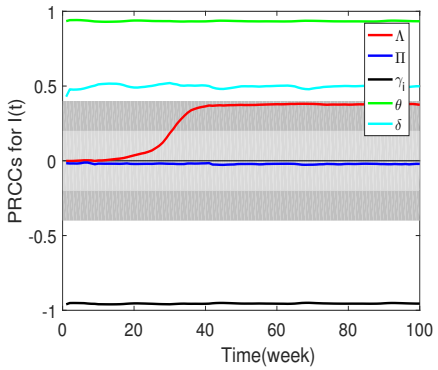


Figure 7. The sensitivity of the parameters changes as the dynamics of model (4.1) progress.

(4.1) on the variables $I(t)$ from January 2014 to June 2017. The 1000 simulations of the output variables $I(t)$ is periodic, which reflects the periodicity of dengue in Singapore.

From Figure 7, it can be seen that the changes of several parameters with time have an impact on the reported new cases. In particular, there is strong negative correlation between the recover rate γ_i and the number of new cases. This means that the public health department should strengthen the treatment work and the patients with dengue should go to the hospital for treatment rather than treatment in family. There is a little negative correlation between the recruitment ratio Π

and the number of new cases. This means that reducing the mosquito birth rate has a role in controlling disease. Then, parameters θ and δ are strongly positively correlated throughout the time period. This indicates that the active case detection and timely reporting case cannot be overlooked.

Further, we can obtain the sensitivity of some parameters to each population, such as the infected individual (seen Figure 8). Figure 8 shows that the infected

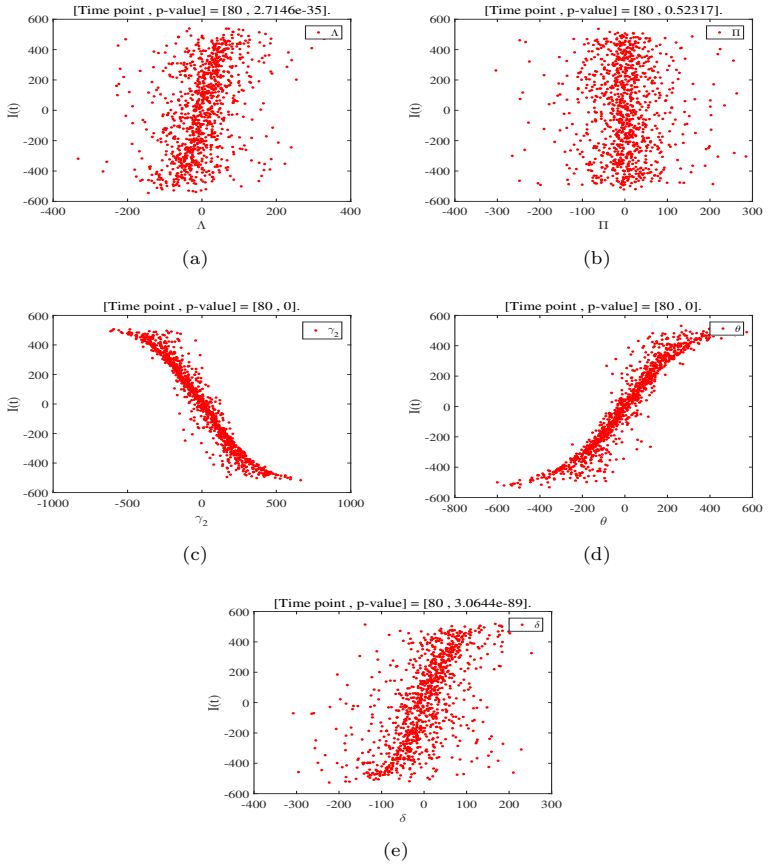
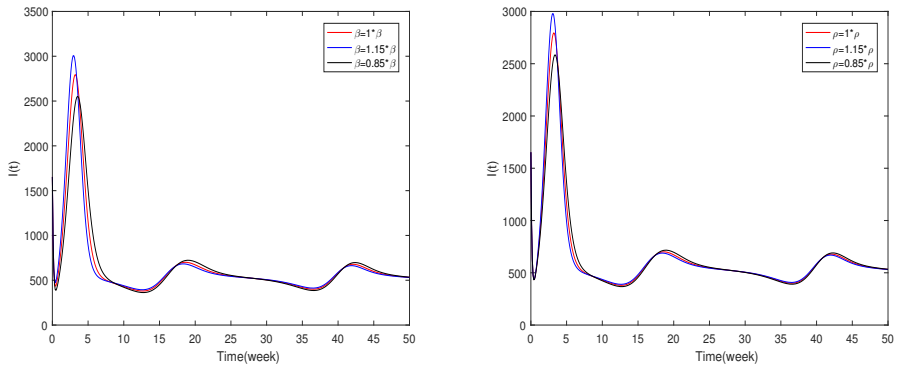


Figure 8. P values of each parameter on the 80th days. (a) Λ, (b) Π, (c) γ_a, (d) θ, (e) δ.

individual ($I(t)$) is sensitive to parameters Λ ($p-value = 2.7146 \times 10^{-35}$), Π($p-value = 0.52317$), γ_a ($p-value = 0$), θ ($p-value = 0$) and δ ($p-value = 3.0644 \times 10^{-89}$), which indicates that they excepted Π have significant effects on model (2.1). Therefore, dengue fever epidemic can be effectively controlled under the appropriate control strategies.

5.2. Sensitivity of the infection rate

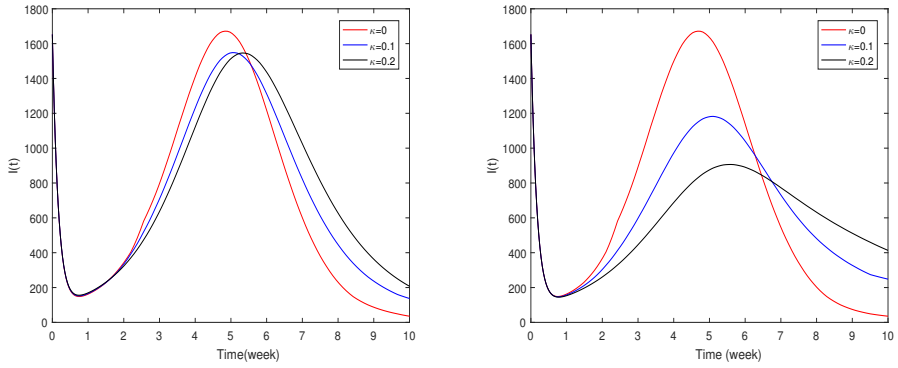
In order to study the effects of human-to-mosquito contact transmission rate and mosquito-to-human contact transmission rate, Figure 9 shows the impact of infection rates $\beta(t)$ and $\rho(t)$ on disease transmission respectively. According to Figure 9(a), the infection rate $\beta(t)$ is increased and then decreased by 0.15 times, respec-



(a) (b)

Figure 9. The impact of infection rates $\beta(t)$ and $\rho(t)$ on disease transmission. (a) $\beta(t)$, (b) $\rho(t)$.

tively, and the transmission trend of the disease is obtained. Figure 9(b) reflects that the infection rate $\rho(t)$ is increased and then decreased by 0.15 times respectively, and the transmission trend of the disease is obtained. According to the Figure 9, changing the mosquito-borne transmission rate can significantly change the intensity of infection. The rate of transmission increases, which makes the peak of infection earlier and larger. Inverse, it delays and decrease the peak of infection.



(a) (b)

Figure 10. The number of the reported infected individuals with different vaccination. (a) 50%, (b) 80%.

5.3. Effects of vaccination on dengue control

In this part, we study the effect of the vaccine on dengue fever. According to model (2.1), we assume that the vaccine is 50 percent effective and 80 percent effective, respectively ($\xi = 0.8/0.5$). Hence, the effect of inoculation ratio of 0.1 and 0.2 on disease control is considered respectively. When the vaccine is 50 percent effective, the post-vaccination results are shown in Figure 10 (a). When the vaccine is 80 percent effective, the results after vaccination are shown in Figure 10 (b).

According to Figure 10 (a), when the vaccine is 50 percent effective, with the vaccination rate increasing, the peak of disease development can be reduced to a certain extent. However, when the vaccination ratio is 10% and 20%, respectively, the vaccine has little effect on the peak, but only plays a certain role of delay, which is conducive to the preparation of epidemic prevention and control. According to Figure 10 (b), we can easily obtain that when the vaccine is 80 percent effective, with the inoculation rate increasing, the peak of disease is significantly delayed and the peak of disease is significantly reduced, and the number of infected people decreases significantly. Therefore, the government should increase investment in the research and development of the dengue vaccine to improve the effectiveness of the vaccine and increase the proportion of vaccinated people, so that the disease can be effectively controlled.

6. Discussions and conclusions

When we investigate the infectious diseases, some characteristics of such diseases should be considered into the corresponding model. Cheng et al. [7] created different scenarios to investigate the dengue outbreak in Guangzhou, focusing on the timing of imported cases, climate, vertical transmission among mosquitoes, and the impact of intervention measures on the model. The results indicated that the early appearance of imported cases was the most important factor in the characteristics of the 2014 outbreak. Precipitation and temperature also altered the transmission dynamics, indicating that dengue transmission has a seasonal pattern. Wang et al. [38] collected weekly dengue incidence data, daily mean temperature, and rainfall from 30 locations in Singapore, Sri Lanka, and Malaysia between 2012 and 2020. They estimated the peak transmission potential and epidemic duration of dengue fever in the future. Their study showed that the variation in dengue transmission potential and epidemic duration differs by location, with varying transmission rates under different temperatures. Therefore, it is important to consider the seasonal characteristics of dengue fever and construct a cyclical mathematical model for dengue fever. Therefore, our model takes into account the periodic transmission. In our paper, in order to study the dynamic relationship among periodic transmission, vaccinated cases in dengue fever, we propose a novel non-autonomous differential equation model (2.1) with periodic factors and vaccinated cases.

The basic reproduction number is obtained. We estimate that the basic reproduction number R_0 is 1.602 (95% CI: (1.248, 1.958)). The global asymptotic stability of the disease-free periodic solution is proved. The existence of the disease periodic solution and the uniform persistence of model (2.1) are also given. The unknown parameters and initial values of model (4.1) are estimated by using the MCMC algorithm based on the basis of the dengue data in Singapore from 2014 to 2017. The uncertainty and sensitivity of all parameters are evaluated by using the Latin Hypercube Sampling and the Partial Rank Correlation Coefficient. The sensitivity of the parameters suggests that the transmission rate is a possible intervention to reduce dengue infection. Our results show that improving vaccine effectiveness and vaccination coverage are beneficial to the control of the dengue fever. This is consistent with the results in Shim [34] and Pratchaya et al. [31]. Musa et al. [29] also focused on Taiwan and analyzed the impact of different vaccination coverage rates on dengue transmission. Our model results align with the findings [29], showing that high coverage vaccination can effectively control dengue

outbreaks.

In addition, time delay has a significant effect on the dengue fever, and the disease can be effectively prevented by controlling the mosquito population. Therefore, it is possible to consider the dynamics of a dengue fever model with impulsive effects and delay, and propose a better control strategy. This will be investigated in the future.

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Conflict of interest

The authors declare there is no conflict of interest.

References

[1] M. Andraud, N. Hens and P. Beutels, *A simple periodic-forced model for dengue fitted to incidence data in Singapore*, Math. Biosci., 2013, 244(1), 22–28.

[2] G. Aronsson and R. B. Kellogg, *On a differential equation arising from compartmental analysis*, Math. Biosci., 1978, 38(1–2), 113–122.

[3] L. M. Cai, S. M. Guo, X. Li, et al., *Global dynamics of a dengue epidemic mathematical model*, Chaos Soliton. Fract., 2009, 42(4), 2297–2304.

[4] K. K. Chang, Q. M. Zhang and H. M. Yuan, *Stationary distribution and control strategy of a stochastic dengue model with spatial diffusion*, J. Appl. Anal. Comput., 2022, 12(1), 153–178.

[5] K. K. Chang, Z. Y. Zhang and G. Z. Liang, *Dynamics analysis of a nonlocal diffusion dengue model*, Sci. Rep., 2023, 13(1), 15239.

[6] S. Chen and M. H. Hsieh, *Modeling the transmission dynamics of dengue fever: Implications of temperature effects*, Sci. Total. Environ., 2012, 431, 385–391.

[7] Q. Cheng, Q. L. Jing, R. C. Spear, et al., *Climate and the timing of imported cases as determinants of the dengue outbreak in Guangzhou, 2014: Evidence from a mathematical model*, PLoS Neglect Trop. D., 2016, 10(2), e0004417.

[8] F. Coutinhoa, M. Burattinia, L. Lopeza, et al., *Threshold conditions for a non-autonomous epidemic system describing the population dynamics of dengue*, Bull. Math. Biol., 2006, 68(8), 2263–2282.

[9] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, *On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations*, J. Math. Biol., 1990, 28(4), 365–382.

[10] P. Van den Dreessche and J. Watmough, *Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission*, Math. Biosci., 2002, 180(1–2), 29–48.

[11] L. Esteva and C. Vargas, *Coexistence of different serotypes of dengue virus*, J. Math. Biol., 2003, 46(1), 31.

[12] D. Fischer and S. Halstead, *Observations related to pathogenesis of dengue hemorrhagic fever V. examination of agspecific sequential infection rates using a mathematical model*, Yale. J. Biol. Med., 1970, 42(5), 329–349.

[13] S. M. Garba, A. B. Gumel and M. Bakar, *Backward bifurcation in dengue transmission dynamics*, Math. Biosci., 2008, 215(1), 11–25.

[14] H. Haario, M. Laine, A. Mira, et al., *Dram: Efficient adaptive MCMC*, Stat. Comput., 2006, 16(4), 339–354.

[15] H. Haario and S. J. Tamminen, *An adaptive metropolis algorithm*, Bernoulli., 2001, 7(2), 223–242.

[16] M. G. Huang, L. C. Hu and B. Zheng, *Comparing the efficiency of Wolbachia driven Aedes mosquito suppression strategies*, J. Appl. Anal. Compt., 2019, 9(1), 211–230.

[17] H. F. Huo, K. D. Cao and H. Xiang, *Modelling the effects of the vaccination on seasonal influenza in Gansu, China*, J. Appl. Anal. Comput., 2022, 12(1), 407–435.

[18] H. Jagbir, J. S. Malik, S. K. Shashikantha, et al., *Dengue vaccine: A valuable asset for the future*, Human Vaccines, 2014, 10(8), 2245–2246.

[19] C. Y. Kuo, W. W. Yang and E. C.-Y. Su, *Improving dengue fever predictions in Taiwan based on feature selection and random forests*, BMC Infect. Dis., 2024, 24(Suppl 2), 334.

[20] J. Kyle and E. Harris, *Global spread and persistence of dengue*, Ann. Rev. Microbiol., 2008, 62(1), 71–92.

[21] M. Li, G. Sun, Y. Laith, et al., *The driving force for 2014 dengue outbreak in Guangdong, China*, Plos One, 2016, 11(11), e0166211.

[22] S. H. Ma, T. Tian and H. F. Huo, *Global stability and optimal control of an age-structured $SVEIR$ epidemic model with waning immunity and relapses*, J. Math. Biol., 2024, 89(3), 1–38.

[23] P. Magal and G. Webb, *The parameter identification problem for SIR epidemic models: Identifying unreported cases*, J. Math. Biol., 2018, 77(10), 1–20.

[24] S. Marino, I. B. Hogue and C. J. Ray, *A methodology for performing global uncertainty and sensitivity analysis in systems biology*, J. Theor. Biol., 2008, 254(1), 178–196.

[25] A. Li-Martín, R. Reyes-Carreto and C. Vargas-De-León, *Dynamics of a dengue disease transmission model with two-stage structure in the human population*, Math. Biosci. Eng., 2023, 20(1), 955–974.

[26] X. Y. Meng and L. Xiao, *Hopf bifurcation and Turing instability of a delayed diffusive zooplankton-phytoplankton model with hunting cooperation*, Int. J. Bifurcat. Chaos, 2024, 34(7), 106–123.

[27] X. Y. Meng and C. Y. Yin, *Dynamics of a dengue fever model with unreported cases and asymptomatic infected classes in Singapore, 2020*, J. Appl. Anal. Comput., 2023, 13(2), 782–808.

[28] *Ministry of Health Singapore*, http://www.moh.gov.sg., April, 2024.

[29] S. S. Musa, S. Zhao, H. Chan, et al., *A mathematical model to study the 2014-2015 large-scale dengue epidemics in Kaohsiung and Tainan cities in Taiwan, China*, Math. Biosci. Eng., 2019, 16(5), 3841–3863.

[30] J. G. Rigau-Perez, G. G. Clark, D. J. Gubler, et al., *Dengue and dengue haemorrhagic fever*, Lancet, 1998, 352(9132), 971–977.

[31] C. Pratchaya, T. I. Ming and P. Puntani, *SIR model for dengue disease with effect of dengue vaccination*, Comput. Math. Meth. Med., 2018, 2018, 1–14.

[32] M. S. Rahman, F. Mehejabin, M. Arafat. Rahman, et al., *A case-control study to determine the risk factors of dengue fever in Chattogram, Bangladesh*, Pub. Heal. Prac., 2022, 4, 100288.

[33] S. Shah, R. Tyagi and P. Shah, *Case study review on dengue fever: An emerging public health issue*, Int. J. Per. Pub. Heal., 2018, 2(1), 1–7.

[34] E. Shim, *Dengue dynamics and vaccine cost-effectiveness analysis in the Philippines*, Am. J. Trop. Med. Hyg., 2016, 1137–1147.

[35] J. F. Siler, M. W. Hall and A. P. Hitchens, *Dengue: Its history, epidemiology, mechanism of transmission, etiology, clinical manifestations, immunity, and prevention*, Philipp. J. Sci., 1926, 29, 1–302.

[36] D. C. Speirs, H. L. Smith and P. Waltman, *The theory of the chemostat: Dynamics of microbial competition*, J. Appl. Ecol., 1996, 33(3), 651.

[37] W. D. Wang and X. Q. Zhao, *Threshold dynamics for compartmental epidemic models in periodic environments*, J. Dyn. Differ. Equ., 2008, 20(3), 699–717.

[38] Y. W. Wang, C. L. Li, S. Zhao, et al., *Projection of dengue fever transmissibility under climate change in South and Southeast Asian countries*, PLoS Neglect Trop. D., 2024, 18(4), e0012158.

[39] *Weekly Infectious Diseases Bulletin*, http://www.moh.gov.sg., April, 2024.

[40] P. Wu, J. Lay, H. Guo, et al., *Higher temperature and urbanization affect the spatial patterns of dengue fever transmission in subtropical Taiwan*, Sci. Total Environ., 2009, 407(7), 2224–2233.

[41] L. Xue, X. Ren, F. Magpantay, et al., *Optimal control of mitigation strategies for dengue virus transmission*, Bull. Math. Biol., 2021, 83(2), s11538.

[42] Y. J. Zha and W. H. Jiang, *Global dynamics and asymptotic profiles for a degenerate dengue fever model in heterogeneous environment*, J. Differ. Equations, 2023, 348, 278–319.

[43] F. Zhang and X. Q. Zhao, *A periodic epidemic model in a patchy environment*, J. Math. Anal. Appl., 2007, 325(1), 496–516.

[44] X. H. Zhang, X. N. Liu, Y. Z. Li, et al., *Modelling the effects of Wolbachia-carrying male augmentation and mating competition on the control of dengue fever*, J. Dyn. Differ. Equ., 2023, 1–41.

[45] X. Q. Zhao, *Dynamical Systems in Population Biology*, Springer, Switzerland, 2017.

[46] B. Zheng, W. Guo, L. Hu, et al., *Complex Wolbachia infection dynamics in mosquitoes with imperfect maternal transmission*, Math. Biosci. Eng., 2018, 15(2), 523–541.

[47] Z. C. Zhu, X. M. Feng and L. C. Hu, *Global dynamics of a mosquito population suppression model under a periodic release strategy*, J. Appl. Anal. Comput., 2023, 13(4), 2297–2314.