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MODELLING AND ANALYSIS OF AN HIV/AIDS MODEL WITH DIFFERENT WINDOW PERIOD AND TREATMENT*

Hai-Feng Huo[1,†], Li-Na Gu[1] and Hong Xiang[1]

Abstract A novel HIV/AIDS model with different window period and treatment is proposed. Window period individuals and latent individuals are divided into two types: treated and untreated in our model. The basic reproduction number R_0 is obtained by using the next generation matrix. Stability of the disease-free equilibrium and existence of the endemic equilibrium is derived. Using the theory of central manifold, the generation of forward bifurcation is established. Existence of the optimal control pair is analyzed and the mathematical expression of the optimal control is also given by the Pontryagin maximum principle. The best-fit parameter values in our model are identified by the MCMC algorithm on the basis of the AIDS data in Gansu province of China from 2004 to 2019. We also estimate that the basic reproduction number R_0 is 2.1985 (95%CI: (1.3535-3.0435)). Numerical simulation and sensitivity analysis of several parameters are also presented. Our results suggest that individuals who are in the stage of window period for AIDS should receive treatment, and this plays a key role in the prevention and control of HIV/AIDS.

Keywords Treatment, window period, forward bifurcation, optimal control.

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1. Introduction

AIDS is an infectious disease without effective treatment and high mortality, causing more than 32 million deaths so far. According to the report by the World Health Organization on HIV/AIDS [3], an estimated 79% of people living with HIV were aware of their status at the end of 2018. To determine whether a person is infected with HIV, the current common test method is to go to the local health institutions for HIV antibody detection in the blood. People develop antibodies to HIV within 28 days of infection in most cases [3]. During this time, people experience the so-called "window" period − the time between the infection and first detection of HIV [9]. Although HIV antibodies are not produced and may not show signs of HIV infection, they may transmit HIV to others. A person develops some symptoms in the weeks following a high-risk behavior, including high fever of 38 degrees or more

†The corresponding author. Email: hfhuo@lut.edu.cn(H. F. Huo)
[1]Department of Applied Mathematics, Lanzhou University of Technology, Lanzhou, Gansu, 730050, China
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(4 days or more) that does not respond to antibiotic treatment, persistent diarrhea over several days, and viral rashes after or during fever. At this time, the patient may have been infected with HIV. If this is confirmed, immediate antiretroviral treatment should be provided. Current antiretroviral therapy (ART) has become an important measure to control the epidemic since ART can decline the mortality rate [23] and thus improve their life quality of HIV-infected individuals. The WHO [2] makes it clear that once HIV patients are on antiretroviral therapy, they will not transmit the disease on to others.

Many mathematical models for HIV infection have been studied [12,22,30,32,34] recently. May et al. [22] came up with the original model of AIDS. Xiao et al. [32] formulated a baseline model to predict the HIV/AIDS epidemic and measure the effect of mobility in mainland of China. Zhang et al. [34] studied on a HIV/AIDS model with application to Yunnan province. Wang et al. [30] developed an HIV latent infection model including both virus-to-cell infection and cell-to-cell transmission. Huo, Guo and Xiang [12] introduced an age-structured HIV infection model with logistic target-cell growth, in which testified Hopf bifurcation occurred at the positive steady state when bifurcating parameter crossed some critical values. Other mathematical models about HIV have been considered in [4, 11, 26, 35].

Medical treatment is one of the effective ways to control diseases, many authors have studied HIV/AIDS or epidemic models with medical treatment [13–15, 17, 24, 25, 27, 33]. Yang et al. [33] introduced pulse HIV vaccination which gave feasibility for virus eradication and optimal vaccination schedule. Chen and Wang [13] studied an HIV/AIDS epidemic model with treatment which constructed Lyapunov function to prove the stability of equilibria. An HIV/AIDS epidemic model with different latent stages and treatment is presented in [15]. Kgosimore et al. [17] constructed a model which included treatment for juveniles infected with HIV/AIDS through vertical transmission and adults infected with HIV/AIDS.

The purpose of this paper is to extend the known models in order to describe the individuals who are in the stage of window period for AIDS by introducing a new compartment, furthermore the treatment of the individuals who are in the stage of window period for AIDS are also considered. We derive the basic reproduction number R_0 by using the next generation matrix and study forward bifurcation. We also study stability of the disease-free equilibrium and existence of the endemic equilibrium, and further investigate optimal control strategies. The best-fit parameter values in our model are identified by the MCMC algorithm on the basis of the AIDS data in Gansu province of China from 2004 to 2019. We also estimate that the basic reproduction number R_0 is 2.1985 (95%CI: (1.3535-3.0435)).

The structure of this paper is organized as follows. In Section 2, we introduce a novel model of AIDS/HIV with different window period and treatment. In Section 3, we obtain the stability of the disease-free equilibrium and the existence of the endemic equilibrium. We also study the basic reproduction number and forward bifurcation. In Section 4, we further investigate the optimal control strategy by Pontryagin's Maximum Principle. In Section 5, we give a case study and numerical results. Some discussions and conclusion are given in last section.

2. The model formulation

The whole population $N(t)$ is divided into six compartments: $S(t)$, $W_1(t)$, $W_2(t)$, $E_1(t)$, $E_2(t)$, $A(t)$. $S(t)$ represents the number of susceptible individuals, $W_1(t)$

represents the number of untreated individuals who are in the stage of window period for AIDS, and these individuals are infectious. $W_2(t)$ represents the number of treated individuals who are in the stage of window period for AIDS, and these individuals are not infectious. $E_1(t)$ represents the number of untreated individuals in the latent compartment. $E_2(t)$ represents the number of treated individuals in the latent compartment. $A(t)$ represents the number of individuals with full-blown AIDS. The total number of population at time t is given by

$$N(t) = S(t) + W_1(t) + W_2(t) + E_1(t) + E_2(t) + A(t).$$

These parameters are described in Table 1. The transfer dynamic of those compartments in the model is shown in the following figure (Figure 1).

Table 1. The parameters description of the HIV/AIDS model.

Parameter	Description(Units)
Λ	The constant recruitment rate of the population ($year^{-1}$)
p	The part of S being infected with W_1 and entering W_1 ($none$)
q	The part of S being infected with E_1 and entering W_1 ($none$)
β_1	Transmission coefficient from W_1 ($year^{-1}$)
β_2	Transmission coefficient from E_1 ($year^{-1}$)
δ_1	Progression coefficient from W_1 to E_1 ($year^{-1}$)
δ_2	Progression coefficient from W_2 to E_2 ($year^{-1}$)
ε_1	Treatment rate to W_2 for W_1 ($year^{-1}$)
ε_2	Treatment rate to E_2 for E_1 ($year^{-1}$)
γ_1	Progression rate from E_1 to A ($year^{-1}$)
γ_2	Progression rate from E_2 to A ($year^{-1}$)
α	The mortality rate due to disease ($year^{-1}$)
μ	The natural mortality rate ($year^{-1}$)

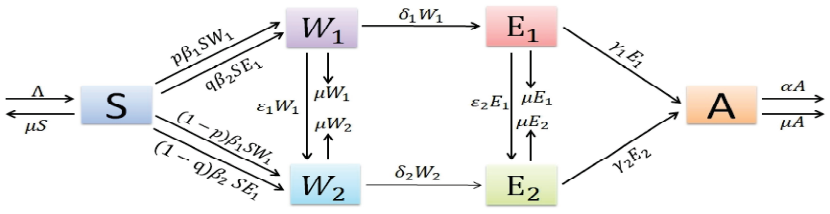


Figure 1. Transfer diagram for the dynamics of HIV/AIDS.

This diagram results in the following system of ordinary differential equations:

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta_1 S W_1 - \beta_2 S E_1 - \mu S, \\ \dfrac{\mathrm{d}W_1}{\mathrm{d}t} = p\beta_1 S W_1 + q\beta_2 S E_1 - \varepsilon_1 W_1 - \delta_1 W_1 - \mu W_1, \\ \dfrac{\mathrm{d}W_2}{\mathrm{d}t} = (1-p)\beta_1 S W_1 + (1-q)\beta_2 S E_1 + \varepsilon_1 W_1 - \delta_2 W_2 - \mu W_2, \\ \dfrac{\mathrm{d}E_1}{\mathrm{d}t} = \delta_1 W_1 - \varepsilon_2 E_1 - \gamma_1 E_1 - \mu E_1, \\ \dfrac{\mathrm{d}E_2}{\mathrm{d}t} = \delta_2 W_2 + \varepsilon_2 E_1 - \gamma_2 E_2 - \mu E_2, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = \gamma_1 E_1 + \gamma_2 E_2 - \alpha A - \mu A. \end{cases} \tag{2.1}$$

For simplicity, we let $b_1 = \varepsilon_1 + \delta_1 + \mu, b_2 = \delta_2 + \mu, b_3 = \varepsilon_2 + \gamma_1 + \mu, b_4 = \gamma_2 + \mu, b_5 = \alpha + \mu$. Then the system (2.1) becomes

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta_1 S W_1 - \beta_2 S E_1 - \mu S, \\ \dfrac{\mathrm{d}W_1}{\mathrm{d}t} = p\beta_1 S W_1 + q\beta_2 S E_1 - b_1 W_1, \\ \dfrac{\mathrm{d}W_2}{\mathrm{d}t} = (1-p)\beta_1 S W_1 + (1-q)\beta_2 S E_1 + \varepsilon_1 W_1 - b_2 W_2, \\ \dfrac{\mathrm{d}E_1}{\mathrm{d}t} = \delta_1 W_1 - b_3 E_1, \\ \dfrac{\mathrm{d}E_2}{\mathrm{d}t} = \delta_2 W_2 + \varepsilon_2 E_1 - b_4 E_2, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = \gamma_1 E_1 + \gamma_2 E_2 - b_5 A. \end{cases} \tag{2.2}$$

Lemma 2.1. *If $S(0) \geq 0, W_1(0) \geq 0, W_2(0) \geq 0, E_1(0) \geq 0, E_2(0) \geq 0, A(0) \geq 0$, the solutions $S(t), W_1(t), W_2(t), E_1(t), E_2(t), A(t)$ of system (2.2) are positive for all $t > 0$.*

Proof. For the given initial conditions, it can easily testify that the solutions of the system (2.2) are positive; if not, we suppose a contradiction: that there exists a first time t_1 such that

$$S(t_1)=0, S^{'}(t_1)<0, W_1(t)\geq 0, W_2(t)\geq 0, E_1(t)\geq 0, E_2(t)\geq 0, A(t)\geq 0, 0\leq t\leq t_1,$$

or there exists a t_2,

$$W_1(t_2)=0, W_1^{'}(t_2)<0, S(t)\geq 0, W_2(t)\geq 0, E_1(t)\geq 0, E_2(t)\geq 0, A(t)\geq 0, 0\leq t\leq t_2,$$

or there exists a t_3,

$$W_2(t_3)=0, W_2^{'}(t_3)<0, S(t)\geq 0, W_1(t)\geq 0, E_1(t)\geq 0, E_2(t)\geq 0, A(t)\geq 0, 0\leq t\leq t_3,$$

or there exists a t_4,

$$E_1(t_4)=0, E_1^{'}(t_4)<0, S(t)\geq 0, W_1(t)\geq 0, W_2(t)\geq 0, E_2(t)\geq 0, A(t)\geq 0, 0\leq t\leq t_4,$$

or there exists a t_5,

$$E_2(t_5)=0, E_2^{'}(t_5)<0, S(t)\geq 0, W_1(t)\geq 0, W_2(t)\geq 0, E_1(t)\geq 0, A(t)\geq 0, 0\leq t\leq t_5,$$

or there exists a t_6,

$$A(t_6)=0, A^{'}(t_6)<0, S(t)\geq 0, W_1(t)\geq 0, W_2(t)\geq 0, E_1(t)\geq 0, E_2(t)\geq 0, 0\leq t\leq t_6.$$

For the first case, we have

$$S^{'}(t_1) = \Lambda > 0,$$

which is contradiction implying that $S(t) \geq 0, t \geq 0$. For the second case, we have

$$W_1^{'}(t_2) = q\beta_2 S(t_2)E_1(t_2) \geq 0,$$

which is contradiction implying that $W_1(t) \geq 0, t \geq 0$. Similarly, it can be proven that $W_2(t) \geq 0, E_1(t) \geq 0, E_2(t) \geq 0, A(t) \geq 0$ for all $t \geq 0$.

Therefore, the solutions $S(t), W_1(t), W_2(t), E_1(t), E_2(t), A(t)$ of system (2.2) are still positive for all $t > 0$. This completes the proof. □

Lemma 2.2. *Define*

$$\Omega = \{(S, W_1, W_2, E_1, E_2, A) \in R_+^6 : 0 \leq S, W_1, W_2, E_1, E_2, A \leq N(t) = \frac{\Lambda}{\mu}\} \quad (2.3)$$

The solutions of model (2.1) or (2.2) are bounded and the set Ω *is a positive invariant set.*

Proof. Adding the six equations of system (2.1) or (2.2), we have

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \frac{\mathrm{d}S}{\mathrm{d}t} + \frac{\mathrm{d}W_1}{\mathrm{d}t} + \frac{\mathrm{d}W_2}{\mathrm{d}t} + \frac{\mathrm{d}E_1}{\mathrm{d}t} + \frac{\mathrm{d}E_2}{\mathrm{d}t} + \frac{\mathrm{d}A}{\mathrm{d}t} = \Lambda - \alpha A - \mu N \leq \Lambda - \mu N.$$

That means

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} + N(0)e^{-\mu t},$$

where $N(0)$ represents the initial values of the total population. Then $0 \leq \lim\limits_{t\to\infty} \sup N(t) \leq \frac{\Lambda}{\mu}$. So, we get a positive invariant set of system (2.1) or (2.2) which is

$$\Omega = \{(S, W_1, W_2, E_1, E_2, A) \in R_+^6 : 0 \leq S, W_1, W_2, E_1, E_2, A \leq N = \frac{\Lambda}{\mu}\}.$$

This completes the proof. □

Thus we consider dynamics of system (2.2) on the set Ω in this paper.

3. Analysis of the model

3.1. Disease-free equilibrium and the basic reproductive number

Obviously, the system (2.2) always has a disease-free equilibrium which is given by:

$$P_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0).$$

In this part, the basic reproduction number will be obtained through the method of the next generation matrix in [29]. System (2.2) can be written as

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

where $x = (W_1, W_2, E_1, E_2, A, S)^T$,

$$\mathcal{F}(x) = \begin{pmatrix} p\beta_1 SW_1 + q\beta_2 SE_1 \\ (1-p)\beta_1 SW_1 + (1-q)\beta_2 SE_1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \mathcal{V}(x) = \begin{pmatrix} b_1 W_1 \\ b_2 W_2 - \varepsilon_1 W_1 \\ b_3 E_1 - \delta_1 W_1 \\ b_4 E_2 - \varepsilon_2 E_1 - \delta_2 W_2 \\ b_5 A - \gamma_1 E_1 - \gamma_2 E_2 \\ \beta_1 SW_1 + \beta_2 SE_1 + \mu S - \Lambda \end{pmatrix}. \tag{3.1}$$

The Jacobian matrices of $\mathcal{F}(x)$ and $\mathcal{V}(x)$ at the disease-free equilibrium P_0 are

$$D\mathcal{F}(P_0) = \begin{pmatrix} F_{5\times 5} & 0 \\ 0 & 0 \end{pmatrix}, \text{and } D\mathcal{V}(P_0) = \begin{pmatrix} V_{5\times 5} & 0 \\ \beta_1 \frac{\Lambda}{\mu}\ 0\ \beta_2 \frac{\Lambda}{\mu}\ 0\ 0 & \mu \end{pmatrix}, \tag{3.2}$$

where

$$F = \begin{pmatrix} p\beta_1 \frac{\Lambda}{\mu} & 0 & q\beta_2 \frac{\Lambda}{\mu} & 0 & 0 \\ (1-p)\beta_1 \frac{\Lambda}{\mu} & 0 & (1-q)\beta_2 \frac{\Lambda}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \text{and } V = \begin{pmatrix} b_1 & 0 & 0 & 0 & 0 \\ -\varepsilon & b_2 & 0 & 0 & 0 \\ -\delta_1 & 0 & b_3 & 0 & 0 \\ 0 & -\delta_2 & -\varepsilon_2 & b_4 & 0 \\ 0 & 0 & -\gamma_1 & -\gamma_2 & b_5 \end{pmatrix}. \tag{3.3}$$

Therefore, the basic reproduction number R_0 is

$$R_0 = \rho(FV^{-1}) = \frac{\Lambda(p\beta_1 b_3 + q\beta_2 \delta_1)}{\mu b_1 b_3}, \tag{3.4}$$

where $b_1 = \varepsilon_1 + \delta_1 + \mu, b_3 = \varepsilon_2 + \gamma_1 + \mu$. We all know that the ability of a virus to spread in the early stages of an epidemic is measured by the basic reproductive number R_0, which refers to the average number of secondary cases produced by a case during its infection period. Further, using the Theorem 2 of [29], we can get the local stability of the disease-free equilibrium.

Theorem 3.1. *The disease-free equilibrium P_0 is locally asymptotically stable for $R_0 < 1$ and is unstable for $R_0 > 1$.*

3.2. Global stability of disease-free equilibrium

Theorem 3.2. *The disease-free equilibrium P_0 is globally asymptotically stable for $R_0 < 1$.*

Proof. We prove the global stability of the disease-free equilibrium by comparison theorem. System (2.2) can be re-written as

$$\begin{pmatrix} \dot{W}_1 \\ \dot{W}_2 \\ \dot{E}_1 \\ \dot{E}_2 \\ \dot{A} \end{pmatrix} = (F-V) \begin{pmatrix} W_1 \\ W_2 \\ E_1 \\ E_2 \\ A \end{pmatrix} - (1-\frac{\mu}{\Lambda}S) \begin{pmatrix} p\beta_1\frac{\Lambda}{\mu} & 0 & q\beta_2\frac{\Lambda}{\mu} & 0\ 0 \\ (1-p)\beta_1\frac{\Lambda}{\mu} & 0 & (1-q)\beta_2\frac{\Lambda}{\mu} & 0\ 0 \\ 0 & 0 & 0 & 0\ 0 \\ 0 & 0 & 0 & 0\ 0 \\ 0 & 0 & 0 & 0\ 0 \end{pmatrix} \begin{pmatrix} W_1 \\ W_2 \\ E_1 \\ E_2 \\ A \end{pmatrix}, \tag{3.5}$$

where F and V are the same as that in the next generation matrix. Since S$\leq \frac{\Lambda}{\mu}$ for all t≥ 0 in Ω, then

$$\begin{pmatrix} \dot{W}_1 \\ \dot{W}_2 \\ \dot{E}_1 \\ \dot{E}_2 \\ \dot{A} \end{pmatrix} = (F-V) \begin{pmatrix} W_1 \\ W_2 \\ E_1 \\ E_2 \\ A \end{pmatrix}.$$

Where $F-V$ is cooperative, that is, its off-diagonal elements are non-negative. From the Theorem 3.1, the system (2.2) is stable when $R_0 < 1$. Thus, $(W_1, W_2, E_1, E_2, A) \to (0,0,0,0,0)$ as $t \to \infty$. By the comparison theorem [19, 28], it's easy to see $(W_1, W_2, E_1, E_2, A) \to (0,0,0,0,0)$ and $S \to \frac{\Lambda}{\mu}$ as $t \to \infty$. Then $(S, W_1, W_2, E_1, E_2, A) \to P_0$ as $t \to \infty$. Therefore, P_0 is globally asymptotically stable for $R_0 < 1$. This completes the proof. □

3.3. Endemic equilibrium

3.3.1. Existence of endemic equilibrium

If $R_0 > 1$, system has a unique endemic equilibrium $P^*(S^*, W_1^*, W_2^*, E_1^*, E_2^*, A^*)$, where

$$\begin{aligned} S^* &= \frac{\Lambda}{\mu R_0}, \\ W_1^* &= \frac{\mu b_3(R_0-1)}{b_3\beta_1 + \beta_2\delta_1}, \\ W_2^* &= \frac{(R_0-1)}{b_2}[\frac{\Lambda}{R_0} + \frac{\mu b_3(\varepsilon_1 - b_1)}{\beta_1 b_3 + \beta_2\delta_1}], \\ E_1^* &= \frac{\mu\delta_1(R_0-1)}{b_3\beta_1 + \beta_2\delta_1}, \\ E_2^* &= \frac{1}{b_4}[\frac{\mu\delta_1\varepsilon_2(R_0-1)}{b_3\beta_1 + \beta_2\delta_1} + \delta_2 W_2^*], \\ A^* &= \frac{1}{b_4 b_5}[\frac{\mu\delta_1(R_0-1)(b_4\gamma_1 + \gamma_2\varepsilon_2)}{b_3\beta_1 + \beta_2\delta_1} + \gamma_2\delta_2 W_2^*]. \end{aligned}$$

3.3.2. Stability of the endemic equilibrium for a special case

Theorem 3.3. *If $\beta_2 = 0$ and $R_0 > 1$, the endemic equilibrium P^* is locally asymptotically stable.*

Proof. For the endemic equilibrium P^*, the matrix at P^* can be written as

$$\begin{pmatrix} -\beta_1 W_1^* - \beta_2 E_1^* - \mu & -\beta_1 S^* & 0 & -\beta_2 S^* & 0 & 0 \\ p\beta_1 W_1^* + q\beta_2 E_1^* & p\beta_1 S^* - b_1 & 0 & q\beta_2 S^* & 0 & 0 \\ (1-p)\beta_1 W_1^* + (1-q)\beta_2 E_1^* & (1-p)\beta_1 S^* + \varepsilon_1 & -b_2 & (1-q)\beta_2 S^* & 0 & 0 \\ 0 & \delta_1 & 0 & -b_3 & 0 & 0 \\ 0 & 0 & \delta_2 & \varepsilon_2 & -b_4 & 0 \\ 0 & 0 & 0 & \gamma_1 & \gamma_2 & -b_5 \end{pmatrix}. \tag{3.6}$$

Where $b_1 = \varepsilon_1 + \delta_1 + \mu, b_2 = \delta_2 + \mu, b_3 = \varepsilon_2 + \gamma_1 + \mu, b_4 = \gamma_2 + \mu, b_5 = \alpha + \mu$. So, when $\beta_2 = 0$, the characteristic equation can be written as

$$(\lambda + b_5)(\lambda + b_4)(\lambda + b_3)(\lambda + b_2) \begin{vmatrix} \lambda + \beta_1 W_1^* + \mu & \beta_1 S^* \\ -p\beta_1 W_1^* & \lambda - p\beta_1 S^* + b_1 \end{vmatrix} = 0. \tag{3.7}$$

Thus, the four eigenvalues of the Eq.(3.7) are $\lambda_1 = -b_2$, $\lambda_2 = -b_3$, $\lambda_3 = -b_4$, $\lambda_4 = -b_5$, and the other eigenvalues are decided by the equation

$$(\lambda + \beta_1 W_1^* + \mu)(\lambda - p\beta_1 S^* + b_1) + p\beta_1^2 S^* W_1^* = 0. \tag{3.8}$$

So, the Eq.(3.8) can be written as

$$\lambda^2 + a_1\lambda + a_2 = 0,$$

where

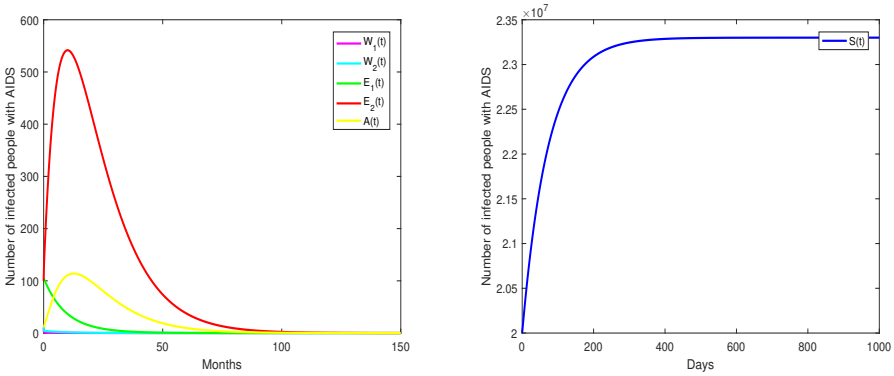
$$a_1 = b_1 - p\beta_1 S^* + \beta_1 W_1^* + \mu,$$
$$a_2 = b_1(\beta_1 W_1^* + \mu) - \mu p\beta_1 S^*.$$

When $\beta_2 = 0$, $R_0 = \frac{\Lambda p\beta_1}{\mu b_1}$, and $S^* = \frac{\Lambda}{\mu R_0}$. Therefore, $b_1 - p\beta_1 S^* = 0$, $\mu b_1 - \mu p\beta_1 S^* = 0$. Then, we can get

$$a_1 > 0, \quad a_1 a_2 > 0.$$

According to the Routh-Hurwitz [18], all the characteristic equation are negative and the endemic equilibrium $P^*(S^*, W_1^*, W_2^*, E_1^*, E_2^*, A^*)$ is locally asymptotically stable. □

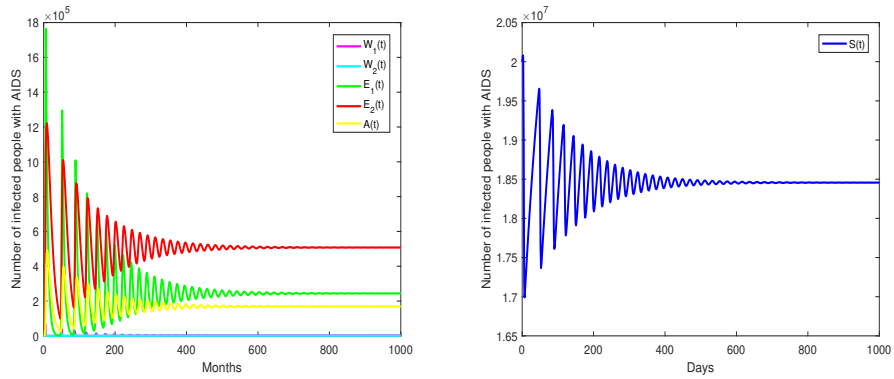
It is difficult to prove the global stability of endemic equilibrium theoretically. We can only give some numerical simulation to illustrate and extend our results. The parameter values are $\Lambda = 319179$, $p = 0.37802$, $q = 0.31761$, $\beta_1 = 1.0607 \times 10^{-06}$, $\beta_2 = 4.8333 \times 10^{-08}$, $\delta_1 = 365/18$, $\delta_2 = 365/15$, $\varepsilon_1 = 24.721$, $\varepsilon_2 = 0.18694$, $\gamma_1 = 1/11$, $\gamma_2 = 1/15$, $\alpha = 0.318$, $\mu = 1/73$. We know that $R_0 = 0.7602 < 1$. Then the disease free equilibrium P_0 of system (2.1) is globally asymptotically stable by theorem 3.2(Figure 2).



(a) (b)

Figure 2. Disease free equilibrium P_0 is globally asymptotically stable.

Next, we study the local stability of the endemic equilibrium P^* numerically. We select the parameter values as following. $\Lambda = 319179$, $p = 0.87802$, $q = 0.61761$, $\beta_1 = 1.5607 \times 10^{-06}$, $\beta_2 = 0$, $\delta_1 = 365/18$, $\delta_2 = 365/15$, $\varepsilon_1 = 5$, $\varepsilon_2 = 0.08694$, $\gamma_1 = 1/11$, $\gamma_2 = 1/15$, $\alpha = 0.318$, $\mu = 1/73$. So, $R_0 = 2.0926 > 1$. (Figure 3) show that the endemic equilibrium P^* of system (2.1) is locally asymptotically stable.



(a) (b)

Figure 3. Endemic equilibrium P^* is locally asymptotically stable.

3.4. Forward Bifurcation Analysis

In this section, the occurrence of a forward bifurcation is studied by the central manifold theory [7].

Theorem 3.4. *When $R_0 = 1$, the system (2.2) appears a forward bifurcation.*

Proof. By the central manifold theory described in [7]. Let $x_1 = S$, $x_2 = W_1$,

$x_3 = W_2$, $x_4 = E_1$, $x_5 = E_2$, $x_6 = A$. Then the system (2.2) becomes

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta_1 S W_1 - \beta_2 S E_1 - \mu S := f_1, \\ \dfrac{\mathrm{d}W_1}{\mathrm{d}t} = p\beta_1 S W_1 + q\beta_2 S E_1 - \varepsilon_1 W_1 - \delta_1 W_1 - \mu W_1 := f_2, \\ \dfrac{\mathrm{d}W_2}{\mathrm{d}t} = (1-p)\beta_1 S W_1 + (1-q)\beta_2 S E_1 + \varepsilon_1 W_1 - \delta_2 W_2 - \mu W_2 := f_3, \\ \dfrac{\mathrm{d}E_1}{\mathrm{d}t} = \delta_1 W_1 - \varepsilon_2 E_1 - \gamma_1 E_1 - \mu E_1 := f_4, \\ \dfrac{\mathrm{d}E_2}{\mathrm{d}t} = \delta_2 W_2 + \varepsilon_2 E_1 - \gamma_2 E_2 - \mu E_2 := f_5, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = \gamma_1 E_1 + \gamma_2 E_2 - \alpha A - \mu A := f_6. \end{cases} \tag{3.9}$$

Therefore, the disease-free equilibrium P_0 is

$$P_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0).$$

The Jacobian matrix $J(P_0)$ of the system (3.9) in the disease-free equilibrium is

$$J(P_0) = \begin{pmatrix} -\mu & -\beta_1\frac{\Lambda}{\mu} & 0 & -\beta_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & p\beta_1\frac{\Lambda}{\mu} - b_1 & 0 & q\beta_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & (1-p)\beta_1\frac{\Lambda}{\mu} + \varepsilon_1 & -(\mu+\delta_2) & (1-q)\beta_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & \delta_1 & 0 & -b_3 & 0 & 0 \\ 0 & 0 & \delta_2 & \varepsilon_2 & -(\mu+\gamma_2) & 0 \\ 0 & 0 & 0 & \gamma_1 & \gamma_2 & -(\mu+\alpha) \end{pmatrix}.$$

We choose β_1 as bifurcation parameter, when $R_0 = 1$ corresponding to $\beta_1 = \beta_1^* = \frac{\mu b_1}{\Lambda p} - \frac{q\beta_2\delta_1}{pb_3}$. Therefore, we have

$$J(P_0) = \begin{pmatrix} -\mu & -(\frac{b_1}{p} - \frac{\Lambda q\beta_2\delta_1}{\mu p b_3}) & 0 & -\beta_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & -\frac{\Lambda q\beta_2\delta_1}{\mu} & 0 & q\beta_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & \frac{(1-p)b_1}{p} - \frac{\Lambda(1-p)q\beta_2\delta_1}{\mu p b_3} + \varepsilon_1 & -(\mu+\delta_2) & (1-q)\beta_2\frac{\Lambda}{\mu b_3} & 0 & 0 \\ 0 & \delta_1 & 0 & -b_3 & 0 & 0 \\ 0 & 0 & \delta_2 & \varepsilon_2 & -(\mu+\gamma_2) & 0 \\ 0 & 0 & 0 & \gamma_1 & \gamma_2 & -(\mu+\alpha) \end{pmatrix}.$$

It is obviously that 0 is a simple eigenvalue of $J(P_0)$. So, the right eigenvector corresponding to the 0 eigenvalue is $V = (v_1, v_2, v_3, v_4, v_5, v_6)^T$, the left eigenvector corresponding to the 0 eigenvalue is $U = (u_1, u_2, u_3, u_4, u_5, u_6)$, and it needs to

satisfy $UV = 1$. So, the right eigenvector is

$$V = \begin{pmatrix} \frac{\Lambda\beta_2\delta_1(q-p)-\mu b_1 b_3}{\mu^2 p} \\ b_3 \\ \frac{\mu b_3[(1-p)b_1+\varepsilon_1 p]+\Lambda\beta_2\delta_1(p-q)}{\mu p b_2} \\ \delta_1 \\ \frac{\mu b_3\delta_2[(1-p)b_1+\varepsilon_1 p]+\Lambda\beta_2\delta_1\delta_2(p-q)}{\mu p b_2 b_4} + \frac{\varepsilon_2\delta_1}{b_4} \\ \frac{\mu b_3\delta_2\gamma_2[(1-p)b_1+\varepsilon_1 p]+\Lambda\beta_2\delta_1\delta_2\gamma_2(p-q)}{\mu p b_2 b_4 b_5} + \frac{b_5\gamma_1\delta_1+\varepsilon_2\delta_1\gamma_2}{b_4 b_5} \end{pmatrix},$$

the left eigenvector is

$$U = \Big(0, \frac{\mu b_3}{\mu b_3^2 + \Lambda q\beta_2\delta_1}, 0, \frac{\Lambda q\beta_2}{\mu b_3^2 + \Lambda q\beta_2\delta_1}, 0, 0\Big).$$

In viewpoint of Theorem 4.1 [7], we know that

$$a = \sum_{k,i,j=1}^{6} u_k v_i v_j \frac{\partial^2 f_k(P_0)}{\partial x_i \partial x_j}, \quad b = \sum_{k,i=1}^{6} u_k v_i \frac{\partial^2 f_k(P_0)}{\partial x_i \partial \beta_1}.$$

Therefore, we have

$$\begin{aligned} a =& u_2 v_1 v_2 \frac{\partial^2 f_2(P_0)}{\partial x_1 \partial x_2} + u_2 v_1 v_4 \frac{\partial^2 f_2(P_0)}{\partial x_1 \partial x_4} + u_2 v_2 v_1 \frac{\partial^2 f_2(P_0)}{\partial x_2 \partial x_1} + u_2 v_4 v_1 \frac{\partial^2 f_2(P_0)}{\partial x_4 \partial x_1} \\ =& 2u_2\Big(v_1 v_2 \frac{\partial^2 f_2(P_0)}{\partial x_1 \partial x_2} + v_1 v_4 \frac{\partial^2 f_2(P_0)}{\partial x_1 \partial x_4}\Big) \\ =& \frac{2\mu b_3}{\mu b_3^2 + \Lambda q\beta_2\delta_1}\Big(\frac{\Lambda\beta_2\delta_1(q-p)}{\mu^2 p} - \frac{b_1 b_3}{\mu p}\Big)[p b_3\Big(\frac{\mu b_1}{\Lambda p} - \frac{q\beta_2\delta_1}{p b_3}\Big) + q\beta_2\delta_1] \\ =& \frac{2\mu b_3}{\mu b_3^2 + \Lambda q\beta_2\delta_1}\Big(\frac{-\Lambda p\beta_2\delta_1 - \Lambda p b_3\delta_1}{\mu^2 p}\Big)\frac{\mu b_1 b_3}{\Lambda} < 0. \\ b =& u_2 v_2 \frac{\partial^2 f_2(P_0)}{\partial x_2 \partial \beta_1} = \frac{\Lambda p b_3^2}{\mu b_3^2 + \Lambda q\beta_2\delta_1} > 0. \end{aligned}$$

We find that the coefficient a is always negative and b is always positive. According to Theorem 4.1 of [7], the system (2.2) at $R_0 = 1$ appears a forward bifurcation. This completes the proof. □

The forward bifurcation diagram of system (2.2) is shown in Figure 4.

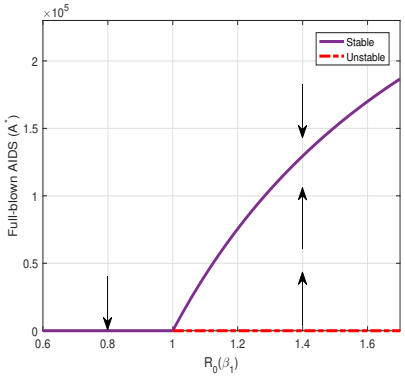


Figure 4. Illustration of forward bifurcation when one parameter β_1 in R_0 is varied.

4. The optimal control problems

4.1. The existence of optimal control

In the previous part, we mainly study the dynamical behavior in the system (2.1). In this section, we use two control variables $u_1(t)$ and $u_2(t)$ to reduce the number of HIV/AIDS($W_1(t)$ and $E_1(t)$). The control $u_1(t)$ represents efforts intended to keep the susceptible from contacting with the HIV/AIDS($W_1(t)$), for example, the media report and educational programs are included. The control $u_2(t)$ represents the effort to encourage HIV/AIDS ($E_1(t)$) through proper treatment, such as taking medicine or looking for other medical help. The optimal control problems to minimize the objective function is given by

$$J(u_1, u_2) = \int_0^{t_f} [W_1(t) + E_1(t) + \frac{1}{2}c_1 u_1^2(t) + \frac{1}{2}c_2 u_2^2(t)]dt. \tag{4.1}$$

In order to obtain the optimal control strategy, the following optimal model is established

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - (1-u_1(t))\beta_1 S W_1 - (1-u_2(t))\beta_2 S E_1 - \mu S, \\ \dfrac{\mathrm{d}W_1}{\mathrm{d}t} = (1-u_1(t))p\beta_1 S W_1 + (1-u_2(t))q\beta_2 S E_1 - \varepsilon_1 W_1 - \delta_1 W_1 - \mu W_1, \\ \dfrac{\mathrm{d}W_2}{\mathrm{d}t} = (1-u_1(t))(1-p)\beta_1 S W_1 + (1-u_2(t))(1-q)\beta_2 S E_1 \\ \qquad\qquad + \varepsilon_1 W_1 - \delta_2 W_2 - \mu W_2, \\ \dfrac{\mathrm{d}E_1}{\mathrm{d}t} = \delta_1 W_1 - \varepsilon_2 E_1 - \gamma_1 E_1 - \mu E_1, \\ \dfrac{\mathrm{d}E_2}{\mathrm{d}t} = \delta_2 W_2 + \varepsilon_2 E_1 - \gamma_2 E_2 - \mu E_2, \\ \dfrac{\mathrm{d}A}{\mathrm{d}t} = \gamma_1 E_1 + \gamma_2 E_2 - \alpha A - \mu A. \end{cases} \tag{4.2}$$

with initial conditions

$$S(0) \geq 0, W_1(0) \geq 0, W_2(0) \geq 0, E_1(0) \geq 0, E_2(0) \geq 0, A(0) \geq 0,$$

where $U = \{(u_1, u_2)|u_i(t)$ *is a Lebesgue measurable and* $0 \leq u_i(t) \leq 1, for\ all\ t \in [0, t_f]\}$ and t_f is the final time. The constant $c_i \geq 0, i = 1, 2$ are relative weight coefficients that balance the cost and the number of AIDS.

Next, the existence of the optimal control pair in the system (2.1) is studied by using the results of Fleming and Rishel [10].

Theorem 4.1. *Under the initial conditions, the system (4.2) exists an optimal control pair* $(u_1^*, u_2^*) \in U, t \in [0, t_f]\}$ *such that*

$$J(u_1^*, u_2^*) = \min_{u_1(t), u_2(t) \in U} J(u_1, u_2).$$

Proof. To prove the existence of optimal control, the following conditions must be satisfied:
(1) The control and related state variables are non-negative values.
(2) The control set U is convex and closed.
(3) The right-hand of the state system (4.2) is bounded and it is a linear function of the control and the state variable.
(4) The integrand of the objective function on U is convex.
(5) There exist constants $b_1, b_2 > 0$ and $\alpha > 1$ such that the integrant of the objective functional

$$L(t, u_1, u_2) = W_1(t) + E_1(t) + \frac{1}{2}c_1 u_1^2(t) + \frac{1}{2}c_2 u_2^2(t)$$

satisfies

$$L(t, u_1, u_2) \geq b_1[u_1^2(t) + u_2^2(t)]^{\frac{\alpha}{2}} - b_2.$$

Obviously the conditions (1), (2) and (4) are satisfied. As for condition (3), we have already proved that six state variable are bounded, therefore

$$\begin{aligned}
&\frac{\mathrm{d}S}{\mathrm{d}t} \leq \Lambda, \qquad \frac{\mathrm{d}W_1}{\mathrm{d}t} \leq (1 - u_1(t))p\beta_1 S W_1 + (1 - u_2(t))q\beta_2 S E_1, \\
&\frac{\mathrm{d}W_2}{\mathrm{d}t} \leq (1 - u_1(t))(1 - p)\beta_1 S W_1 + (1 - u_2(t))(1 - q)\beta_2 S E_1 + \varepsilon_1 W_1, \\
&\frac{\mathrm{d}E_2}{\mathrm{d}t} \leq \delta_2 W_2 + \varepsilon_2 E_1, \qquad \frac{\mathrm{d}E_1}{\mathrm{d}t} \leq \delta_1 W_1, \qquad \frac{\mathrm{d}A}{\mathrm{d}t} \leq \gamma_1 E_1 + \gamma_2 E_2.
\end{aligned}$$

For the condition (5), there exist $b_1 = min\{\frac{c_1}{2}, \frac{c_2}{2}\}, b_2 \in R^+$ and $\alpha = 2$, such that

$$L(t, u_1, u_2) \geq b_1[u_1^2(t) + u_2^2(t)]^{\frac{\alpha}{2}} - b_2,$$

which completes the existence of an optimal control. □

4.2. Characterization of optimal controls

According to the Pontryagin¡¯s Maximum Principle in [8], the necessary conditions for the existence of optimal control of the system (2.1) are obtained. Now, we will formulate the Hamiltonian from the governing dynamics and the objective

functional to get the optimality conditions. So, we have

$$\begin{aligned} H &= W_1(t) + E_1(t) + \frac{1}{2}c_1u_1^2(t) + \frac{1}{2}c_2u_2^2(t) \\ &\quad + \lambda_S[\Lambda - (1-u_1(t))\beta_1 SW_1 - (1-u_2(t))\beta_2 SE_1 - \mu S], \\ &\quad + \lambda_{W_1}[(1-u_1(t))p\beta_1 SW_1 + (1-u_2(t))q\beta_2 SE_1 - \varepsilon_1 W_1 - \delta_1 W_1 - \mu W_1] \\ &\quad + \lambda_{W_2}[(1-u_1(t))(1-p)\beta_1 SW_1 + (1-u_2(t))(1-q)\beta_2 SE_1 + \varepsilon_1 W_1 - \delta_2 W_2 - \mu W_2] \\ &\quad + \lambda_{E_1}[\delta_1 W_1 - \varepsilon_2 E_1 - \gamma_1 E_1 - \mu E_1] \\ &\quad + \lambda_{E_2}[\delta_2 W_2 + \varepsilon_2 E_1 - \gamma_2 E_2 - \mu E_2] \\ &\quad + \lambda_A[\gamma_1 E_1 + \gamma_2 E_2 - \alpha A - \mu A]. \end{aligned} \tag{4.3}$$

Where $\lambda_S,\ \lambda_{W_1},\ \lambda_{W_2},\ \lambda_{E_1},\ \lambda_{E_2},\ \lambda_A$ are the associated adjoints for the states $S,\ W_1,\ W_2,\ E_1,\ E_2,\ A$. The system of adjoint equations is found by taking the proper partial derivatives of the Hamiltonian with respect to the associated state and control variables.

Theorem 4.2. *There is an optimal control pairs $(u_1^*,\ u_2^*)$ and solutions $S(t)^*$, $W_1^*(t)$, $W_2^*(t)$, $E_1^*(t)$, $E_2^*(t)$, $A^*(t)$ of the corresponding state system (4.2) that minimizes the objective functional $J(u_1^*,\ u_2^*)$ over U. Then there exist adjoint variables $\lambda_S,\ \lambda_{W_1},\ \lambda_{W_2},\ \lambda_{E_1},\ \lambda_{E_2},\ \lambda_A$, satisfying*

$$-\frac{d\lambda_i}{dt} = \frac{\partial H}{\partial i} \tag{4.4}$$

and with the terminal conditions

$$\lambda_i(t_f) = 0,\ \textit{where } i = S,\ W_1,\ W_2,\ E_1,\ E_2,\ A. \tag{4.5}$$

The optimality conditions is given by

$$\frac{\partial H}{\partial u_j} = 0,\ j = 1,\ 2. \tag{4.6}$$

Further, the control $(u_1^*,\ u_2^*)$ can be obtained from the following equations:

$$\begin{aligned} u_1^* &= \min\{1,\ \max\{0,\ \frac{[-\lambda_S + p\lambda_{W_1} + (1-p)\lambda_{W_2}]\beta_1 S^* W_1^*}{c_1}\}\}, \\ u_2^* &= \min\{1,\ \max\{0,\ \frac{[-\lambda_S + q\lambda_{W_1} + (1-q)\lambda_{W_2}]\beta_2 S^* E_1^*}{c_2}\}\}. \end{aligned} \tag{4.7}$$

Proof. By differentiating the Hamiltonian, we obtain the adjoint system can be written as:

$$\begin{aligned} &-\frac{\mathrm{d}\lambda_S}{\mathrm{d}t} = \frac{\partial H}{\partial S},\ \lambda_S(t_f) = 0, && -\frac{\mathrm{d}\lambda_{W_1}}{\mathrm{d}t} = \frac{\partial H}{\partial W_1},\ \lambda_{W_1}(t_f) = 0, \\ &-\frac{\mathrm{d}\lambda_{W_2}}{\mathrm{d}t} = \frac{\partial H}{\partial W_2},\ \lambda_{W_2}(t_f) = 0, && -\frac{\mathrm{d}\lambda_{E_1}}{\mathrm{d}t} = \frac{\partial H}{\partial E_1},\ \lambda_{E_1}(t_f) = 0, \\ &-\frac{\mathrm{d}\lambda_{E_2}}{\mathrm{d}t} = \frac{\partial H}{\partial E_2},\ \lambda_{E_2}(t_f) = 0, && -\frac{\mathrm{d}\lambda_A}{\mathrm{d}t} = \frac{\partial H}{\partial A},\ \lambda_A(t_f) = 0, \end{aligned} \tag{4.8}$$

the state adjoint system is given by

$$\begin{aligned}
\frac{\mathrm{d}\lambda_S}{\mathrm{d}t} &= [\lambda_S - p\lambda_{W_1} - (1-p)\lambda_{W_2}](1-u_1(t))\beta_1 W_1^* + [\lambda_S - q\lambda_{W_1} - (1-q)\lambda_{W_2}] \\
&\quad \times (1-u_2(t))\beta_2 E_1^* + \mu\lambda_S, \\
\frac{\mathrm{d}\lambda_{W_1}}{\mathrm{d}t} &= -1 + [\lambda_S - p\lambda_{W_1} - (1-p)\lambda_{W_2}](1-u_1(t))\beta_1 S^* + (\lambda_{W_1} - \lambda_{W_2})\varepsilon_1 \\
&\quad + (\lambda_{W_1} - \lambda_{E_1})\delta_1 + \mu\lambda_{W_1}, \\
\frac{\mathrm{d}\lambda_{W_2}}{\mathrm{d}t} &= (\lambda_{W_2} - \lambda_{E_2})\delta_2 + \mu\lambda_{W_2}, \\
\frac{\mathrm{d}\lambda_{E_1}}{\mathrm{d}t} &= -1 + [\lambda_S - q\lambda_{W_1} - (1-q)\lambda_{W_2}](1-u_2(t))\beta_2 S^* + (\lambda_{E_1} - \lambda_{E_2})\varepsilon_2 \\
&\quad + (\lambda_{E_1} - \lambda_A)\gamma_1 + \mu\lambda_{E_1}, \\
\frac{\mathrm{d}\lambda_{E_2}}{\mathrm{d}t} &= (\lambda_{E_2} - \lambda_A)\gamma_2 + \mu\lambda_{E_2}, \\
\frac{\mathrm{d}\lambda_A}{\mathrm{d}t} &= \alpha\lambda_A + \mu\lambda_A.
\end{aligned}$$

Further, by differentiating the Hamiltonian with respect to the controls, we have the following optimality conditions:

$$\begin{aligned}
\frac{\partial H}{\partial u_1} &= c_1 u_1^*(t) + \beta_1 S^* W_1^* \lambda_S - p\beta_1 S^* W_1^* \lambda_{W_1} - (1-p)\beta_1 S^* W_1^* \lambda_{W_2} = 0, \\
\frac{\partial H}{\partial u_2} &= c_2 u_2^*(t) + \beta_2 S^* E_1^* \lambda_S - q\beta_2 S^* E_1^* \lambda_{W_1} - (1-q)\beta_2 S^* E_1^* \lambda_{W_2} = 0.
\end{aligned}$$

For the u_1^* and u_2^*, we have

$$\begin{aligned}
u_1^* &= \frac{[-\lambda_S + p\lambda_{W_1} + (1-p)\lambda_{W_2}]\beta_1 S^* W_1^*}{c_1}, \\
u_2^* &= \frac{[-\lambda_S + q\lambda_{W_1} + (1-q)\lambda_{W_2}]\beta_2 S^* E_1^*}{c_2}.
\end{aligned}$$

The completes the proof. □

5. A case study

5.1. Numerical results

Numerical experiments are carried out using MATLAB in this section. We estimate the parameters of our model on the basis of the AIDS data in Gansu province of China from 2004 to 2019 by carrying out the Markov Chain Monte Carlo (MCMC) procedure. The actual infection is shown in Figure 5. In order to calculate the basic reproduction number R_0 of HIV/AIDS in Gansu Province and predict changes in the next few years, it is essential to estimate the unknown parameters of the model (2.1). The population size of the Gansu Province at the end of 2003 is 25.3719 million. According to the relevant data of the Gansu Provincal Bureau of Statistics (2019), we can get the birth rate in Gansu Province at the end of 2003 is 12.58 per thousand. Therefore, we have the yearly birth population of Gansu Province is about 319179

by calculation. We know that the average life expectancy of the population of Gansu Province is 73. So, we conclude that the yearly natural mortality rate of the population in Gansu Province is approximately $\mu = 1/73$. We get the mortality rate due to HIV is 0.318 $year^{-1}$ [32]. We know that the incubation period of HIV/AIDS is $10 - 15$ years [3]. So, we assume that the average progress time of latent individuals without treatment $(1/\gamma_1)$ is 11 years and with treatment $(1/\gamma_2)$ is 15 years, then the yearly progress rate γ_1 is 1/11 and γ_2 is 1/15. We know that the window period for HIV/AIDS is $14 - 21$ days [3]. Therefore, we assume that the average progress time of "window" period individuals without treatment $(1/\delta_1)$ is 18 days and with treatment $(1/\delta_2)$ is 15 days, then the yearly progress rate δ_1 is 365/18 and δ_2 is 365/15. We choose a set of values of parameters in Table 2.

Table 2. The parameters description of the HIV/AIDS model.

Parameters	Mean value	Std	95% CI	Reference
Λ	319179	-	-	[1]
δ_1	365/18	-	-	Estimate
δ_2	365/15	-	-	Estimate
γ_1	1/11	-	-	Estimate
γ_2	1/15	-	-	Estimate
α	0.318	-	-	[32]
μ	1/73	-	-	[16]
p	0.57802	0.2431	[0.1015, 1]	MCMC
q	0.61761	0.21623	[0.1938, 1]	MCMC
β_1	1.0607×10^{-06}	8.5234×10^{-07}	$[0, 0.2731\times10^{-05}]$	MCMC
β_2	4.8333×10^{-08}	1.3772×10^{-08}	$[0.2134\times10^{-07}, 0.7533\times10^{-07}]$	MCMC
ε_1	21.721	13.4	[0, 47.9850]	MCMC
ε_2	0.08694	0.081435	[0, 0.2466]	MCMC

According to the Table 2, infection rate of untreated window individuals to susceptible persons is $\beta_1 = 1.0607\times10^{-06}$. Infection rate of untreated latent individuals to susceptible individuals is $\beta_2 = 4.8333\times10^{-08}$. We know that β_1 is more than β_2. This suggests that people with HIV in the window period may be more infectious than those with HIV in the latent. This is consistent with the results of in [6,31].

We give the number of samples and the frequency distribution of R_0 by using Markov Chain Monte Carlo (MCMC) procedure. From Figure 6(b), we can clearly know that the basic reproductive number R_0 satisfies the normal distribution. Hence, we can obtain the confidence interval and mean value of R_0. The basic reproduction number R_0 is estimated to be $R_0 = 2.1985$ (95%CI: (1.3535-3.0435)), as shown in Figure 6. This means that AIDS should be taken seriously in Gansu Province.

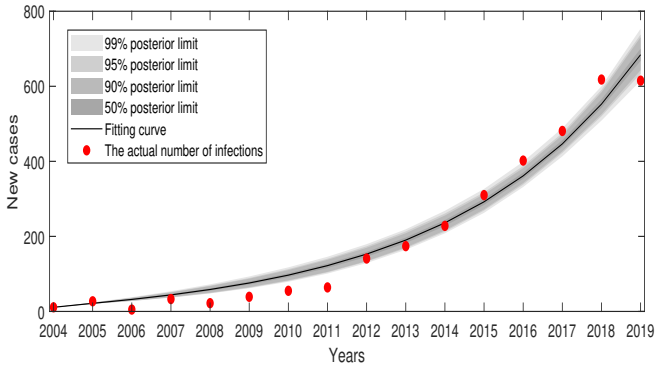
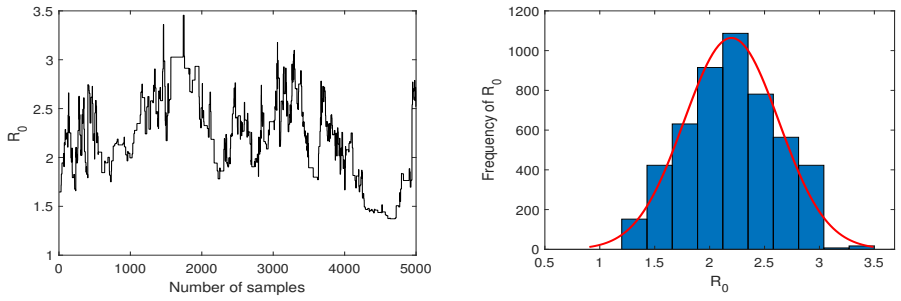


Figure 5. The actual number of people infected in Gansu Province from 2004 to 2019.



(a) (b)

Figure 6. (a) The number of Markov chain samples of R_0. The curve represents the size of the R_0 value. (b) The frequency distribution of R_0. The red curve is the probability density function curve of R_0.

5.2. Uncertainty and Sensitivity analysis

We study uncertainty and sensitivity analysis by using a Latin hypercube sampling (LHS) method and evaluating the partial rank correlation coefficients (PRCCs) [5, 21] in this section.

Figure 7 shows that the parameters have the positive influence on basic reproduction number R_0 are the proportion of susceptible individuals infected by untreated window period individuals (p), the proportion of susceptible individuals infected by untreated latent individuals (q), the transmission coefficient from the window period individuals without treatment (β_1) and the transmission coefficient from the latent individuals without treatment (β_2). Lowering these parameters can effectively reduce the number of infections. While parameters have a negative effect on basic reproduction number R_0 are the treatment rate in untreated window period individuals (ε_1) and the treatment rate in untreated latent individuals (ε_2).

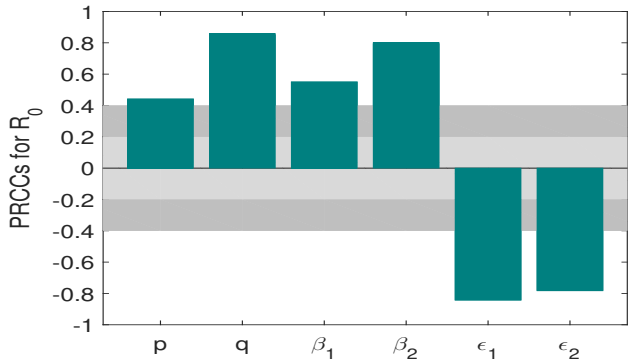


Figure 7. The Partial Rank Coefficients (PRCCs) of R_0 in system (2.1).

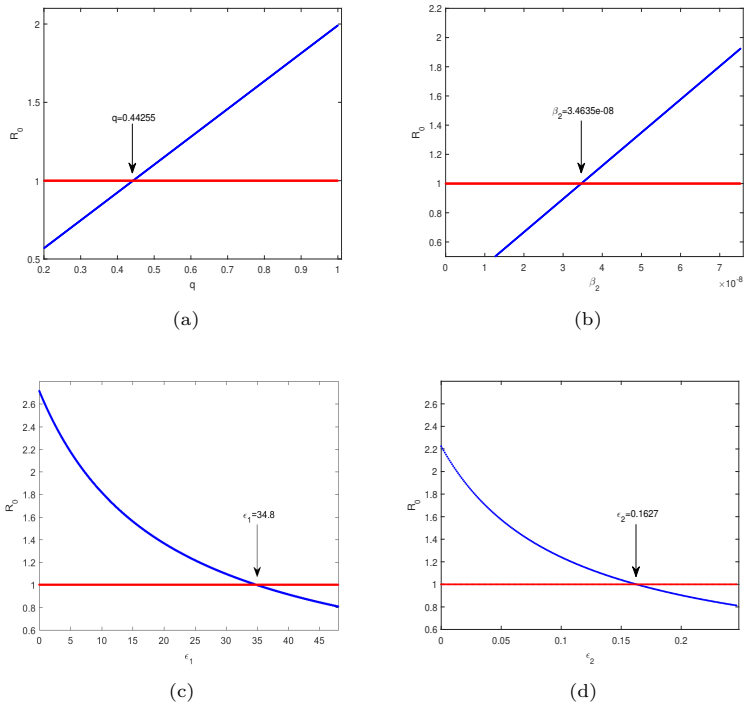


Figure 8. The variation trend between four parameters and the basic regeneration number R_0.

According to the Figure 7, we already know the effect of the parameters q, β_2, ε_1, ε_2 on the base number of reproduction R_0. However, Figure 8 demonstrates that the changing trend of single parameter and R_0 more clearly and intuitively. In each subgraph, we change only one parameter and the other parameters are shown in Table 2. It can be seen from Figure 8(a) that R_0 is less than 1 only when $q < 0.44255$, which means that the disease can be controlled only when the number of infected people is less than 44255 per 100000 people. Figure 8(b) reveals that the transmission rate of the patients with latent period must be controlled within

$3.4635e^{-08}$. This can effectively reduce the spread of the disease. In Figure 8(c) and (d), with the gradual increase of ε_1 and ε_2, we can see that R_0 is gradually decreasing. Especially, the treatment rate in window period is more than 200 times of that in latent period at $R_0 = 1$, which indicates that it is necessary to increase the treatment of infected individuals in window period in order to control the disease.

Figure 9 shows that the effects of several parameters over time on infected individuals. Obviously, there is a strong negative correlation between the treatment rate of individuals in the untreated window individuals (ε_1) and the infected individuals. This suggests that the Chinese Center for Disease Control and Prevention should increase the treatment of diseases as early as possible to reduce the number of infected people. This plays a key role in the prevention and control of disease. The change of parameter ε_2 over time from the initial insignificant correlation to a moderate negative correlation indicates that the public health departments should take some measures (for example, strengthen the publicity of AIDS knowledge) to control treatment rate among untreated latent individuals. The parameters p and β_1 have a strong positive correlation throughout the period. So we know that when p and β_1 are smaller, the number of people infected by untreated window-period individuals is smaller. Similarly, the parameters q and β_2 have a strong positive effect on infected individuals.

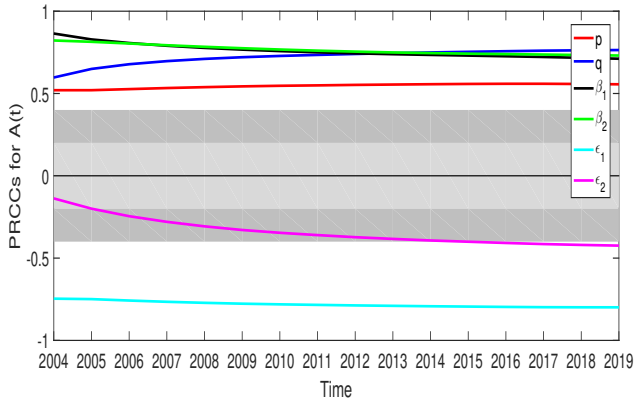


Figure 9. The sensitivity of several parameters changes on infected individuals.

Figure 10 shows that infected individuals (i.e., $A(t)$) is sensitive to parameters p ($p-value = 1.4866\times10^{-157}$), q ($p-value = 0$), β_1 ($p-value = 5.0138\times10^{-260}$), β_2 ($p-value = 4.9901\times10^{-288}$), ε_1 ($p-value = 0$) and ε_2 ($p-value = 1.0006\times10^{-60}$).

5.3. Optimal control analysis

We will study the optimal solution of the our model by using the numerical method [20] in this section.

For this simulation, the initial values of system (2.1) is assumed to be $S(0) = 20000000$, $W_1(0) = 10$, $W_2(0) = 10$, $E_1(0) = 100, E_2(0) = 100$ and $A(0) = 11$. We also select the parameter values are as follow, $\Lambda = 319179$, $p = 0.57802$, $q = 0.61761$, $\beta_1 = 1.0607\times10^{-06}$, $\beta_2 = 4.8333\times10^{-08}$, $\delta_1 = 365/18$, $\delta_2 = 365/15$, $\varepsilon_1 = 21.721$, $\varepsilon_2 = 0.08694$, $\gamma_1 = 1/11$, $\gamma_2 = 1/15$, $\alpha = 0.318$, $\mu = 1/73$. The period

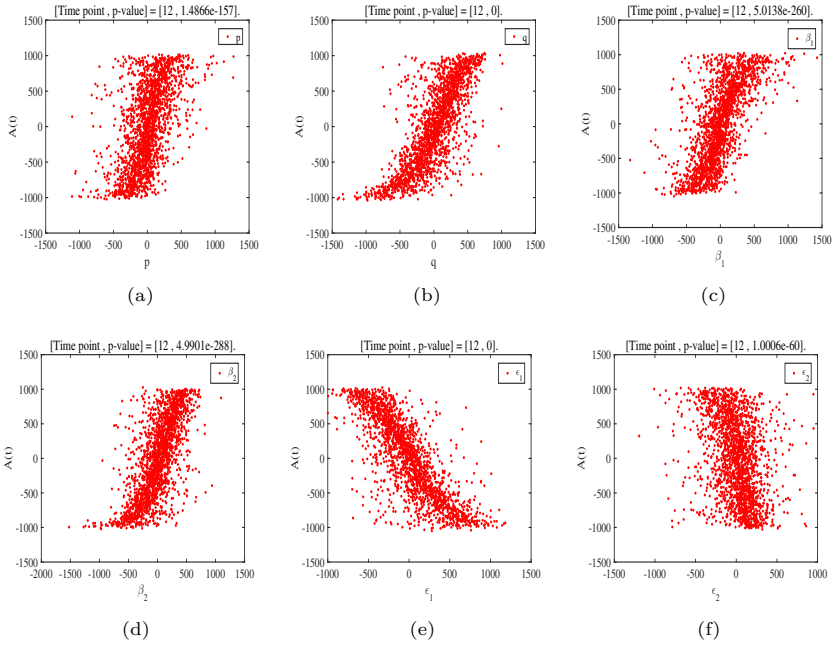


Figure 10. P values of each parameter in the 12th year.

of the control is 16 years. In order to reveals the effect of the control strategies considered in our paper, we will give the graphes of evolution with time in different compartment populations under different controls.

Figure 11 shows that the number of people in different compartments when we select the weights on objective function are $c_1 = 100; c_2 = 1000$ and the different values of u_1, u_2. It can be seen from Figure 11(a) that different optimal control strategies have little effect on the susceptibles. Figure 11(b)-(f) show that the system with control is obviously better than the system without control. When $u_1 = 0, u_2 = 0$, the number of people in different compartment is always the highest. However, when $u_1 = 0.5, u_2 = 0$, the number of people decreased significantly. But, single control u_2, middle control and optimal control have almost the same effect and they are better than single control u_1, while u_1 is better than no control.

Figure 12 shows that the influence of different weights in the objective function on u_1 and u_2. We change the weights in the objective function from $c_1 = 100$, $c_2 = 1000$ to $c_1 = 1000$, $c_2 = 100$. In Figure 12(a), when we choose $c_1 = 100$, and $c_2 = 1000$, the simulation shows that the control u_1 decreases rapidly from 1 to 0.78, then continues to decline slowly and finally tends to 0. The control u_2 reaches a peak value of about 0.54 at the time about 0.3 years, and then gradually decreases with the increase of time. In Figure 12(b), when we choose $c_1 = 1000$, and $c_2 = 100$, the control u_1 decreases sharply from about 0.47 to 0 and is relatively stable approaching to 0. The control u_2 remains unchanging at about 1 and lasts for about 6.5 years. Then it gradually decreases with the increase of time and finally reaches 0.

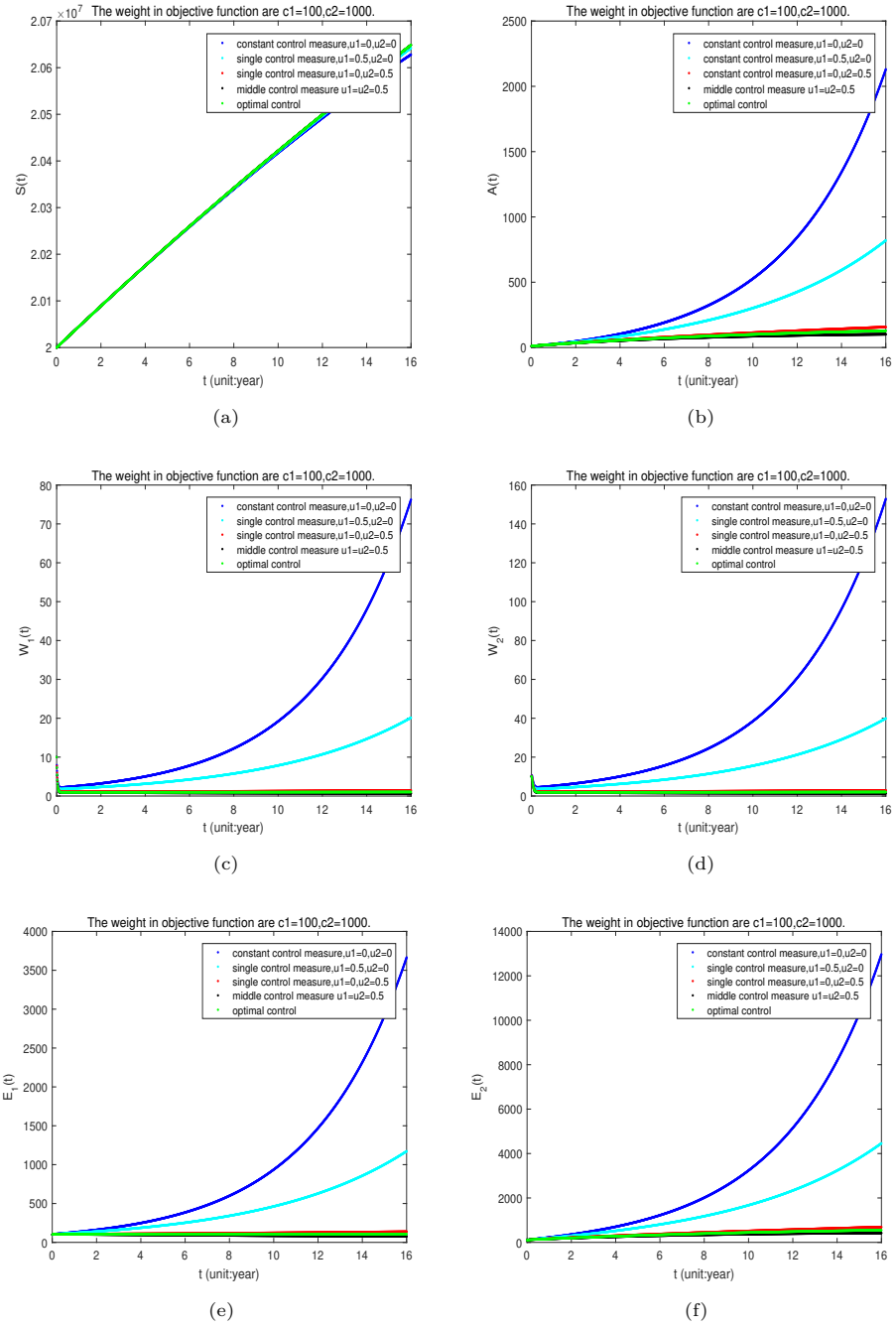
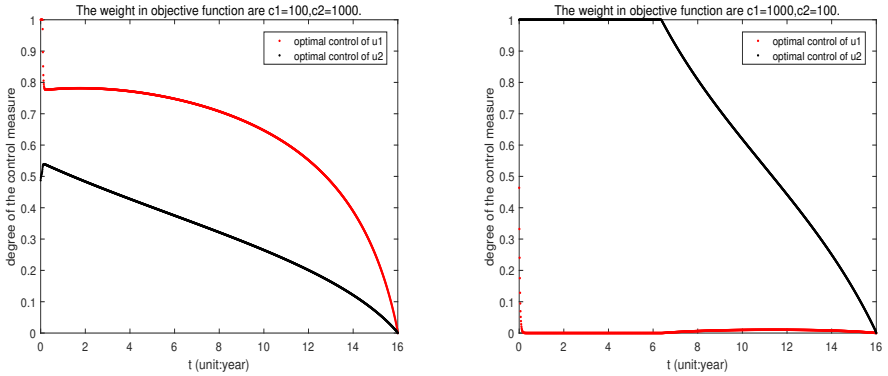


Figure 11. Number of people in different compartment when we select the weights on objective function are $c_1 = 100; c_2 = 1000$ and under different optimal control strategies, that is, (1) without $u_1 = 0, u_2 = 0$;(2) single control $u_1 = 0.5, u_2 = 0$; (3) single control $u_1 = 0, u_2 = 0.5$; (4) middle control $u_1 = u_2 = 0.5$; (5) optimal control $u_1 = u_1^*, u_2 = u_2^*$.



(a) (b)

Figure 12. The impact of different weight coefficients on optimal control u_1, u_2: (a)$c_1 = 100, c_2 = 1000$; (b)$c_1 = 1000, c_2 = 100$.

6. Discussion and conclusion

We formulate a novel HIV/AIDS model with different window periods and treatment. The basic reproduction number R_0 is obtained by using the next generation matrix. Stability of the disease-free equilibrium and existence of the endemic equilibrium is derived. We also study the emergence of forward branches by the theory of central manifold. Using the Pontryagin¡¯s maximum principle, we get the existence of the optimal control pair and the mathematical expression of the optimal control. The best-fit parameter values in our model are identified by the MCMC algorithm on the basis of the AIDS data in Gansu province of China from 2004 to 2019. We also estimate that the basic reproduction number R_0 is 2.1985 (95%CI: (1.3535-3.0435)). Some numerical simulations and sensitivity analysis are carried out to illustrate our main results. Our results show that treatment for individuals who are in the stage of window period for AIDS is necessary and meaningful for the control of HIV/AIDS.

Conflict of interest

The authors declare that they have no conflict of interest.

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