



Research article

Modelling and analysis of the HIV/AIDS epidemic with fast and slow asymptomatic infections in China from 2008 to 2021

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Abstract: The aim of this paper is to investigate the spread of the HIV/AIDS epidemic in China during 2008–2021. A new mathematical model is proposed to study the dynamics of HIV transmission with acute infection, fast asymptomatic infections, and slow asymptomatic infections. The basic reproduction number is obtained by the next-generation matrix method. A quantitative analysis of the model, including the local behavior, global behavior, and permanence, is performed. Numerical simulations are presented to enhance the results of these analyses. The behavior or the model's parameters are estimated from real data. A sensitivity analysis shows that the proportion of asymptomatic infections co-infected with other diseases significantly affects the basic reproduction number. We further analyze the impact of implementing single and multiple measure(s) in parallel with the epidemic. The study results conclude that multiple measures are more effective in controlling the spread of AIDS compared to just one. The HIV epidemic can be effectively curbed by reducing the contact rate between fast asymptomatic infected individuals and susceptible populations, increasing the early diagnosis and screening of HIV-infected individuals co-infected with other diseases, and treating co-infected patients promptly.

Keywords: HIV/AIDS; asymptomatic infection; global stability; sensitivity analysis

1. Introduction

Human Immunodeficiency Virus (HIV) is a virus that attacks the human immune system. When the virus severely compromises the body's immune system [1], it results in acquired immunodeficiency syndrome (AIDS), which is an advanced stage of HIV infection. AIDS caused by HIV infection has been widely spread in different countries and regions since the first HIV case was discovered in the United States in 1981 [2]. In 2021, 38.4 million people were living with HIV globally, and as many as 650,000 people have died from HIV-related causes [3]. In China, Yunnan Province was the first region to experience an AIDS epidemic, which has continuously spread through most of China since

then [4–6]. In the past few years, the number of people living with HIV in China has rapidly increased. By the end of 2020, 1,053,000 people have been diagnosed with HIV, with 351,000 cumulative deaths reported in China. Moreover, an increasing number of HIV-infected patients are beginning to develop clinical AIDS [7]. More details on the evolution of the HIV/AIDS epidemic in China can be found in [8–12].

In recent years, many scholars have adopted the idea of compartment modelling, which divides the total population into corresponding categories, to study the transmission and development of AIDS within the population and to reflect the dynamics of the HIV epidemic. These models can provide short- or long-term predictions of HIV/AIDS incidences and have become an important tool in analyzing the transmission and control of HIV/AIDS. Hyman et al. [13] developed a staged progression model which subdivided the infected population into n subgroups. Each infected subgroup has a different impact on disease transmission. Mccluskey [14] studied an HIV/AIDS model with multistage infection. Naresh et al. [15] proposed a nonlinear mathematical model to analyze the effect of contact tracing to reduce the transmission of HIV/AIDS in a homogeneous population. In the model, the population was divided into four subcategories: susceptible individuals, HIV-positive infected individuals who did not know they were infected, HIV-positive infected individuals who knew they were infected, and people living with AIDS. Hattaf and Dutta [16] developed an epidemic model with three classes and considered the cure of infected individuals during the latent phase. Wattanasirikosone et al. [17] considered two groups of infected individuals-HIV and AIDS-and introduced a mathematical model with treated and monitored patients. Xue and Sun et al. [18] developed a six-dimensional compartmental model to study the dynamics of HIV transmission; the population was divided into susceptible, latent, consciously infected, unconsciously infected, treated, and AIDS patients. They proved the existence and stability of disease-free and endemic equilibria. Cheneke et al. [19] constructed a susceptible-window period-HIV-AIDS (SWIA) model of HIV/AIDS transmission incorporating stage progression. Suppose that a population N is divided into susceptible (S), window stage (W), HIV-stage (I), and AIDS-stage (A) individuals. Their model is shown below:

$$\begin{cases} \dot{S}(t) = \lambda - \frac{\lambda}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - \mu S, \\ \dot{W}(t) = \frac{\lambda}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - (\rho + \mu)W, \\ \dot{I}(t) = \rho W - (\eta + \mu)I, \\ \dot{A}(t) = \eta I - (\delta + \mu)A, \end{cases}$$

where λ is the recruitment rate of the susceptible population, β_1 , β_2 and β_3 are the transmission rates of W , I and A , respectively, the parameter ρ is the transfer rate of individuals from the window phase to the HIV phase, and η is the transfer rate of individuals from the HIV phase to transfer to the AIDS phase. Here, μ and δ are the natural mortality rate and the AIDS mortality rate, respectively. Through the aforementioned analysis, these models often ignore the impact of asymptomatic infection. Thus, asymptomatic infections should be considered in HIV/AIDS transmission.

In practice, HIV/AIDS patients can develop multiple opportunistic infections due to immunodeficiency, and diseases such as tuberculosis and hepatitis C are secondary infections with both high morbidity and mortality [20–22]. The co-infection may increase the risk of AIDS and seriously affects HIV/AIDS patients [23–25]. Compared to HIV/AIDS patients without other diseases, the patients co-infected with HIV/AIDS have a shorter asymptomatic period. Thus, it should distinguish between HIV/AIDS patients with or without co-infection by either describing the fast or

slow progression, respectively. Now that co-infections have become a serious public health challenge, our findings can provide effective recommendations to public health authorities and have important implications in terms of improving the quality of patient survival. In our work, a five-dimensional mathematical model is developed to describe a more complex system of HIV transmission dynamics. Two different asymptomatic infections are emphasized, generally agreeing with the actual epidemic. This paper differs from other models of HIV/AIDS infections in that it takes the fast and slow asymptomatic phases that characterize the course of HIV infection due to co-infection into account for the model.

The remaining sections are organized as follows. Section 2 collects data on the number of HIV/AIDS patients and death cases reported in China from January 2008 to December 2021. In Section 3, we establish a five-dimensional system focusing on asymptomatic compartments, considering a model of the HIV epidemic with two asymptomatic infections. Moreover, the global asymptotic stability of disease-free and endemic equilibria is analyzed. Based on the data set, a parameter estimation is performed in Section 4 using a genetic algorithm. The parameter estimation results are used to analyze the model in Section 5. A concluding remark is provided in Section 6.

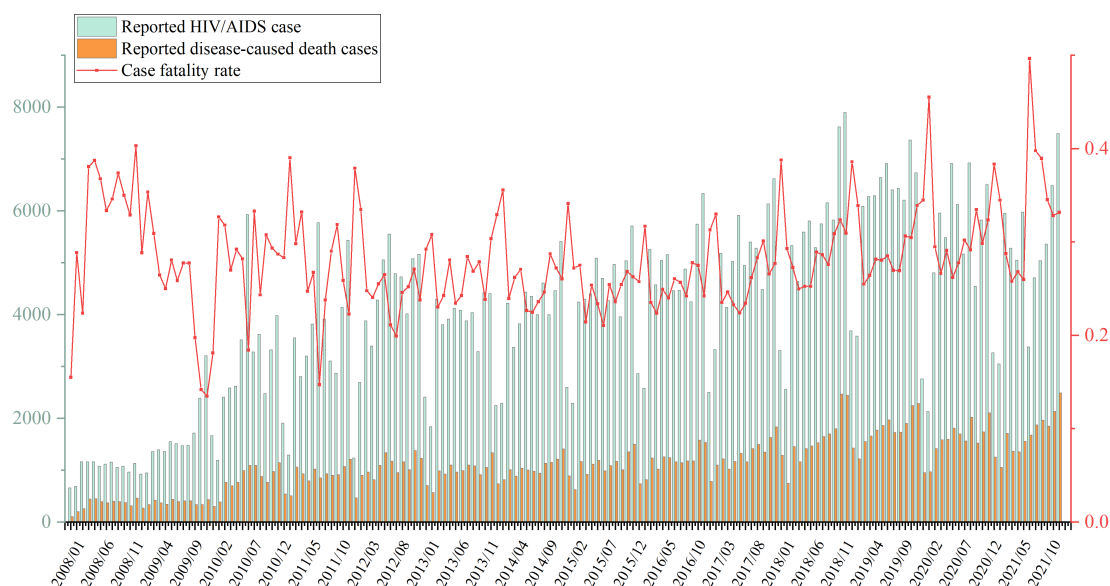


Figure 1. Reported HIV/AIDS individuals by month, 2008.1–2021.12.

2. HIV/AIDS data

HIV is mainly transmitted through blood, from mother-to-child, and by sexual contact. It will attack the immune system after entering the human body, resulting in different degrees of immune dysfunction. Generally, HIV has an average incubation period of 10 years within the human body. The progression for HIV-infected patients to AIDS usually requires a natural process. It is clinically divided into three stages. (i) The first stage of the acute infection period, usually classified as the primary HIV infection, includes body symptoms such as fevers, sore throats, and rashes, of which usually return to normal after two to three weeks. (ii) The second stage is classified as the asymptomatic infection period, where individuals infected with HIV do not have any symptoms; infection is only detected

by positive HIV antibodies within blood tests. Patients do not display any symptoms and live and work for many years as normal. (iii) The third stage is classified as the AIDS period, in which the immune function is completely broken down and the patient develops various severe syndromes until their inevitable death. Thus, mathematical models are used to study the developmental process of HIV and HIV co-infection with other diseases, reveal the infection pattern, and predict the changing trend.

With the expansion of HIV testing, the number of AIDS patients has been increasing. The number of AIDS patients in 2021 was 4.9 times that of 2008. The number of living HIV and AIDS patients has officially exceeded 1 million. For HIV-infected and AIDS patients, male cases were higher than female ones. Curbing the AIDS epidemic is crucial for China. The onset and death data from the National Health Commission of the People's Republic of China was collected from January 1, 2008, to December 31, 2021. According to the Chinese Center for Disease Control and Prevention, by March 31, 2018, the number of living HIV/AIDS patients reached 789,617, and the number of death cases reached 245,498. By calculation, the cumulative number of surviving HIV/AIDS cases was approximately 361,270, and the number of deaths was approximately 245,000 by the end of 2007. Figure 1 shows the cumulative number of HIV/AIDS survivors, deaths from the disease, and the case fatality rate.

3. An HIV/AIDS model and dynamic properties

In our work, infected individuals are divided into acutely, slowly, and rapidly asymptomatic infected individuals. Suppose that all AIDS patients will self-isolate and not spread the infection. Patients with HIV/AIDS can develop multiple opportunistic infections due to immunodeficiency. When HIV-infected patients are co-infected with other diseases, the disease progresses rapidly, and the asymptomatic period becomes shorter. Unless HIV-infected patients are promptly screened and treated for other diseases, the progression to AIDS will be accelerated. In contrast to other models of HIV/AIDS epidemics, this paper considers the course of infection in HIV co-infection with other diseases. We will distinguish between co-infected and unco-infected AIDS patients by describing the rapid and slow progression of HIV/AIDS. An HIV/AIDS epidemiological model containing two different asymptomatic infections is developed to analyze the transmission of HIV between individuals. The population is divided into five compartments: susceptible (S), acute infection (W), fast asymptomatic infection (I_s), slow asymptomatic infection (I_l), and AIDS (A). The total number of individuals at time t is $N(t)$, that is, $N(t) = S(t) + W(t) + I_s(t) + I_l(t) + A(t)$. The model is established as follows:

$$\begin{cases} \dot{S}(t) = b - \mu S(t) - \beta_1 S(t)W(t) - \beta_2 S(t)I_s(t) - \beta_3 S(t)I_l(t), \\ \dot{W}(t) = \beta_1 S(t)W(t) + \beta_2 S(t)I_s(t) + \beta_3 S(t)I_l(t) - (\varepsilon + \mu)W(t), \\ \dot{I}_s(t) = p\varepsilon W(t) - (\omega_1 + \sigma_1 + \mu)I_s(t) + \omega_2 I_l(t), \\ \dot{I}_l(t) = (1 - p)\varepsilon W(t) - (\omega_2 + \sigma_2 + \mu)I_l(t) + \omega_1 I_s(t), \\ \dot{A}(t) = \sigma_1 I_s(t) + \sigma_2 I_l(t) - (d + \mu)A(t), \end{cases} \quad (1)$$

where all parameters of model (1) are defined in Table 1. Figure 2 shows a schematic diagram of the HIV/AIDS model for the two asymptomatic infections.

For convenience, let $p_1 = p\varepsilon$, $p_2 = (1 - p)\varepsilon$, $m = -(\omega_1 + \sigma_1 + \mu)$, $n = -(\omega_2 + \sigma_2 + \mu)$. Then, model

(1) is rewritten as follows:

$$\begin{cases} \dot{S}(t) = b - \mu S(t) - \beta_1 S(t)W(t) - \beta_2 S(t)I_s(t) - \beta_3 S(t)I_l(t), \\ \dot{W}(t) = \beta_1 S(t)W(t) + \beta_2 S(t)I_s(t) + \beta_3 S(t)I_l(t) - (\varepsilon + \mu)W(t), \\ \dot{I}_s(t) = p_1 W(t) + mI_s(t) + \omega_2 I_l(t), \\ \dot{I}_l(t) = p_2 W(t) + nI_l(t) + \omega_1 I_s(t), \\ \dot{A}(t) = \sigma_1 I_s(t) + \sigma_2 I_l(t) - (d + \mu)A(t). \end{cases} \quad (2)$$

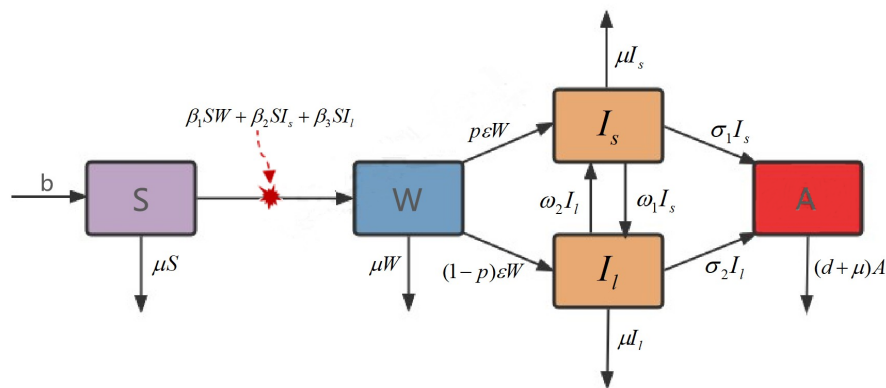


Figure 2. Flow diagram of the model with two asymptomatic infections.

Table 1. The definition of parameters in model (1).

| Parameter | Description |
|---------------|---|
| b | The birth rate of population |
| μ | The natural death rate of population |
| d | The death-diseased rate of population |
| β_1 | The infection rate of acute infection period |
| β_2 | The infection rate of fast asymptomatic infection |
| β_3 | The infection rate of slow asymptomatic infection |
| p | The proportion of individuals with co-infection detected by early diagnosis and screening |
| ε | The conversion rate from the acute infection period to the asymptomatic infection |
| σ_1 | The conversion rate from fast asymptomatic infection to the AIDS period |
| σ_2 | The conversion rate from slow asymptomatic infection to the AIDS period |
| ω_1 | The cure rate of other diseases |
| ω_2 | The proportion of HIV asymptomatic infected individuals co-infected with other diseases |
| W_0 | The initial value of the acute infection period compartment |
| I_{s0} | The initial value of the fast asymptomatic infection compartment |
| I_{l0} | The initial value of the slow asymptomatic infection compartment |

In model (2), the disease-free equilibrium point is $E_0 = (\frac{b}{\mu}, 0, 0, 0, 0)$. Based on the model, it is easy to obtain the following result.

Lemma 1. Let $S(0) \geq 0$, $W(0) \geq 0$, $I_s(0) \geq 0$, $I_l(0) \geq 0$, $A(0) \geq 0$ be the initial values of model (2). Then, the feasible region

$$X = \left\{ (S(t), W(t), I_s(t), I_l(t), A(t)) \in \mathbb{R}_+^5, N(t) \leq \frac{b}{\mu} \right\}$$

is a positive invariant set, where $N(t) = S(t) + W(t) + I_s(t) + I_l(t) + A(t)$.

Lemma 1 shows that $\limsup_{t \rightarrow \infty} N(t) \leq \frac{b}{\mu}$. It means that $S(t)$, $W(t)$, $I_s(t)$, $I_l(t)$ and $A(t)$ are ultimately bounded. The basic reproduction number R_0 is the threshold parameter of the epidemic models. Here, we calculate it using the next-generation matrix method [26]. Let $Y = (W(t), I_s(t), I_l(t), A(t))^T$; model (2) can be written as follows:

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

where

$$\mathcal{F}(x) = \begin{pmatrix} \beta_1 S(t)W(t) + \beta_2 S(t)I_s(t) + \beta_3 S(t)I_l(t) \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad \mathcal{V}(x) = \begin{pmatrix} (\varepsilon + \mu)W(t) \\ -mI_s(t) - p_1W(t) - \omega_2I_l(t) \\ -nI_l(t) - p_2W(t) - \omega_1I_s(t) \\ (d + \mu)A(t) - \sigma_1I_s(t) - \sigma_2I_l(t) \end{pmatrix}.$$

The Jacobian matrix of $\mathcal{F}(x)$ and $\mathcal{V}(x)$ can be obtained as follows:

$$F = D\mathcal{F}(E_0) = \begin{pmatrix} \beta_1 \frac{b}{\mu} & \beta_2 \frac{b}{\mu} & \beta_3 \frac{b}{\mu} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad V = D\mathcal{V}(E_0) = \begin{pmatrix} \varepsilon + \mu & 0 & 0 & 0 \\ -p_1 & -m & -\omega_2 & 0 \\ -p_2 & -\omega_1 & -n & 0 \\ 0 & -\sigma_1 & -\sigma_2 & d + \mu \end{pmatrix}.$$

Thus, the basic reproduction number R_0 of model (2) is as follows:

$$R_0 = \rho(FV^{-1}) = \frac{\beta_1 b}{\mu(\varepsilon + \mu)} + \frac{\beta_2 b(p_2 \omega_2 - p_1 n) + \beta_3 b(p_1 \omega_1 - p_2 m)}{\mu(\varepsilon + \mu)(mn - \omega_1 \omega_2)}.$$

Since $mn - \omega_1 \omega_2 = (\omega_1 + \sigma_1 + \mu)(\omega_2 + \sigma_2 + \mu) - \omega_1 \omega_2 > 0$, $p_2 \omega_2 - p_1 n = (1 - \varepsilon)p\omega_2 + p\varepsilon(\omega_2 + \sigma_2 + \mu) > 0$, $p_1 \omega_1 - p_2 m = p\varepsilon\omega_1 + (1 - p)\varepsilon(\omega_1 + \sigma_1 + \mu) > 0$, we have $R_0 > 0$.

If $R_0 > 1$, model (2) has a positive equilibrium $E^* = (S^*, W^*, I_s^*, I_l^*, A^*)$ given by the following:

$$\begin{cases} S^* = \frac{(\varepsilon + \mu)(mn - \omega_1 \omega_2)}{\beta_1(mn - \omega_1 \omega_2) + \beta_2(\omega_2 p_2 - p_1 n) + \beta_3(\omega_1 p_1 - p_2 m)}, \\ W^* = \frac{b}{\varepsilon + \mu} + \frac{\mu(mn - \omega_1 \omega_2)}{\beta_1(mn - \omega_1 \omega_2) + \beta_2(\omega_2 p_2 - p_1 n) + \beta_3(\omega_1 p_1 - p_2 m)}, \\ I_s^* = \frac{b(\omega_2 p_2 - p_1 n)}{(\varepsilon + \mu)(mn - \omega_1 \omega_2)} + \frac{\mu(\omega_2 p_2 - p_1 n)}{\beta_1(mn - \omega_1 \omega_2) + \beta_2(\omega_2 p_2 - p_1 n) + \beta_3(\omega_1 p_1 - p_2 m)}, \\ I_l^* = \frac{b(\omega_1 p_1 - p_2 m)}{(\varepsilon + \mu)(mn - \omega_1 \omega_2)} + \frac{\mu(\omega_1 p_1 - p_2 m)}{\beta_1(mn - \omega_1 \omega_2) + \beta_2(\omega_2 p_2 - p_1 n) + \beta_3(\omega_1 p_1 - p_2 m)}, \\ A^* = \frac{1}{d + \mu} \left(\frac{\sigma_1(\omega_2 p_2 - p_1 n) + \sigma_2(\omega_1 p_1 - p_2 m)}{mn - \omega_1 \omega_2} \right) W^*. \end{cases} \quad (3)$$

Theorem 1. If $R_0 < 1$, the disease-free equilibrium $E_0 = (\frac{b}{\mu}, 0, 0, 0, 0)$ of model (2) is locally asymptotically stable.

Proof. If $R_0 < 1$, we have $\frac{\beta_1 b}{\mu(\varepsilon + \mu)} < 1$. Denote $f = \beta_1 \frac{b}{\mu} - (\varepsilon + \mu) < 0$, $l = -(d + \mu) < 0$. The Jacobian matrix of model (2) at E_0 can be obtained as follows:

$$J(E_0) = \begin{pmatrix} -\mu & -\beta_1 \frac{b}{\mu} & -\beta_2 \frac{b}{\mu} & -\beta_3 \frac{b}{\mu} & 0 \\ 0 & f & \beta_2 \frac{b}{\mu} & \beta_3 \frac{b}{\mu} & 0 \\ 0 & p & m & \omega_2 & 0 \\ 0 & q & \omega_1 & n & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & l \end{pmatrix}.$$

Let

$$J_1(E_0) = \begin{pmatrix} f & \beta_2 \frac{b}{\mu} & \beta_3 \frac{b}{\mu} \\ p_1 & m & \omega_2 \\ p_2 & \omega_1 & n \end{pmatrix}.$$

The characteristic equation is formed by the following:

$$f(\lambda) = |\lambda E - J_1(E_0)| = \begin{vmatrix} \lambda - f & -\beta_2 \frac{b}{\mu} & -\beta_3 \frac{b}{\mu} \\ -p_1 & \lambda - m & -\omega_2 \\ -p_2 & -\omega_1 & \lambda - n \end{vmatrix} = a_0 \lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3,$$

where $a_0 = 1$, $a_1 = -(m + n + f) > 0$, $a_2 = mf + mn + nf - \omega_1 \omega_2 - p_1 \beta_2 \frac{b}{\mu} - p_2 \beta_3 \frac{b}{\mu}$, $a_3 = (\omega_1 \omega_2 - mn)f + n p_1 \beta_2 \frac{b}{\mu} - p_2 \omega_2 \beta_2 \frac{b}{\mu} + m p_2 \beta_3 \frac{b}{\mu} - p_1 \omega_1 \beta_3 \frac{b}{\mu}$.

When $R_0 < 1$, we can calculate the following:

$$\begin{aligned} & \beta_1 \frac{b}{\mu} (mn - \omega_1 \omega_2) + \beta_2 \frac{b}{\mu} (p_2 \omega_2 - p_1 n) + \beta_3 \frac{b}{\mu} (p_1 \omega_1 - p_2 m) < (\varepsilon + \mu) (mn - \omega_1 \omega_2), \\ & (\beta_1 \frac{b}{\mu} - (\varepsilon + \mu)) (mn - \omega_1 \omega_2) - p_1 \beta_2 \frac{b}{\mu} n - p_2 \beta_3 \frac{b}{\mu} m + p_2 \omega_2 \beta_2 \frac{b}{\mu} + p_1 \omega_1 \beta_3 \frac{b}{\mu} < 0, \\ & (mn - \omega_1 \omega_2) f + p_2 \omega_2 \beta_2 \frac{b}{\mu} + p_1 \omega_1 \beta_3 \frac{b}{\mu} < p_1 \beta_2 \frac{b}{\mu} n + p_2 \beta_3 \frac{b}{\mu} m. \end{aligned}$$

There is $\tau \in N^*$ such that $(-p_1 \beta_2 \frac{b}{\mu} - p_2 \beta_3 \frac{b}{\mu}) \tau = p_1 \beta_2 \frac{b}{\mu} n + p_2 \beta_3 \frac{b}{\mu} m$. Hence, we obtain the following:

$$\begin{aligned} a_2 &= mf + mn + nf - \omega_1 \omega_2 + p_1 \beta_2 \frac{b}{\mu} n + p_2 \beta_3 \frac{b}{\mu} m \\ &> mn - \omega_1 \omega_2 + (m + n) f + (mn - \omega_1 \omega_2) f + p_2 \omega_2 \beta_2 \frac{b}{\mu} + p_1 \omega_1 \beta_3 \frac{b}{\mu} \\ &= (mn - \omega_1 \omega_2) (1 + f) + (m + n) f + p_2 \omega_2 \beta_2 \frac{b}{\mu} + p_1 \omega_1 \beta_3 \frac{b}{\mu}. \end{aligned}$$

If $-1 < f < 0$, then $1 + f > 0$. Clearly, $a_2 > 0$. If

$$\frac{(m + n) f + p_2 \omega_2 \beta_2 \frac{b}{\mu} + p_1 \omega_1 \beta_3 \frac{b}{\mu}}{-(mn - \omega_1 \omega_2)} - 1 < f < -1,$$

we have $a_2 > 0$. Since $R_0 < 1$, we obtain the following:

$$\begin{aligned} \frac{\beta_2 \frac{b}{\mu}(p_2\omega_2 - p_1n) + \beta_3 \frac{b}{\mu}(p_1\omega_1 - p_2m)}{mn - \omega_1\omega_2} &< -f, \\ -p_1\beta_2 \frac{b}{\mu}n + p_2\omega_2\beta_2 \frac{b}{\mu} - p_2\beta_3 \frac{b}{\mu}m + p_1\omega_1\beta_3 \frac{b}{\mu} &< -(mn - \omega_1\omega_2)f, \\ p_1\beta_2 \frac{b}{\mu}n - p_2\omega_2\beta_2 \frac{b}{\mu} + p_2\beta_3 \frac{b}{\mu}m - p_1\omega_1\beta_3 \frac{b}{\mu} &> -(\omega_1\omega_2 - mn)f, \\ p_1\beta_2 \frac{b}{\mu}n - p_2\omega_2\beta_2 \frac{b}{\mu} + p_2\beta_3 \frac{b}{\mu}m - p_1\omega_1\beta_3 \frac{b}{\mu} + (\omega_1\omega_2 - mn)f &> 0. \end{aligned}$$

Then, $a_3 = (\omega_1\omega_2 - mn)f + np_1\beta_2 \frac{b}{\mu} - p_2\omega_2\beta_2 \frac{b}{\mu} + mp_2\beta_3 \frac{b}{\mu} - p_1\omega_1\beta_3 \frac{b}{\mu} > 0$. It follows that

$$\begin{aligned} a_1a_2 - a_0a_3 &= -(m+n+f)(mf+mn+nf - \omega_1\omega_2 - p_1\beta_2 \frac{b}{\mu} - p_2\beta_3 \frac{b}{\mu}) - (\omega_1\omega_2 - mn)f \\ &\quad - np_1\beta_2 \frac{b}{\mu} + p_2\omega_2\beta_2 \frac{b}{\mu} - mp_2\beta_3 \frac{b}{\mu} + p_1\omega_1\beta_3 \frac{b}{\mu} \\ &= -m^2f - m^2n - n^2f - n^2m - mf^2 - nf^2 - 2mnf + (m+n)\omega_1\omega_2 \\ &\quad + (m+f)p_1\beta_2 \frac{b}{\mu} + (n+f)p_2\beta_3 \frac{b}{\mu} + p_2\omega_2\beta_2 \frac{b}{\mu} + p_1\omega_1\beta_3 \frac{b}{\mu} \\ &= (m+n)(\omega_1\omega_2 - f^2) + (m+f)(p_1\beta_2 \frac{b}{\mu} - n^2) + (n+f)(p_2\beta_3 \frac{b}{\mu} - m^2) \\ &\quad + p_2\omega_2\beta_2 \frac{b}{\mu} + p_1\omega_1\beta_3 \frac{b}{\mu}. \end{aligned}$$

If $f \leq \min\{\omega_1, \omega_2\}$, $n \leq \min\{p_1, \beta_2, \frac{b}{\mu}\}$, and $m \leq \min\{p_2, \beta_3, \frac{b}{\mu}\}$, then we have $a_1a_2 - a_0a_3 > 0$. According to the Hurwitz criterion, the disease-free equilibrium E_0 of model (2) is locally asymptotically stable. \square

Theorem 2. If $R_0 < 1$, the disease-free equilibrium $E_0 = (\frac{b}{\mu}, 0, 0, 0, 0)$ of model (2) is globally asymptotically stable.

Proof. Let H and K be two positive constants. We construct a Lyapunov function $V = W + HI_s + KI_l$. The derivative of V is calculated as follows:

$$\dot{V} = \dot{W} + HI_s + KI_l. \quad (4)$$

Substituting the model equations into Eq (4), we obtain the following:

$$\dot{V} = \beta_1 S W + \beta_2 S I_s + \beta_3 S I_l - (\epsilon + \mu)W + H(p_1 W + m I_s + \omega_2 I_l) + K(p_2 W + n I_l + \omega_1 I_s).$$

With $S_0 = \frac{b}{\mu}$, we have the following:

$$\dot{V} = \frac{b\beta_1}{\mu} W + \frac{b\beta_2}{\mu} I_s + \frac{b\beta_3}{\mu} I_l - (\epsilon + \mu)W + H(p_1 W + m I_s + \omega_2 I_l) + K(p_2 W + n I_l + \omega_1 I_s)$$

$$= \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + Hp_1 + Kp_2 \right) W + \left(\frac{b\beta_2}{\mu} + mH + \omega_1 K \right) I_s + \left(\frac{b\beta_3}{\mu} + \omega_2 H + nK \right) I_l.$$

To obtain the values of H and K , we can use the following:

$$\frac{b\beta_2}{\mu} + mH + \omega_1 K = 0, \quad \frac{b\beta_3}{\mu} + \omega_2 H + nK = 0. \quad (5)$$

From Eq (5), we can calculate the following:

$$K = \frac{b\beta_2\omega_2 - b\beta_3m}{\mu(mn - \omega_1\omega_2)}, \quad H = \frac{b\beta_3\omega_1m - b\beta_2mn}{\mu(mn - \omega_1\omega_2)}.$$

Hence, we obtain the following:

$$\begin{aligned} \dot{V} &= \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + \frac{bp_1\beta_3\omega_1m - bp_1\beta_2mn}{\mu(mn - \omega_1\omega_2)} + \frac{bp_2\beta_2\omega_2 - bp_2\beta_3m}{\mu(mn - \omega_1\omega_2)} \right) W \\ &= \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + \frac{bp_1\beta_3\omega_1m - bp_1\beta_2mn + bp_2\beta_2\omega_2m - bp_2\beta_3m^2}{\mu(mn - \omega_1\omega_2)} \right) W \\ &= \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + \frac{b\beta_3m(p_1\omega_1 - p_2m) + b\beta_2m(p_2\omega_2 - p_1n)}{\mu(mn - \omega_1\omega_2)} \right) W \\ &= \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + \frac{b\beta_3(p_1\omega_1 - p_2m) + b\beta_2(p_2\omega_2 - p_1n)}{\mu(mn - \omega_1\omega_2)} \right) W. \end{aligned}$$

When $R_0 < 1$, we have the following:

$$\begin{aligned} \frac{\beta_1 b}{\mu(\varepsilon + \mu)} + \frac{\beta_2 b(p_2\omega_2 - p_1n) + \beta_3 b(p_1\omega_1 - p_2m)}{\mu(\varepsilon + \mu)(mn - \omega_1\omega_2)} &< 1, \\ \frac{\beta_2 b(p_2\omega_2 - p_1n) + \beta_3 b(p_1\omega_1 - p_2m)}{\mu(mn - \omega_1\omega_2)} &< (\varepsilon + \mu) - \frac{\beta_1 b}{\mu}, \\ \frac{\beta_2 b(p_2\omega_2 - p_1n) + \beta_3 b(p_1\omega_1 - p_2m)}{\mu(mn - \omega_1\omega_2)} - (\varepsilon + \mu) + \frac{\beta_1 b}{\mu} &< 0. \end{aligned}$$

It follows that

$$\dot{V} = \left(\frac{b\beta_1}{\mu} - (\varepsilon + \mu) + \frac{b\beta_3(p_1\omega_1 - p_2m) + b\beta_2(p_2\omega_2 - p_1n)}{\mu(mn - \omega_1\omega_2)} \right) W < 0.$$

According to LaSalle's invariance principle, the disease-free equilibrium E_0 of model (2) is globally asymptotically stable. \square

Theorem 3. *If $R_0 > 1$, then system (2) is a uniform persistence with respect to $(X_0, \partial X_0)$, i.e., there exists $\xi > 0$ such that any positive solution $(S(t), W(t), I_s(t), I_l(t), A(t))$ of system (2) in X_0 satisfies the following:*

$$\begin{aligned} \liminf_{t \rightarrow \infty} W(t) &\geq \xi, \quad \liminf_{t \rightarrow \infty} I_s(t) \geq \xi, \\ \liminf_{t \rightarrow \infty} I_l(t) &\geq \xi, \quad \liminf_{t \rightarrow \infty} A(t) \geq \xi. \end{aligned}$$

Proof. We begin by defining the following symbols:

$$\begin{aligned} X &= \{(S, W, I_s, I_l, A) \mid S \geq 0, W \geq 0, I_s \geq 0, I_l \geq 0, A \geq 0\}, \\ X_0 &= \{(S, W, I_s, I_l, A) \in X \mid W > 0, I_s > 0, I_l > 0, A > 0\}, \\ \partial X_0 &= X \setminus X_0. \end{aligned}$$

It is obvious that X and X_0 are positivity invariants and system (2) is a point dissipative. In the following, we will show that system (2) is uniformly persistent with respect to $(X_0, \partial X_0)$. For this purpose, we denote the following:

$$M_\partial = \{(S(0), W(0), I_s(0), I_l(0)), A(0) \mid S(t), W(t), I_s(t), I_l(t), A(t) \in \partial X_0, \forall t \geq 0\}.$$

Now, we prove that $M_\partial = \{(S(0), 0, 0, 0, 0) \mid S(0) \geq 0\}$. For convenience, let $M = \{(S(0), 0, 0, 0, 0) \mid S(0) \geq 0\}$. It is clear that $M \subset M_\partial$ and it is only necessary to show that $M_\partial \subset M$. If $(S(0), W(0), I_s(0), I_l(0), A(0)) \in M_\partial$, then $W(0) = I_s(0) = I_l(0) = A(0) = 0$. By contradiction, assume at least one of $W(0)$, $I_s(0)$, $I_l(0)$ or $A(0)$ is greater than zero (e.g., $W(0) > 0$), then we can obtain $I_s(0)$, $I_l(0)$ and $A(0)$, which are all greater than zero in a certain interval, such as $[0, T_1]$. In fact, for $t \in [0, T_1]$, from the inequality $\frac{dW(t)}{dt}|_{(2)} \geq -(\varepsilon + \mu)W(t)$, we have the following:

$$W(t) \geq W(0)e^{-(\varepsilon + \mu)T_1} > 0, \text{ for } t \in [0, T_1].$$

Similarly, we have $I_s(t) \geq I_s(0)e^{mT_1} > 0$, $I_l(t) \geq I_l(0)e^{nT_1} > 0$, and $A(t) \geq A(0)e^{-(d + \mu)T_1} > 0$.

Consequently, $W(0) > 0$ implies that $I_s(t) > 0$, $I_l(t) > 0$ and $A(t) > 0$ for $t \in [0, T_1]$. From the definition of M_∂ , we know that any point in ∂X_0 with $W(t) > 0$ can not belong to M_∂ . A similar idea and procedure shows that any point in ∂X_0 other than $(S(0), 0, 0, 0, 0)$ can not belong to M_∂ . Hence, it is obvious that $M_\partial = \{(S(0), 0, 0, 0, 0) \mid S(0) \geq 0\}$.

The disease-free equilibrium point E_0 is the only equilibrium point in M_∂ . Next, we prove that $W^s(E_0) \cap X_0 = \emptyset$ when $R_0 > 1$, where $W^s(E_0)$ is a stable manifold of E_0 . If it is not true, then there exists a solution (S, W, I_s, I_l, A) in X_0 such that

$$S(t) \rightarrow S(0), W(t) \rightarrow 0, I_s(t) \rightarrow 0, I_l(t) \rightarrow 0, A(t) \rightarrow 0 \text{ as } t \rightarrow \infty.$$

Thus, for any constant $\epsilon > 0$, there exists a $T^* > 0$ such that for any $t \geq T^*$, there is $S(t) \geq S(0) - \epsilon$. Define the following functions $U(t) = W(t)$. When $t \geq T^*$, we have the following:

$$\begin{aligned} \frac{dU(t)}{dt} &= \beta_1 S(t)W(t) + \beta_2 S(t)I_s(t) + \beta_3 S(t)I_l(t) - (\varepsilon + \mu)W(t) \\ &= [\beta_1 S(t) - (\varepsilon + \mu)]W(t) + \beta_2 S(t)I_s(t) + \beta_3 S(t)I_l(t) \\ &\geq [\beta_1(S(0) - \epsilon) - (\varepsilon + \mu)]W(t) + \beta_2(S(0) - \epsilon)I_s(t) + \beta_3(S(0) - \epsilon)I_l(t). \end{aligned}$$

Since $R_0 > 1$, we have $\beta_1 S(0) - (\varepsilon + \mu) > \frac{\beta_2 b(p_2 \omega_2 - p_1 n) + \beta_3 b(p_1 \omega_1 - p_2 m)}{\mu(mn - \omega_1 \omega_2)}$, and it is possible to pick ϵ small enough so that $\beta_1(S(0) - \epsilon) - (\varepsilon + \mu) > 0$, $\beta_2(S(0) - \epsilon) > 0$ and $\beta_3(S(0) - \epsilon) > 0$. Therefore, $U(t)$ is an increasing function on $t \geq T^*$. It follows that $U(t)$ does not tend to be zero when $t \rightarrow \infty$, which is a contradiction. Thus, we have $W^s(E_0) \cap X_0 = \emptyset$. Since E_0 is globally asymptotically stable in M_∂ , E_0 is an isolated invariant set and is acyclic. According to [27], system (2) is uniformly persistent with respect to $(X_0, \partial X_0)$. \square

Theorem 4. If $R_0 > 1$ and $\frac{\beta_2 \omega_2}{p_1} \leq \frac{\beta_3 \omega_1}{p_2}$, the endemic equilibrium $E^* = (S^*, W^*, I_s^*, I_l^*, A^*)$ of model (2) is globally asymptotically stable.

Proof. By Theorem 3, we know that variables S, W, I_s, I_l and A are positive when $R_0 > 1$. We let B and $C > 0$, and construct the following Lyapunov function:

$$V(S, W, I_s, I_l) = (S - S^* - S^* \ln S) + (W - W^* - W^* \ln W) + B(I_s - I_s^* - I_s^* \ln I_s) + C(I_l - I_l^* - I_l^* \ln I_l),$$

where $B = \frac{\beta_2 S^* I_s^*}{p_1 W^*}$, $C = \frac{\beta_3 S^* I_l^*}{p_2 W^*}$.

Let $V(S) = S - S^* - S^* \ln S$, $V(W) = W - W^* - W^* \ln W$, $V(I_s) = I_s - I_s^* - I_s^* \ln I_s$, $V(I_l) = I_l - I_l^* - I_l^* \ln I_l$. The four functions $V(S)$, $V(W)$, $V(I_s)$, and $V(I_l)$ are derived alongside the solution of system (2):

$$\begin{aligned} \dot{V}(S) &= \left(1 - \frac{S^*}{S}\right) (\mu S^* + \beta_1 S^* W^* + \beta_2 S^* I_s^* + \beta_3 S^* I_l^* - \mu S - \beta_1 S W - \beta_2 S I_s - \beta_3 S I_l) \\ &= (\mu S^* + \beta_1 S^* W^* + \beta_2 S^* I_s^* + \beta_3 S^* I_l^* - \mu S - \beta_1 S W - \beta_2 S I_s - \beta_3 S I_l) \\ &\quad - \left(\mu \frac{S^*}{S} + \beta_1 \frac{S^*}{S} W^* + \beta_2 \frac{S^*}{S} I_s^* + \beta_3 \frac{S^*}{S} I_l^* - \mu S^* - \beta_1 S^* W - \beta_2 S^* I_s - \beta_3 S^* I_l\right) \\ &= \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \beta_1 S^* W^* \left(1 - \frac{S W}{S^* W^*} - \frac{S^*}{S} + \frac{W}{W^*}\right) + \beta_2 S^* I_s^* \left(1 - \frac{S I_s}{S^* I_s^*} - \frac{S^*}{S} + \frac{I_s}{I_s^*}\right) \\ &\quad + \beta_3 S^* I_l^* \left(1 - \frac{S I_l}{S^* I_l^*} - \frac{S^*}{S} + \frac{I_l}{I_l^*}\right). \end{aligned}$$

$$\begin{aligned} \dot{V}(W) &= \left(1 - \frac{W^*}{W}\right) \left(\beta_1 S W + \beta_2 S I_s + \beta_3 S I_l - (\beta_1 S^* W^* + \beta_2 S^* I_s^* + \beta_3 S^* I_l^*) \frac{W}{W^*}\right) \\ &= \beta_1 S W + \beta_2 S I_s + \beta_3 S I_l - \beta_1 S^* W^* \frac{W}{W^*} - \beta_2 S^* I_s^* \frac{W}{W^*} - \beta_3 S^* I_l^* \frac{W}{W^*} - \beta_1 S W^* - \beta_2 S I_s \frac{W^*}{W} - \beta_3 S I_l \frac{W^*}{W} \\ &\quad + \beta_1 S^* W^* + \beta_2 S^* I_s^* + \beta_3 S^* I_l^* \\ &= \beta_1 S^* W^* \left(1 + \frac{S W}{S^* W^*} - \frac{S}{S^*} - \frac{W}{W^*}\right) + \beta_2 S^* I_s^* \left(1 + \frac{S I_s}{S^* I_s^*} - \frac{S I_s W^*}{S^* I_s^* W} - \frac{W}{W^*}\right) \\ &\quad + \beta_3 S^* I_l^* \left(1 + \frac{S I_l}{S^* I_l^*} - \frac{S I_l W^*}{S^* I_l^* W} - \frac{W}{W^*}\right). \end{aligned}$$

$$\begin{aligned} \dot{V}(I_s) &= \left(1 - \frac{I_s^*}{I_s}\right) \left(p_1 W + \omega_2 I_l - (p_1 W^* + \omega_2 I_l^*) \frac{I_s}{I_s^*}\right) \\ &= p_1 W + \omega_2 I_l - p_1 W^* \frac{I_s}{I_s^*} - \omega_2 I_l^* \frac{I_s}{I_s^*} - p_1 W \frac{I_s^*}{I_s} - \omega_2 I_l \frac{I_s^*}{I_s} + p_1 W^* + \omega_2 I_l^* \\ &= p_1 W^* \left(1 + \frac{W}{W^*} - \frac{I_s}{I_s^*} - \frac{W I_s^*}{W^* I_s}\right) + \omega_2 I_l^* \left(1 + \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} - \frac{I_s I_l}{I_s I_l^*}\right). \end{aligned}$$

$$\begin{aligned} \dot{V}(I_l) &= \left(1 - \frac{I_l^*}{I_l}\right) \left(p_2 W + \omega_1 I_s - (p_2 W^* + \omega_1 I_s^*) \frac{I_l}{I_l^*}\right) \\ &= p_2 W + \omega_1 I_s - p_2 W^* \frac{I_l}{I_l^*} - \omega_1 I_s^* \frac{I_l}{I_l^*} - p_2 W \frac{I_l^*}{I_l} - \omega_1 I_s \frac{I_l^*}{I_l} + p_2 W^* + \omega_1 I_s^* \\ &= p_2 W^* \left(1 + \frac{W}{W^*} - \frac{I_l}{I_l^*} - \frac{W I_l^*}{W^* I_l}\right) + \omega_1 I_s^* \left(1 + \frac{I_s}{I_s^*} - \frac{I_l}{I_l^*} - \frac{I_s I_l}{I_s I_l^*}\right). \end{aligned}$$

Hence,

$$\begin{aligned}
\dot{V} &= \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_1 S^* W^* \left(1 - \frac{S W}{S^* W^*} - \frac{S^*}{S} + \frac{W}{W^*} \right) + \beta_2 S^* I_s^* \left(1 - \frac{S I_s}{S^* I_s^*} - \frac{S^*}{S} + \frac{I_s}{I_s^*} \right) \\
&\quad + \beta_3 S^* I_l^* \left(1 - \frac{S I_l}{S^* I_l^*} - \frac{S^*}{S} + \frac{I_l}{I_l^*} \right) + \beta_1 S^* W^* \left(1 + \frac{S W}{S^* W^*} - \frac{S}{S^*} - \frac{W}{W^*} \right) \\
&\quad + \beta_2 S^* I_s^* \left(1 + \frac{S I_s}{S^* I_s^*} - \frac{S I_s W^*}{S^* I_s^* W} - \frac{W}{W^*} \right) + \beta_3 S^* I_l^* \left(1 + \frac{S I_l}{S^* I_l^*} - \frac{S I_l W^*}{S^* I_l^* W} - \frac{W}{W^*} \right) \\
&\quad + B p_1 W^* \left(1 + \frac{W}{W^*} - \frac{I_s}{I_s^*} - \frac{W I_s^*}{W^* I_s} \right) + B \omega_2 I_l^* \left(1 + \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} - \frac{I_s^* I_l}{I_s I_l^*} \right) + C p_2 W^* \left(1 + \frac{W}{W^*} - \frac{I_l}{I_l^*} - \frac{W I_l^*}{W^* I_l} \right) \\
&\quad + C \omega_1 I_s^* \left(1 + \frac{I_s}{I_s^*} - \frac{I_l}{I_l^*} - \frac{I_s I_l^*}{I_s^* I_l} \right) \\
&= \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_1 S^* W^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_2 S^* I_s^* \left(2 - \frac{S^*}{S} - \frac{W}{W^*} + \frac{I_s}{I_s^*} - \frac{S I_s W^*}{S^* I_s^* W} \right) \\
&\quad + \beta_3 S^* I_l^* \left(2 - \frac{S^*}{S} - \frac{W}{W^*} + \frac{I_l}{I_l^*} - \frac{S I_l W^*}{S^* I_l^* W} \right) + B p_1 W^* \left(1 + \frac{W}{W^*} - \frac{I_s}{I_s^*} - \frac{W I_s^*}{W^* I_s} \right) \\
&\quad + B \omega_2 I_l^* \left(1 + \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} - \frac{I_s^* I_l}{I_s I_l^*} \right) + C p_2 W^* \left(1 + \frac{W}{W^*} - \frac{I_l}{I_l^*} - \frac{W I_l^*}{W^* I_l} \right) + C \omega_1 I_s^* \left(1 + \frac{I_s}{I_s^*} - \frac{I_l}{I_l^*} - \frac{I_s I_l^*}{I_s^* I_l} \right).
\end{aligned}$$

Using the inequality $1 - x + \ln x \leq 0$ for $x > 0$ with equality holding if and only if $x = 1$ yield,

$$\begin{aligned}
\dot{V} &\leq \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_1 S^* W^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) \\
&\quad + \beta_2 S^* I_s^* \left(1 - \frac{S^*}{S} - \ln \frac{S}{S^*} + \frac{I_s}{I_s^*} - \ln \frac{I_s}{I_s^*} - \frac{W}{W^*} + \ln \frac{W}{W^*} \right) \\
&\quad + \beta_3 S^* I_l^* \left(1 - \frac{S^*}{S} - \ln \frac{S}{S^*} + \frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - \frac{W}{W^*} + \ln \frac{W}{W^*} \right) + \beta_2 S^* I_s^* \left(\frac{W}{W^*} - \ln \frac{W}{W^*} - \frac{I_s}{I_s^*} + \ln \frac{I_s}{I_s^*} \right) \\
&\quad + \frac{\beta_2 \omega_2 S^* I_s^* I_l^*}{p_1 W^*} \left(\frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} + \ln \frac{I_s}{I_s^*} \right) + \beta_3 S^* I_l^* \left(\frac{W}{W^*} - \ln \frac{W}{W^*} - \frac{I_l}{I_l^*} + \ln \frac{I_l}{I_l^*} \right) \\
&\quad + \frac{\beta_3 \omega_1 S^* I_s^* I_l^*}{p_2 W^*} \left(\frac{I_s}{I_s^*} - \ln \frac{I_s}{I_s^*} - \frac{I_l}{I_l^*} + \ln \frac{I_l}{I_l^*} \right) \\
&\leq \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_1 S^* W^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_2 S^* I_s^* \left(1 - \frac{S^*}{S} + \ln \frac{S}{S^*} \right) \\
&\quad + \beta_3 S^* I_l^* \left(1 - \frac{S^*}{S} + \ln \frac{S}{S^*} \right) + \frac{\beta_2 \omega_2 S^* I_s^* I_l^*}{p_1 W^*} \left(\frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} + \ln \frac{I_s}{I_s^*} \right) \\
&\quad - \frac{\beta_3 \omega_1 S^* I_s^* I_l^*}{p_2 W^*} \left(\frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - \frac{I_s}{I_s^*} + \ln \frac{I_s}{I_s^*} \right) \\
&\leq \mu S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_1 S^* W^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S} \right) + \beta_2 S^* I_s^* \left(1 - \frac{S^*}{S} + \ln \frac{S}{S^*} \right) \\
&\quad + \beta_3 S^* I_l^* \left(1 - \frac{S^*}{S} + \ln \frac{S}{S^*} \right) + \left(\frac{\beta_2 \omega_2}{p_1} - \frac{\beta_3 \omega_1}{p_2} \right) \frac{S^* I_s^* I_l^*}{W^*} \left(\frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - 1 \right).
\end{aligned}$$

From the basic inequality, $2 - \frac{S}{S^*} - \frac{S^*}{S} \leq 0$. Based on the inequality $1 - x + \ln x \leq 0$ for $x > 0$, we obtain $1 - \frac{S^*}{S} + \ln \frac{S^*}{S} \leq 0$ and $\frac{I_l}{I_l^*} - \ln \frac{I_l}{I_l^*} - 1 \geq 0$. If $\frac{\beta_2 \omega_2}{p_1} \leq \frac{\beta_3 \omega_1}{p_2}$, then $\frac{\beta_2 \omega_2}{p_1} - \frac{\beta_3 \omega_1}{p_2} \leq 0$. Thus, $\dot{V} \leq 0$, and $\dot{V} = 0$ if and only if $S = S^*$, $W = W^*$, $I_s = I_s^*$ and $I_l = I_l^*$. The endemic equilibrium point E^* is globally asymptotically stable for $R_0 > 1$ by LaSalle's invariance principle. \square

4. Parameter estimation

For model (1), there is a total of fifteen unknown parameters in Table 1. Some of them are determined from population data, and the remaining parameters are estimated from AIDS patient data. The birth and natural mortality rates from 2008 to 2021 were obtained from the National Bureau of Statistics of China [28], see Table 2. The mean values of birth and natural mortality rates are 0.01187 and 0.0071, respectively. The whole population of China in 2007 was 1,321,290,000 [28]. Based on the mean of birth and death rates, the recruitment rate can be estimated by the following:

$$b = \frac{0.01187}{12} \times 1321290000 = 1306976,$$

and the natural death rate is $\mu = \frac{0.0071}{12} = 0.00059$. The rate of AIDS death is $d = 0.35$ [29].

Table 2. The birth and natural death rates from 2008 to 2021.

| Year | Birth rate (‰) | Natural death rate (‰) | Year | Birth rate (‰) | Natural death rate (‰) |
|------|----------------|------------------------|------|----------------|------------------------|
| 2008 | 12.14 | 7.06 | 2015 | 11.99 | 7.12 |
| 2009 | 11.95 | 7.08 | 2016 | 13.57 | 7.07 |
| 2010 | 11.90 | 7.11 | 2017 | 12.64 | 7.04 |
| 2011 | 13.27 | 7.14 | 2018 | 10.86 | 7.06 |
| 2012 | 14.57 | 7.13 | 2019 | 10.41 | 7.08 |
| 2013 | 13.03 | 7.13 | 2020 | 8.52 | 7.09 |
| 2014 | 13.83 | 7.12 | 2021 | 7.52 | 7.07 |

Table 3. The parameters of the model (1), and their ranges for PRCC sensitivity analysis.

| Parameter | Unit | Range | Estimated value | The parameter range for PRCC |
|---------------|-------------------------|--|--------------------------|---|
| W_0 | Person | $[5 \times 10^4, 5 \times 10^5]$ | 3.6733×10^5 | - |
| I_{s0} | Person | $[5 \times 10^4, 5 \times 10^5]$ | 3.6506×10^5 | - |
| I_{l0} | Person | $[5 \times 10^4, 5 \times 10^5]$ | 2.5150×10^5 | - |
| β_1 | Per month ⁻¹ | $[1 \times 10^{-13}, 1 \times 10^{-10}]$ | 4.7125×10^{-12} | $\beta_1 \pm \kappa, \kappa \in [0, 5 \times 10^{-14}]$ |
| β_2 | Per month ⁻¹ | $[1 \times 10^{-13}, 1 \times 10^{-9}]$ | 4.4246×10^{-10} | $\beta_2 \pm \kappa, \kappa \in [0, 5 \times 10^{-14}]$ |
| β_3 | Per month ⁻¹ | $[1 \times 10^{-13}, 1 \times 10^{-9}]$ | 2.1748×10^{-11} | $\beta_3 \pm \kappa, \kappa \in [0, 5 \times 10^{-14}]$ |
| p | Per month ⁻¹ | [0,0.1301] | 0.0089 | $p \pm \kappa, \kappa \in [0, 0.0001]$ |
| ε | Per month ⁻¹ | [0,0.218] | 0.2161 | $\varepsilon \pm \kappa, \kappa \in [0, 0.001]$ |
| σ_1 | Per month ⁻¹ | [0.10,0.18] | 0.1689 | $\sigma_1 \pm \kappa, \kappa \in [0, 0.001]$ |
| σ_2 | Per month ⁻¹ | [0.20,0.34] | 0.2953 | $\sigma_2 \pm \kappa, \kappa \in [0, 0.0001]$ |
| ω_1 | Per month ⁻¹ | [0.10,0.27] | 0.2461 | $\omega_1 \pm \kappa, \kappa \in [0, 0.001]$ |
| ω_2 | Per month ⁻¹ | [0.201,0.350] | 0.2733 | $\omega_2 \pm \kappa, \kappa \in [0, 0.0001]$ |

Other unknown parameters include $\beta_1, \beta_2, \beta_3, p, \varepsilon, \sigma_1, \sigma_2, \omega_1, \omega_2$, and three initial values W_0, I_{s0} , and I_{l0} . A genetic algorithm [30] is an optimization algorithm for adaptive searching. Compared with other algorithms, the genetic algorithm has better estimation results. It has been applied to neural networks [31], combinatorial optimization [32], artificial intelligence [33], genetic programming [34], data mining, and other fields. For the given parameter ranges (see Table 3), all parameters are randomly generated with a certain number of initial populations. The fitness index is an important indicator to evaluate whether the parameters conform to the HIV/AIDS model. Generally, the square sum of the difference between the real HIV/AIDS data and the simulated data of the model is used as a fitness index, defined as follows:

$$fitness = \sum_{l=1}^{168} (\bar{A}_l(t) - A_l(t))^2,$$

where $A_l(t)$ denotes the real cumulative HIV/AIDS infection data and $\bar{A}_l(t)$ denotes the cumulative infection data in the model (1). In genetic evolution, it is simulated for the parameter set using three genetic operators. Each generation's set of parameters is recorded and compared with the updated set of parameters in the next generation. The updated set of parameters is always recorded until the evolution is completed with the final global optimal set. The accuracy and validity of the method are verified by fitting it to the real cumulative case data of HIV/AIDS. The results of the parameter estimation are shown in Table 3.

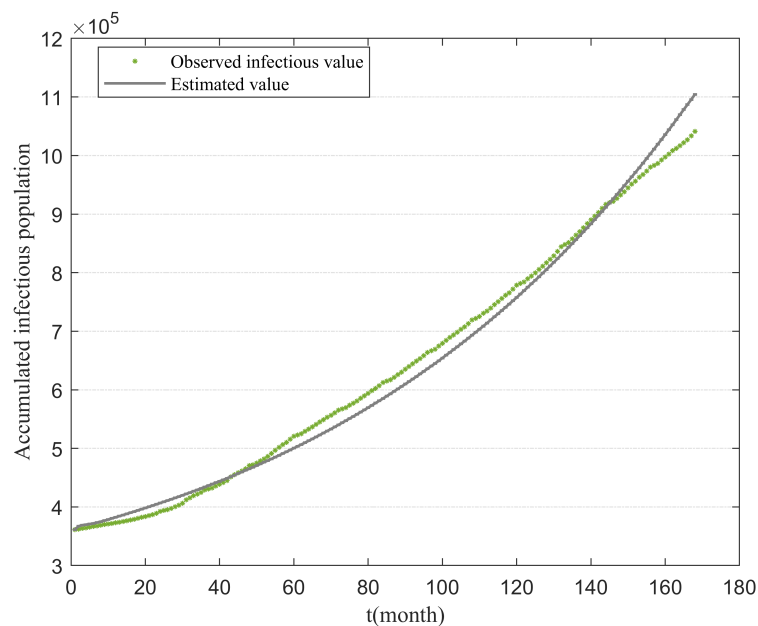


Figure 3. Fitting of the cumulative infected cases.

5. Model analysis

5.1. Validation of the model

The initial values and parameter estimators are brought into model (1), according to Table 3. First, we validate the fitting model with the observed HIV data from January 2008 to December 2021.

Figure 3 shows the curves of the observed HIV cases and the model. The green dots indicate the observed real data and the gray curve is the fitting curve of model (1). As shown by the real data, the cumulative number of HIV cases has been increasing since 2008, and the model better reflects this trend.

Figure 4 shows the residual analysis of the fitting results of model (1). When the confidence interval of the residuals contains a zero, it reveals that the model can fit the original data well. Otherwise, it can be considered as an outlier. As can be seen from Figure 4, the residual confidence interval almost contains zero points. It reflects that model (1) fits well and further indicates the validity of the genetic algorithm.

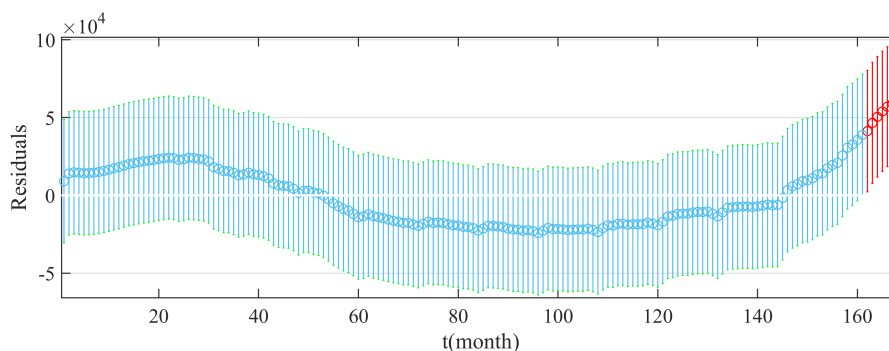


Figure 4. Residual analysis.

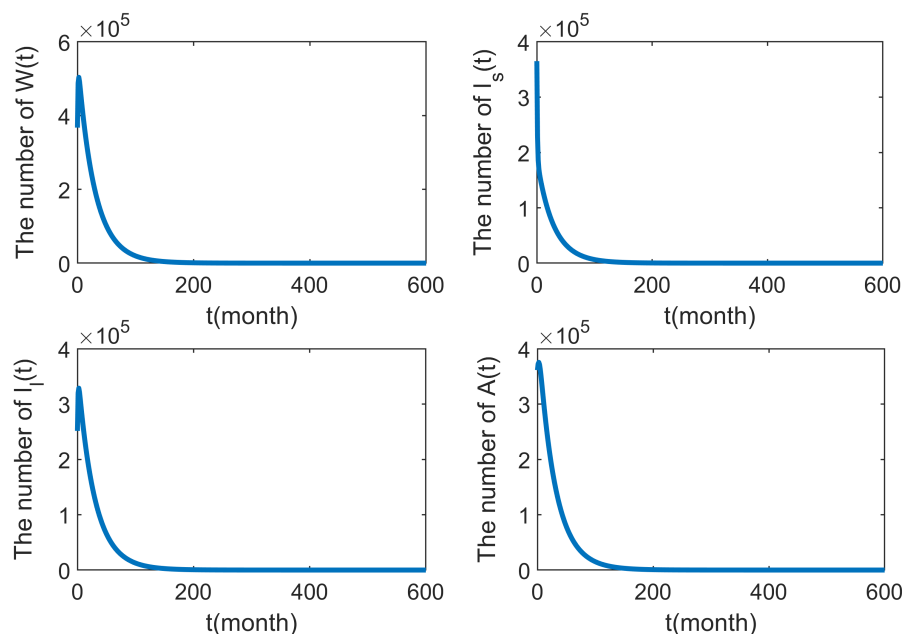


Figure 5. Stability analysis of disease-free equilibrium when $R_0 < 1$.

The stability of the model is shown in Figures 5 and 6. Figure 5 shows the global asymptotic stability of the disease-free equilibrium point. When $R_0 < 1$, the disease-free equilibrium first decreases and

then stabilizes. In Figure 6, the epidemic equilibrium point tends to stabilize when $R_0 > 1$. The values of W , I_s , I_l and A fluctuate and then stabilize.

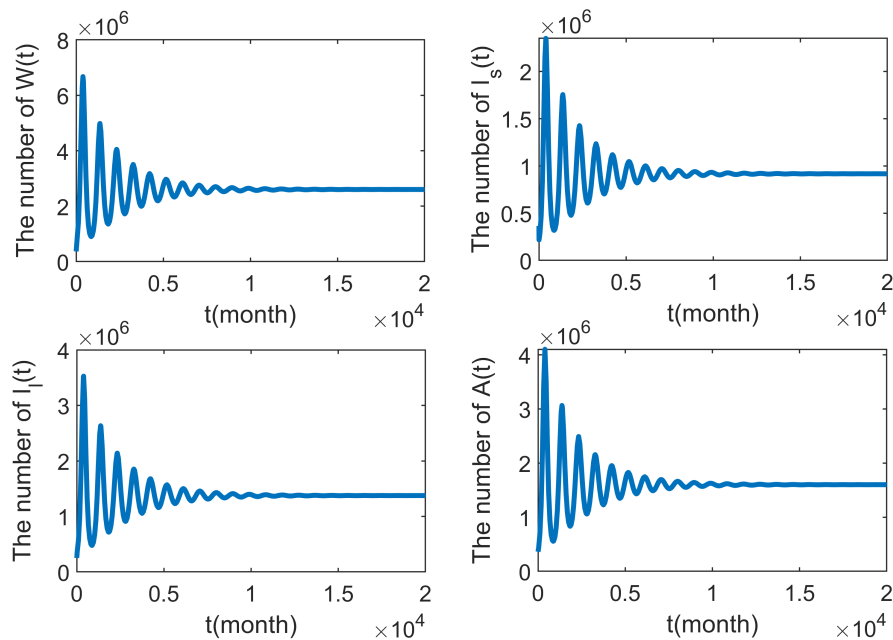


Figure 6. Stability analysis of the endemic equilibrium when $R_0 > 1$.

5.2. Sensitivity analysis

The basic reproduction number R_0 is an important threshold value for the spread of HIV and is closely related to the parameters $\beta_1, \beta_2, \beta_3, p, \varepsilon, \sigma_1, \sigma_2, \omega_1$ and ω_2 . Considering all other parameters, Figure 7 shows that R_0 gradually increases when $\beta_1, \beta_2, \beta_3, p$ or ω_2 is larger, but gradually decreases when $\varepsilon, \sigma_1, \sigma_2$ or ω_1 increases. This means that reducing the rate of effective contacts with HIV-infected people and raising the rate of treatment for co-infections could curb the AIDS epidemic in China.

To identify the most influential parameters associated with HIV-infected populations, we use the partial rank correlation coefficient (PRCC) to investigate the global sensitivity of the parameters of model (1). The PRCC measures the relationship between the state variables and each model parameter and helps to identify the most important parameters that affect HIV transmission. The sensitivity analysis of PRCC depends on the range of values of the parameters to a large extent. There exists an $\kappa \in (0, 0.1)$, and the range of parameter values is shown in Table 3. Thus, the PRCC value entirely depends on the range of κ . The results of the PRCC are shown in Figure 8. These parameters $\beta_1, \beta_2, \beta_3, p$ and ω_2 are positively correlated with R_0 , and $\varepsilon, \sigma_1, \sigma_2$ and ω_1 are negatively correlated with R_0 . Furthermore, we observe that $\beta_2, \sigma_2, \omega_1$ and ω_2 are more sensitive to R_0 than other parameters. Therefore, decreasing β_2 and ω_2 , increasing ω_1 and σ_1 can reduce R_0 and thus effectively slow down HIV transmission. Therefore, it is of great applied value to study the effect of changing these four parameters on the basic reproduction number. The results presented in Figure 8 suggest that lowering the proportion of asymptotically infected individuals co-infected with other diseases is the more critical measure.

In addition, we investigate the effect of parameters on R_0 by the contour plot with parameters β_2 , σ_1 , ω_1 and ω_2 in Figure 9. The contour plots show a significant increase for R_0 with a higher β_2 and ω_2 . The burden of AIDS is usually exacerbated by co-infectious diseases. This means that if the public does not take preventive measures, the disease will persist in the population and spread through the community. In order to control R_0 , it is necessary to lower β_2 and ω_2 , and raise σ_1 and ω_1 . Therefore, it is important to strengthen early diagnosis, symptom screening, and timely treatment of HIV/AIDS combined with other diseases.

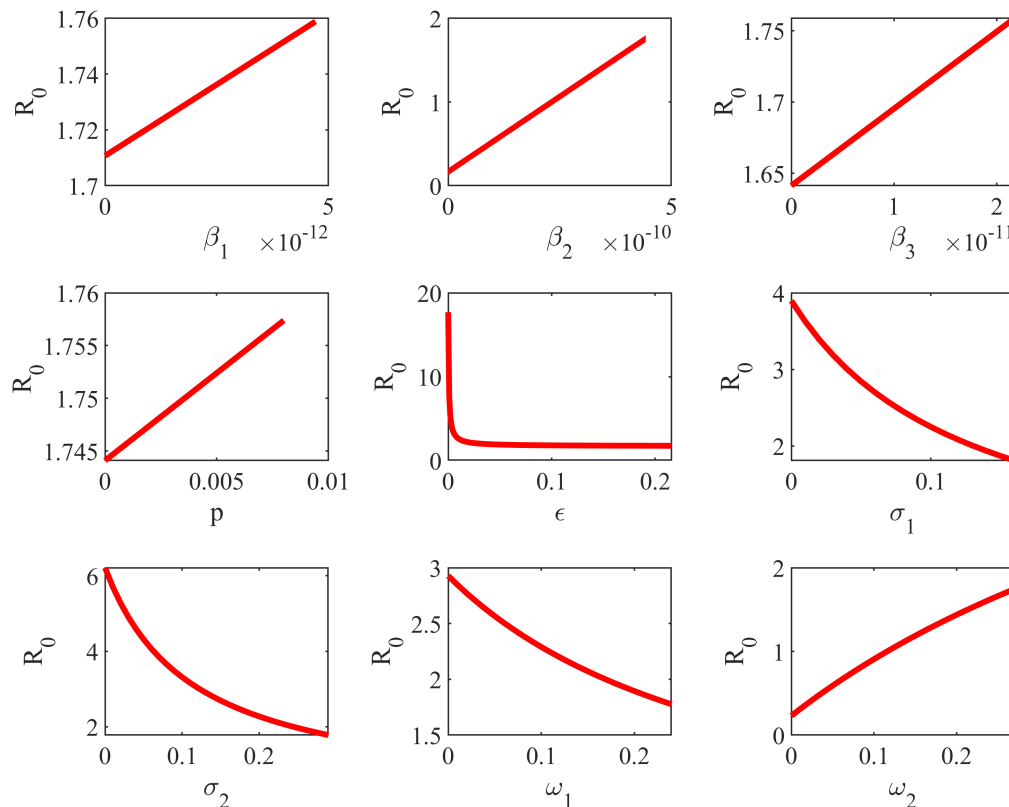


Figure 7. The sensitivity analysis of parameters.

5.3. Predictions of the model

In the next numerical simulations, an uncertainty analysis is performed for two compartmental I_s and I_l based on the parameters in Table 3. Figure 10(a),(b) show the trends of I_s and I_l through the coefficient of variation (CV) 3% of these parameters. The mean values of I_s and I_l (solid line) and the 95% confidence intervals (dotted line) are shown at the bottom of Figure 10.

Then, we analyze the impact of various parameters on the AIDS epidemic. We take the fitting value of each compartment at the end of December 2021 as the initial value, and the estimated value of b , d , β_1 , β_2 , β_3 , p , ϵ , σ_1 , σ_2 , ω_1 and ω_2 in Table 3 as the standard. When one parameter changes and other parameters are fixed, we use model (1) to analyze the trend of patients in the next 29 years. We investigate the effect of the transmission rate β_2 on the epidemic. In Figure 11(a), the number of infected persons in the HIV acute infection phase can be effectively controlled by reducing the

transmission rate β_2 . In addition, the epidemic dies out more quickly when the transmission rate of β_2 decreases to $0.8\beta_2$. Hence, public health organizations can enhance their control efforts by diminishing the transmission rate. For example, publicizing the dangers of AIDS can be used to slow the spread of the disease. Figure 11(b) shows the impact of reducing the proportion of HIV-infected patients with other co-infections through early diagnosis and screening, with little change in the number of rapidly asymptomatic patients. This suggests that early diagnosis and screening is not a key factor in controlling HIV transmission. Figure 12 suggests that growing the proportion of ω_1 and cutting down the proportion of ω_2 can significantly lessen the number of fast asymptomatic individuals, thereby inhibiting HIV transmission.

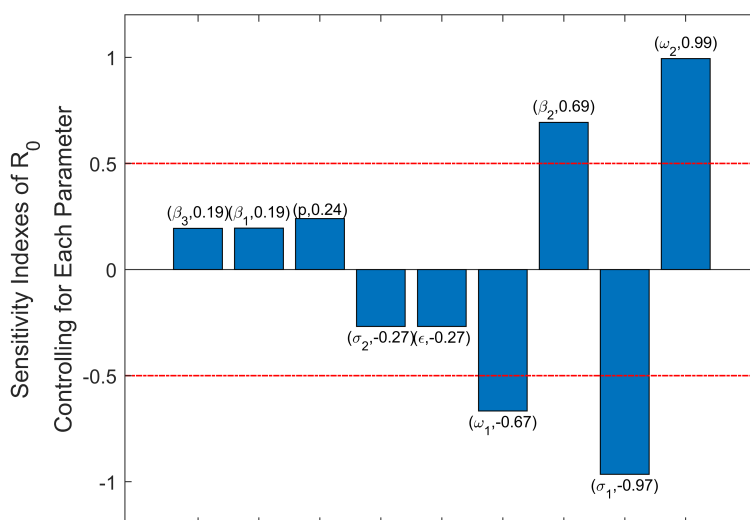


Figure 8. The global sensitivity analysis of parameters.

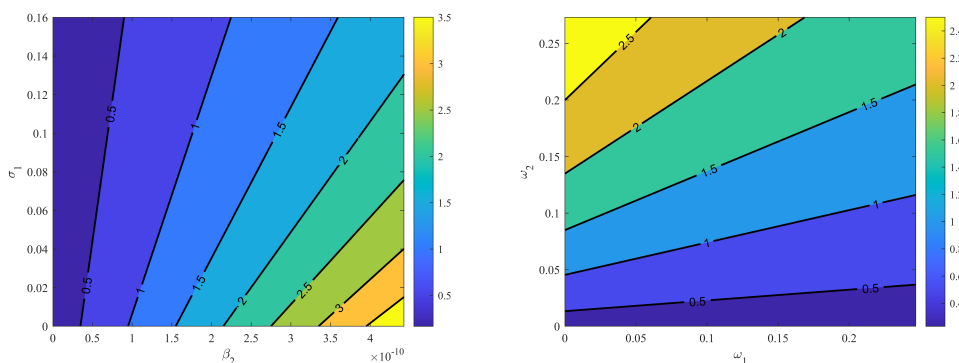


Figure 9. Contour plots of basic reproduction number R_0 .

To assess the combined effect of β_2 , ω_1 and ω_2 on HIV transmission, we use different combinations of these three parameters to model the number of infected individuals, as given in Figure 13. Figure 13(a),(b) show that the number of individuals in the acute infection and fast asymptomatic phases

gradually decline as β_2 and ω_2 diminishes, and ω_1 expands. However, Figure 13(c),(d) reflect that the number of individuals in the acute infection and fast asymptomatic phases first tends to improve and then gradually diminishes. Figure 14 explores the trend of infected individuals for different parameter values. When $\beta_2 < 0.95\beta_2$, $\omega_1 > 1.05\omega_1$, and $\omega_2 < 0.95\omega_2$ there is a declining trend of HIV/AIDS. This means that the spread of HIV/AIDS can be effectively curbed as the transmission rate β_2 and the number of co-infected patients decreases, and the cure rate of other diseases increases.

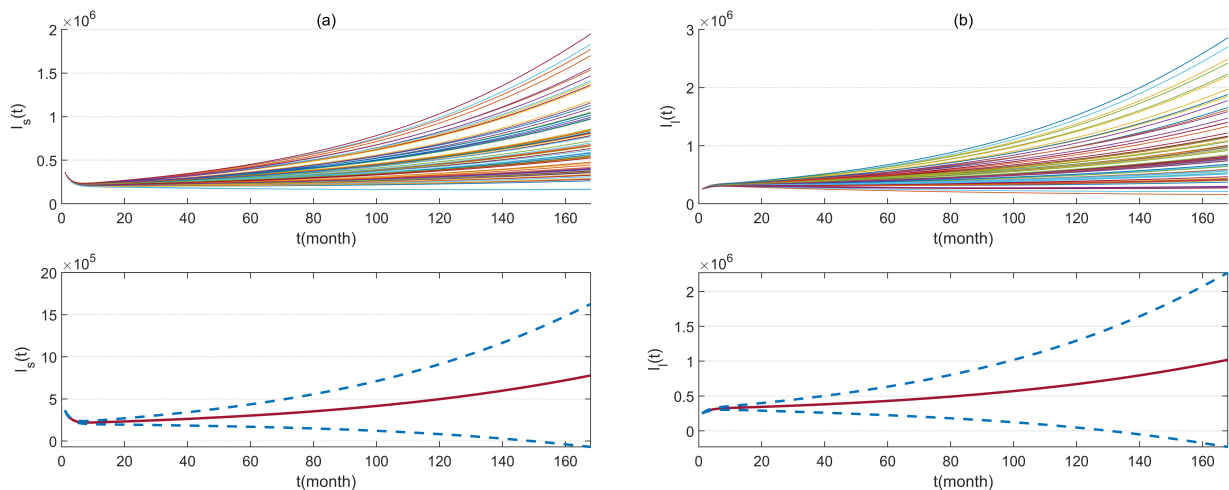


Figure 10. Uncertainty analysis and 95% confidence intervals for fast and slow asymptomatic infection.

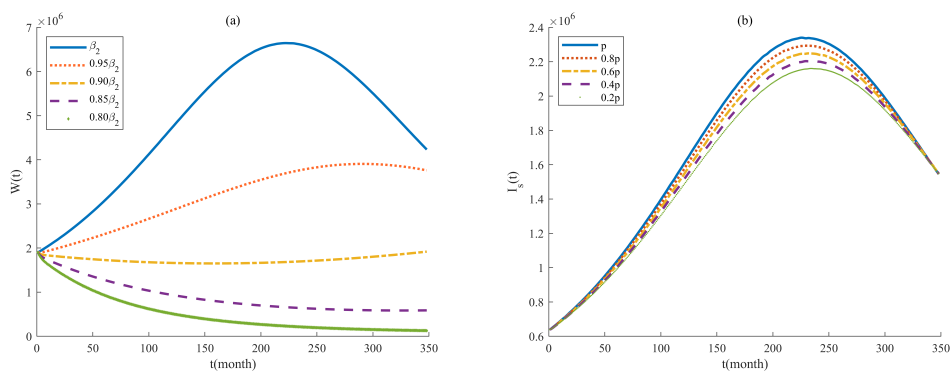


Figure 11. (a) The number of HIV acute infections W for β_2 . (b) The number of rapid asymptomatic infections I_s for p .

Based on the above numerical simulations, we know $R_0 = 1.7593 > 1$ for the given parameters in Table 3. If the previous control measures do not change, the HIV epidemic will be persistent and approach epidemic equilibrium. In addition, we have found that the effective rate of exposure to the disease and the proportion of co-infections in HIV/AIDS have a significant impact on reducing the number of infected individuals. When more HIV-infected people are either protected or screened, the number of people receiving treatment increases. Therefore, it needs to improve early diagnoses and screenings of HIV patients co-infected with other diseases. By increasing awareness of co-infection

and improving the rate of treatment for co-infected patients, the incidence and transmission of HIV can significantly decrease, thereby alleviating pressure on public health organizations.

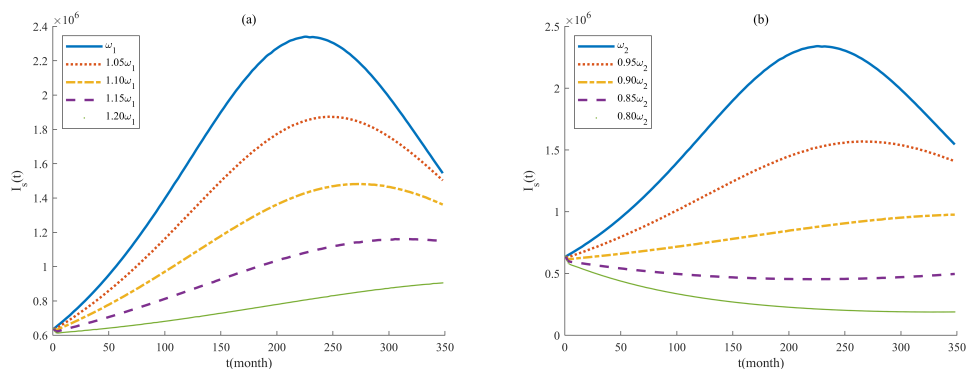


Figure 12. (a) The number of fast asymptomatic infections I_s for ω_1 . (b) The number of fast asymptomatic infections I_s for ω_2 .

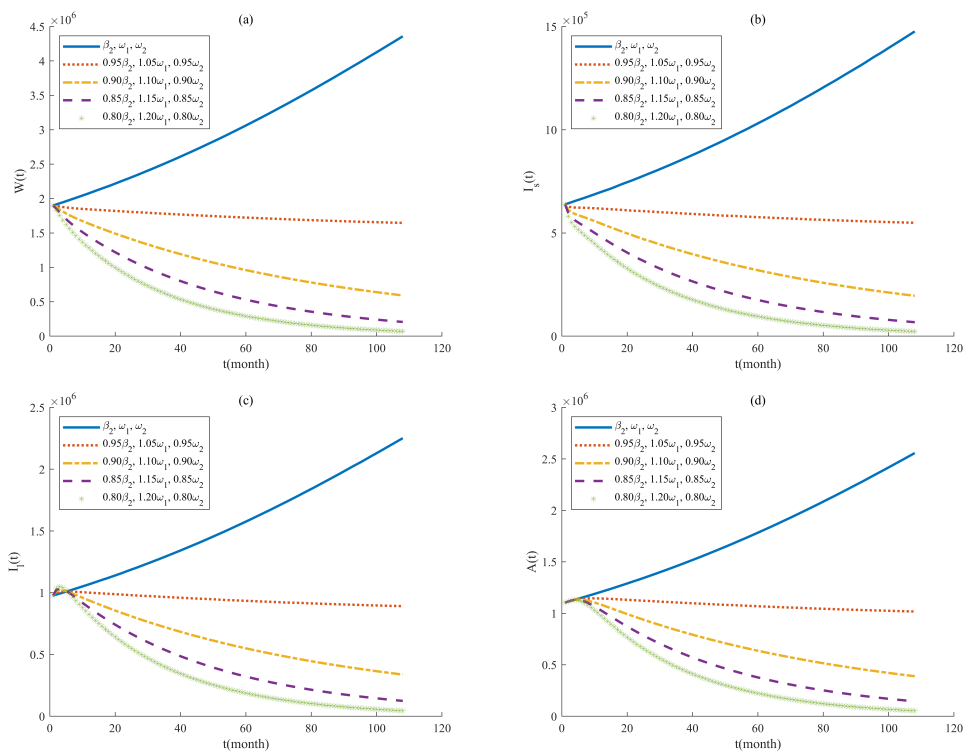


Figure 13. The number of infections for $\beta_2 = 4.4246 \times 10^{-10}$, $\omega_1 = 0.2461$ and $\omega_2 = 0.2733$.

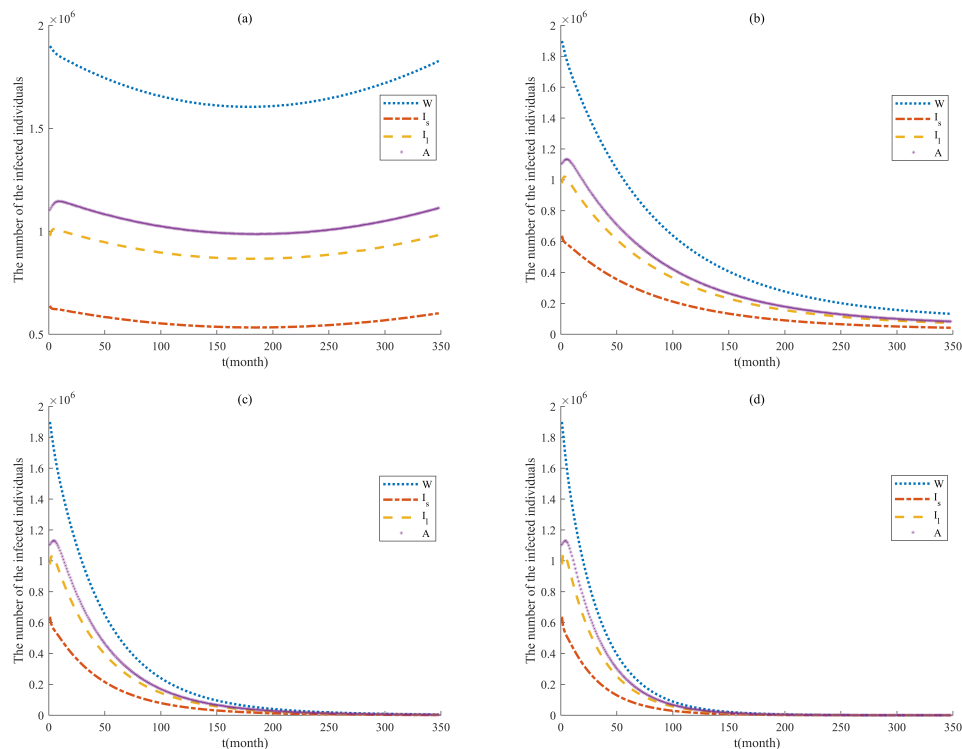


Figure 14. The number of infected individuals for $\beta_2 = 4.4246 \times 10^{-10}$, $\omega_1 = 0.2461$ and $\omega_2 = 0.2733$. (a) $0.95\beta_2$, $1.05\omega_1$ and $0.95\omega_2$. (b) $0.90\beta_2$, $1.10\omega_1$ and $0.90\omega_2$. (c) $0.85\beta_2$, $1.15\omega_1$ and $0.85\omega_2$. (d) $0.80\beta_2$, $1.20\omega_1$ and $0.80\omega_2$.

6. A concluding remark

In this paper, we developed a five-dimensional mathematical model including susceptible infection, acute infection, fast asymptomatic infection, slow asymptomatic infection, and AIDS. A theoretical analysis and application were conducted based on this model. The basic reproduction number R_0 was obtained by the next-generation matrix method. The stability of the model was studied using the Lyapunov method. When $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable and the disease gradually disappears. When $R_0 > 1$, the endemic equilibrium is globally asymptotically stable and the disease continues to spread.

We collected the number of reported HIV/AIDS cases in China from 2008 to 2021. The unknown parameters were estimated by a genetic algorithm, and the basic reproduction number $R_0 = 1.7593$ was finally calculated, which indicated that the model we built was consistent with the actual HIV/AIDS epidemic. Furthermore, a sensitivity analysis of the parameters was performed to analyze the effect of individual parameters on R_0 , and global sensitivity was performed from the PRCC approach. We found that parameters associated with fast asymptomatic infection had a more significant effect on R_0 . The studied results showed that the spread of the HIV/AIDS epidemic could be effectively controlled by decreasing the contact rate β_2 and improving early diagnosis, screening rates, and treatment rates for co-infected patients. Therefore, we further analyzed the impact of single and multiple measures on disease transmission. Multiple measures can be more effective in controlling the spread of HIV than one.

In summary, public health organizations can lower transmission rates by publicizing the dangers of AIDS, reduce the risk of co-infections by strengthening the awareness of self-protection among HIV-infected individuals, and improve treatment rates for co-infections by upgrading medical technology. Reference [18] suggests that HIV transmission can be mitigated by improving medical technology, increasing testing rates, and intensify education for unaware infected individuals. Our proposed program focuses more on the impact of co-infections on the course of AIDS than those proposed in the [18].

In the work, we focus on studying the HIV/AIDS epidemic with either fast or slow asymptomatic infections. However, there are still some unsolved and interesting problems. For example, some factors, such as age structure and gender, often play important roles in HIV/AIDS transmission [35–37]. The theoretical methods of the aforementioned results are important references for our subsequent research and practice.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare that they have no conflict of interest.

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References

1. AIDS.gov, 2022. Available from: <https://aids.gov/index.html>.
2. M. S. Gottlieb, Pneumocystis Pneumonia—Los Angeles, *Am. J. Public Health*, **96** (2006), 980–981. <https://doi.org/10.2105/AJPH.96.6.980>
3. HIV, 2023. Available from: <https://www.who.int/data/gho/data/themes/hiv-aids>.
4. X. Sun, N. Wang, D. Li, X. Zheng, S. Qu, L. Wang, et al., The development of HIV/AIDS surveillance in China, *Aids*, **21** (2007), S33–S38. <https://doi.org/10.1097/01.aids.0000304694.54884.06>

5. Y. Xiao, S. Kristensen, J. Sun, L. Lu, S. H. Vermund, Expansion of HIV/AIDS in China: lessons from Yunnan Province, *Soc. Sci. Med.*, **64** (2007), 665–675. <https://doi.org/10.1016/j.socscimed.2006.09.019>
6. M. Jia, H. Luo, Y. Ma, N. Wang, K. Smith, J. Mei, et al., The HIV epidemic in Yunnan province, China, 1989–2007, *J. Acquired Immune Defic. Syndr.*, **53** (2010), S34–S40. <https://doi.org/10.1097/QAI.0b013e3181c7d6ff>
7. N. He, Research progress in the epidemiology of HIV/AIDS in China, *China CDC Wkly.*, **3** (2021), 1022. <https://doi.org/10.46234/ccdcw2021.249>
8. Y. Ding, Z. Ma, J. He, X. Xu, S. Qiao, L. Xu, et al., Evolving HIV epidemiology in mainland China: 2009–2018, *Curr. HIV/AIDS Rep.*, **16** (2019), 423–430. <https://doi.org/10.1007/s11904-019-00468-z>
9. Z. Wu, J. Chen, S. R. Scott, J. M. McGoogan, History of the HIV epidemic in China, *Curr. HIV/AIDS Rep.*, **16** (2019), 458–466. <https://doi.org/10.1007/s11904-019-00471-4>
10. Y. Lu, S. Tang, Y. Qin, V. Harypursat, H. Wu, Y. Chen, Changes of human immunodeficiency virus (HIV) burden globally and in China over three decades: a secondary analysis of global HIV statistics, *Chin. Med. J.*, **10** (2022), 1097. <https://doi.org/10.1097/CM9.0000000000002500>
11. H. Yang, Y. Li, F. He, F. Yuan, L. Liu, L. Li, et al., Demographic characteristics and hot-spot areas of recent infections among new HIV diagnoses in Sichuan, China, between 2018 and 2020, *Infect. Drug Resist.*, **16** (2023), 779–789. <https://doi.org/10.2147/IDR.S394828>
12. L. Wang, N. Zhao, Y. Wang, K. Sun, Y. Wang, S. Huang, et al., Impact of the COVID-19 pandemic and the dynamic COVID-zero strategy on HIV incidence and mortality in China, *BMC Public Health*, **23** (2023), 1–11. <https://doi.org/10.1186/s12889-023-15268-9>
13. J. M. Hyman, J. Li, E. A. Stanley, The differential infectivity and staged progression models for the transmission of HIV, *Math. Biosci.*, **155** (1999), 77–109. [https://doi.org/10.1016/S0025-5564\(98\)10057-3](https://doi.org/10.1016/S0025-5564(98)10057-3)
14. C. C. McCluskey, A model of HIV/AIDS with staged progression and amelioration, *Math. Biosci.*, **181** (2003), 1–16. [https://doi.org/10.1016/S0025-5564\(02\)00149-9](https://doi.org/10.1016/S0025-5564(02)00149-9)
15. R. Naresh, A. Tripathi, D. Sharma, A nonlinear HIV/AIDS model with contact tracing, *Appl. Math. Comput.*, **217** (2011), 9575–9591. <https://doi.org/10.1016/j.amc.2011.04.033>
16. K. Hattaf, H. Dutta, Modeling the dynamics of viral infections in presence of latently infected cells, *Chaos Solitons Fractals*, **136** (2020), 109916. <https://doi.org/10.1016/j.chaos.2020.109916>
17. R. Wattanasirikosone, C. Modnak, Analysing transmission dynamics of HIV/AIDS with optimal control strategy and its controlled state, *J. Biol. Dyn.*, **16** (2022), 499–527. <https://doi.org/10.1080/17513758.2022.2096934>
18. L. Xue, Y. Sun, X. Ren, W. Sun, Modelling the transmission dynamics and optimal control strategies for HIV infection in China, *J. Biol. Dyn.*, **17** (2023), 2174275. <https://doi.org/10.1080/17513758.2023.2174275>
19. K. R. Cheneke, K. P. Rao, G. K. Edessa, Bifurcation and stability analysis of HIV transmission model with optimal control, *J. Math.*, **2021** (2021), 1–14. <https://doi.org/10.1155/2021/7471290>

20. World Health Organization HIV/AIDS, 2023. Available from: <http://www.who.int/mediacentre/factsheets/fs360/en/>.
21. L. B. Shrestha, G. K. Yadav, S. Pradhan, A. Sharma, T. Pandit, R. Chhetry, et al., Co-infection of Hepatitis B and Hepatitis C among HIV-infected patients: A cross-sectional study from tertiary care hospital of eastern Nepal, *Plos One*, **17** (2022), e0264791. <https://doi.org/10.1371/journal.pone.0264791>
22. T. Getaneh, A. Negesse, G. Dessie, M. Desta, The impact of tuberculosis co-infection on virological failure among adults living with HIV in Ethiopia: a systematic review and meta-analysis, *J. Clin. Tuberc. Other Mycobact. Dis.*, **27** (2022), 100310. <https://doi.org/10.1016/j.jctube.2022.100310>
23. J. Bruchfeld, M. Correia-Neves, G. Källenius, Tuberculosis and HIV coinfection, *Cold Spring Harbor Perspect. Med.*, **5** (2015), a017871. <https://doi.org/10.1101/cshperspect.a017871>
24. L. C. K. Bell, M. Noursadeghi, Pathogenesis of HIV-1 and Mycobacterium tuberculosis co-infection, *Nat. Rev. Microbiol.*, **16** (2018), 80–90. <https://doi.org/10.1038/nrmicro.2017.128>
25. S. D. Lawn, AIDS in Africa: the impact of coinfections on the pathogenesis of HIV-1 infection, *J. Infect.*, **48** (2004), 1–12. <https://doi.org/10.1016/j.jinf.2003.09.001>
26. P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.*, **180** (2002), 29–48. [https://doi.org/10.1016/S0025-5564\(02\)00108-6](https://doi.org/10.1016/S0025-5564(02)00108-6)
27. X. Q. Zhao, *Dynamical Systems in Population Biology*, Springer, New York, 2003.
28. National Bureau of Statistics, 2023. Available from: <https://data.stats.gov.cn/index.html>.
29. Z. Li, Z. Teng, H. Miao, Modeling and control for HIV/AIDS transmission in China based on data from 2004 to 2016, *Comput. Math. Methods Med.*, **2017** (2017), 8935314. <https://doi.org/10.1016/j.jctube.2022.100310>
30. L. Li, L. X. Du, Z. Yan, J. Zhang, Y. P. Wu, A method for parameters estimation in a dynamical model of Ebola virus transmission in Sierra Leone, *Complexity*, **2020** (2020), 1–9. <https://doi.org/10.1155/2020/9172835>
31. N. Chen, C. Xiong, W. Du, C. Wang, X. Lin, Z. Chen, An improved genetic algorithm coupling a back-propagation neural network model (IGA-BPNN) for water-level predictions, *Water*, **11** (2019), 1795. <https://doi.org/10.3390/w11091795>
32. A. Misevičius, D. Kuznecovaitė, J. Platužienė, Some further experiments with crossover operators for genetic algorithms, *Informatica*, **29** (2018), 499–516. <https://doi.org/10.15388/Informatica.2018.178>
33. Z. Chen, J. Zhou, R. Sun, L. Kang, A new evolving mechanism of genetic algorithm for multi-constraint intelligent camera path planning, *Soft Comput.*, **25** (2021), 5073–5092. <https://doi.org/10.1007/s00500-020-05510-6>
34. A. Ragalo, N. Pillay, Evolving dynamic fitness measures for genetic programming, *Expert Syst. Appl.*, **109** (2018), 162–187. <https://doi.org/10.1016/j.eswa.2018.03.060>

35. P. Wu, H. Zhao, Mathematical analysis of an age-structured HIV/AIDS epidemic model with HAART and spatial diffusion, *Nonlinear Anal. Real World Appl.*, **60** (2021), 103289. <https://doi.org/10.1016/j.nonrwa.2021.103289>
36. H. Zhao, P. Wu, S. Ruan, Dynamic analysis and optimal control of a three-age-class HIV/AIDS epidemic model in China, *Discrete Contin. Dyn. Syst. Ser. B*, **25** (2020). <https://doi.org/10.3934/dcdsb.2020070>
37. P. Wu, S. Ahmed, X. Wang, H. Wang, PrEP intervention in the mitigation of HIV/AIDS epidemics in China via a data-validated age-structured model, *Bull. Math. Biol.*, **85** (2023), 41. <https://doi.org/10.1007/s11538-023-01145-4>



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