

MODELING THE EFFECTS OF EXTERNAL PROTECTION MEASURES AND OPTIMAL CONTROL ON SEASONAL LASSA FEVER OUTBREAKS IN NIGERIA*

Teng-Fei Jin¹, Hai-Feng Huo^{2,3,†}, Shuanglin Jing^{2,3} and Hong Xiang¹

Abstract Lassa fever, also referred to as Lassa hemorrhagic fever, is an endemic viral disease that frequently triggers epidemics in West Africa. This study presents a disease transmission dynamics model of Lassa fever that integrates external protective measures, the dynamics of rodent reproductive cycles, and the periodic nature of transmission from rodents to humans, aiming to provide a comprehensive understanding of the disease. The basic reproduction number \mathcal{R}_0 can be deduced and as a threshold parameter for global dynamics. The disease-free periodic solution is globally asymptotically stable when $\mathcal{R}_0 < 1$, and the disease persists when $\mathcal{R}_0 > 1$. Based on the data provided by the Nigerian Center for Disease Control and Prevention, the Markov Chain Monte Carlo algorithm is used to simulate the model to find the baseline values of the unknown parameters and the exact value of \mathcal{R}_0 is calculated as 1.6237. Next, the optimal control problem associated with the model is solved through the application of the Pontryagin maximum principle, implementing optimal control strategies for mitigating the transmission of Lassa fever virus. Finally, sensitivity analyses is conducted to determine the key parameters affecting the number of the infectious individuals. The findings suggest that enhancing the rate of external protection and optimizing protective efficiency have a substantial impact on the incidence of Lassa fever infections, serving as effective measures for disease control. However, these measures alone cannot completely eliminate disease transmission. If both measures to reduce rodent transmission and increase mortality rates are implemented, it will be possible to control the epidemic.

Keywords Lassa fever, external protection, mathematical model, parameter estimation, optimal control.

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[†]The corresponding author.

¹Department of Applied Mathematics, Lanzhou University of Technology, Lanzhou, Gansu 730050, China

²School of Mathematics and Physics, Lanzhou Jiaotong University, Lanzhou, Gansu 730070, China

³Gansu Center for Fundamental Research in Complex Systems Analysis and Control, Lanzhou Jiaotong University, Lanzhou, Gansu 730070, China

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Email: 1935260203@qq.com(T.-F. Jin), hfhuo@lut.edu.cn(H.-F. Huo), shuanglinjing@lztu.edu.cn(S. Jing), xiangh1969@163.com(H. Xiang)

1. Introduction

Lassa fever is an acute viral hemorrhagic disease caused by the Lassa virus [2]. The disease has its origins in the 1950s but was officially identified and named after the town Lassa of Nigeria's Benue State in 1969 [13]. The transmission of Lassa fever to humans primarily occurs through direct contact with infected multimammate rodents or through food and household items that are contaminated by the urine or feces of infected rodents [32, 35, 40]. The virus is transmitted to humans through cuts and scratches, or via inhalation of airborne dust particles. Human-to-human transmission can occur through direct contact with the blood or body fluids of an infected individual [3]. According to the World Health Organization, transmission from infected rodents to humans occurs mainly during the dry season (December–April), with annual peaks in human cases usually observed after the mouse breeding cycle during the rainy season (May–November) [4, 42]. Lassa fever is endemic in Benin, Guinea, Ghana, Liberia, Mali, Sierra Leone and Nigeria, with an annual incidence of infection ranging from 100,000 to 300,000 cases and approximately 5,000 fatalities reported [29]. These countries collectively bear a significant burden of Lassa fever. The Lassa virus primarily poses a significant threat to individuals living in regions with inadequate sanitation and densely populated conditions.

Approximately 80% of individuals infected with the Lassa virus remain asymptomatic [2, 21]. One out of every five infections progresses to severe disease, characterized by multi-organ infection, including the liver, spleen, and kidneys [25]. The primary clinical manifestations encompass pyrexia, rigors, pharyngitis, productive cough, emesis, diarrheal episodes, myalgia and thoracoabdominal discomfort [2]. Especially in late pregnancy, the symptoms are severe, with an alarming rate of over 80% maternal mortality or miscarriage in affected cases [39]. Early supportive care, including fluid replacement and symptomatic treatment, is crucial for improving survival rates. The antiviral ribavirin has been utilized in the treatment of Lassa fever [3, 18]; however, its efficacy remains unproven.

Lassa fever is included in the World Health Organization Blueprint for Epidemiological Research and Development, which means that Lassa fever is recognized as an important disease area [20]. However, the number of studies on mathematical modeling of Lassa fever remains relatively small compared to other infectious diseases. Onah et al. [36] extended the SIR-SI compartment model by incorporating various control interventions and employed optimal control theory to identify cost-effective strategies for reducing disease transmission. Mariéen et al. [28] combined empirical field data and mathematical models to evaluate the impact of rodent control measures on the prevalence of Lassa fever. Musa et al. [33] established a model to describe the interaction between humans and rodents, incorporating quarantine, isolation, and hospitalization measures, and conducted a comprehensive study on the Lassa fever outbreak in Nigeria from 2016 to 2019. Akhmetzhanov et al. [7] investigated the seasonal drivers of Lassa fever epidemics in Nigeria by employing a mathematical model to analyze datasets on human infections, rodent population dynamics, and climate change. The study revealed that rainfall exerted an indirect influence on Lassa fever transmission, while the periodicity of Lassa fever was significantly influenced by seasonal rodent migration. Davies et al. [14] employed mathematical models that captured seasonal transmission of rodents to humans in order to evaluate the potential outcomes of implementing vaccination programs in affected regions. Ibrahim et al. [23] developed a model to differentiate individuals

based on disease severity, incorporating the birth rate and environmental carrying capacity of rodents as temporal parameters. The basic reproduction number was also introduced and proved to be an important factor in determining whether Lassa fever can be transmitted among people. McKendrick et al. [30] introduced an approximate Bayesian computational scheme to fit the model to the 2018-2020 case data provided by the NCDC and analyzed the impact of changes in rodent birth rates on the number of infected cases.

Previous studies have modeled the seasonality of cases in Nigeria, but have not captured the seasonal variations in zoonotic host reproduction and their impact on the number of new cases. In light of the aforementioned considerations, this paper establishes and investigates the dynamics of a non-autonomous model of Lassa transmission. The model incorporates external protective measures taken by susceptible individuals and accounts for the impact of human-to-human, mouse-to-mouse, mouse-to-human, and human-to-mouse transmissions [12]. We introduce periodic birth rates of rodents and periodic transmission rates from rodents to humans into the model. Then, optimal control analysis is carried out to obtain the best strategy. The Markov chain Monte Carlo (MCMC) method is employed for parameter estimation, while the analysis of sensitivity is conducted to assess the influence of different parameters on the number of new infections.

We refer to any external measures taken for personal protection against viral exposure as external protective measures. The external protection can be effectively ensured by utilizing personal protective equipment (PPE) and condoms, among other measures [9, 36]. However, improper use of protective equipment does not guarantee prevention of Lassa fever infection. Since Lassa fever incidence shows a strong seasonal behavior: the number of human Lassa cases peaks during the dry season through both direct and indirect contact between rodents and humans [7, 34]. At this time of year, rats move closer to humans in search of food, increasing rodents' contact with humans. The rat population itself is also heavily affected by the annual weather changes. Thus, we introduce periodic parameters to represent the birth and transmission rates, where $\Pi(t)$ is the time-dependent per capita birth rate of Knott's suckling mice, and $\beta_{ph}(t)$ represents the periodic transmission rate of rodents to humans.

The structure of this paper is as follows: In Section 2, we present a non-autonomous mathematical model of Lassa virus transmission dynamics. In Section 3, we calculate basic reproduction number of the model. In Section 4, we analyze the dynamic behavior of the model. In Section 5, we analyze and discuss the optimal control strategy. In Section 6, we use the MCMC algorithm to fit the real Nigerian data to the model and perform sensitivity analysis for some parameters. In Section 7, we summarize and discuss this paper.

2. Seasonal models of Lassa fever transmission

We divide the human population into six compartments: susceptible individuals $S_h(t)$, susceptible individuals using external protection $G(t)$, exposed individuals $E(t)$, mildly infected individuals $I_a(t)$, severely infected individuals $I_m(t)$, and recovered individuals $R(t)$. We divide the rodent population into two compartments: susceptible $S_p(t)$ and infectious $I_p(t)$. Thus, the total human and rodent popula-

tions at any moment t are denoted respectively as

$$\begin{aligned} N_h(t) &= S_h(t) + G(t) + E(t) + I_a(t) + I_m(t) + R(t), \\ N_p(t) &= S_p(t) + I_p(t). \end{aligned}$$

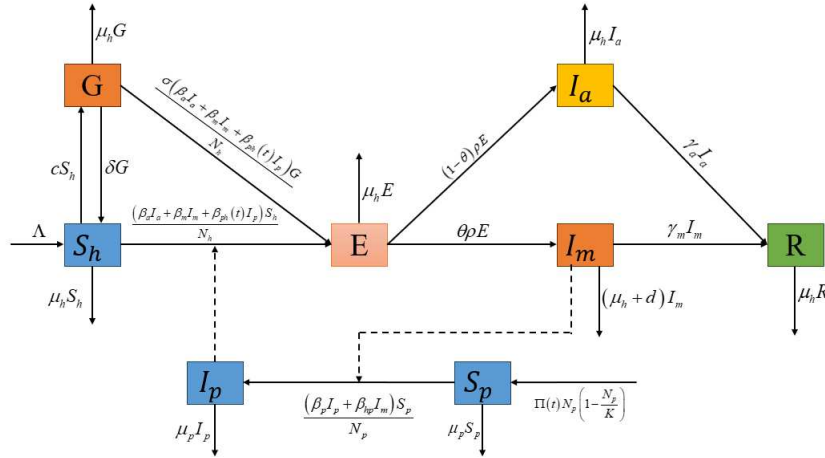


Figure 1. Flow chart of Lassa fever transmission between rodents and humans, where dashed arrows indicate the direction of transmission between humans and rodents.

The flow between the compartments is shown in Figure 1, and the model is established based on the flow chart of the compartments.

$$\begin{cases} \dot{S}_p(t) = \Pi(t)N_p(1 - \frac{N_p}{K}) - \frac{(\beta_p I_p + \beta_{hp} I_m)S_p}{N_p} - \mu_p S_p, \\ \dot{I}_p(t) = \frac{(\beta_p I_p + \beta_{hp} I_m)S_p}{N_p} - \mu_p I_p, \\ \dot{S}_h(t) = \Lambda - \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)S_h}{N_h} - \mu_h S_h - cS_h + \delta G, \\ \dot{G}(t) = cS_h - \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)G}{N_h} - \mu_h G - \delta G, \\ \dot{E}(t) = \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)S_h}{N_h} + \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)G}{N_h} \\ \quad - \rho E - \mu_h E, \\ \dot{I}_a(t) = (1 - \theta)\rho E - \gamma_a I_a - \mu_h I_a, \\ \dot{I}_m(t) = \theta\rho E - \gamma_m I_m - (\mu_h + d)I_m, \\ \dot{R}(t) = \gamma_a I_a + \gamma_m I_m - \mu_h R. \end{cases} \quad (2.1)$$

An individual may transmit from susceptible (S_h) to exposed (E) upon contracting the disease. It is also possible for an individual to go from susceptible (G) with external protection to exposed (E). Exposed individuals have not yet developed symptoms. After the incubation period, exposed individuals are transferred to the severe infection category (I_m) or mild infection category (I_a), depending on whether

or not the person is showing symptoms. After the infection period, individuals who recover move to the recovered category R . The detailed meaning of the parameters is shown in Table 1.

Table 1. Parameter description in the model.

Parameters	Description
σ	Measuring the efficiency of condoms and personal protective equipment
δ	Probability of failure to use external protection
K	Rodent maximum environmental capacity
Λ	Human recruitment rate
μ_h	Human natural mortality rate
μ_p	Rodent natural mortality rate
β_p	Rodent-to-rodent transmission rate
β_a, β_m	Human-to-human transmission rate
β_{hp}	Human-to-rodent transmission rates
θ	Proportion of severe infections
c	The probability of external protection in susceptible individuals
ρ	Human incubation rate
γ_a, γ_m	Infection recovery rate
d	Disease-induced death rates for humans

In our model, while the use of external protection may reduce infections by protecting susceptible individuals, it may not be fully effective. Using σ to measure the efficiency of condoms and PPE as a multiplier for infection rates, where $\sigma = 0$ means that condoms and PPE are fully effective, while $\sigma = 1$ means that condoms and PPE have no effect at all [27, 46]. In our model, we assume that $\Pi(t)$ and $\beta_{ph}(t)$ are continuous, positive T -periodic functions [10, 11]. We denote the human birth rate and death rate by Λ and μ_h , respectively. There is also an additional mortality due to the disease, which is denoted by d in the compartment I_m .

3. Basic properties of the model

To determine the disease-free periodic solution of system (2.1), consider

$$\frac{dS_p}{dt} = \Pi(t)S_p \left(1 - \frac{S_p}{K}\right) - \mu_p S_p, \quad (3.1)$$

equation (3.1) has a unique positive T -periodic solution

$$S_p^0(t) = \frac{e^{\int_0^t (\Pi(s) - \mu_p) ds}}{\int_0^t \frac{\Pi(\tau)}{K} e^{\int_0^\tau (\Pi(s) - \mu_p) ds} d\tau + \frac{\int_0^T \frac{\Pi(\tau)}{K} e^{\int_0^\tau (\Pi(s) - \mu_p) ds} d\tau}{e^{\int_0^T (\Pi(s) - \mu_p) ds} - 1}} > 0. \quad (3.2)$$

Thus, system (2.1) has a unique disease-free periodic solution $P_0 = (S_p^0(t), 0, S_h^0, G^0, 0, 0, 0, 0)$, where $S_h^0 = \frac{\Lambda(\mu_h + \delta)}{\mu_h(\mu_h + c + \delta)}$ and $G^0 = \frac{c\Lambda}{\mu_h(\mu_h + c + \delta)}$.

3.1. Positively invariant set

Lemma 3.1. (Lemma 3.1, [24]) *Define*

$$\Omega = \left\{ \Delta_1 \times \Delta_2 | N_p \leq N_p^0, N_h \leq \frac{\Lambda}{\mu_h} \right\},$$

where $\Delta_1 = \{(S_p, I_p) \in \mathbb{R}_+^2, N_p \leq N_p^0\}$, $\Delta_2 = \{(S_h, E, G, I_a, I_m, R) \in \mathbb{R}_+^6, N_h \leq \frac{\Lambda}{\mu_h}\}$, $N_p^0 = \limsup_{t \rightarrow \infty} \frac{K(\Pi(t) - \mu_p)}{\Pi(t)} > 0$. Then the solution of system (2.1) is uniformly bounded and non-negative, and the set Ω is a positively invariant set.

Proof. At any time, the total populations of humans and rodents are given by

$$\begin{aligned} N_p &= S_p + I_p, \\ N_h &= S_h + G + E + I_a + I_m + R. \end{aligned} \quad (3.3)$$

By summing the last six equations of system (2.1), since $d > 0$ and $I_m \geq 0$ for all $t \geq 0$, we obtain

$$\frac{dN_h}{dt} = \Lambda - \mu_h N_h - dI_m \leq \Lambda - \mu_h N_h. \quad (3.4)$$

Based on the integral performed on the (3.4), we can get the following inequality:

$$N_h(t) \leq \frac{\Lambda}{\mu_h} + \left(N_h(0) - \frac{\Lambda}{\mu_h} \right) e^{-\mu_h t} \leq \frac{\Lambda}{\mu_h} + N_h(0) e^{-\mu_h t},$$

where $N_h(0)$ represents the initial value of the total number of people, which indicates $0 \leq \limsup_{t \rightarrow \infty} N_h(t) \leq \frac{\Lambda}{\mu_h}$.

From system (2.1), we have

$$\begin{aligned} \frac{dN_p(t)}{dt} &= \Pi(t)N_p(t) \left(1 - \frac{N_p(t)}{K} \right) - \mu_p N_p(t) \\ &\leq \left(\Pi(t) - \mu_p - \frac{\Pi(t)}{K} N_p(t) \right) N_p(t) \\ &\leq 0, \text{ if } N_p(t) \geq N_p^0, \end{aligned}$$

which implies that Δ_1 is positively invariant. Assume that the rodent birth rate is greater than the death rate, therefore, we get $\lim_{t \rightarrow \infty} (N_p(t) - N_p^0) = 0$. Thus, from the above proof, we can conclude

$$\begin{aligned} \Delta_1 &= \{(S_p, I_p) \in \mathbb{R}_+^2, N_p \leq N_p^0\}, \\ \Delta_2 &= \left\{ (S_h, E, G, I_a, I_m, R) \in \mathbb{R}_+^6, N_h \leq \frac{\Lambda}{\mu_h} \right\}, \\ \Omega &= \left\{ \Delta_1 \times \Delta_2 | N_p \leq N_p^0, N_h \leq \frac{\Lambda}{\mu_h} \right\}, \end{aligned}$$

and the set Ω is a positively invariant set. □

3.2. The basic reproduction number for the periodic system

To gain further insight into the disease transmission dynamics, we analyze the basic reproduction number \mathcal{R}_0 , which is an important threshold to determine whether an infectious disease will spread. Moreover, based on the work of Wang and Zhao [44], we introduce the theory of periodic systems and define $x = (I_p, E, I_a, I_m, R, S_p, S_h, G)$, thus the system (2.1) can be represented in the following form:

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

where

$$\mathcal{F}(t, x) = \begin{pmatrix} \frac{(\beta_p I_p + \beta_{hp} I_m) S_p}{N_p} \\ \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)(\sigma G + S_h)}{N_h} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

and

$$\mathcal{V}(t, x) = \begin{pmatrix} \mu_p I_p \\ \rho E + \mu_h E \\ -(1 - \theta)\rho E + \gamma_a I_a + \mu_h I_a \\ -\theta\rho E + \gamma_m I_m + (\mu_h + d)I_m \\ -\gamma_a I_a - \gamma_m I_m + \mu_h R \\ -\Pi(t)N_p(1 - \frac{N_p}{K}) + \frac{(\beta_p I_p + \beta_{hp} I_m) S_p}{N_p} + \mu_p S_p \\ -\Lambda + \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) S_h}{N_h} + \mu_h S_h + cS_h - \delta G \\ -cS_h + \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) G}{N_h} + \mu_h G + \delta G \end{pmatrix}.$$

We now consider whether the model satisfies conditions (A1)-(A7) of the theory proposed by Wang and Zhao [44] for finding the fundamental reproduction number of periodic systems. It is clear that conditions (A1)-(A5) are satisfied. Next, let

$$f(t, x(t)) = \mathcal{F}(t, x) - \mathcal{V}(t, x),$$

and define

$$M(t) := \left(\frac{\partial f_i(t, x^0(t))}{\partial x_j} \right), \quad (5 \leq i, j \leq 8).$$

For matrix chunking, $x^0(t) = (0, 0, 0, 0, 0, S_p^0(t), S_h^0, G^0)$ is obtained by transforming the disease-free equilibrium P_0 . Let $\Phi_M(t)$ represent the solution matrix for the linear T -periodic system $\frac{dz}{dt} = M(t)z$. Therefore, we can obtain

$$\rho(\Phi_M(T)) = \max \left\{ e^{-\mu_h t}, e^{-\mu_p t}, e^{-(\mu_h + c + \delta)t}, e^{-\mu_h t} \right\} < 1.$$

This suggests that $\rho(\Phi_M(t))$ the spectral radius of $\Phi_M(t)$ less than 1. Clearly, condition (A6) in the theory of Wang and Zhao [44] is satisfied.

To verify that condition (A7) in the theoretical framework proposed by Wang and Zhao [44] is satisfied, the system (2.1) is linearized at the disease-free equilibrium P_0 , yielding the following linear periodic subsystem of infectious diseases.

$$\begin{cases} \dot{I}_p(t) = \frac{(\beta_p I_p + \beta_{hp} I_m) S_p}{N_p} - \mu_p I_p, \\ \dot{E}(t) = \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)(\sigma G + S_h)}{N_h} - \rho E - \mu_h E, \\ \dot{I}_a(t) = (1 - \theta)\rho E - \gamma_a I_a - \mu_h I_a, \\ \dot{I}_m(t) = \theta\rho E - \gamma_m I_m - (\mu_h + d)I_m. \end{cases} \quad (3.5)$$

After performing a simple calculation, we obtain

$$F(t) = \begin{pmatrix} \beta_p & 0 & 0 & \beta_{hp} \\ \frac{\beta_{ph}(t)S_h^0 + \sigma\beta_{ph}(t)G^0}{S_h^0 + G^0} & 0 & \frac{\beta_a S_h^0 + \sigma\beta_a G^0}{S_h^0 + G^0} & \frac{\beta_m S_h^0 + \sigma\beta_m G^0}{S_h^0 + G^0} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V(t) = \begin{pmatrix} \mu_p & 0 & 0 & 0 \\ 0 & \rho + \mu_h & 0 & 0 \\ 0 & -(1 - \theta)\rho & \gamma_a + \mu_h & 0 \\ 0 & -\theta\rho & 0 & \gamma_m + \mu_h + d \end{pmatrix},$$

clearly, it follows that $F(t)$ is nonnegative, and that the off-diagonal elements of $-V(t)$ are nonnegative, meaning that the system is cooperative. Thus, $F(t) - V(t)$ is irreducible.

Let $Z(t, s)$ be the evolution operator of a T -periodic system

$$\frac{dy}{dt} = -V(t)y. \quad (3.6)$$

That is, for any $s \in R$, the 4×4 matrix $Z(t, s)$ satisfies

$$\frac{dZ(t, s)}{dt} = -V(t)Z(t, s), \forall t \geq s, Z(s, s) = I, \quad (3.7)$$

where I is the 4×4 identity matrix. Let $\Phi_{-V}(t)$ and $\rho(\Phi_{-V}(T))$ denote the monodromy matrix of the linear T -periodic system (3.6) and the spectral radius of $\Phi_{-V}(t)$, respectively. Hence, we obtain

$$\rho(\Phi_{-V}(T)) = \max \{ e^{-\mu_p t}, e^{-(\rho + \mu_h)t}, e^{-(\gamma_a + \mu_h)t}, e^{-(\gamma_m + \mu_h + d)t} \} < 1.$$

Therefore, the theoretical condition (A7) is satisfied.

According to the theory proposed by Wang and Zhao [44], a linear operator $L : C_T \rightarrow C_T$ can be defined as follows, assuming that $\phi(s)$ represents the initial distribution of infectious individuals and that $\phi(s)$ is T -periodic. Thus, $F(s)\phi(s)$ represents the distribution of new infections produced by the infected individuals introduced at time s . Given $t \geq s$, then $Z(t, s)F(s)\phi(s)$ gives the distribution of those infected individuals who were newly infected at time s and remain in the infected compartments at time t , then define

$$\psi(t) := \int_{-\infty}^t Z(t, s)F(s)\phi(s)ds = \int_0^\infty Z(t, t-a)F(t-a)\phi(t-a)da,$$

where $\psi(t)$ denotes the distribution of cumulative newly infected individuals resulting from all previously introduced infected individuals $\phi(s)$ at time t .

Let C_T be the ordered Banach space of all T -period functions from \mathbb{R} to \mathbb{R}^4 , where the maximum norm is $\|\cdot\|$, and the cones are

$$C_T^+ := \{\phi \in C_T : \phi(t) \geq 0, \forall t \in \mathbb{R}\}.$$

According to the method proposed by Wang and Zhao [44], a linear operator $L : C_T \rightarrow C_T$ can be defined as follows:

$$(L\phi)(t) = \int_0^\infty Z(t, t-a)F(t-a)\phi(t-a)da, \forall t \in \mathbb{R}, \phi \in C_T.$$

L is called the next generation infection operator, and the spectral radius of L is defined as the basic reproduction number \mathcal{R}_0 . Therefore, the basic reproduction number \mathcal{R}_0 of system (2.1) can be expressed as follows:

$$\mathcal{R}_0 := \rho(L).$$

To estimate the basic reproduction number \mathcal{R}_0 of system (2.1) in the periodic case, it is assumed that $W(t, \lambda)$ is the evolution operator of the T -periodic system, given as follows:

$$\frac{dw}{dt} = \left(\frac{F(t)}{\lambda} - V(t) \right) w, \forall t \in \mathbb{R},$$

and the parameter $\lambda \in (0, \infty)$, it follows that $\Phi_{F-V}(t) = W(t, 1)$. Hence, we derive

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

where

$$\begin{aligned} & -V(t) + \frac{F(t)}{\lambda} \\ &= \begin{pmatrix} \frac{\beta_p}{\lambda} - \mu_p & 0 & 0 & \frac{\beta_{hp}}{\lambda} \\ \frac{\beta_{ph}(t)S_h^0 + \sigma\beta_{ph}(t)G^0}{\lambda(S_h^0 + G^0)} & -(\rho + \mu_h) & \frac{\beta_a S_h^0 + \sigma\beta_a G^0}{\lambda(S_h^0 + G^0)} & \frac{\beta_m S_h^0 + \sigma\beta_m G^0}{\lambda(S_h^0 + G^0)} \\ 0 & (1 - \theta)\rho & -(\gamma_a + \mu_h) & 0 \\ 0 & \theta\rho & 0 & -(\gamma_m + \mu_h + d) \end{pmatrix}. \end{aligned}$$

Next, we present the following Lemma 3.2.

Lemma 3.2. (Theorem 2.1, [44]) *The following statements are valid:*

- (1) *If $\rho(W(t, \lambda)) = 1$ has a positive solution λ_0 , then λ_0 is an eigenvalue of L , and hence $\mathcal{R}_0 > 0$.*
- (2) *If $\mathcal{R}_0 > 0$, then $\lambda = \mathcal{R}_0$ is the unique solution of $\rho(W(t, \lambda)) = 1$.*
- (3) *$\mathcal{R}_0 = 0$ if and only if $\rho(W(t, \lambda)) < 1$ for all $\lambda > 0$.*

Therefore, it is clear that the basic reproduction number \mathcal{R}_0 can be estimated by the numerical solution of this equation. Regarding the stability of the disease-free periodic solution, the following conclusions can be derived from Theorem 2.2 of Wang and Zhao [44].

Lemma 3.3. (Theorem 2.2, [44]) *The following statements are valid:*

- (1) *$\mathcal{R}_0 = 1$ if and only if $\rho(\Phi_{F-V}(t)) = 1$.*
- (2) *$\mathcal{R}_0 > 1$ if and only if $\rho(\Phi_{F-V}(t)) > 1$.*
- (3) *$\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(t)) < 1$.*

Therefore, the disease-free periodic solution P_0 of system (2.1) is locally asymptotically stable if $\mathcal{R}_0 < 1$, whereas it is unstable if $\mathcal{R}_0 > 1$, where $\Phi_{F-V}(t)$ is the monodromy matrix of the linear periodic system (3.5).

Since the biological significance of \mathcal{R}_0 in a periodic system is not straightforward to interpret, the following discussion aims to clarify its biological meaning. Using the generalized approach introduced by van den Driessche and Watmough [17] and Diekmann and Heesterbeek [15], we compute the basic reproduction number for the autonomous model derived from system (2.1) by setting the time-varying parameters $\Pi(t) = a_1$ and $\beta_{ph}(t) = a_3$ as constants. Here, a_1 represents the baseline average birth rate of rodents, and a_3 represents the baseline transmission rate from rodents to humans. We then obtain the Jacobian matrix F , given by

$$F = \begin{pmatrix} \beta_p & 0 & 0 & \beta_{hp} \\ \frac{a_3 S_h^0 + \sigma a_3 G^0}{S_h^0 + G^0} & 0 & \frac{\beta_a S_h^0 + \sigma \beta_a G^0}{S_h^0 + G^0} & \frac{\beta_m S_h^0 + \sigma \beta_m G^0}{S_h^0 + G^0} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and the Jacobian matrix V , given by

$$V = \begin{pmatrix} \mu_p & 0 & 0 & 0 \\ 0 & \rho + \mu_h & 0 & 0 \\ 0 & -(1 - \theta)\rho & \gamma_a + \mu_h & 0 \\ 0 & -\theta\rho & 0 & \gamma_m + \mu_h + d \end{pmatrix},$$

thus the characteristic polynomial of FV^{-1} is

$$\lambda^2(\lambda^2 - (\mathcal{R}_{hh} + \mathcal{R}_{pp})\lambda + \mathcal{R}_{hh}\mathcal{R}_{pp} - \mathcal{R}_{hp}\mathcal{R}_{ph}) = 0,$$

where

$$\mathcal{R}_{hh} = \frac{\beta_a(\sigma c + \mu_h + \delta)(1 - \theta)\rho}{(\mu_h + c + \delta)(\rho + \mu_h)(\gamma_a + \mu_h)} + \frac{\beta_m(\sigma c + \mu_h + \delta)\theta\rho}{(\mu_h + c + \delta)(\rho + \mu_h)(\gamma_m + \mu_h + d)},$$

$$\begin{aligned}\mathcal{R}_{hp} &= \frac{\beta_{hp}\theta\rho}{(\rho + \mu_h)(\gamma_m + \mu_h + d)}, \\ \mathcal{R}_{ph} &= \frac{a_3(\sigma c + \mu_h + \delta)}{(\mu_h + c + \delta)\mu_p}, \\ \mathcal{R}_{pp} &= \frac{\beta_p}{\mu_p}.\end{aligned}$$

The characteristic polynomial can therefore be written as the quadratic equation

$$\lambda^2 - (\mathcal{R}_{hh} + \mathcal{R}_{pp})\lambda + \mathcal{R}_{hh}\mathcal{R}_{pp} - \mathcal{R}_{hp}\mathcal{R}_{ph} = 0. \quad (3.8)$$

According to Diekmann and Heesterbeek [15], the basic reproduction number is the largest absolute eigenvalue of FV^{-1} , and therefore, it is given by the root of the quadratic equation (3.8),

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\mathcal{R}_{hh} + \mathcal{R}_{pp} + \sqrt{(\mathcal{R}_{hh} - \mathcal{R}_{pp})^2 + 4\mathcal{R}_v^2}}{2}, \quad (3.9)$$

where \mathcal{R}_{hh} , \mathcal{R}_{pp} and $\mathcal{R}_v = \sqrt{\mathcal{R}_{hp}\mathcal{R}_{ph}}$ are the basic reproduction numbers of human-to-human transmission, rodent-to-rodent transmission, and vectorial transmission, respectively.

4. Dynamics analysis of the model

4.1. Extinction of disease

Assume that $(\mathbb{R}^n, \mathbb{R}_+^n)$ is a standard n -dimensional Euclidean space. For $u, v \in \mathbb{R}^n$, if $u - v \in \mathbb{R}_+^n$, then $u \geq v$; if $u - v \in \mathbb{R}_+^n \setminus \{0\}$, then $u > v$; if $u - v \in \text{Int}(\mathbb{R}_+^n)$, then $u \gg v$.

First, assume that $A(t)$ is a continuous, cooperative, and irreducible $n \times n$ T -periodic matrix function, and that $\Phi_A(t)$ is the fundamental solution matrix of system (4.1).

$$\frac{dx(t)}{dt} = A(t)x(t). \quad (4.1)$$

In the system, $\rho(\Phi_A(t))$ is defined as the spectral radius of $\Phi_A(t)$, therefore, each element of the matrix $\Phi_A(t)$ is positive for $T > 0$ [8, 22]. From the Perron-Frobenius theorem [41], it follows that $\rho(\Phi_A(t))$ is the principal eigenvalue of $\Phi_A(t)$, which means it is simple and has an eigenvector $v^* \gg 0$. Hence, we conclude the following.

Lemma 4.1. (Lemma 2.1, [45]) *Let $\mu = \frac{1}{T} \ln \rho(\Phi_A(T))$, then there is a positive T -periodic function $v(T)$, such that $e^{\mu t} v(t)$ is the solution of $\frac{dx(t)}{dt} = A(t)x(t)$.*

Theorem 4.1. *When $\mathcal{R}_0 < 1$, the disease-free periodic solution P_0 of system (2.1) is globally asymptotically stable, and when $\mathcal{R}_0 > 1$, it is unstable.*

Proof. From the previous process, we can see that for any $\epsilon > 0$, there exists $t_0 > 0$ such that

$$S_h(t) \leq S_h^0 + \epsilon, \quad G(t) \leq G^0 + \epsilon, \quad N_h(t) \geq \frac{\Lambda}{\mu_h} - \epsilon = S_h^0 + G^0 - \epsilon, \quad \text{for } t > t_0.$$

Therefore, we have

$$\frac{S_p(t)}{N_p(t)} \leq 1 + \epsilon, \frac{S_h(t)}{N_h(t)} \leq \frac{S_h^0 + \epsilon}{S_h^0 + G^0 - \epsilon}, \text{ and } \frac{G(t)}{N_h(t)} \leq \frac{G^0 + \epsilon}{S_h^0 + G^0 - \epsilon}.$$

This introduces the comparison system

$$\begin{cases} \dot{\bar{I}}_p(t) = (\beta_p \bar{I}_p + \beta_{hp} \bar{I}_m)(1 + \epsilon) - \mu_p \bar{I}_p, \\ \dot{\bar{E}}(t) = (\beta_a \bar{I}_a + \beta_m \bar{I}_m + \beta_{ph}(t) \bar{I}_p) \frac{S_h^0 + \epsilon + \sigma(G^0 + \epsilon)}{S_h^0 + G^0 - \epsilon} - \rho \bar{E} - \mu_h \bar{E}, \\ \dot{\bar{I}}_a(t) = (1 - \theta) \rho \bar{E} - \gamma_a \bar{I}_a - \mu_h \bar{I}_a, \\ \dot{\bar{I}}_m(t) = \theta \rho \bar{E} - \gamma_m \bar{I}_m - (\mu_h + d) \bar{I}_m. \end{cases} \quad (4.2)$$

Let $B_\epsilon(t)$ be the following 4×4 matrix function

$$B_\epsilon(t) = \begin{pmatrix} \beta_p(1 + \epsilon) - \mu_p & 0 & 0 & \beta_{hp}(1 + \epsilon) \\ \beta_{ph}(t) \frac{S_h^* + \epsilon + \sigma(G^0 + \epsilon)}{S_h^0 + G^0 - \epsilon} & -(\rho + \mu_h) & \beta_a \frac{S_h^* + \epsilon + \sigma(G^0 + \epsilon)}{S_h^0 + G^0 - \epsilon} & \beta_m \frac{S_h^* + \epsilon + \sigma(G^0 + \epsilon)}{S_h^0 + G^0 - \epsilon} \\ 0 & (1 - \theta) \rho & -(\gamma_a + \mu_h) & 0 \\ 0 & \theta \rho & 0 & -(\gamma_m + \mu_h + d) \end{pmatrix}.$$

Set $u = (\bar{I}_p, \bar{E}, \bar{I}_a, \bar{I}_m)^T$, from this, it can be seen that system (4.2) is equivalent to system (4.3)

$$\frac{du(t)}{dt} = B_\epsilon(t)u. \quad (4.3)$$

According to Lemma 4.1, there is always a T -period function $v(t) = (v_1, v_2, v_3, v_4)$ such that $u(t) = e^{\mu t} v(t)$ is the solution of system (4.3), where $\mu = \frac{1}{T} \ln \rho(\Phi_{B_\epsilon}(T))$, therefore, $t' > t^0$ and there exists a sufficiently small number κ satisfying the following inequality:

$$\bar{I}_p(t') \leq \kappa v_1(0), \bar{E}(t') \leq \kappa v_2(0), \bar{I}_a(t') \leq \kappa v_3(0), \bar{I}_m(t') \leq \kappa v_4(0).$$

According to the principle of comparison, the following inequality can be obtained.

$$\begin{aligned} I_p(t) &\leq \bar{I}_p(t) \leq \kappa e^{\mu(t-t')} v_1(t-t'), \quad E(t) \leq \bar{E}(t) \leq \kappa e^{\mu(t-t')} v_2(t-t'), \\ I_a(t) &\leq \bar{I}_a(t) \leq \kappa e^{\mu(t-t')} v_3(t-t'), \quad I_m(t) \leq \bar{I}_m(t) \leq \kappa e^{\mu(t-t')} v_4(t-t'). \end{aligned}$$

Lemma 3.3 shows that $\rho(\Phi_{F-V}(t)) < 1$ if and only if $\mathcal{R}_0 < 1$. Then, by choosing a sufficiently small number $\epsilon > 0$ such that $\rho(\Phi_{B_\epsilon}(t)) < 1$, we can obtain $\mu < 0$. Thus, $u(t) \rightarrow 0$ as $t \rightarrow \infty$. Using the standard comparison principle, we deduce that

$$\lim_{t \rightarrow \infty} (I_p(t), E(t), I_a(t), I_m(t)) = (0, 0, 0, 0).$$

Based on the asymptotic periodic half-flow theory [43], we can deduce that

$$\lim_{t \rightarrow \infty} (S_p(t) - S_p^0(t), S_h(t) - S_h^0, G(t) - G^0, R(t)) = (0, 0, 0, 0).$$

Therefore, when $\mathcal{R}_0 < 1$, the disease-free periodic solution P_0 is globally asymptotically stable. \square

4.2 Uniform persistence of disease

Lemma 4.2. *Let $u = (u_i(t, x_0))$ ($i = 1, 2, \dots, 8$) be the solution of system (2.1), where $x_0 = (S_p(0), I_p(0), S_h(0), E(0), G(0), I_a(0), I_m(0), R(0)) \in \Omega$ is the initial condition of system (2.1). If there exists some $t_0 \geq 0$ such that $u_i(t_0) > 0$ for a certain $i \in \{2, 5, 6, 7\}$, then $u_i(t) > 0$ for all $i = 2, 5, 6, 7$ with $t > t_0$.*

Proof. If $E(t_0) > 0$ for some $t_0 \geq 0$, then $E(t)$ satisfies

$$\frac{dE}{dt} \geq -(\rho + \mu_h)E.$$

Hence, for $\forall t > t_0$, $E(t) > 0$, according to the expressions of I_a , I_m in system (2.1), when $\forall t > t_0$, $I_a(t) > 0$ and $I_m(t) > 0$, based on the expression of I_p in system (2.1) and the positivity of S_p , it is easy to see that when $\forall t > t_0$, $I_p(t) > 0$.

If $I_a(t_0) > 0$ for some $t_0 \geq 0$, then $I_a(t)$ satisfies

$$\frac{dI_a}{dt} \geq -(\gamma_a + \mu_h)I_a.$$

Therefore, according to the expression of E in system (2.1) and the positivity of S_h, G , when $\forall t > t_0$, $E(t) > 0$, and from the expressions of I_m, I_p in system (2.1), we can see that when $\forall t > t_0$, $I_m(t) > 0$ and $I_p(t) > 0$.

If $I_p(t_0) > 0$ for some $t_0 \geq 0$, then $I_p(t)$ satisfies

$$\frac{dI_p}{dt} \geq -\mu_p I_p.$$

Therefore, according to the expressions of E in system (2.1) and the positivity of S_h, G , when $\forall t > t_0$, $E(t) > 0$, and by the expressions of I_m, I_a in system (2.1), we can conclude that when $\forall t > t_0$, $I_a(t) > 0$ and $I_m(t) > 0$. \square

Theorem 4.2. *If $\mathcal{R}_0 > 1$, the disease is consistently persistent, that is, there is a positive constant $\eta > 0$ such that any solution $(S_p(t), I_p(t), S_h(t), E(t), G(t), I_a(t), I_m(t), R(t))$ in system (2.1) with $I_p(0) > 0, E(0) > 0, I_a(0) > 0$ or $I_m(0) > 0$ satisfies*

$$\liminf_{t \rightarrow \infty} (I_p, E, I_a, I_m) \geq (\eta, \eta, \eta, \eta).$$

Moreover, there is at least one positive periodic solution of system (2.1) when $\mathcal{R}_0 > 1$.

Proof. Define

$$\begin{aligned} X &:= \Omega, \\ X_0 &:= \{(S_p, I_p, S_h, E, G, I_a, I_m, R) \in X : I_p > 0, E > 0, I_a > 0, I_m > 0\}, \\ \partial X_0 &:= X \setminus X_0. \end{aligned}$$

Let $f : X \rightarrow X$ be the Poincaré map associated with system (2.1), and we get

$$f(x_0) = u(T, x_0), \quad \forall x_0 \in X,$$

where $x_0 \in X$ is the initial condition of system (2.1). According to the existence and uniqueness theorem for solutions [37], $u(t, x_0)$ is the unique solution of system (2.1) in $(0, x_0)$.

In order to prove that system (2.1) is consistently persistent, the set X, X_0 are all positively invariant. Let $\forall x_0 \in X_0$ be any initial condition; then, the solution for system (2.1) can be obtained. Set

$$\begin{aligned} a_1 &= \frac{\beta_p I_p}{N_p} + \frac{\beta_h I_m}{N_h}, \\ a_2 &= \frac{\beta_a I_a + \beta_m I_m + \beta_{ph}(s) I_p}{N_h}, \\ a_3 &= \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(s) I_p)}{N_h}, \end{aligned}$$

thus, for all $t > 0$ the following inequality can be obtained.

$$\begin{aligned} S_p(t) &= e^{-\int_0^t (a_1(s) + \mu_p) ds} \left[S_p(0) + \int_0^t \Pi(s) N_p(s) \left(1 - \frac{N_p(s)}{K} \right) e^{\int_0^s (a_1(\tau) + \mu_p) d\tau} ds \right] \geq 0, \\ I_p(t) &= e^{-\int_0^t (\mu_p - \frac{\beta_p S_p(s)}{N_p}) ds} \left[I_p(0) + \int_0^t \frac{\beta_{hp} I_m(s) S_p(s)}{N_h} e^{\int_0^s (\mu_p - \frac{\beta_p S_p(\tau)}{N_p}) d\tau} ds \right] > 0, \\ S_h(t) &= e^{-\int_0^t (a_2(s) + \mu_h + c) ds} \left[S_h(0) + \int_0^t (\Lambda + \delta G(s)) e^{\int_0^s (a_2(\tau) + \mu_h + c) d\tau} ds \right] \geq 0, \\ G(t) &= e^{-\int_0^t (a_3(s) + \mu_h + \delta) ds} \left[G(0) + \int_0^t c S_h(s) e^{\int_0^s (a_3(\tau) + \mu_h + \delta) d\tau} ds \right] \geq 0, \\ E(t) &= e^{-(\rho + \mu_n)t} \left[E(0) + \int_0^t (a_2(s) S_h(s) + a_3(s) G(s)) e^{(\rho + \mu_h)s} ds \right] > 0, \quad (4.4) \\ I_a(t) &= e^{-(\gamma_a + \mu_h)t} \left[I_a(0) + \int_0^t (1 - \theta) \rho E(s) e^{(\gamma_a + \mu_h)s} ds \right] > 0, \\ I_m(t) &= e^{-(\gamma_m + \mu_h + d)t} \left[I_m(0) + \int_0^t \theta \rho E(s) e^{(\gamma_m + \mu_h + d)s} ds \right] > 0, \\ R(t) &= e^{-\mu_h t} \left[R(0) + \int_0^t (\gamma_a I_a(s) + \gamma_m I_m(s)) e^{\mu_h s} ds \right] \geq 0. \end{aligned}$$

Hence, both X and X_0 are positive invariant sets, and ∂X_0 is relatively closed in X .

From the continuous dependence of the solution on the initial value, we can see that we have

$$\lim_{x_0 \rightarrow P_0} \|u(t, x_0) - P_0\| = 0.$$

It's uniform on $(0, T)$, with the norm $\|\cdot\|$ representing the Euclidean distance on \mathbb{R}^8 . Therefore, for any $\epsilon > 0$, there exists $\rho > 0$, such that when $\|x_0 - P_0\| < \rho$, we have

$$\|u(t, x_0) - u(t, P_0)\| < \epsilon, \quad \forall t \in [0, T].$$

Now, prove that $\lim_{n \rightarrow \infty} \|f^n(x_0) - P_0\| \geq \rho$ with $x_0 \in X_0$.

If this assertion is false, then there exists $\bar{x}_0 \in X_0$ such that

$$\limsup_{n \rightarrow \infty} \|f^n(\bar{x}_0) - P_0\| < \rho.$$

Suppose there exists $n_0 > 0$ such that $\|f^n(\bar{x}_0) - P_0\| < \rho$ for all $n \geq n_0$, through the continuous dependence of the solution on the initial value, for any $t \in [0, T]$, we have

$$\|u(t, f^n(\bar{x}_0)) - u(t, P_0)\| < \epsilon, \quad \forall t \in [0, T].$$

Assume $n \geq n_0$, for any $t \geq n_0 T$, let $m = [\frac{t}{T}]$ be the largest integer less than or equal to $\frac{t}{T}$, we have $t = \bar{t} + mT$, where $\bar{t} \in [0, T]$ and $m \geq n_0$, therefore,

$$\|u(t, \bar{x}_0) - u(t, P_0)\| = \|u(\bar{t}, f^n(\bar{x}_0)) - u(\bar{t}, P_0)\| < \epsilon.$$

There exists $t_1 > 0$ such that for all $t \geq t_1$, we have the following results.

$$\begin{aligned} |S_p(t, \bar{x}_0) - S_p^0(t)| &< \epsilon, \quad |S_h(t, \bar{x}_0) - S_h^0| < \epsilon, \\ |G(t, \bar{x}_0) - G^0| &< \epsilon, \quad 0 \leq I_p(t, \bar{x}_0) \leq \epsilon, \quad 0 \leq E(t, \bar{x}_0) \leq \epsilon, \\ 0 \leq I_a(t, \bar{x}_0) &\leq \epsilon, \quad 0 \leq I_m(t, \bar{x}_0) \leq \epsilon, \quad 0 \leq R(t, \bar{x}_0) \leq \epsilon. \end{aligned} \quad (4.5)$$

Hence, for all $t \geq t_1$, we have

$$\begin{aligned} \frac{S_p(t)}{N_p(t)} &\geq \frac{S_p^0(t) - \epsilon}{S_p^0(t) + 2\epsilon} \geq 1 - \frac{3\epsilon}{S_p^0(t) + 2\epsilon}, \\ \frac{S_h(t)}{N_h(t)} &\geq \frac{S_h^0 - \epsilon}{S_h^0 + G^0 + 6\epsilon}, \quad \frac{G(t)}{N_h(t)} \geq \frac{G^0 - \epsilon}{S_h^0 + G^0 + 6\epsilon}. \end{aligned}$$

Next, it is similar to the proof of Theorem 4.1, which follows from the comparison theorem

$$\begin{cases} \dot{\tilde{I}}_p(t) = (\beta_p \tilde{I}_p + \beta_{hp} \tilde{I}_m) \left(1 - \frac{3\epsilon}{S_p^0(t) + 2\epsilon}\right) - \mu_p \tilde{I}_p, \\ \dot{\tilde{E}}(t) = (\beta_a \tilde{I}_a + \beta_m \tilde{I}_m + \beta_{ph}(t) \tilde{I}_p) \frac{S_h^0 - \epsilon + \sigma(G^0 - \epsilon)}{S_h^0 + G^0 + 6\epsilon} - \rho \tilde{E} - \mu_h \tilde{E}, \\ \dot{\tilde{I}}_a(t) = (1 - \theta) \rho \tilde{E} - \gamma_a \tilde{I}_a - \mu_h \tilde{I}_a, \\ \dot{\tilde{I}}_m(t) = \theta \rho \tilde{E} - \gamma_m \tilde{I}_m - (\mu_h + d) \tilde{I}_m. \end{cases} \quad (4.6)$$

Let $C_\epsilon(t)$ be the following 4×4 matrix function

$$C_\epsilon(t) = \begin{pmatrix} \beta_p \left(1 - \frac{3\epsilon}{S_p^0(t) + 2\epsilon}\right) - \mu_p & 0 & 0 & \beta_{hp}(t) \left(1 - \frac{3\epsilon}{S_p^0(t) + 2\epsilon}\right) \\ \beta_{ph}(t) \frac{S_h^0 - \epsilon + \sigma(G^0 - \epsilon)}{S_h^0 + G^0 + 6\epsilon} & -(\rho + \mu_h) & \beta_a \frac{S_h^0 - \epsilon + \sigma(G^0 - \epsilon)}{S_h^0 + G^0 + 6\epsilon} & \beta_m \frac{S_h^0 - \epsilon + \sigma(G^0 - \epsilon)}{S_h^0 + G^0 + 6\epsilon} \\ 0 & (1 - \theta) \rho & -(\gamma_a + \mu_h) & 0 \\ 0 & \theta \rho & 0 & -(\gamma_m + \mu_h + d) \end{pmatrix},$$

set $u = (\tilde{I}_p, \tilde{E}, \tilde{I}_a, \tilde{I}_m)^T$, from this, we can see that system (4.6) is equivalent to system (4.7)

$$\frac{du(t)}{dt} = C_\epsilon(t)u. \quad (4.7)$$

According to Lemma 4.1, there is always a T -period function $w(t) = (w_1, w_2, w_3, w_4)$ such that $e^{\mu t}w(t)$ is the solution of the system (4.7), where $\mu = \frac{1}{T}\ln\rho(\Phi_{C_\varepsilon}(T))$, therefore, we choose $t_3 > t_2$ and a sufficiently small number $\bar{\kappa}$ satisfying the following inequality:

$$\tilde{I}_p(t_3) \geq \bar{\kappa}w_1(0), \quad \tilde{E}(t_3) \geq \bar{\kappa}w_2(0), \quad \tilde{I}_a(t_3) \geq \bar{\kappa}w_3(0), \quad \tilde{I}_m(t_3) \geq \bar{\kappa}w_4(0).$$

Using the comparison principle, the following inequality can be derived.

$$\begin{aligned} \tilde{I}_p(t) &\geq \bar{\kappa}e^{\mu(t-t_3)}w_1(t-t_3), \quad \tilde{E}(t) \geq \bar{\kappa}e^{\mu(t-t_3)}w_2(t-t_3), \\ \tilde{I}_a(t) &\geq \bar{\kappa}e^{\mu(t-t_3)}w_3(t-t_3), \quad \tilde{I}_m(t) \geq \bar{\kappa}e^{\mu(t-t_3)}w_4(t-t_3). \end{aligned}$$

Therefore, the following equation holds

$$\begin{aligned} \lim_{t \rightarrow \infty} I_p(t) &= \infty, \quad \lim_{t \rightarrow \infty} E(t) = \infty, \\ \lim_{t \rightarrow \infty} I_a(t) &= \infty, \quad \lim_{t \rightarrow \infty} I_m(t) = \infty. \end{aligned}$$

This contradicts inequality (4.5), thus, we can get $\lim_{n \rightarrow \infty} \|f^n(x_0) - P_0\| \geq \rho$. Then, P_0 is an isolated invariant set of Poincaré mapping f in X , then $W^s(P_0) \cap X_0 = \emptyset$ is proved, where $W^s(P_0)$ is a stable manifold of P_0 .

Define

$$M_\partial := \{x_0 \in \partial X_0 : f^n(x_0) \in \partial X_0, \forall n > 0\}.$$

The following proves that P_0 is globally stable for the Poincaré map f in M_∂ .

Set $\overline{M_\partial} := \{x_0 \in X : I_p = E = I_a = I_m = 0\}$, we first prove that $M_\partial = \overline{M_\partial}$, obviously, $\overline{M_\partial} \subset M_\partial$. So next we only need to prove $M_\partial \subset \overline{M_\partial}$, that is, it is only necessary to prove that for any $x_0 \in \partial X_0$ under the condition of the initial value $(0, x_0)$ the solution $u(t, x_0) = (S_p(t, x_0), I_p(t, x_0), S_h(t, x_0), V(t, x_0), E(t, x_0), I_a(t, x_0), I_m(t, x_0), R(t, x_0))$ satisfies $I_p(t, x_0) = E(t, x_0) = I_a(t, x_0) = I_m(t, x_0) = 0$. If it is not true, then there exists $t^* > 0$ such that $I_p(t^*, x_0) > 0, E(t^*, x_0) > 0, I_a(t^*, x_0) > 0$, or $I_m(t^*, x_0) > 0$, we only prove the case of $I_a(t^*, x_0) > 0$, the other cases are similar. The inequality $\frac{dI_a}{dt} \geq -(\gamma_a + \mu_h)I_a$ means that for all $t \geq t^*$, there is $I_a(t, x_0) > 0$. For all $t \geq t^*$, based on the inequality (4.4), we can derive

$$E(t, x_0) > 0, \quad I_p(t, x_0) > 0, \quad I_m(t, x_0) > 0, \quad \text{for all } t > t^*.$$

This implies that for each $t > t^*$, $u(t, x_0) \notin \partial X_0$, this means that $x_0 \notin M_\partial$. Thus, we arrive at a contradiction, $M_\partial \subset \overline{M_\partial}$ is proved.

Next, we prove that for any $x_0 \in M_\partial$, the omega limit set $T(x_0) = P_0$, where $T(x_0)$ is the omega limit set of the forward orbit $\gamma^+(x_0) = \{f^n(x_0) : \forall n > 0\}$. Since $M_\partial = \overline{M_\partial}$, we have $I_p(t, x_0) = E(t, x_0) = I_a(t, x_0) = I_m(t, x_0) = 0$, for all $x_0 \in \overline{M_\partial}$ and $t \geq 0$. According to system (2.1), it follows that S_p, S_h, G and R satisfy the following system:

$$\begin{cases} \dot{S}_p(t) = \Pi(t)N_p(1 - \frac{N_p}{K}) - \mu_p S_p, \\ \dot{S}_h(t) = \Lambda - \mu_h S_h - cS_h + \delta G, \\ \dot{G}(t) = cS_h - \mu_h G - \delta G, \\ \dot{R}(t) = -\mu_h R. \end{cases} \quad (4.8)$$

Therefore, $\lim_{t \rightarrow \infty} (S_p(t) - S_p^0(t), S_h(t) - S_h^0, V(t) - G^0, R(t)) = (0, 0, 0, 0)$ is uniform. For any $x_0 \in M_\partial$, there is $T(x_0) = P_0$, which means that P_0 has a global attraction to f in M_∂ . Since system (4.8) is cooperative, it can be concluded from Zhao (Lemma 2.2.1, [47]) that P_0 is globally asymptotically stable in set M_∂ .

Since f has a global attractor on X , from the previous Lemma 3.1 it follows that the solution of system (2.1) is uniformly bounded, it also implies that f is point-dissipative on X . It is also proved earlier that P_0 is isolated in X , each solution in M_∂ tends to P_0 . It then follows from Zhao (Theorem 1.3.1 and Note 1.3.1, [47]) that f is consistently persistent for $(X_0, \partial X_0)$. Thus, by Zhao (Theorem 3.1.1, [47]), the solution of system (2.1) remains consistently persistent under $I_p(0) > 0, E(0) > 0, I_a(0) > 0$, and $I_m(0) > 0$.

If $I_p(0) > 0, E(0) > 0, I_a(0) > 0$, or $I_m(0) > 0$, it follows from Lemma 4.2 that there exists an integer $n_0 \geq 0$ such that $f^{n_0}(x_0) \in X_0$. Since $f(t)x_0 = f(t - n_0T)f^{n_0}(x_0)$ for all $t \geq n_0T$, consistent persistence also holds.

According to Zhao (Theorem 1.3.10, [47]), the Poincaré map f has a fixed point $(S_p^*(0), I_p^*(0), S_h^*(0), E^*(0), G^*(0), I_a^*(0), I_m^*(0), R^*(0))$. Then the corresponding periodic solution is $(S_p^*(t), I_p^*(t), S_h^*(t), E^*(t), G^*(t), I_a^*(t), I_m^*(t), R^*(t))$, due to $I_p^*(0) > 0, E^*(0) > 0, I_a^*(0) > 0$, and $I_m^*(0) > 0$, apparently

$$I_p^*(t) > 0, E^*(t) > 0, I_a^*(t) > 0, I_m^*(t) > 0, \text{ for all } t > 0.$$

Next, we prove that $S_p^*(0) > 0, S_h^*(0) > 0, G^*(0) > 0$, and $R^*(0) > 0$. Using the counter-evidence method, assume that $S_p^*(0) = 0, S_h^*(0) = 0, G^*(0) = 0$, and $R^*(0) = 0$, using the periodicity of the solution, we have

$$\begin{aligned} S_p^*(0) &= S_p^*(nT) = 0, S_h^*(0) = S_h^*(nT) = 0, \\ G^*(0) &= G^*(nT) = 0, R^*(0) = R^*(nT) = 0. \end{aligned}$$

From the inequality (4.4), we have

$$S_p^*(t) > 0, S_h^*(t) > 0, G^*(t) > 0, R^*(t) > 0, \text{ for all } t > 0.$$

It's easy to derive

$$S_p^*(nT) > 0, S_h^*(nT) > 0, G^*(nT) > 0, R^*(nT) > 0, \text{ for all } t > 0,$$

which yields a contradiction. Thus, $(S_p^*(t), I_p^*(t), S_h^*(t), E^*(t), G^*(t), I_a^*(t), I_m^*(t), R^*(t))$ is the positive T periodic solution of system (2.1). \square

5. The optimal control problems

We have conducted mathematical research and exploration on the proposed model in the previous section. We introduce four time-dependent control variables into the model, corresponding to the four intervention strategies in system (2.1). Pontryagin's maximum principle [38] is used to derive the necessary conditions for the existence of optimal control. We introduce four control strategies, $u_1(t), u_2(t), u_3(t), u_4(t)$, to extend system (2.1) into system (5.1), where $u_1(t)$ means controlling rodents (e.g., extermination, expulsion, etc.), $u_2(t)$ means increasing resource investment to encourage more people to adopt external protection, $u_3(t)$ represents full vaccination, and $u_4(t)$ represents increasing treatment rates.

Based on these assumptions, the optimal control model is as follows:

$$\left\{ \begin{array}{l} \dot{S}_p(t) = \Pi(t)N_p(1 - \frac{N_p}{K}) - \frac{(\beta_p I_p + \beta_{hp} I_m)S_p}{N_p} - \mu_p S_p - u_1(t)S_p, \\ \dot{I}_p(t) = \frac{(\beta_p I_p + \beta_{hp} I_m)S_p}{N_p} - \mu_p I_p - u_1(t)I_p, \\ \dot{S}_h(t) = \Lambda - \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t)I_p)S_h}{N_h} - \mu_h S_h - c(1 + u_2(t))S_h \\ \quad + \delta G - u_3(t)S_h, \\ \dot{G}(t) = c(1 + u_2(t))S_h - \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t)I_p)G}{N_h} - \mu_h G - \delta G, \\ \dot{E}(t) = \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t)I_p)S_h}{N_h} + \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t)I_p)G}{N_h} \\ \quad - \rho E - \mu_h E, \\ \dot{I}_a(t) = (1 - \theta)\rho E - \gamma_a(1 + u_4(t))I_a - \mu_h I_a, \\ \dot{I}_m(t) = \theta\rho E - \gamma_m(1 + u_4(t))I_m - (\mu_h + d)I_m, \\ \dot{R}(t) = \gamma_a(1 + u_4(t))I_a + \gamma_m(1 + u_4(t))I_m - \mu_h R + u_3(t)S_h, \end{array} \right. \quad (5.1)$$

with initial value conditions

$$\begin{aligned} S_p(0) &\geq 0, \quad I_p(0) \geq 0, \quad S_h(0) \geq 0, \quad G(0) \geq 0, \\ E(0) &\geq 0, \quad I_a(0) \geq 0, \quad I_m(0) \geq 0, \quad R(0) \geq 0. \end{aligned}$$

To solve the optimal control problem for the system (5.1), where T denotes the given control period, the objective function is defined as

$$J = \int_0^T [A_1 I_p + A_2 I_a + A_3 I_m + \frac{1}{2}(\eta_1 u_1^2 + \eta_2 u_2^2 + \eta_3 u_3^2 + \eta_4 u_4^2)] dt,$$

where A_1, A_2 and A_3 are the accompanying variables associated with I_p, I_a and I_m , respectively, while η_1, η_2, η_3 and η_4 represent the costs of implementing control variables u_1, u_2, u_3 and u_4 . Let $u = (u_1, u_2, u_3, u_4)$ be the control vector associated with the state vector $S_p, I_p, S_h, E, G, I_a, I_m, R$, and the control vector is bounded, expressed as

$$\Omega = \{(u_1, u_2, u_3, u_4) | u_i(t) \in L[0, M], \quad 0 \leq u_i(t) \leq u_{i,\max}, (i = 1, 2, 3, 4)\}.$$

Considering practical factors such as the cost of vaccines, we set the upper limit for effective vaccination in susceptible populations to 0.5, which is difficult to implement due to challenges in rodent control. The upper limit for rodent control is set to 0.2. Increasing the number of people protected externally and increasing treatment rates are health measures that are an order of magnitude less costly than vaccines, so we set the upper limits for sanitation facilities to 2. Thus, the upper limits are: $u_{1,\max} = 0.2, u_{2,\max} = 2, u_{3,\max} = 0.5, u_{4,\max} = 2$. According to the findings of Fleming and Rishel [19], the corresponding state and control variables are non-negative and linear functions of Ω , and the integral of the objective function J with respect to u_1, u_2, u_3 , and u_4 over Ω is convex. Therefore, the following conclusions can be obtained.

Theorem 5.1. Assume that there is an optimal control $u^* = \{u_1^*, u_2^*, u_3^*, u_4^*\} \in \Omega$ of the control system such that the objective function J achieves its minimum in Ω .

$$J(u_1^*, u_2^*, u_3^*, u_4^*) = \min \{J(u_1, u_2, u_3, u_4) | (u_1, u_2, u_3, u_4) \in \Omega\}.$$

To verify the correctness of this optimal control, we assume the existence of a continuous function $\lambda_i(t)$ ($i = 1, 2, 3, 4, 5, 6$) satisfying

$$\begin{aligned} \frac{d\lambda_1}{dt} &= (\lambda_1 - \lambda_2) \left(\frac{\beta_p I_P}{N_p} + \frac{\beta_{hp} I_m}{N_p} \right) + u_1(\lambda_1 + \lambda_2) + \lambda_1 \mu_p, \\ \frac{d\lambda_2}{dt} &= -A_1 + (\lambda_1 - \lambda_2) \frac{\beta_p S_p}{N_p} + (\lambda_3 - \lambda_5) \frac{\beta_{ph}(t) S_h}{N_h} + (\lambda_4 - \lambda_5) \frac{\sigma \beta_{ph}(t) G}{N_h} + \lambda_2 \mu_p, \\ \frac{d\lambda_3}{dt} &= \frac{(\lambda_3 - \lambda_5)(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)}{N_h} + (\lambda_3 - \lambda_4)(1 + u_2)c \\ &\quad + (\lambda_3 - \lambda_8)u_3 + \lambda_3(\mu_h - \Lambda), \\ \frac{d\lambda_4}{dt} &= (\lambda_4 - \lambda_3)\delta + \frac{\sigma(\lambda_4 - \lambda_5)(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p)}{N_h} + \lambda_4 \mu_h, \\ \frac{d\lambda_5}{dt} &= \lambda_5(\rho + \mu_h) - \lambda_6(1 - \theta)\rho - \lambda_7\theta\rho, \\ \frac{d\lambda_6}{dt} &= -A_2 + \frac{(\lambda_3 - \lambda_5)\beta_a S_h}{N_h} + (\lambda_4 - \lambda_5) \frac{\sigma \beta_a G}{N_h} + (\lambda_6 - \lambda_8)(1 + u_4)\gamma_a + \lambda_6 \mu_h, \\ \frac{d\lambda_7}{dt} &= -A_3 + (\lambda_1 - \lambda_2) \frac{\beta_{hp} I_m}{N_p} + \frac{(\lambda_3 - \lambda_5)\beta_m S_h}{N_h} + (\lambda_4 - \lambda_5) \frac{\sigma \beta_m G}{N_h} \\ &\quad + (\lambda_7 - \lambda_8)(1 + u_4)\gamma_m + \lambda_7(\mu_h + d), \\ \frac{d\lambda_8}{dt} &= \lambda_8 \mu_h. \end{aligned} \tag{5.2}$$

The boundary conditions are

$$\lambda_i(t) = 0 \quad (i = 1, 2, 3, 4, 5, 6, 7, 8).$$

Further, the optimal controls u_1^*, u_2^*, u_3^* and u_4^* are expressed as

$$\begin{aligned} u_1^*(t) &= \min \{ \max \{ u_1^*, 0 \}, 0.05 \}, \\ u_2^*(t) &= \min \{ \max \{ u_2^*, 0 \}, 2 \}, \\ u_3^*(t) &= \min \{ \max \{ u_3^*, 0 \}, 0.5 \}, \\ u_4^*(t) &= \min \{ \max \{ u_4^*, 0 \}, 2 \}, \end{aligned}$$

where

$$\begin{aligned} u_1^* &= \frac{(\lambda_1 + \lambda_2) S_p^*}{\eta_1}, \\ u_2^* &= \frac{(\lambda_3 - \lambda_4) c S_h^*}{\eta_2}, \\ u_3^* &= \frac{(\lambda_5 + \lambda_8) S_h^*}{\eta_3}, \\ u_4^* &= \frac{(\lambda_6 - \lambda_8) \gamma_a I_a^* + (\lambda_7 - \lambda_8) \gamma_m I_m^*}{\eta_4}. \end{aligned}$$

Proof. To prove the above theorem, the system is analyzed by constructing a Hamiltonian function and applying Pontryagin's maximum principle [38], where the Hamiltonian function H is defined as follows:

$$\begin{aligned}
 H = & A_1 I_p + A_2 I_a + A_3 I_m + \frac{1}{2}(\eta_1 u_1^2 + \eta_2 u_2^2 + \eta_3 u_3^2 + \eta_4 u_4^2) \\
 & + \lambda_1 \left[\Pi(t) N_p \left(1 - \frac{N_p}{K} \right) - \frac{\beta_p S_p I_p}{N_p} - \frac{\beta_{hp} I_m S_p}{N_p} - \mu_p S_p - u_1(t) S_p \right] \\
 & + \lambda_2 \left[\frac{\beta_p S_p I_p}{N_p} + \frac{\beta_{hp} I_m S_p}{N_p} - \mu_p I_p - u_1(t) I_p \right] \\
 & + \lambda_3 \left[\Lambda - \frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) S_h}{N_h} - \mu_h S_h - c(1 + u_2(t)) S_h \right. \\
 & \left. + \delta G - u_3(t) S_h \right] \\
 & + \lambda_4 \left[c(1 + u_2(t)) S_h - \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) G}{N_h} - \mu_h G - \delta G \right] \\
 & + \lambda_5 \left[\frac{(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) S_h}{N_h} + \frac{\sigma(\beta_a I_a + \beta_m I_m + \beta_{ph}(t) I_p) G}{N_h} \right. \\
 & \left. - \rho E - \mu_h E \right] \\
 & + \lambda_6 [(1 - \theta) \rho E - \gamma_a (1 + u_4(t)) I_a - \mu_h I_a] \\
 & + \lambda_7 [\theta \rho E - \gamma_m (1 + u_4(t)) I_m - (\mu_h + d) I_m] \\
 & + \lambda_8 [\gamma_a (1 + u_4(t)) I_a + \gamma_m (1 + u_4(t)) I_m - \mu_h R + u_3(t) S_h].
 \end{aligned}$$

Then the adjoint equation with cross-sectional condition $\lambda_i(t) = 0$ ($i = 1, 2, 3, 4, 5, 6, 7, 8$) satisfies

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial y},$$

where $y = (S_p, I_p, S_h, E, G, I_a, I_m, R)$. Now, consider the optimality conditions, we have

$$\begin{aligned}
 \frac{\partial H}{\partial u_1} &= \eta_1 u_1^*(t) - \lambda_1 S_p^* - \lambda_2 I_p^* = 0, \\
 \frac{\partial H}{\partial u_2} &= \eta_2 u_2^*(t) - \lambda_3 c S_h^* + \lambda_4 c S_h^* = 0, \\
 \frac{\partial H}{\partial u_3} &= \eta_3 u_3^*(t) - \lambda_3 S_h^* + \lambda_8 S_h^* = 0, \\
 \frac{\partial H}{\partial u_4} &= \eta_4 u_4^*(t) - \lambda_6 \gamma_a I_a^* - \lambda_7 \gamma_m I_m^* + \lambda_8 (\gamma_a I_a^* + \gamma_m I_m^*) = 0, \\
 u_1^* &= \frac{\lambda_1 S_p^* + \lambda_2 I_p^*}{\eta_1}, \\
 u_2^* &= \frac{(\lambda_3 - \lambda_4) c S_h^*}{\eta_2}, \\
 u_3^* &= \frac{(\lambda_5 + \lambda_8) S_h^*}{\eta_3}, \\
 u_4^* &= \frac{(\lambda_6 - \lambda_8) \gamma_a I_a^* + (\lambda_7 - \lambda_8) \gamma_m I_m^*}{\eta_4}.
 \end{aligned}$$

Thus, we get the above results, this completes the proof. \square

6. A case study-Lassa fever in Nigeria from 2020-2024

6.1. Data source

In this section, we use our model to study the spread of Lassa fever in Nigeria during the outbreak period from March 2020 to February 2024, using data obtained from the Centers for Disease Control and Prevention(CDC) in Nigeria [1]. This is shown in the figure below.

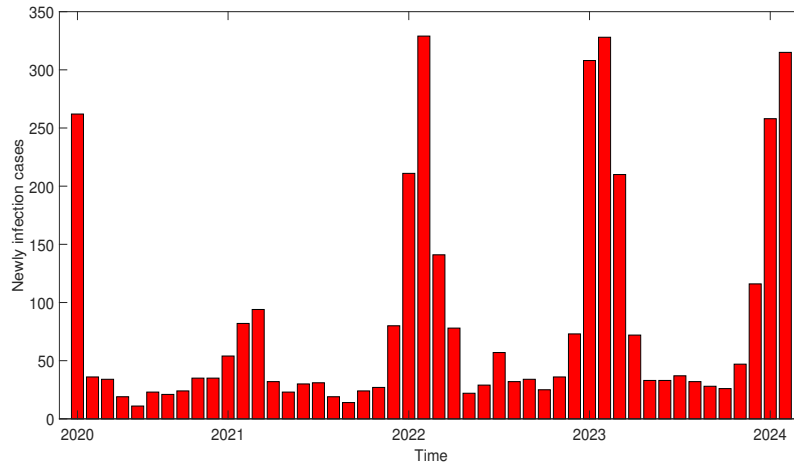


Figure 2. Monthly number of cases of seasonal Lassa fever from March 2020 to February 2024 from Nigeria CDC.

6.2. Parameter estimation of the model

Suppose the functions $\Pi(t)$ and $\beta_{ph}(t)$ are time-periodic, with a period of twelve months, according to Bakare and Are [10] and Bai and Zhou [11], they are of the forms

$$\Pi(t) = a_1 \left(1 + a_2 \sin \left(\frac{2\pi}{12}t + \phi \right) \right), \quad \beta_{ph}(t) = a_3 \left(1 + a_4 \sin \left(\frac{2\pi}{12}t + \phi \right) \right),$$

where $\frac{2\pi}{12}$ indicates that the period is twelve months, a_1 indicates the baseline value of rodents birth rate, a_3 indicates the baseline values for average rodent-to-human transmission rates, a_2 and a_4 indicate the amplitude or degree of seasonality, and ϕ indicates the initial phase. Next, we use the MCMC algorithm to fit the model reasonably well to the real infection data and estimate all parameters and initial values of system (2.1).

- (i) Human recruitment rate (i.e., Λ): Based on data from the World Bank Nigeria and the study by Ibrahim [5, 23], the daily birth rate in Nigeria at the end of 2019 was estimated to be 10,000 individuals. Through simple calculations, the monthly birth rate in Nigeria is approximately 300,000 individuals.

- (ii) Rodent maximum environmental capacity (i.e., K): Based on the study by Barua [12], the maximum environmental carrying capacity of rodents is assumed to be $K = 4 \times 10^8$.
- (iii) Rodent natural mortality rate (i.e., μ_p): According to the study by Ibrahim [23], the daily natural mortality rate of rodents is 0.003. Therefore, the monthly natural mortality rate of rodents in Nigeria can be calculated as $\mu_p = 0.09$.
- (iv) Human natural mortality rate (i.e., μ_h): Data from the World Bank Nigeria indicates that the average life expectancy in Nigeria is 55 years [5]. Thus, the monthly natural mortality rate of humans can be calculated as $\mu_h = 0.0015$.
- (v) Proportion of severe infections (i.e., θ): According to reports from the World Health Organization (WHO) [2], the ratio of mild to severe cases of Lassa fever is 1:4. Therefore, the proportion of severe infections is $\theta = 0.2$.
- (vi) Human incubation rate (i.e., ρ): Based on Barua's article [12], different latent rates of Lassa fever are proposed in the presence and absence of isolation measures. Therefore, we take into comprehensive consideration the protective measures, and we assume $\rho = 1.2$.
- (vii) Progression rates from I_a and I_m to R (i.e., γ_a, γ_m) and disease-induced death rates for humans (i.e., d): Based on studies by Musa [33] and Abidemi [6], we assume $\gamma_a = 2$, $\gamma_m = 0.369$, and $d = 6.3$.

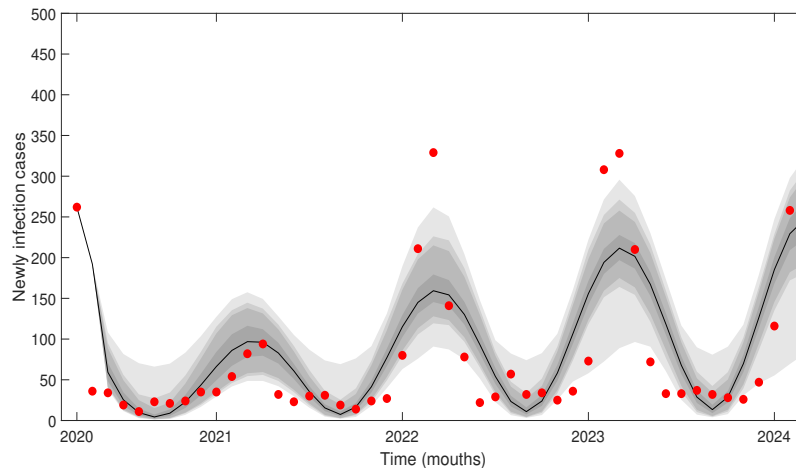


Figure 3. Fitting results of Lassa fever infection cases in Nigeria.

The known data in Table 2 includes a representative sample set of all parameters, which were generated from the literature and the range of parameters obtained from the World Bank website [5, 16]. Based on article [36], we can obtain the initial values for each compartment: $S_p(0) = 3 \times 10^8$, $I_p(0) = 1 \times 10^6$, $S_h(0) = 2 \times 10^8$, $I_a(0) = 210$, $I_m(0) = 52$, $R(0) = 1.4 \times 10^4$. Using the actual data in Table 2, the unknown parameters in the model are estimated by fitting through the MCMC algorithm. The fitting result is shown in Figure 3, where the red dots represent the actual

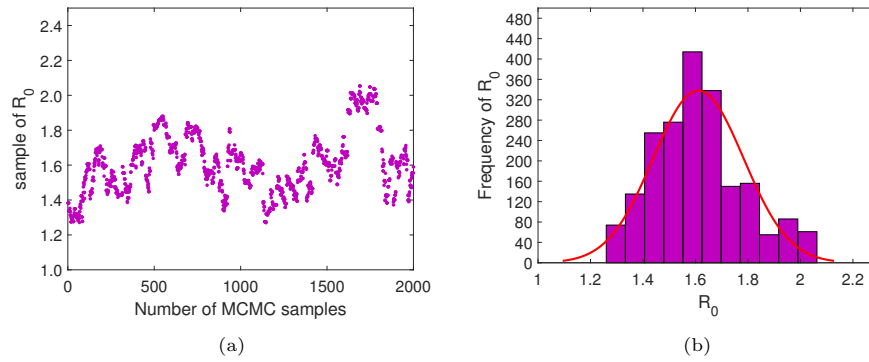


Figure 4. (a) Markov chain for the last 2000 samples of \mathcal{R}_0 . The purple dots represent the size of the \mathcal{R}_0 values. (b) The frequency distribution of \mathcal{R}_0 . The red curve is the probability density function curve for \mathcal{R}_0 .

Table 2. The value of the parameter of system (2.1).

Parameters	Units	Std	Mean Value	Reference
K	-	-	4×10^8	ii
Λ	Persons month ⁻¹	-	300000	i
μ_p	month ⁻¹	-	0.09	iii
μ_h	month ⁻¹	-	0.0015	iv
θ	-	-	0.2	v
ρ	month ⁻¹	-	1.2	vi
γ_a	month ⁻¹	-	2	vii
γ_m	month ⁻¹	-	0.369	vii
d	month ⁻¹	-	6.3	vii
a_1	-	0.14664	0.3078	MCMC
a_2	-	0.39415	0.1721	MCMC
a_3	-	8.737×10^{-6}	1.462×10^{-5}	MCMC
a_4	-	0.081795	0.90097	MCMC
ϕ	-	0.15879	8.7792	MCMC
δ	month ⁻¹	0.095324	0.14815	MCMC
σ	-	0.24791	0.32681	MCMC
c	-	0.052982	0.14236	MCMC
β_p	-	0.065942	0.24076	MCMC
β_{hp}	-	0.14163	0.2211	MCMC
β_a	-	0.053247	0.1494	MCMC
β_m	-	0.10312	0.16968	MCMC
$G(0)$	Number	5.3403×10^5	1.0735×10^7	MCMC
$E(0)$	Number	26	216	MCMC

infection data, the black lines represent the fitted cases, and the gray areas, ranging from the brightest to the darkest, represent the posterior distribution limits of 50%, 90%, 95%, and 99% of the system (2.1).

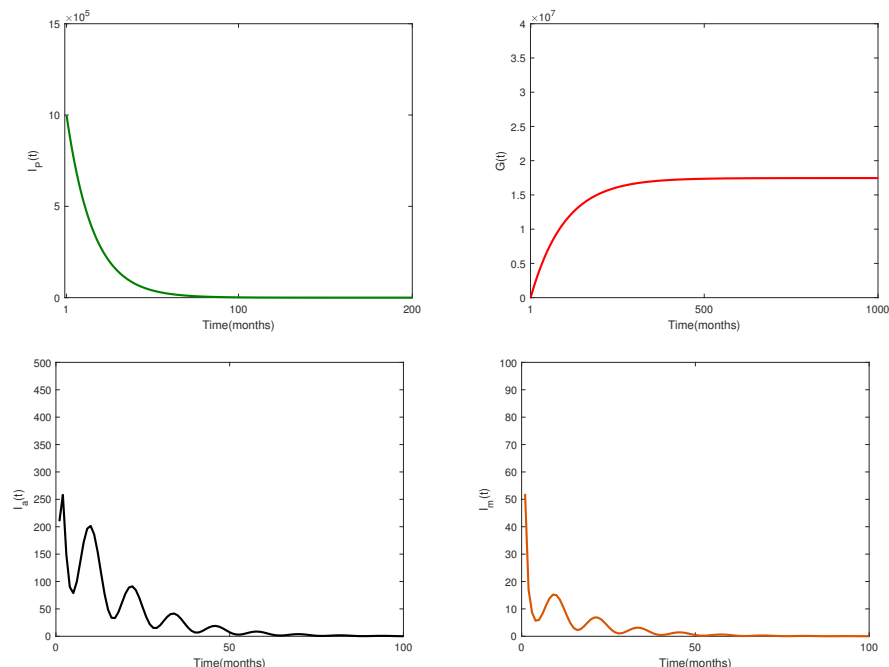


Figure 5. Lassa fever will gradually disappear, when $\mathcal{R}_0 < 1$.

From the fitted curve in Figure 3, it is evident that the number of Lassa fever infections in Nigeria has been increasing year by year, showing a clear periodic pattern. Using the parameters in Table 2, we apply the theory proposed by Wang and Zhao [44] to calculate the basic reproduction number for the periodic system (2.1). The basic reproduction number \mathcal{R}_0 can be calculated by Lemma 3.2(2), and the estimated value of \mathcal{R}_0 is 1.6237, as shown in Figure 4. From Figure 4(b), we can see that the basic reproduction number \mathcal{R}_0 follows a normal distribution. Therefore, we can easily obtain the confidence interval and mean value of \mathcal{R}_0 .

We use the method of Wang and Zhao [44] to numerically calculate the basic reproduction number \mathcal{R}_0 . According to Theorem 4.1, we know that when $\mathcal{R}_0 < 1$, the disease will disappear, in which case the long-term dynamics of Lassa fever infection between humans and rodents are shown in Figure 5. This indicates that when $\mathcal{R}_0 < 1$, the only disease-free equilibrium point P_0 is globally asymptotically stable.

According to Theorem 4.2, when $\mathcal{R}_0 > 1$, the system (2.1) has a positive T -period solution, Figure 6 shows the persistence of the disease at $\mathcal{R}_0 = 1.6237$. Obviously, the simulation results are in agreement with our theoretical results.

Figure 6 also illustrates the long-term behavior of Lassa fever infectivity between humans and rodents. These results suggest that Lassa fever in Nigeria will persist and fluctuate cyclically in the coming years unless additional measures are taken.

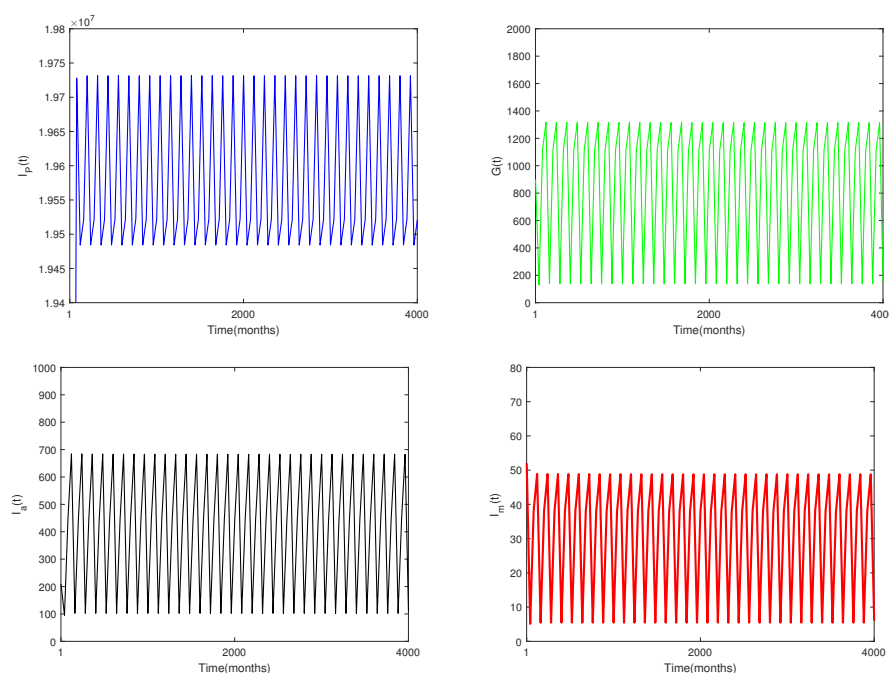


Figure 6. The uniform persistence of Lassa fever $\mathcal{R}_0 = 1.6237 > 1$, the parameters are shown in Table 2.

6.3. Simulation of optimal control

In this section, the influence of several control measures on the epidemic and the change in the number of infected persons under optimal control are studied. For the numerical simulation, assume that the initial values of the system (2.1) are: $S_p(0) = 3 \times 10^8$, $I_p(0) = 1 \times 10^6$, $S_h(0) = 2 \times 10^8$, $G(0) = 1.0002 \times 10^7$, $E(0) = 227$, $I_a(0) = 210$, $I_m(0) = 52$, $R(0) = 1.4 \times 10^4$, and the values of other parameters are shown in Table 2. To compare the effectiveness of the measures, the following simulation analysis is conducted.

To study the effects of different control measures on Lassa fever infection, the number of infected people under various control measures will be simulated over time. Figure 7(a) and Figure 7(b) show how the number of infected people changes over time when only control measure u_1 is applied, without other control measures. From the figure, it can be observed that controlling rodents can effectively reduce the number of infected people. As the control intensity (i.e., u_1) increases, the number of infected people decreases more significantly. Figure 7(c) and Figure 7(d) show the implementation of the single control variable u_3 (i.e., vaccination). It can be observed that as the vaccination rate increases, the number of infected people decreases more significantly.

Further, we discuss the impact of control measures on reducing the number of Lassa fever cases. Figure 8(a) shows that the number of infections decreases significantly with two control measures (i.e., increased use of external protection and vaccination), but it does not make the disease extinct in a short period. Figure 8(b) shows that when three control measures are implemented (i.e., increasing the rate of external protection, vaccination, and increasing treatment rates), the number of

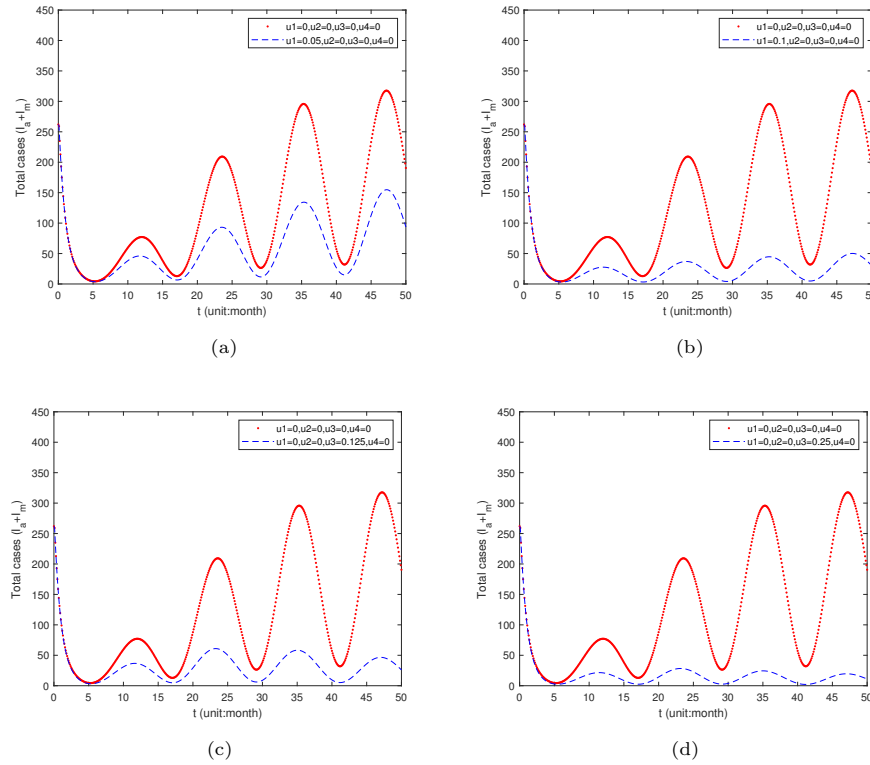


Figure 7. The number of individuals infected with Lassa fever over time when a control measure u_1 or u_3 is implemented.

infections decreases rapidly and shows a more pronounced effect. Figure 8(c) shows the implementation of the four control measures. Even weaker control measures are sufficient to effectively control and eradicate the spread of the disease within 25 months. Figure 8(d) shows the change in the number of infected people over time under optimal control. In this case, the disease does not break out and can be controlled in a short time, demonstrating that optimal control is more effective than the previous measures.

6.4. Effect of changes in model parameters on disease

In this section, in order to find more effective control measures, we compare the impact of parameters on the number of new infections. Firstly, in the absence of external protection ($\sigma = 1$), external protection has no effect. Then, the impact of external protection efficiency (σ) and other parameters on the number of new infections is analyzed [26]. Finally, we analyze the effect of the rate of external protection and the efficiency of external protection of susceptible individuals on the population of new infections.

Figure 9(a) shows the effect of changes in rodent-to-rodent transmission rates (β_p) on new infections, Figure 9(b) shows the effect of changes in rodent-to-human transmission rates ($\beta_{ph}(t)$) on new infections, Figure 9(c) shows the effect of changes

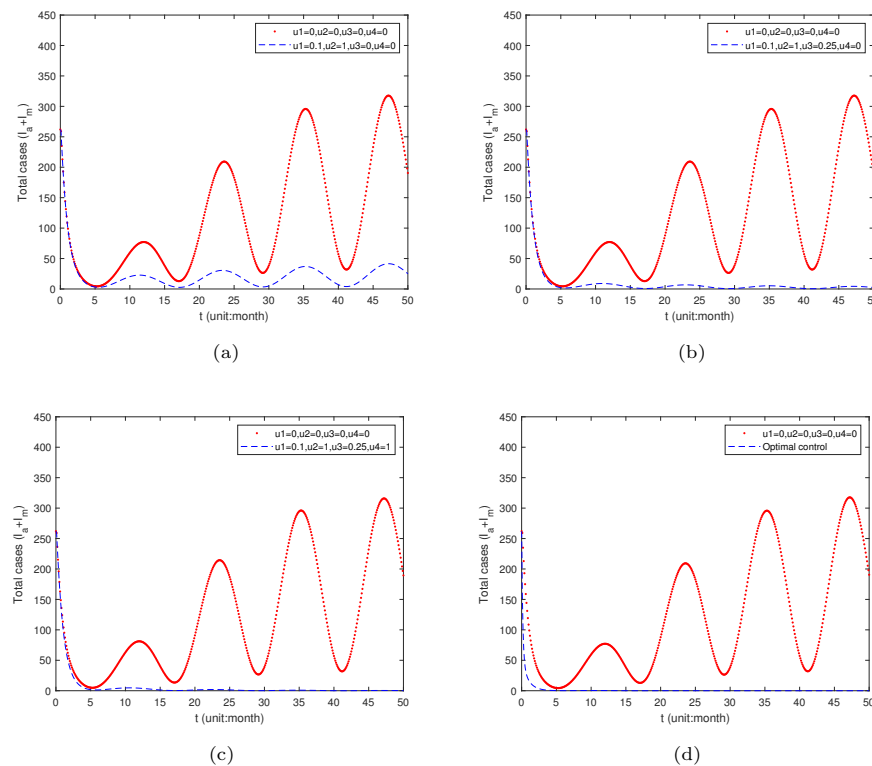


Figure 8. (a) The number of infected individuals over time with the implementation of two control measures u_2 and u_3 . (b) The number of infected individuals over time with the implementation of the three control measures u_2 , u_3 and u_4 . (c) The number of infected individuals over time with the implementation of the four control measures. (d) The number of infected individuals over time with optimal control.

in external protection efficiency (σ) on new infections, Figure 9(d) shows the effect of changes in rodent birth rate ($\Pi(t)$) on new infections, Figure 9(e) shows the effect of changes in the transmission rate (β_a) among mildly infected individuals on new infections, and Figure 9(f) shows the effect of changes in the external protection failure rate (δ) on new infections. The figures show that the rate of rodent-to-rodent transmission (β_p), rodent-to-human transmission rate ($\beta_{ph}(t)$) and the efficiency of external protection (σ) have a significant impact on new infections. In particular, changes in the transmission rate between rodents can lead to a large increase or decrease in new infections, which show cyclical fluctuations annually. However, the external protection failure rate (δ), rodent birth rate ($\Pi(t)$) and transmission rate (β_a) among mildly infected individuals have little effect on new infections, particularly the change in the external protection failure rate.

As can be observed from Figure 10(a) and Figure 10(b), as the external protection efficiency and the external protection rate of susceptible individuals increase, the infection level decreases, the number of new infections declines, and the seasonal fluctuations in infection levels at high coverage of external protection diminish. When the external protection efficiency increases from 20% to 80%, there is a significant reduction in the number of new infections, especially during the peak

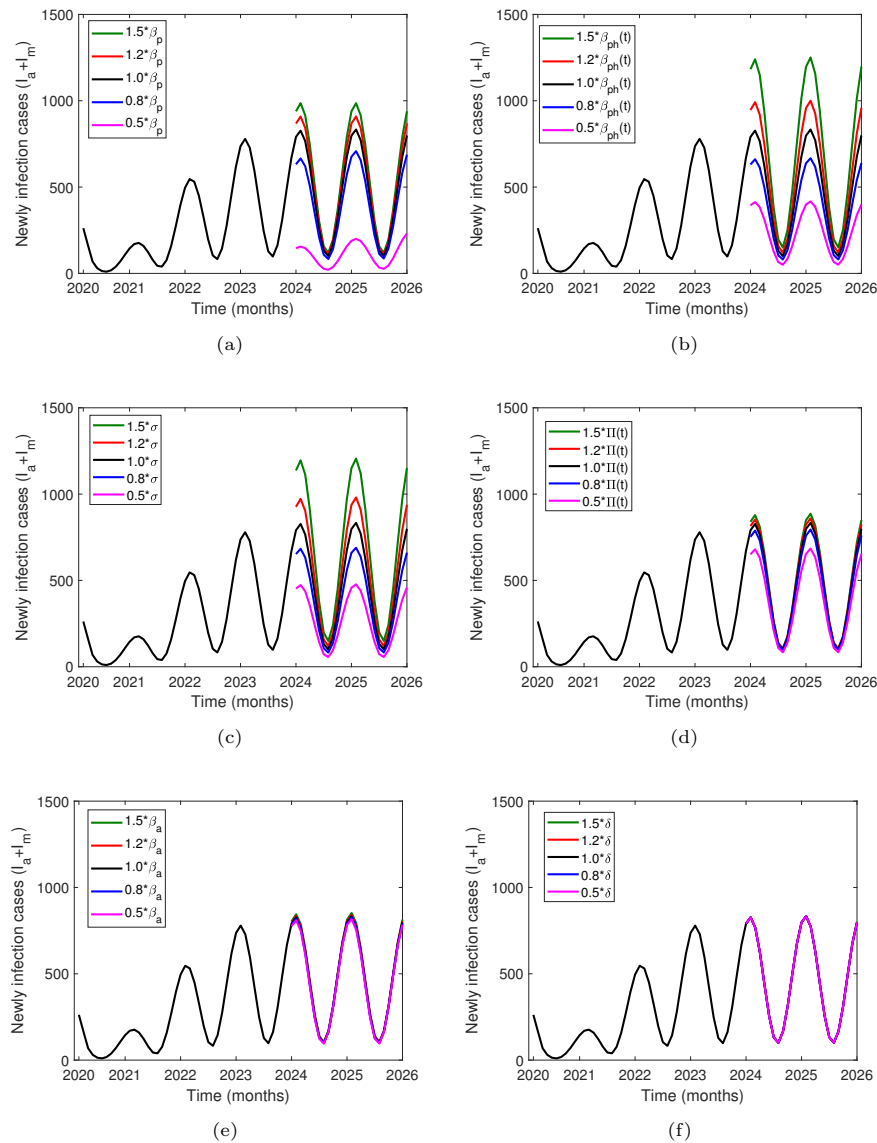


Figure 9. Effect of parameter changes in the system (2.1) on new infections.

period, where the number drops from about 500 new infections per month to around 100. Therefore, external protection efficiency has a significant impact on the number of new infections, and efficient external protection measures can effectively slow down the development of the epidemic.

7. Discussion

In this paper, our main work is to study a mathematical model of the periodic transmission of Lassa fever between humans and rodents, and to analyze the effect

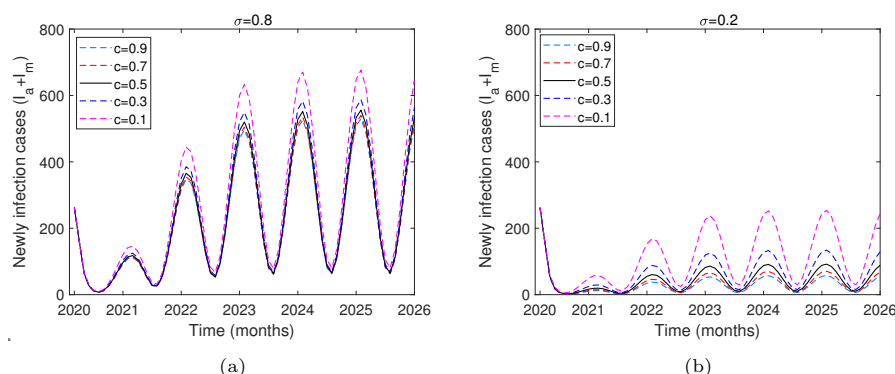


Figure 10. Changes over time in the number of newly infected individuals at different levels of external protection efficiency and external protection rate of susceptible individuals.

of external protection on the spread of the disease. We conclude that the use of external protection can help reduce the spread of Lassa fever and is an effective means of controlling the outbreak. Moreover, we derive the basic reproduction number \mathcal{R}_0 , and compute it numerically [31]. It is proved that the Lassa fever outbreak dynamics are determined by the basic reproduction number \mathcal{R}_0 . As shown in Figure 5 and Figure 6, if $\mathcal{R}_0 > 1$, the disease is persistently endemic, with at least one positive periodic solution. If $\mathcal{R}_0 < 1$, the disease-free periodic solution P_0 is globally asymptotically stable, and the disease becomes extinct.

The baseline values of the unknown parameters of system (2.1) and the initial values of the compartments were estimated using the MCMC algorithm, with data obtained from the Lassa fever infection data for the period of March 2020 to February 2024 provided by the Nigerian Centers for Disease Control and Prevention. Our study analyzes the changes in the extent of disease infection under different interventions, showing that even weaker control measures are sufficient to effectively control and eradicate the spread of the disease over a 25-month period when multiple measures are implemented simultaneously. Subsequently, an optimal solution is provided, where the disease does not break out and can be controlled within a short period.

To identify more effective control measures, we analyzed the effects of different parameters on the number of new infections and observed the impact of external protection efficiency and transmission rates on the Lassa fever outbreak through numerical simulations. The efficiency of external protection has a significant impact on the number of new infections, and seasonal fluctuations are reduced under high coverage of external protection, as shown in Figure 10. As observed in Figures 9(a) and 7(b), the most important factors influencing the cyclical recurrence of Lassa fever are the rodent transmission rate and mortality.

The simulation results suggest that, without additional interventions, Lassa fever will persist and continue to fluctuate cyclically in Nigeria for the foreseeable future. Therefore, we hypothesize that complete eradication of the disease will require not only controlling human contact with zoonotic hosts but also addressing rodent transmission—either by strengthening external protective measures, improving personal diet and hygiene, or implementing more effective rodent control and rat extermination strategies. This control approach is equally applicable to the spread

of Lassa fever in other countries and regions.

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