Dynamics and optimal control of a spatial diffusion HIV/AIDS model with ART and PrEP treatments

Liping Wang[1], Anwarud Din[2], Peng Wu[3*]

[1] School of Mathematics-Physics and Finance, Anhui Polytechnic University, Wuhu 241000, PR China
[2] Department of Mathematics, Sun Yat-sen University, Guangzhou 510275, PR China

[3] School of Data Sciences, Zhejiang University of Finance & Economics, Hangzhou 310018, PR China

Abstract In this paper, to investigate the synthetic effect of PrEP (pre-exposure prophylaxis) and ART (antiretrovial therapy) on HIV transmission among MSM (men who have sex with men) in heterogenous environment, an realistic HIV epidemic model with spatial diffusion is established. Here, HIV infectious people are divided into three immunity based compartments, i.e., CD4+ T cell count less than 350, between 350 and 500, and more than 500, respectively. The basic reproduction number R_0 is established and proved as a threshold parameter: The global asymptotic stability of the disease-free steady state holds for $R_0 < 1$, and the disease will be present if $R_0 > 1$. Considering the substantial advantages of PrEP and ART in controlling HIV transmissions among MSM, the optimal control problem is presented for the case of positive constant diffusion coefficients, which minimize the total population of susceptible individual and HIV infected individual, the cost of PrEP and ART thearpy. As an illustration of our theoretical results, we conduct numerical simulations. We also conduct an optimal control case study where model parameters are estimated from the demographic and epidemiological data from China. This work suggests: (1) Spatial factors cannot be ignored during the HIV intervention; (2)Taking the PrEP intervention measure for HIV transmissions among MSM as early as possible will help to improve the control efficiency and reduces its cost; (3) Reducing the PrEP drug costs will promote the efficiency of PrEP treatment in preventing the spread of HIV among MSM.

Keywords HIV/AIDS· Spatial diffusion· MSM · PrEP· Optimal control

2020 AMS Subject Classification: 92D30;35B40; 93C95.

---

*Corresponding authors: Peng Wu, Email: HZPengWu@163.com

1 Introduction

The total number of HIV notifications in China has steadily increased in recent years [1]. MSM group (men who have sex with men) turn out to be a crucial driving force of the increase in HIV infection. In 2017, there were 34,385 new cases within the MSM group, accounting for one quarter of the total new HIV/AIDS cases in China [2]. Hence, the Chinese government has strengthened its intervention and control efforts, developed national working policies and guidelines and control among MSM.

On the one hand, development of clinic treatment has made AIDS as a treatable chronic disease [3]. There exist some models are presented to investigated the influence of ART on HIV incidence [4, 5] and many compartment models also have been applied to studying the impact of ART treatment on HIV infection [6, 7]. As one of the earliest mathematical models, Williams et al.[?] established a model to investigated the effect of ART on the transmission of HIV based on the HIV infected cases in adults in South Africa, and to show how it could help to control the epidemic. Hosseini et al.[6] formulated a multi-scale model of HIV infection in vitro and APOBEC3G-based ART to study the impact of ART to HIV virus infection. However, the above work only studies the impact of ART therapy on HIV infection, and did not consider the medical standards of ART treatment. This is an important factor that cannot be ignored in mathematical modeling. In fact, in clinical treatment, a decision as to whether a therapy should begin or not is dependent on CD4+ T cell count in patients. The report of World Heath Organization (WHO) suggests [8] that ART should start when CD4+ T cell < 350. Meanwhile, infected persons having 350-500 CD4+ T cell within the host, then they are suggested to start ART, they should moderately suggest to begin ART when CD4+ T cell > 500. Hence, the infected individuals immunity can be divided into three levels: normal (> 500), moderate (350-500), and weak (< 350). Based on the above discussions, Rahman et al.[9] divided the total HIV infected population into three compartments dependent to their immunity level. Soon afterwards, Ishaku et al.[10] established an HIV model to analysis and optimal control problem based on CD4+ T cell count. Shen et al.[11] presented an infection-age structured HIV-1 model linking within-host and between-host dynamics, they divided the total infection population into three stages with similar way in [9]. The results of those works have provided some useful suggestions for the design of the clinical treatment strategy.

On the other hand, current studies have found that daily use of a fixed dose of Tenofovir and Entreptabine (Truvada) can effectively prevent HIV infection effectively [12]. CDC (centers for Disease Control) of the United States accepted the proposal and wrote it into the latest edition of the guidelines. According to the guidelines, the CDC recommends the following four measures for high-risk groups to receive PrEP: MSM (men who have sex with men), IDUs (inject drugs users), Heterosexual sex workers with high-risk behaviors, People in HIV-discordant couples [13]. Meanwhile, the medical results suggest that individuals at substantial risk of HIV infection should be offered PrEP as an additional prevention choice [14], it is an effective and safe mechanism for preventing HIV-infection [15]. In recent times, there are many studies that focus on PrEP prevention. Rahman [16] divided the total population into two groups: study group and general group to study the impact of Tenofovir gel as a PrEP on HIV infection. Akudibillah et al.[17] considered a model to study the benefits of ART and PrEP in resource-limited settings. Silva et al. [18] presented

a compartment model with PrEP to cumulative cases of HIV infection from 1987 to 2014 in Cape Verde. Kim et al. [19] investigated HIV prevention strategies including PrEP on HIV incidences in South Korea. Pinto et al. [20] presented a model that combine PrEP with HCT (HIV counselling and testing).

Note that these works mentioned above are mainly based on ordinary differential equations (ODE) models to study the effect of PrEP treatment on the HIV transmission. Epidemiologically, the spacial heterogeneity can not be ignored in epidemiological compartment model. That is, it is necessary to investigate the whole process of HIV/AIDS transmission by mathematical modeling and experiment when heterogenous environment and population diffusion are considered. In fact, reaction-diffusion epidemic models are effective tools to understanding those situations [21, 22, 23]. Furthermore, Shen et al.[24] studied the cost-effectiveness of oral HIV PrEP and early ART in the presence of drug resistance among MSM in San Francisco, and they verified that high PrEP coverage and earlier ART are expected to provide the greatest benefit. Therefore, in addition to considering the heterogeneous spatial diffusion, it is also necessary to consider the optimal control strategies that combines PrEP with ART treatments in this paper. Actually, optimal strategy theory has been successfully applied to some reaction-diffusion epidemiological and population models, e.g., general SIS model [25], SIR model [26], prey-predator model [28], Cancer invasion model [29]. However, as far as we know, few HIV/AIDS epidemic models have been formulated to study the adjoint effect of PrEP and ART treatments, optimal control, and spatial heterogeneity on HIV infection among MSM group. Here, we will consider those factors all together by investigating the following spatial diffusion MSM HIV/AIDS model in a heterogeneous environment.

$$
\begin{cases}
\dfrac{\partial S(x,t)}{\partial t} = \nabla\left(\theta_0(x)\nabla S(x,t)\right) + \Lambda(x) - (\mu(x) + r(x))S(x,t) \\
\qquad\qquad - \left(\beta_1(x)I_1(x,t) + \beta_2(x)I_2(x,t) + \beta_3(x)I_3(x,t)\right)S(x,t), \\[2mm]
\dfrac{\partial I_1(x,t)}{\partial t} = \nabla\left(\theta_1(x)\nabla I_1(x,t)\right) + \eta_2(x)I_2(x,t) - (\mu(x) + \alpha_1(x))I_1(x,t) \\
\qquad\qquad + \left(\beta_1(x)I_1(x,t) + \beta_2(x)I_2(x,t) + \beta_3(x)I_3(x,t)\right)S(x,t), \\[2mm]
\dfrac{\partial I_2(x,t)}{\partial t} = \nabla\left(\theta_2(x)\nabla I_2(x,t)\right) + \alpha_1(x)I_1(x,t) \\
\qquad\qquad - (\alpha_2(x) + \eta_2(x) + \mu(x))I_2(x,t) + \eta_3(x)I_3(x,t), \\[2mm]
\dfrac{\partial I_3(x,t)}{\partial t} = \nabla\left(\theta_3(x)\nabla I_3(x,t)\right) + \alpha_2(x)I_2(x,t) - (\eta_3(x) + \mu(x) + d(x))I_3(x,t), \\[2mm]
\dfrac{\partial P(x,t)}{\partial t} = \nabla\left(\theta_4(x)\nabla P(x,t)\right) + r(x)S(x,t) - \mu(x)P(x,t),
\end{cases}
\tag{1.1}
$$

with $(x,t) \in \Omega_T = \Omega \times (0,T)$. It is supplemented with the no-flux conditions

$$
[\theta_0(x)\nabla S(x,t)] \cdot \vartheta = [\theta_i(x)\nabla I_i(x,t)] \cdot \vartheta = [\theta_4(x)\nabla P(x,t)] \cdot \vartheta = 0, \ (x,t) \in \partial\Omega \times \in (0,T),
\tag{1.2}
$$

and positive initial conditions

$$
S(x,0) = S_0(x), \ P(x,0) = P_0(x), \ I_i(x,0) = I_{i0}(x), \ i = 1,2,3, \ x \in \Omega,
\tag{1.3}
$$

In this paper, we consider a MSM population and divide it into five groups at time t and location x: a healthy compartment, $S(t, x)$, three infected compartments (dependent on CD4+ T cell count) with ART treatment, $I_1(t, x), I_2(t, x), I_3(t, x)$, and a susceptible group under PrEP, $P(t, x)$ (see Table 1). The meaning and symbols of the model parameters and variables are summarized in Table 2. Since we mainly focus on the disease infected among MSM in China.

Table 1. Biological meaning of variables in model (1.1)-(1.3)

Variables	Description
$S(x, t)$	Susceptible at time t and location x
$P(x, t)$	Individuals under PrEP treatment at t and location x
$I_1(x, t)$	Infected compartment with $CD4+$ T cell count> 500
$I_2(x, t)$	Infected compartment with $CD4+$ T cell count $350 - 500$
$I_3(x, t)$	Infected compartment with $CD4+$ T cell count< 350

Table 2. Description of parameters in model (1.1)-(1.3)

Parameters	Description	Mean value (year^{-1})	Sources
$\Lambda(\cdot)$	Recruitment rate of susceptible	830,000	[44]
$\beta_1(\cdot)$	Infection rate of for $I_1(x, t)$	–	–
$\beta_2(\cdot)$	Infection rate of for $I_2(x, t)$	–	–
$\beta_3(\cdot)$	Infection rate of for $I_3(x, t)$	–	–
$\mu(\cdot)$	Natural death of individuals	0.0246	[45]
$d(\cdot)$	The rate of death-related AIDS	0.7114	[45]
$\alpha_1(\cdot)$	Transfer rate of $I_1(x, t)$	0.33	[9]
$\alpha_2(\cdot)$	Transfer rate of $I_2(x, t)$	0.34	[9]
$\eta_2(\cdot)$	The ART failure rate of $I_2(x, t)$	0.57	[9]
$\eta_3(\cdot)$	The ART failure rate of $I_3(x, t)$	0.32	[9]
$r(\cdot)$	Rate of individuals under PrEP treatment	0.2	[47]
$\theta_0(\cdot)$	Diffusion of susceptible	0.08	[23]
$\theta_1(\cdot)$	Diffusion of $I_1(x, t)$	0.02	[23]
$\theta_2(\cdot)$	Diffusion of $I_2(x, t)$	0.01	[23]
$\theta_3(\cdot)$	Diffusion of $I_3(x, t)$	0.03	[23]
$\theta_4(\cdot)$	Diffusion of $P(x, t)$	0.1	Estimate

We first set $\underline{b} = \min_{x \in \bar{\Omega}} b(\cdot)$ and $barb = \max_{x \in \bar{\Omega}} b(\cdot)$, where $b(\cdot) = \Lambda(\cdot), \beta_i(\cdot), \mu(\cdot), d(\cdot), \alpha_1(\cdot), \alpha_2(\cdot), r(\cdot), \eta_2(\cdot), \eta_3(\cdot)$.

2 Preliminaries

In this section, we are devoted to studying the well-posedness of system (1.1)-(1.3). Moreover, the existence of the global attractor of system (1.1)-(1.3) can be also established.

Consider the system as follows

$$\begin{cases} \dfrac{\partial w}{\partial \vartheta} = \nabla \left(\mathscr{A}(x)\nabla w \right) - \mathscr{B}(x)w + \mathscr{F}(x), \ t > 0, \ x \in \Omega, \\ \dfrac{\partial w}{\partial \vartheta} = 0, \hspace{5cm} x \in \partial\Omega, \end{cases} \tag{2.4}$$

where

$$w = \left(\begin{array}{c} S(\cdot,t) \\ P(\cdot,t) \end{array} \right), \mathscr{A}(\cdot) = \left(\begin{array}{cc} \theta_0(\cdot) & 0 \\ 0 & \theta_4(\cdot) \end{array} \right), \ \mathscr{F} = \left(\begin{array}{c} \Lambda(\cdot) \\ 0 \end{array} \right), \mathscr{B}(\cdot) = \left(\begin{array}{cc} \mu(\cdot) + r(\cdot) & 0 \\ -r(\cdot) & \mu(\cdot) \end{array} \right),$$

Using the similar methods in Lemma 1 in [30] , one has the following lemma

Lemma 2.1. *System (2.4) has a globally asymptotically stable positive steady state $w^*(x) = (S^*(x), P^*(x))^T$ in $C\left(\bar{\Omega}, \mathbb{R} \right)$. Moreover, $w^* = \left(\frac{\Lambda}{\mu+r}, \frac{r\Lambda}{\mu(\mu+r)} \right)^T$ if Λ, r, and μ are all positive constants.*

Set $\mathbb{X} = C\left(\bar{\Omega}, \mathbb{R}^5 \right)$ equip with the supermum norm $|| \cdot ||_{\mathbb{X}}$, $\mathbb{X}^+ = C\left(\bar{\Omega}, \mathbb{R}_+^5 \right)$. Then $(\mathbb{X}, \mathbb{X}^+)$ is an ordered Banach space. Define $y_j(t) : C\left(\bar{\Omega}, \mathbb{R} \right) \to C\left(\bar{\Omega}, \mathbb{R} \right)$ $(j = 0, 1, 2, 3, 4)$ as C_0 semigroups with respect to $\nabla \left(\theta(x)\nabla \right) - m_j(\cdot)$ with the Neumann boundary conditions, where $m_0(\cdot) = \mu(\cdot) + r(\cdot), m_1(\cdot) = \mu(\cdot) + \alpha_1(\cdot), m_2(\cdot) = \mu(\cdot) + \alpha_2(\cdot) + \eta_2(\cdot), m_3(\cdot) = \mu(\cdot) + d(\cdot) + \eta_3(\cdot), m_4(\cdot) = \mu(\cdot)$. Then we have

$$\left(y_j(t)\varphi \right)(x) = \int_\Omega G_j(x,t,a)\varphi(a)da, \ t > 0, \ \phi \in C\left(\bar{\Omega}, \mathbb{R} \right),$$

where $G_j(x,t,a)$ is the Green function with respect to $\nabla \left(\theta(x)\nabla \right) - m_j(\cdot), \ j = 0, 1, 2, 3, 4$. Based on the conclusion in [31], it is obvious that $y_j(t) \ (j = 0, 1, 2, 3, 4)$ is strongly positive and compact for all $t > 0$. Then there admits an $Q > 0$ such that $||y_i(t)|| \leqslant Qe^{\epsilon_j t}$ for each $t \geqslant 0$. Here $\epsilon_j < 0$ is the principal eigenvalue of $\nabla \left(\theta(x)\nabla \right) - m_j(\cdot)$ with the no-flux condition.

Define $Z = (Z_0, Z_1, Z_2, Z_3, Z_4)^T : \mathbb{X}^+ \to \mathbb{X}$ by

$$\begin{aligned} Z_0(\psi)(\cdot) &= \Lambda(x) - \left(\beta_1(\cdot)\psi_1(\cdot) + \beta_2(\cdot)\psi_2(\cdot) + \beta_3(\cdot)\psi_3(\cdot) \right)\psi_0(\cdot), \\ Z_1(\psi)(\cdot) &= \left(\beta_1(\cdot)\psi_1(\cdot) + \beta_2(\cdot)\psi_2(\cdot) + \beta_3(\cdot)\psi_3(\cdot) \right)\psi_0(\cdot) + \eta_2(\cdot)\psi_2(\cdot), \\ Z_2(\psi)(\cdot) &= \alpha_1(\cdot)\psi_1(\cdot) + \eta_3(\cdot)\psi_3(\cdot), \\ Z_3(\psi)(\cdot) &= \alpha_2(\cdot)\psi_2(\cdot), \\ Z_4(\psi)(\cdot) &= r(\cdot)\psi_0(\cdot), \end{aligned}$$

where $\psi = (\psi_0, \psi_1, \psi_2, \psi_3, \psi_4)^T \in \mathbb{X}^+$. Then we can rewrite system (1.1)-(1.3) as follows

$$B(t) = B^*(t)\psi + \int_0^t B^*(t-s)Z(B(s))ds, \tag{2.5}$$

where $B(t) = (S(t), E(t), I_1(t), I_2(t), I_3(t), P(t))^T$, $B^*(t) = diag(y_0(t), y_1(t), y_2(t), y_3(t), y_4(t))$. Thus, similar with the result of Corollary 4 in [32], we have the following lemma

Lemma 2.2. *For system (1.1)-(1.3) with initial value $\psi \in \mathbb{X}^+$, it has a unique mild solution $B(t, \psi) \in \mathbb{X}^+$ on $[0, \sigma_\infty)$, $\sigma_\infty \leqslant +\infty$. Furthermore, the solution is a classical solution.*

2.1 Well-posedness and global attractor of system (1.1)-(1.3)

Theorem 2.3. *For system (1.1)-(1.3) with initial value $\psi \in \mathbb{X}^+$, it admits a unique solution $B(x, t, \psi) \in \mathbb{X}^+$ for $t \geq 0$, and the semi-flow of solution $\Psi(t) = B(t, \cdot, \psi) : \mathbb{X}^+ \to \mathbb{X}^+$ admits a global attractor.*

Proof. We complete the proof by the following two steps.

Step 1: The uniqueness, existence, and positivity of the solutions can be obtained from Lemma 2.2. Assume $\sigma_\infty < +\infty$, $\|B(t, x, \psi)\| \to +\infty (t \to +\infty)$ (see Theorem 2 in [32]). It follows from $S(x, t)$ equation of system (1.1) that

$$\frac{\partial S(x, t)}{\partial t} \leqslant \nabla\left(\theta(x)\nabla S(x, t)\right) + \bar{\Lambda} - (\underline{\mu} + \underline{r})S(x, t), \ x \in \Omega, \ t \in [0, \sigma_\infty). \qquad (2.6)$$

From Lemma 2.1, we obtain that there admits $M_1 > 0$ such that $S(x, t) \leqslant M_1$, $x \in \bar{\Omega}$, $t \in [0, \sigma_\infty)$. Next, we consider the following system

$$\begin{cases} \dfrac{\partial \omega_1}{\partial t} = \nabla\left(\theta_1(x)\nabla\omega_1\right) + M_1 \displaystyle\sum_{i=1}^{3} \bar{\beta}_i \omega_i + \bar{\eta_2}\omega_2 - (\underline{\mu} + \underline{\alpha_1})\omega_1, \ x \in \Omega, t > 0, \\[3mm] \dfrac{\partial \omega_2}{\partial t} = \nabla\left(\theta_2(x)\nabla\omega_2\right) + \bar{\alpha_1}\omega_1 - (\underline{\alpha_2} + \underline{\eta}_2 + \bar{\mu})\omega_2 + \bar{\eta_3}\omega_3, \ x \in \Omega, t > 0, \\[3mm] \dfrac{\partial \omega_3}{\partial t} = \nabla\left(\theta_3(x)\nabla\omega_3\right) + \bar{\alpha_2}\omega_2 - (\underline{d} + \underline{\eta}_3 + \underline{\mu})\omega_3, \ x \in \Omega, t > 0, \\[3mm] \dfrac{\partial \omega_4}{\partial t} = \nabla\left(\theta_4(x)\nabla\omega_4\right) + \bar{r}M_1 - \underline{\mu}\omega_4, \ x \in \Omega, t > 0, \\[3mm] \dfrac{\partial \omega_1}{\vartheta} = \dfrac{\partial \omega_2}{\vartheta} = \dfrac{\partial \omega_3}{\vartheta} = \dfrac{\partial \omega_4}{\vartheta} = 0, \ x \in \partial\Omega. \end{cases} \qquad (2.7)$$

From Theorem 7.6.1 in [31], we know that the eigenvalue problem associated with system (2.7) admits a principal eigenvalue λ with respect to a strongly positive eigenfunction $\varphi = (\varphi_1, \varphi_2, \varphi_3, \varphi_4)$. Hence, system (2.7) admits a solution $\delta e^{\lambda t}\varphi(t)$ for $t \geqslant 0$, where δ satisfies

$$\delta\phi = (\omega_1(0, x), \omega_2(0, x), \omega_3(0, x), \omega_4(0, x)) \geqslant (I_{10}(x), I_{20}(x), I_{30}(x), I_{40}(x), p_0(x)) \ for \ x \in \bar{\Omega}.$$

Thus, we obtain that

$$(I_1(x, t), I_2(x, t), I_3(x, t), P(x, t)) \leqslant \delta e^{\lambda t}\varphi(x), \ t \in [0, \sigma_\infty), \ x \in \bar{\Omega},$$

which indicates that there has a positive constant Q_2, such that $P(t, x) \leqslant Q_2$, $I_i(t, x) \leqslant Q_2$, $i = 1, 2, 3$, $x \in \bar{\Omega}, t \in [0, \sigma_\infty)$. If $\sigma_\infty < +\infty$, it leads to a contradiction. Accordingly, the global existence of solution follows.

Step 2: We further prove that the dissipativeness of the semiflow of solution. Applying the standard comparison principle, formula (2.6) and Lemma 2.1, it can be verified that there exist N_0, $t_0 > 0$ such that $S(t,x) \leqslant N_0, t \geqslant t_0, \ x \in \bar{\Omega}$.

Denote $\mathcal{N}(t) = \int_\Omega (S(t,x) + I_1(t,x) + I_2(t,x) + I_3(t,x) + P(t,x)) dx$, then we have that

$$\frac{\partial \mathcal{N}}{\partial t} \leqslant \int_\Omega \Lambda(x) dx - (\mu(x) + d(x)) \mathcal{N}(x), \ t \geqslant 0.$$

Thus, there admits $N^* > 0$ and $t_1 > 0$ such that $\mathcal{N} \leqslant N^*$ for all $t \geqslant t_1$. It follows from Chapter 5 in [34] that $G_1(t,x,y) = \sum_{n \geqslant 1} e^{\sigma_n t} \phi_n(x) \varphi_n(y)$. Here σ_i is the eigenvalue for $\nabla(\theta_1(x)\nabla) - m_1(x)$ subjects to the no-flux condition associated with $\phi_n(x)$, and $\sigma_1 \geqslant \sigma_2 \geqslant \sigma_3 \geqslant ... \geqslant \sigma_n \geqslant ....$ Since φ_n is uniformly bounded, then we know that $G_1(t,x,y) \leqslant \varpi_1 \sum_{n \geqslant 1} e^{\sigma_n t}, \ t > 0$, for some $\phi_1 > 0$.

Let ϑ_n (n=1,2,3...) be the eigenvalue of $\nabla(\theta_1(x)\nabla) - \underline{m}_1$ with the no-flux condition and satisfy $\vartheta_1 = -\underline{m}_1 \geqslant \vartheta_2 \geqslant \vartheta_3 \geqslant ... \geqslant \vartheta_n \geqslant ...$, we obtain that $\vartheta_i \geqslant \tau_i$ for any $i \in \mathbb{N}_+$ from Theorem 2.4.7 in [35], For ϑ_n decreases like $-n^2$, then we have

$$G_1(t,x,y) \leqslant \varpi_1 \sum_{n \geqslant 1} e^{\vartheta_n t} \leqslant \varpi e^{\vartheta_1 t} = \varpi e^{-\underline{m}_1 t}, \ t > 0,$$

for $t > 0$ and some $\varpi > 0$.

Set $t_3 = \max\{t_0, t_1\}$. From (2.5), we have

$$I_1(t,x) = y_1(t) I_1(t_3, x) + \int_{t_3}^t y_1(t-s) \left(S(s,x) \sum_{i=1}^3 \beta_i(x) I_i(s,x) + \sum_{k=2}^3 \eta_k(x) I_k(s,x) \right) ds$$

$$\leqslant M_1 e^{\epsilon_1(t-t_3)} ||I_1(t_3, x)|| + \int_{t_3}^t \int_\Omega G_1(t-s,x,y) \left(S(s,y) \sum_{i=1}^3 \beta_i(y) I_i(s,y) + \sum_{k=2}^3 \eta_k(y) I_k(s,y) \right) dy ds$$

$$\leqslant M_1 e^{\epsilon_1(t-t_3)} ||I_1(t_3, x)|| + \int_{t_3}^t \varpi e^{-\underline{m}_1(t-s)} \int_\Omega \left(N_0 \sum_{i=1}^3 \beta_i(y) I_i(s,y) + N^* \sum_{k=2}^3 \eta_k(y) \right) dy ds$$

$$\leqslant M_1 e^{\epsilon_1(t-t_3)} ||I_1(t_3, x)|| + \varpi N^* \left(N_0 \sum_{i=1}^3 \bar{\beta}_i + \sum_{k=2}^3 \bar{\eta}_k \right) \int_{t_3}^t e^{-\underline{m}_1(t-s)} ds$$

$$\leqslant \varpi N^* \left(N_0 \sum_{i=1}^3 \bar{\beta}_i + \sum_{k=2}^3 \bar{\eta}_k \right) \Big/ \underline{m}_1,$$

for $t \geqslant t_3$, which implies $\limsup_{t \to \infty} ||I_1(t,x)|| \leqslant \varpi N^* \left(N_0 \sum_{i=1}^3 \bar{\beta}_i + \sum_{k=2}^3 \bar{\eta}_k \right) \Big/ \underline{m}_1$. Similarly, there exists N_1, N_2, N_3, $N_4 > 0$ such that

$$\limsup_{t \to \infty} ||I_2(t,x)|| \leqslant N_2, \ \limsup_{t \to \infty} ||I_3(t,x)|| \leqslant N_3, \ \limsup_{t \to \infty} ||P(t,x)|| \leqslant N_4.$$

Thus, the dissipativeness of the system follows. Accordingly, the compactness of $\Psi(t)$ holds for all $t > 0$ (Theorem 2.2.6 in [35]). Hence, the existence of the global attractor of $\Psi(t)$ follows (Theorem 3.4.8 in [36]). $\square$

3   The basic reproduction ratio R_0 and the dynamics of disease-free steady state E_0

In fact, Lemma 2.1 implies that system (1.1)-(1.3) always has a disease-free steady state $E_0 = (S^0(x), 0, 0, 0, P^0(x))$, where $\left(S^0(x), P^0(x)\right)^T = w^*(x)$.

The linearized system (1.1) around E_0 is given by

$$\begin{cases} \dfrac{\partial q_1}{\partial t} = \nabla\left(\theta_1(x)\nabla q_1\right) + S^0 \sum_{i=1}^{3}\beta_i(x)q_i + \eta_2(x)q_2 - (\mu(x) + \alpha_1(x))q_1, \ t > 0, x \in \Omega, \\[2mm] \dfrac{\partial q_2}{\partial t} = \nabla\left(\theta_2(x)\nabla q_2\right) + \alpha_1(x)q_1 - (\alpha_2(x) + \eta_2(x) + \mu(x))q_2 + \eta_3(x)q_3, \ t > 0, \ x \in \Omega, \\[2mm] \dfrac{\partial q_3}{\partial t} = \nabla\left(\theta_3(x)\nabla q_3\right) + \alpha_2(x)q_2 - (d(x) + \eta_3(x) + \mu(x))q_3, \ t > 0, \ x \in \Omega, \\[2mm] \dfrac{\partial q_1}{\vartheta} = \dfrac{\partial q_2}{\vartheta} = \dfrac{\partial q_3}{\vartheta} = 0, \ x \in \partial\Omega. \end{cases}$$

Set $(q_1, q_2, q_3) = e^{\lambda t}(\psi_1(x), \psi_2(x), \psi_3(x))$. Then we can rewrite the system as

$$\begin{cases} \lambda\psi_1 = \nabla\left(\theta_1(x)\nabla\psi_1\right) + S^0 \sum_{i=1}^{3}\beta_i(x)\psi_i + \eta_2(x)\psi_2 - (\mu(x) + \alpha_1(x))\psi_1, \ x \in \Omega, \\[2mm] \lambda\psi_2 = \nabla\left(\theta_2(x)\nabla\psi_2\right) + \alpha_1(x)\psi_1 - (\alpha_2(x) + \eta_2(x) + \mu(x))\psi_2 + \eta_3(x)\psi_3, \ x \in \Omega, \\[2mm] \lambda\psi_3 = \nabla\left(\theta_3(x)\nabla\psi_3\right) + \alpha_2\psi_2 - (d(x) + \eta_3(x) + \mu(x))\psi_3, \ x \in \Omega. \end{cases} \tag{3.8}$$

It follows from Theorem 7.6.1 in [31] that system (3.8) has a unique principle eigenvalue $\lambda_0(S_0)$ with a strongly positive eigenfunction $(\psi_1(x), \psi_2(x), \psi_3(x))$.

Define $\Phi(t) : C(\bar{\Omega}, \mathbb{R}^3) \to C(\bar{\Omega}, \mathbb{R}^3)$ as the solution semigroup of the following system

$$\begin{cases} \dfrac{\partial q_1}{\partial t} = \nabla\left(\theta_1(x)\nabla q_1\right) + \eta_2(x)q_2 - (\mu(x) + \alpha_1(x))q_1, \ t > 0, x \in \Omega, \\[2mm] \dfrac{\partial q_2}{\partial t} = \nabla\left(\theta_2(x)\nabla q_2\right) + \alpha_1(x)q_1 - (\alpha_2(x) + \eta_2(x) + \mu(x))q_2 + \eta_3(x)q_3, \ t > 0, \ x \in \Omega, \\[2mm] \dfrac{\partial q_3}{\partial t} = \nabla\left(\theta_3(x)\nabla q_3\right) + \alpha_2(x)q_2 - (d(x) + \eta_3(x) + \mu(x))q_3, \ t > 0, \ x \in \Omega, \\[2mm] \dfrac{\partial q_1}{\vartheta} = \dfrac{\partial q_2}{\vartheta} = \dfrac{\partial q_3}{\vartheta} = 0, \ x \in \partial\Omega, \end{cases}$$

and set

$$\mathbf{H}(x) = \begin{pmatrix} \beta_1(x)S^0 & \beta_2(x)S^0 & \beta_3(x)S^0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Denote the density of initial value as $\psi = (\psi_1(x), \psi_2(x), \psi_3(x))$. Thus, $\Phi(t)\psi$ is the density of those HIV infected individuals as time goes by. Accordingly, the density of total new HIV infective individuals is $\mathscr{L}(\psi)(x) = \int_0^\infty \mathbf{H}(x)\Phi(t)\psi dt$. Thus, the basic reproduction number is obtained $R_0 = \rho(\mathscr{L})$ by the next generation operator.

From [37], we have the lemma as follows

Lemma 3.1. λ_0 *has the same sign as* $R_0 - 1$ *and* E_0 *is stable when* $R_0 < 1$, *otherwise, it is unstable.*

Theorem 3.2. *The disease-free steady state* E_0 *of system* (1.1)-(1.3) *is globally asymptotically stable (g.a.s) when* $R_0 < 1$.

Proof. From lemma 3.1, we can verify that there admits a $\sigma > 0$ such that $\lambda_0(S^0 + \sigma) < 0$ and $\lambda_0(P^0 + \sigma) < 0$. From system (1.1), we can obatin that

$$\frac{\partial S}{\partial t} \leqslant \nabla(\theta_0(x)\nabla S) + \Lambda(x) - (\mu(x) + r(x))S, \ t > 0, \ x \in \Omega,$$

$$\frac{\partial P}{\partial t} \leqslant \nabla(\theta_4(x)\nabla P) + r(x)(S^0 + \sigma) - \mu(x)P, \ t > 0, \ x \in \Omega,$$

which indicates $S(t,x) \leqslant S^0 + \sigma$ and $P(t,x) \leqslant P^0 + \sigma$ for all $t \geqslant t_1 > 0$ and $x \in \bar{\Omega}$. Thus, we obtain

$$\begin{cases} \dfrac{\partial I_1}{\partial t} \leqslant \nabla(\theta_1(x)\nabla I_1) + (S^0 + \sigma) \displaystyle\sum_{i=1}^{3} \beta_i(x)I_i + \eta_2(x)I_2 - (\mu(x) + \alpha_1(x))I_1, \ t > t_1, x \in \Omega, \\[2mm] \dfrac{\partial I_2}{\partial t} \leqslant \nabla(\theta_2(x)\nabla I_2) + \alpha_1(x)I_1 - (\alpha_2(x) + \eta_2(x) + \mu(x))I_2 + \eta_3(x)I_3, \ t > t_1, \ x \in \Omega, \\[2mm] \dfrac{\partial I_3}{\partial t} \leqslant \nabla(\theta_3(x)\nabla I_3) + \alpha_2(x)I_2 - (d(x) + \eta_3(x) + \mu(x))I_3, \ t > t_1, \ x \in \Omega. \end{cases}$$

Assume that $\epsilon(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x)) \geqslant (I_1(t_1,x), I_2(t_1,x), I_3(t_1,x))$, where $(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x))$ is the eigenfunction associated with the principle eigenvalue $\lambda_0(S^0 + \sigma) > 0$. Then, we get

$$(I_1(t,x), I_2(t,x), I_3(t,x)) \leqslant \epsilon(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x)) e^{\lambda_0(S^0 + \sigma)(t - t_1)}.$$

Hence, $\lim_{t \to \infty}(I_1(t,x), I_2(t,x), I_3(t,x)) = 0$, $S(t,x)$ and $P(t,x)$ are asymptotic to Eq. (2.4). Moreover, it is easy to obtain that $\lim_{t \to \infty} S(t,x) = S^0$, $\lim_{t \to \infty} P(t,x) = P^0$. The proof is completed. □

In the next part, we further show that the uniform persistence of the disease. For this purpose, we first give the following denotations.

Let

$$\mathbf{X}_0 = \left\{ \varphi = (S, I_1, I_2, I_3, P) \in \mathbb{X}^+; I_i(\cdot) \neq 0, i = 1, 2, 3 \right\},$$

$$\partial \mathbf{X}_0 = \left\{ (S, I_1, I_2, I_3, P) \in \mathbb{X}^+ : I_1(\cdot) \equiv 0 \ or \ I_2(\cdot) \equiv 0 \ or \ I_3(\cdot) \equiv 0 \right\}.$$

Then, it follows from Hopf boundary lemma [38] and the maximum principle that $\mathbf{X}_0$ is positively invariant of $\Phi(t)$. Let $\mathbf{M}_\partial = \{ \varphi \in \partial \mathbf{X}_0, \ \forall t \geqslant 0 \}$, $\omega(\varphi)$ be the omega limit set of $\gamma^+(\varphi) = \{ \Phi(t)(\varphi) : t \geqslant 0 \}$.

Lemma 3.3. $\cup_{\varphi \in \mathbf{M}_\partial} \omega(\varphi) = E_0$.

Proof. Note that $\phi \in \mathbf{M}_\partial$, it follows that $I_1(x,t,\varphi) \equiv 0$ or $I_2(x,t,\varphi) \equiv 0$ or $I_3(x,t,\varphi) \equiv 0$. Assume that $I_3(x,t,\varphi) \equiv 0$, it follows from the forth equation of system (1.1) that

$I_2(t, x, \varphi) \equiv 0$, and then we obtain that $I_1(t, x, \varphi) \equiv 0$ from the third equation of system (1.1). Therefore, $S(t, x, \varphi) \to S^0, P(t, x, \varphi) \to P^0$ as $t \to \infty$. If there admits a $t_0 > 0$ such that $I_3(t, x, \varphi) \neq 0$, we can verify that $I_3(t, x, \varphi) > 0$ for all $t > t_0$, that is, $I_1(t, x, \varphi) \equiv 0$ or $I_2(t, x, \varphi) \equiv 0$ for all $t \geqslant t_0$. If $I_1(t, x, \varphi) \equiv 0$, then it follows from the second equation of system (1.1) and positivity of $I_i(t, x, \varphi), i = 1, 2, 3$ that $I_3(t, x, \varphi) \to 0$ as $t \to \infty$. If $I_2(t, x, \varphi) \equiv 0$, then it follows from system (1.1) that $I_3(t, x, \varphi) \to 0$ as $t \to \infty$. Then $S(t, x, \varphi), P(t, x, \varphi)$ are asymptotic to Eq. (2.4). Thus, $S(t, x, \varphi) \to S^0$ and $P(t, x, \varphi) \to P^0$ uniformly for $x \in \bar{\Omega}$ as $t \to \infty$.   □

Lemma 3.4. $\limsup\limits_{t \to \infty} ||\Phi(t)(\varphi) - E_0|| \geqslant \varsigma, \ \varphi \in \boldsymbol{X}_0.$

Proof. We proof lemma 3.4 by contradiction. Since $R_0 > 1$, then there admits a $\sigma > 0$ such that $\lambda_0(S^0 - \varsigma) > 0$. Suppose that there exists $\varphi_0 \in \mathbf{X}_0$ such that $\limsup\limits_{t \to \infty} ||\Phi(t)(\varphi_0) - E_0|| \geqslant \varsigma$. Then, we have $S(t, x, \varphi_0) > S^0 - \varsigma, \ \forall t \geqslant t_1$. Hence, we can obtain that

$$
\begin{cases}
\dfrac{\partial I_1}{\partial t} \geqslant \nabla\left(\theta_1(x)\nabla I_1\right) + (S^0 - \varsigma)\sum\limits_{i=1}^{3} \beta_i(x)I_i + \eta_2(x)I_2 - (\mu(x) + \alpha_1(x))I_1, \ t \geqslant t_1, x \in \Omega, \\[3mm]
\dfrac{\partial I_2}{\partial t} \geqslant \nabla\left(\theta_2(x)\nabla I_2\right) + \alpha_1(x)I_1 - (\alpha_2(x) + \eta_2(x) + \mu(x))I_2 + \eta_3(x)I_3, \ t \geqslant t_1, \ x \in \Omega, \\[3mm]
\dfrac{\partial I_3}{\partial t} \geqslant \nabla\left(\theta_3(x)\nabla I_3\right) + \alpha_2(x)I_2 - (d(x) + \eta_3(x) + \mu(x))I_3, \ t \geqslant t_1, \ x \in \Omega,
\end{cases}
$$

Denote the principle eigenvalue $\lambda_0(S^0 - \varsigma) > 0$ as $(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x))$. Suppose $\alpha > 0$ and satisfies $\alpha(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x)) \leqslant (I_1(t_1, x), I_2(t_1, x), I_3(t_1, x))$. Then, $(I_1(x, t), I_2(x, t), I_3(x, t)) \geqslant \alpha(\bar{\varphi}_1(x), \bar{\varphi}_2(x), \bar{\varphi}_3(x))e^{\lambda_0(S^0 - \varsigma)(t - t_1)}, \ t \geqslant t_1$, which implies that $\lim\limits_{t \to \infty}(I_1(t, x), I_2(t, x), I_3(t, x)) = (+\infty, +\infty, +\infty)$, it leads to a contradiction.   □

Theorem 3.5. *If $R_0 > 1$, then there admits a $\varsigma^* > 0$ such that the solution $(S(x, t), I_1(x, t), I_2(x, t), I_3(x, t), P(x, t))$ of system (1.1)-(1.3) with $S_0(x) \neq 0, I_{10}(x) \neq 0, I_{20}(x) \neq 0, I_{30}(x) \neq 0$, and $P_0(x) \neq 0$ satisfies*

$$\liminf_{t \to \infty} S(t, x) \geqslant \varsigma^*, \ \liminf_{t \to \infty} P(t, x) \geqslant \varsigma^*, \ \liminf_{t \to \infty} I_i(t, x) \geqslant \varsigma^*, \ x \in \bar{\Omega}, \ i = 1, 2, 3.$$

Further, system (1.1)-(1.3) admits at least one endemic steady state.

Proof. Define $\mathscr{F} : \mathbb{X}^+ \to [0, \infty]$ by

$$\mathscr{F}(\varphi) = \min\left\{\min_{x \in \bar{\Omega}} \varphi_1(x), \min_{x \in \bar{\Omega}} \varphi_2(x), \min_{x \in \bar{\Omega}} \varphi_3(x)\right\}, \ \varphi \in \mathbb{X}^+.$$

It is obvious that $\mathscr{F}^{-1}(0, \infty) \subseteq \mathbf{X}_0$. Note that $\mathscr{F}(\varphi) = 0$ and $\varphi \in \mathbf{X}_0$ or $\mathscr{F}(\varphi) > 0$. Thus, $\mathscr{F}(\Psi(t), \varphi) > 0$. Therefore, $\mathscr{F}$ is a generalized distance function with respect to $\Psi(t) : \mathbb{X}^+ \to \mathbb{X}^+$. By the above lemmas 3.3-3.4, it indicated that any forward orbit of $\Psi(t)$ in $\mathbf{M}_\partial$ converges to E_0, and $W^s(E_0) \cap \mathbf{X}_0 = \emptyset$. Furthermore, E_0 is an isolated invariant set in $\mathbb{X}^+$ and no set of $\{E_0\}$ from a cycle in $\partial\mathbf{X}_0$. From Theorem 3 in [39] we can verify that there exists a $\varsigma_1 > 0$ such that

$$\liminf_{t \to \infty} I_i(t, x, \varphi) \geqslant \varsigma_1, \forall \ \phi \in \mathbf{X}_0, \ i = 1, 2, 3.$$

By similar discussions as those in Theorem 2.3, we obtain that there exists positive constants $K > 0$ and $t_2 > 0$ such that $I_i(x, t, \varphi) \leqslant K$, $t \geqslant t_2$, $\forall\ x \in \bar{\Omega}$, $i = 1, 2, 3$. Then $S(x, t)$ and $P(x, t)$ satisfies $\frac{\partial S}{\partial t} \geqslant \nabla (\theta_0(x) \nabla S) + \underline{\Lambda} - \left(\bar{\mu} + K \sum_{i=1}^{3} \bar{\beta}_i \right) S$, $t \geqslant t_2$, $x \in \Omega$, which implies $\liminf\limits_{t \to \infty} S(t, x, \phi) \geqslant \varsigma_2 := \underline{\Lambda} / (\bar{\mu} + (\bar{\beta}_1 + \bar{\beta}_2 + \bar{\beta}_3) K)$. Hence

$$\frac{\partial P}{\partial t} \geqslant \nabla (\theta_0(x) \nabla P) + \underline{r}\sigma_2 - \bar{\mu} P,\ t \geqslant t_2,\ x \in \Omega,$$

which implies $\liminf\limits_{t \to \infty} P(t, x, \varphi) \geqslant \varsigma_3 := \underline{r}\sigma_2 / \bar{\mu}$. By the comparison principle, Lemmas 2.1, 3.3,3.4, let $\varsigma^* = \min\{\varsigma_1, \varsigma_2, \varsigma_3\}$, then the uniform persistence follows.

Finally, we show system (1.1)-(1.3) admits at least one positive steady state. From Theorem 3 in [22], it follows that system (1.1)-(1.3) has at least one steady state in $\mathbb{X}_0$. In next, we suppose $(\varphi_0, \varphi_1, \varphi_2, \varphi_3, \varphi_4)$ is a steady state in $\mathbb{X}_0$. Then $\varphi_k \not\equiv 0$ $(k = 1, 2, 3)$. Applying the Hopf lemma and maximum principle, we can obtain that $\varphi_k > 0$, $\varphi_0 > 0$ (or $\varphi_0 \equiv 0$), and $\varphi_4 > 0$ (or $\varphi_4 \equiv 0$). Suppose $\varphi_0 \equiv 0$, then we can obtain that $\varphi_k \equiv 0$ from the first steady state system of system (1.1), which leads to a contradiction. If $\varphi_4 \equiv 0$, then $\varphi_0 \equiv 0$, by the last equation of system (1.1), which implies that $\varphi_k \equiv 0$, a contradiction too. Accordingly, the positivity of $(\varphi_0, \varphi_1, \varphi_2, \varphi_3, \varphi_4)$ holds. This completes the proof.

$\square$

4 Optimal control of model (1.1)-(1.3)

In this section, we study the optimal problems of the following reaction-diffusion HIV model with PrEP and ART treatments. In the rest of the part, we consider the positive constant diffusion coefficients, namely $\theta_j(x) = \theta_j$, $j = 0, 1, 2, 3, 4$. Furthermore, let $\Lambda(x) = \Lambda, r(x) = r, \eta_k(x) = \eta_k$, $k = 2, 3$ as positive constants. We give the following controlled system

$$
\begin{cases}
\begin{aligned}
\frac{\partial S(x,t)}{\partial t} =& \theta_0 \Delta S(x,t) + \Lambda - (\beta_1(x) I_1(x,t) + \beta_2(x) I_2(x,t) + \beta_3(x) I_3(x,t)) S(x,t) \\
& - (\mu(x) + r u_1(x,t)) S(x,t), \\
\frac{\partial I_1(x,t)}{\partial t} =& \theta_1 \Delta I_1(x,t) + (\beta_1(x) I_1(x,t) + \beta_2(x) I_2(x,t) + \beta_3(x) I_3(x,t)) S(x,t) \\
& + \eta_2 u_2(x,t) I_2(x,t) - (\mu(x) + \alpha_1(x)) I_1(x,t), \\
\frac{\partial I_2(x,t)}{\partial t} =& \theta_2 \Delta I_2(x,t) + \alpha_1(x) I_1(x,t) - (\alpha_2(x) + \eta_2 u_2(x,t) + \mu(x)) I_2(x,t) \\
& + \eta_3 u_3(x,t) I_3(x,t), \\
\frac{\partial I_3(x,t)}{\partial t} =& \theta_3 \Delta I_3(x,t) + \alpha_2(x) I_2(x,t) - (\eta_3 u_3(x,t) + \mu(x) + d(x)) I_3(x,t), \\
\frac{\partial P(x,t)}{\partial t} =& \theta_4 \Delta P(x,t) + \alpha_2(x) I_2(x,t) + r u_1(x,t) S(x,t) - \mu(x) P(x,t),
\end{aligned}
\end{cases}
\tag{4.9}
$$

with $(x,t) \in \Omega \times \Omega_T = (0,\tau)$. The corresponding Neumann boundary and initial conditions as follows

$$\frac{\partial S(x,t)}{\partial \vartheta} = \frac{\partial I_1(x,t)}{\partial \vartheta} = \frac{\partial I_2(x,t)}{\partial \vartheta} = \frac{\partial I_3(x,t)}{\partial \vartheta} = \frac{\partial P(x,t)}{\partial \vartheta} = 0, \ (t,x) \in (0,\tau) \times \partial\Omega,$$
$$S(0,x) = S_0(x), \ P(0,x) = P_0(x), \ I_i(0,x) = I_{i0}(x), \ x \in \Omega. \tag{4.10}$$

We let the admissible control set as follows

$$\mathscr{U} = \left\{ u = (u_1,u_2,u_3) \in \left(L^2\left(\Omega_T\right)\right)^3, \ 0 \leqslant u_i \leqslant 1, \ a.e. \ on \ \Omega_T, \ i = 1,2,3 \right\}. \tag{4.11}$$

The optimal control strategy is formulated to minimize the population of susceptible and HIV infected people with different stages and minimize the cost of PrEP and ART. For this purpose, we structure the objective functional as follows

$$\mathscr{J}(S,I_1,I_2,I_3,u) = \int_{\Omega_T} \left[c_0(x,t)S(x,t) + \sum_{i=1}^{3} c_i(x,t)I_i(x,t) + \sum_{i=1}^{3} \omega_i(x,t)u_i(x,t) \right] dxdt$$
$$+ \int_{\Omega} \left[\zeta_0(x)S(\tau,x) + \sum_{i=1}^{3} \zeta_i(x)I_i(\tau,x) + \sum_{i=1}^{3} \rho_i(x)u_i(\tau,x) \right] dx, \tag{4.12}$$

where the positive functions $c_0, c_1, c_2, c_3 \in L^\infty\left(\Omega_T\right)$ and $\omega_i \in L^\infty\left(\Omega_T\right)$, $i = 1,2,3$ are weight functions; $\zeta_0, \zeta_1, \zeta_2, \zeta_3 \in L^\infty\left(\Omega_T\right)$ and $\rho_i \in L^\infty\left(\Omega_T\right)$, $i = 1,2,3$ are the control measures of the cost of HIV intervention among MSM corresponding to the control for PrEP and ART treatments in $(t,x) \in \Omega_T$. (S,I_1,I_2,I_3,P) is the solution for state system (4.9)-(4.10) with the optimal control u. Thus, the purpose of the optimal control strategy is to minimize the control cost functional (4.12) subjects to the state system (4.9)-(4.10), i.e., to find an optimal control $u^* \in \mathscr{U}$ satisfies

$$\mathscr{J}(S,I_1,I_2,I_3,u^*) = \inf_{u \in \mathscr{U}} \mathscr{J}(S,I_1,I_2,I_3,u). \tag{4.13}$$

4.1 Preliminaries and basic assumptions

Define $\Pi = \left(L^2\left(\Omega\right)\right)^5$ as Hilbert space. Suppose that $\mathbf{A} : \mathscr{D}(\mathbf{A}) \subseteq \Pi \to \Pi$ is a linear operator and given by

$$\mathbf{A} = diag(\theta_0\Delta, \theta_1\Delta, \theta_2\Delta, \theta_3\Delta, \theta_4\Delta) \tag{4.14}$$

with

$$\mathscr{D}(\mathbf{A}) \triangleq \left\{ (S,I_1,I_2,I_3) \in \left(\Pi^2\left(\Omega\right)\right)^5, \ \frac{\partial S(x,t)}{\partial \vartheta} = \frac{\partial I_1(x,t)}{\partial \vartheta} = \frac{\partial I_2(x,t)}{\partial \vartheta} = \frac{\partial I_3(x,t)}{\partial \vartheta} = \frac{\partial P(x,t)}{\partial \vartheta} = 0 \right\}. \tag{4.15}$$

Denote by $Q = (S, I_1, I_2, I_3, P)$, $\Theta(t, Q) = (\Theta_0(t, Q), \Theta_1(t, Q), \Theta_2(t, Q), \Theta_3(t, Q), \Theta_4(t, Q))$ with

$$
\begin{cases}
\Theta_0(t, Q) = \Lambda - (\beta_1(x)I_1(x, t) + \beta_2(x)I_2(x, t) + \beta_3(x)I_3(x, t)) S(x, t) \\
\qquad - (\mu(x) + r(x)u_1(x, t))S(x, t), \\
\Theta_1(t, Q) = (\beta_1(x)I_1(x, t) + \beta_2(x)I_2(x, t) + \beta_3(x)I_3(x, t)) S(x, t) + \eta_2 u_2(x, t)I_2(x, t) \\
\qquad - (\mu(x) + \alpha_1(x))I_1(x, t), \\
\Theta_2(t, Q) = \alpha_1(x)I_1(x, t) - (\alpha_2(x) + \eta_2 u_2(x, t) + \mu(x))I_2(x, t) + \eta_3 u_3(x, t)I_3(x, t), \\
\Theta_3(t, Q) = \alpha_2(x)I_2(x, t) - (\eta_3 u_3(x, t) + \mu(x) + d(x))I_3(x, t), \\
\Theta_4(t, Q) = \alpha_2(x)I_2(x, t) + ru_1(x, t)S(x, t) - \mu(x)P(x, t),
\end{cases}
\tag{4.16}
$$

where $Q = (S, I_1, I_2, I_3, P) \in \mathscr{D}(\Theta) \triangleq \{Q \in \Pi, \ \Theta(t, Q) \in \Pi, \ \forall \ t \in [0, \tau]\}$. Then system (4.9)-(4.10) can be rewritten as

$$
\begin{cases}
\dfrac{\partial Q}{\partial t} = \mathbf{A}Q + \Theta(t, Q), \ t \in [0, \tau], \\
Q(0) = Q_0.
\end{cases}
\tag{4.17}
$$

To prove system (4.17) admits a unique strong solution, we introduce the results from literature [40] as follows

Theorem 4.1. *Denote a real Banach space by* $\mathbb{F}$, $\mathbf{A} : \mathscr{D}(\mathbf{A} \subseteq \mathbb{F} \to \mathbb{F}$ *a* C_0-*semigroup infinitesimal generator of continuous* $\{\widetilde{S}(t), \ t \geqslant 0\}$ *on* $\mathbb{F}$. *If* $Q_0 \in \mathbb{F}$, *then system (4.17) has a unique mild solution* $Q \in ([0, \tau]; \mathbb{F})$ *as follows*

$$
Q(t) = \widetilde{S}(t)Q_0 + \int_0^t \widetilde{S}(t - s)\Theta(s, Q(s))ds, \ t \in [0, \tau].
\tag{4.18}
$$

Moreover, if $\mathbb{F}$ *is a Hilbert space,* $\mathbf{A}$ *is dissipative and self-adjoint on* $\mathbb{F}$, *then the mild solution satisfy with* $Q \in W^{1,2}(0, \tau; \mathbb{F}) \cap L^2(0, \tau; \mathscr{D}(\mathbf{A}))$.

Assumption 4.2. *Suppose that* $S_0(x), I_{i0}(x) \in \Pi^2(\Omega)$, *and* $\frac{\partial S_0(x)}{\partial \vartheta} = \frac{\partial P_0(x)}{\partial \vartheta} = \frac{\partial I_{i0}(x)}{\partial \vartheta} = 0$, $x \in \partial\Omega$, $i = 1, 2, 3$.

By the similar arguments as those in [26], we have the following the existence and uniqueness theorem of the solution in state system (4.9)-(4.10). For more details, the reader is referred to Theorem 3.1 in [26].

Theorem 4.3. *For bounded domain* Ω *in* $\mathbb{R}^k$, $k \leqslant 4$, *with the boundary of class* $\mathbb{C}^{2+\xi}$, $\xi > 0$. *Suppose that Assumption 4.2 holds. Then for any optimal control pairs* $u = (u_1, u_2, u_3) \in \mathscr{U}$, *there admits a unique globally positive strong solution* Q *for state system (4.9)-(4.10), satisfying* $Q = (S, I_1, I_2, I_3, P) \in W^{1,2}(0, \tau; \Pi)$ *and*

$$
\begin{aligned}
&S(x, t) \in L^2(0, \tau; \Pi^2(\Omega)) \cap L^\infty(0, \tau; \Pi^1(\Omega)) \cap L^\infty(\Omega_T), \\
&P(x, t) \in L^2(0, \tau; \Pi^2(\Omega)) \cap L^\infty(0, \tau; \Pi^1(\Omega)) \cap \in L^\infty(\Omega_T) \cap L^\infty(\Omega_T), \\
&I_i(x, t) \in L^\infty(0, \tau; \Pi^1(\Omega)) \cap L^2(0, \tau; \Pi^2(\Omega)), \ i = 1, 2, 3.
\end{aligned}
\tag{4.19}
$$

Furthermore, there admits a $\varrho > 0$ such that

$$||\partial S/\partial t||_{L^2(\Omega_T)} + ||S||_{L^2(0,\tau;\Pi^2(\Omega))} + ||S||_{L^\infty(\Omega_T)} \leqslant \varrho,$$
$$||\partial P/\partial t||_{L^2(\Omega_T)} + ||P||_{L^2(0,\tau;\Pi^2(\Omega))} + ||P||_{L^\infty(\Omega_T)} \leqslant \varrho,$$
$$||\partial I_i/\partial t||_{L^2(\Omega_T)} + ||I_i||_{L^2(0,\tau;\Pi^2(\Omega))} + ||I_i||_{L^\infty(\Omega_T)} \leqslant \varrho, \ i = 1, 2, 3,$$
$$||\partial S/\partial t||_{\Pi^1(\Omega_T)} \leqslant \varrho, \ ||\partial P/\partial t||_{\Pi^1(\Omega_T)} \leqslant \varrho, \ ||\partial I_i/\partial t||_{\Pi^1(\Omega_T)} \leqslant \varrho, \ \forall \ t \in [0, \tau], \ i = 1, 2, 3.$$
$$(4.20)$$

4.2 The existence of the optimal control pair of state system (4.9)-(4.10)

Theorem 4.4. *If Assumption 4.2 holds, then there admits an optimal control* $(S^*, I_1^*, I_2^*, I_3^*, P^*, u_1^*, u_2^*, u_3^*)$ *of system (4.9)-(4.10).*

Proof. Let

$$\mathscr{G}(S, I_1, I_2, I_3, u)(x, t) = c_0(x, t)S(x, t) + \sum_{i=1}^{3} c_i(x, t)I_i(x, t) + \sum_{i=1}^{3} \omega_i(x, t)u_i(x, t),$$

$$\mathscr{K}(S, I_1, I_2, I_3, u)(x, T) = \zeta_0(x)S(x, \tau) + \sum_{i=1}^{3} \zeta_i(x)I_i(x, \tau) + \sum_{i=1}^{3} \rho_i(x)u_i(x, \tau).$$

Then

$$\mathscr{J}(S, I_1, I_2, I_3, u) = \int_0^\tau \int_\Omega \mathscr{G}(S, I_1, I_2, I_3, u)(t, x)dxdt + \int_\Omega \mathscr{K}(S, I_1, I_2, I_3, u)(\tau, x)dx.$$

It follows from (4.19) in Theorem 4.3 that the cost functional is bounded blew. Accordingly, there exists a minimizing sequence $\{u_1^m, u_2^m, u_3^m\}_{m \geqslant 1}$ and a positive constant $a_1 = \inf_{u \in \mathscr{U}} \mathscr{J}(S, I_1, I_2, I_3, u)$ such that

$$a_1 = \lim_{m \to \infty} \mathscr{J}(S^m, I_1^m, I_2^m, I_3^m, u^m) = \inf_{u \in \mathscr{U}} \mathscr{J}(S, I_1, I_2, I_3, u), \qquad (4.21)$$

where $(S^m, I_1^m, I_2^m, I_3^m)$ is the solution of the system as follows

$$
\begin{cases}
\dfrac{\partial S^m(x,t)}{\partial t} = \theta_0 \Delta S^m(x,t) + \Lambda - (\beta_1(x)I_1^m(x,t) + \beta_2(x)I_2^m(x,t) + \beta_3(x)I_3^m(x,t))\, S^m(x,t) \\
\qquad\qquad - (\mu(x) + r u_1^m(x,t))S^m(x,t), \\[2mm]
\dfrac{\partial I_1^m(x,t)}{\partial t} = \theta_1 \Delta I_1^m(x,t) + (\beta_1(x)I_1^m(x,t) + \beta_2(x)I_2^m(x,t) + \beta_3(x)I_3^m(x,t))\, S^m(x,t) \\
\qquad\qquad + \eta_2 u_2(x,t) I_2^m(x,t) - (\mu(x) + \alpha_1(x)) I_1^m(x,t), \\[2mm]
\dfrac{\partial I_2^m(x,t)}{\partial t} = \theta_2 \Delta I_2^m(x,t) + \alpha_1(x)I_1^m(x,t) - (\alpha_2(x) + \eta_2 u_2^m(x,t) + \mu(x)) I_2^m(x,t) \\
\qquad\qquad + \eta_3 u_3^m(x,t) I_3^m(x,t), \\[2mm]
\dfrac{\partial I_3^m(x,t)}{\partial t} = \theta_3 \Delta I_3^m(x,t) + \alpha_2(x)I_2^m(x,t) - (\eta_3 u_3^m(x,t) + \mu(x) + d(x)) I_3^m(x,t), \\[2mm]
\dfrac{\partial P^m(x,t)}{\partial t} = \theta_4 \Delta P^m(x,t) + \alpha_2(x)I_2^m(x,t) + r u_1^m(x,t)S^m(x,t) - \mu(x)P^m(x,t), \\[2mm]
\dfrac{\partial S^m(x,t)}{\partial \vartheta} = \dfrac{\partial I_1^m(x,t)}{\partial \vartheta} = \dfrac{\partial I_2^m(x,t)}{\partial \vartheta} = \dfrac{\partial I_3^m(x,t)}{\partial \vartheta} = 0, \\[2mm]
S^m(x,0) = S_0^m(x) > 0, \ \ P^m(x,0) = P_0^m(x) > 0, \ \ I_i^m(x,0) = I_{i0}^m(x) > 0, \ \ i = 1,2,3.
\end{cases}
\tag{4.22}
$$

On basis of the result of Theorem 4.3, we can verify that $S^m, I_i^m, P^m \in W^{1,2}(0,\tau; \Pi)$, $i = 1,2,3$, which means that $S^m, P^m, I_i^m \in C([0,\tau]; L^2(\Omega))$. Further, by (4.19), the uniformly boundedness of S^m, I_i^m follows, i.e., there exists a independent of m positive constant ϖ such that

$$
\begin{aligned}
&||I_i^m||_{\Pi^1(\Omega_T)} + ||\partial I_i^m/\partial t||_{L^2(\Omega_T)} + ||I_i^m||_{L^2(0,\tau;\Pi^2(\Omega))} + ||I_i^m||_{L^\infty(\Omega_T)} \leqslant \varpi, \ \forall\, t \in [0,\tau], \\
&||S^m||_{\Pi^1(\Omega_T)} + ||\partial S^m/\partial t||_{L^2(\Omega_T)} + ||S^m||_{L^2(0,\tau;\Pi^2(\Omega))} + ||S^m||_{L^\infty(\Omega_T)} \leqslant \varpi, \ \forall\, t \in [0,\tau], \\
&||P^m||_{\Pi^1(\Omega_T)} + ||\partial P^m/\partial t||_{L^2(\Omega_T)} + ||P^m||_{L^2(0,\tau;\Pi^2(\Omega))} + ||P^m||_{L^\infty(\Omega_T)} \leqslant \varpi, \ \forall\, t \in [0,\tau].
\end{aligned}
\tag{4.23}
$$

Thus, we have the equicontinuity of the family $\{(S^m(t), P^m(t), I_1^m(t), I_2^m(t), I_3^m(t))\}$ from (4.23). Since $\Pi^1(\Omega)$ is compactly embedded into $L^2(\Omega)$, it follows that $\{(S^m(t), P^m(t), I_1^m(t), I_2^m(t), I_3^m(t),)\}_{m \geqslant 1}$ is relatively compact in $(L^2(\Omega))^5$ and $||S^m||_{L^2(\Omega)} \leqslant \varpi, ||P^m||_{L^2(\Omega)} \leqslant \varpi, ||I_i^m||_{L^2(\Omega)} \leqslant \varpi, \ \forall\, t \in [0,\tau], \ i = 1,2,3$. From Ascoli-Arzela Theorem [41], we obtain there exists $(S^*, P^*, I_1^*, I_2^*, I_3^*) \in (C[0,\tau] : L^2(\Omega))^5$ and a subsequence of $\{(S^m(t), P^m(t), I_1^m(t), I_2^m(t), I_3^m(t),)\}_{m \geqslant 1}$, still defined as itself, such that

$$
\begin{cases}
\lim\limits_{m \to \infty} \sup\limits_{t \in [0,\tau]} ||S^m(t) - S^*(t)||_{L^2(\Omega)} = 0, \\[2mm]
\lim\limits_{m \to \infty} \sup\limits_{t \in [0,\tau]} ||P^m(t) - P^*(t)||_{L^2(\Omega)} = 0, \\[2mm]
\lim\limits_{m \to \infty} \sup\limits_{t \in [0,\tau]} ||I_i^m(t) - I_i^*(t)||_{L^2(\Omega)} = 0, \ i = 1,2,3.
\end{cases}
\tag{4.24}
$$

Therefore, we can show that $(S^*, I_1^*, I_2^*, I_3^*, P^*)$ is an optimal control pair of (4.9)-(4.13) by letting $m \to \infty$ in system (4.22). From (4.23), it can be choose a $\{(S^m(t), I_1^m(t), I_2^m(t), I_3^m(t), P^m(t))\}$

such that

$$
\begin{cases}
\dfrac{\partial S^m}{\partial t} \to \dfrac{\partial S^*}{\partial t}, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \\[2mm]
\dfrac{\partial P^m}{\partial t} \to \dfrac{\partial P^*}{\partial t}, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \\[2mm]
\dfrac{\partial I_i^m}{\partial t} \to \dfrac{\partial I_i^*}{\partial t}, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \ i=1,2,3.
\end{cases}
\tag{4.25}
$$

$$
\begin{cases}
S^m \to S^*, \ \text{weakly in } L^\infty(0,\tau;\Pi^1(\Omega)), \\[2mm]
P^m \to P^*, \ \text{weakly in } L^\infty(0,\tau;\Pi^1(\Omega)), \\[2mm]
I_i^m \to I_i^*, \ \text{weakly in } L^\infty(0,\tau;\Pi^1(\Omega)), \ i=1,2,3.
\end{cases}
\tag{4.26}
$$

$$
\begin{cases}
\Delta S^m \to \Delta S^*, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \\[2mm]
\Delta P^m \to \Delta P^*, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \\[2mm]
\Delta I_i^m \to \Delta I_i^*, \ \text{weakly in } L^2(0,\tau;L^2(\Omega)), \ i=1,2,3.
\end{cases}
\tag{4.27}
$$

Furthermore, note that u_i^m, $i=1,2,3$ are all bounded in $L^2(\Omega_T)$, there admits an optimal control pairs u_i^* and subsequence of $\{u_i^m; m \geqslant 1, \ i=1,2,3\}$, still defined as themselves, such that

$$
u_i^m \to u_i^*, \ weakly \ in \ L^2(\Omega_T), \ i=1,2,3.
\tag{4.28}
$$

Considering $\mathscr{U}$ is convex and closed set in $L^2(\Omega_T)$, which implies it is weakly closed. Therefore, we can obtain that $u_i^* \in \mathscr{U}$ from (4.28). Hence, from (4.20), (4.26), (4.28), we can prove that

$$
S^n I_i^m \to S^* I_i^*, \ in \ L^2(0,\tau;L^2(\Omega)), \ i=1,2,3,
\tag{4.29}
$$

and

$$
S^m u_1^m \to S^* u_1^*, \ I_2^m u_2^m \to I_2^* u_2^*, \ I_3^m u_3^m \to I_3^* u_3^*, \ weakly \ in \ L^2(0,\tau;L^2(\Omega)).
\tag{4.30}
$$

Noting that $S^m I_i^m - S^* I_i^* = S^m(I_i^m - I_i^*) + I_i^*(S^m - S^*)$, $u_1^m S^m - u_1^* S^* = u_1^m(S^m - S^*) + S^*(u_1^m - u_1^*)$ and $I_k^m u_k^m - I_k^* u_k^* = u_k^m(I_k^m - I_k^*) + I_k^*(u_k^m - u_k^*)$, $k=2,3$ and employing the Aubin compactness theorem (Theorem 3.1.1 in [42]), (4.25)-(4.26), we can show that S^n and I_i^n strongly converges to S^* and I_i^* in $L^2(\Omega_T)$, respectively. Moreover, on the basis of the uniformly boundedness of S^m, P^m, I_i^m in $L^\infty(\Omega)$, we have (4.29)-(4.30). Hence, it is obvious to see that $(S^*, I_1^*, I_2^*, I_3^*, P^*)$ is an optimal control pair of state system (4.9)-(4.13) when $m \to +\infty$ in system (4.22). $\qquad\square$

4.3 The first order necessary condition for optimal control

In this subsection, the system which including the adjoint states of the state variables given by

$$
\begin{cases}
\dfrac{\partial \hat{S}}{\partial t} = -\theta_0 \Delta \hat{S} + (\beta_1 I_1^* + \beta_2 I_2^* + \beta_3 I_3^* + \mu + r u_1^*)\hat{S} - \beta_1 I_1^* \hat{I}_1 - \beta_2 I_2^* \hat{I}_2 - \beta_3 I_3^* \hat{I}_3 + c_0, \\[2mm]
\dfrac{\partial \hat{I}_1}{\partial t} = -\theta_1 \Delta \hat{I}_1 + \beta_1 S^* \hat{S} - (\beta_1 I_1^* - \mu - \alpha_1)\hat{I}_1 - \alpha_2 \hat{I}_2 + c_1, \\[2mm]
\dfrac{\partial \hat{I}_2}{\partial t} = -\theta_2 \Delta \hat{I}_2 - \alpha_2 \hat{I}_3 + \beta_2 S^* \hat{S} - \beta_2 I_1^* \hat{I}_1 - \eta_2 u_2^* \hat{I}_1 + \eta_2 u_2^* \hat{I}_2 + (\alpha_2 + \mu)\hat{I}_2 + c_2, \\[2mm]
\dfrac{\partial \hat{I}_3}{\partial t} = -\theta_3 \Delta \hat{I}_3 + \beta_3 S^* \hat{S} - \eta_3 u_3^* \hat{I}_2 + \eta_3 u_3^* \hat{I}_3 + (\mu + d)\hat{I}_3 - \beta_3 S^* \hat{I}_1 + c_3, \\[2mm]
\dfrac{\partial \hat{S}}{\partial \vartheta} = \dfrac{\partial \hat{I}_1}{\partial \vartheta} = \dfrac{\partial \hat{I}_2}{\partial \vartheta} = \dfrac{\partial \hat{I}_3}{\partial \vartheta} = 0, \ on \ (0,\tau) \times \partial\Omega, \\[2mm]
\hat{S}(\tau, x) = -\zeta_0, \ \hat{I}_i(\tau, x) = -\zeta_i, \ in \ \Omega, \ i = 1,2,3,
\end{cases}
\tag{4.31}
$$

where $(S^*, I_1^*, I_2^*, I_3^*, u^*)$ is an optimal pair. Replacing the variable t with $\tau - t$ and setting $\varsigma_0(x,t) = \hat{S}(x, \tau - t)$, $\varsigma_i(x,t) = \hat{I}_i(x, \tau - t)$, $i = 1,2,3$, then we can rewrite system (4.31) as follows

$$
\begin{cases}
\dfrac{\partial \varsigma_0}{\partial t} = -\theta_0 \Delta \varsigma_0 + (\beta_1 I_1^* + \beta_2 I_2^* + \beta_3 I_3^* + \mu + r u_1^*)\varsigma_0 - \beta_1 I_1^* \varsigma_1 - \beta_2 I_2^* \varsigma_2 - \beta_3 I_3^* \varsigma_3 + c_0, \\[2mm]
\dfrac{\partial \varsigma_1}{\partial t} = -\theta_1 \Delta \varsigma_1 + \beta_1 S^* \varsigma_0 - (\beta_1 I_1^* - \mu - \alpha_1)\varsigma_1 - \alpha_1 \varsigma_2 + c_1, \\[2mm]
\dfrac{\partial \varsigma_2}{\partial t} = -\theta_2 \Delta \varsigma_2 - \alpha_2 \varsigma_3 + \beta_2 S^* \varsigma_0 - \beta_2 I_1^* \varsigma_1 - \eta_2 u_2^* \varsigma_1 + \eta_2 u_2^* \varsigma_2 + (\alpha_2 + \mu)\varsigma_2 + c_2, \\[2mm]
\dfrac{\partial \varsigma_3}{\partial t} = -\theta_3 \Delta \varsigma_3 + \beta_3 S^* \varsigma_0 - \eta_3 u_3^* \varsigma_2 + \eta_3 u_3^* \varsigma_3 + (\mu + d)\varsigma_3 - \beta_3 S^* \varsigma_1 + c_3, \\[2mm]
\dfrac{\partial \varsigma_0}{\partial \vartheta} = \dfrac{\partial \varsigma_1}{\partial \vartheta} = \dfrac{\partial \varsigma_2}{\partial \vartheta} = \dfrac{\partial \varsigma_3}{\partial \vartheta} = 0, \ on \ (0,\tau) \times \partial\Omega, \\[2mm]
\varsigma_0(0, x) = -\zeta_0, \ \varsigma_i(0, x) = -\zeta_i, \ in \ \Omega, \ i = 1,2,3.
\end{cases}
\tag{4.32}
$$

Using the similar methods in Theorem 4.3, we show the uniqueness and existence of the solution for (4.32), then the well-posedness of system (4.31) follows. Besides, similar to the proof of Theorem 4.3, we have

Lemma 4.5. *Supposing the conditions for Theorem 4.3 hold, and $(S^*, I_1^*, I_2^*, I_3^*, u^*)$ is an optimal control pair. Then system (4.32) has a unique strong positive solution $(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3)$ such that $\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3 \in W^{1,2}(0, \tau; \Pi)$. Furthermore, $\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3 \in L^\infty(\Omega_T) \cap L^2(0, \tau; \Pi^2(\Omega)) \cap L^\infty(0, \tau; \Pi^1(\Omega))$.*

Lemma 4.6. *Suppose that the conditions of Theorem 4.3 hold. For $\tilde{u} \in L^2(\Omega_T)$ and a positive κ, let $u_i^\kappa = u_i^* + \kappa \tilde{u}_i \in \mathscr{U}$, $i = 1,2,3$. Then optimal control strategy problem (4.9)-(4.13) with $u = u^\kappa$ admits a unique solution $Q^\kappa = (S^\kappa, I_1^\kappa, I_2^\kappa, I_3^\kappa, P^\kappa)$. Further, $\|Q^\kappa\|_{L^\infty(\Omega)}$ is uniformly bounded in regard to κ in Ω_T.*

Proof. Employing the similar methods mentioned in Theorem 4.3, the existence and uniqueness of the positive strong solution immediately follow. To show $||Q^\kappa||_{L^\infty(\Omega)}$ is uniformly bounded, we introduce the system as follows

$$
\begin{cases}
\dfrac{\partial \mathbf{W}(x,t)}{\partial t} = \theta_0 \Delta \mathbf{W}(x,t) + \Lambda, \ in \ \Omega_T, \\
\dfrac{\partial \mathbf{W}(x,t)}{\partial \vartheta} = 0, \ on \ (0,\tau) \times \partial\Omega, \\
\mathbf{W}(x,0) = S_0(x), \ in \ \Omega.
\end{cases}
\tag{4.33}
$$

Together system (4.33) with system (4.9)-(4.12) associated with $u = u^\kappa$ and using Gronwall's inequality and comparison principle, yields

$$
0 \leqslant ||S^\kappa(x,t)||_{L^\infty(\Omega)} \leqslant ||\mathbf{W}(x,t)||_{L^\infty(\Omega)} \leqslant \varpi_1 + \Lambda\tau, \ (t,x) \in \Omega_T,
$$

where $\varpi_1 > 0$ is a constant independent of κ. Thus, we know that $||S^\kappa||_{L^\infty(\Omega)}$ is uniformly bounded with respect to κ in Ω_T. Using similar method, we can obtain $||P^\kappa||_{L^\infty(\Omega)}$, and $||I_i^\kappa||_{L^\infty(\Omega)}$, $i = 1, 2, 3$ are all uniformly bounded in regard to κ in Ω_T. $\qquad\square$

For further analysis, we assumed that $(S^*, I_1^*, I_2^*, I_3^*, P^*, u^*)$ is an optimal pair and $Q^\kappa = (S^\kappa, I_1^\kappa, I_2^\kappa, I_3^\kappa, P^\kappa)$ is the solution of optimal control problem (4.9)-(4.13) subjects to u^κ denoted by in lemma 4.6. Let

$$
Y_0^\kappa = \lim_{\kappa \to 0} \frac{S^\kappa - S^*}{\kappa}, \ Y_4^\kappa = \lim_{\kappa \to 0} \frac{P^\kappa - P^*}{\kappa}, \ Y_i^\kappa = \lim_{\kappa \to 0} \frac{I_i^\kappa - I_i^*}{\kappa}, \ i = 1, 2, 3.
$$

Then we obtain the following system

$$
\begin{cases}
\dfrac{\partial Y_0^\kappa}{\partial t} = \theta_0 \Delta Y_0^\kappa - \displaystyle\sum_{i=1}^{3} \beta_i(I_i^\kappa Y_0^\kappa + S^* Y_i^\kappa) - r(u_1^* Y_0^\kappa + S^\kappa \tilde{u}_1) - \mu Y_0^\kappa, \\
\dfrac{\partial Y_1^\kappa}{\partial t} = \theta_1 \Delta Y_1^\kappa + \displaystyle\sum_{i=1}^{3} \beta_i(I_i^\kappa Y_0^\kappa + S^* Y_i^\kappa) + \eta_2(u_2^* Y_2^\kappa + I_2^\kappa \tilde{u}_2) - (\mu + \alpha_1)Y_1^\kappa, \\
\dfrac{\partial Y_2^\kappa}{\partial t} = \theta_2 \Delta Y_2^\kappa + \alpha_1 Y_1^\kappa - (\alpha_2 + \mu)Y_2^\kappa - \eta_2(u_2^* Y_2^\kappa + I_2^\kappa \tilde{u}_2) + \eta_3(u_3^* Y_3^\kappa + I_3^\kappa \tilde{u}_3), \\
\dfrac{\partial Y_3^\kappa}{\partial t} = \theta_3 \Delta Y_3^\kappa + \alpha_2 Y_2^\kappa - (\mu + d)Y_3^\kappa - \eta_3(u_3^* Y_3^\kappa + I_3^\kappa \tilde{u}_3), \\
\dfrac{\partial Y_4^\kappa}{\partial t} = \theta_4 \Delta Y_4^\kappa - \mu Y_4^\kappa + r(u_1^* Y_0^\kappa + S^\kappa \tilde{u}_1), \\
\dfrac{\partial Y_j^\kappa}{\partial \vartheta} = 0, \ on \ (0,\tau) \times \partial\Omega, \ j = 0, 1, 2, 3, 4, \\
Y_j^\kappa(0,x) = 0, \ in \ \Omega, \ j = 0, 1, 2, 3.
\end{cases}
\tag{4.34}
$$

Lemma 4.7. *If Theorem 4.3 conditions remain hold. The problem (4.34) has a unique strong solution Y^κ which satisfies $Y^\kappa = (Y_0^\kappa, Y_1^\kappa, Y_2^\kappa, Y_3^\kappa, Y_4^\kappa)^T \in W^{1,2}(0,\tau;\Pi)$ and $Y_i^\kappa \in L^2(0,\tau;\Pi^2(\Omega)) \cap L^\infty(0,\tau;\Pi^1(\Omega))$. Furthermore, it can be verified that $S^\kappa \to S^*, P^\kappa \to$*

$P^*, I_i^\kappa \to I_i^*$, in $L^2(\Omega_T)$ and $Y^\kappa \to Y$, in $L^2(\Omega_T)$ as $\kappa \to 0$. Here, $Y = (Y_0, Y_1, Y_2, Y_3, Y_4)^T$ is the solution of the system as follows

$$
\begin{cases}
\dfrac{\partial Y_0}{\partial t} = \theta_0 \Delta Y_0 - \displaystyle\sum_{i=1}^{3} \beta_i(I_i^* Y_0 + S^* Y_i) - r(u_1^* Y_0 + S^* \tilde{u}_1) - \mu Y_0, \\[2mm]
\dfrac{\partial Y_1}{\partial t} = \theta_1 \Delta Y_1 + \displaystyle\sum_{i=1}^{3} \beta_i(I_i^* Y_0 + S^* Y_i) + \eta_2(u_2^* Y_2 + I_2^* \tilde{u}_2) - (\mu + \alpha_1) Y_1, \\[2mm]
\dfrac{\partial Y_2}{\partial t} = \theta_2 \Delta Y_2 + \alpha_1 Y_1 - (\alpha_2 + \mu) Y_2 - \eta_2(u_2^* Y_2 + I_2^* \tilde{u}_2) + \eta_3(u_3^* Y_3 + I_3^* \tilde{u}_3), \\[2mm]
\dfrac{\partial Y_3}{\partial t} = \theta_3 \Delta Y_3 + \alpha_2 Y_2 - (\mu + d) Y_3 - \eta_3(u_3^* Y_3 + I_3^* \tilde{u}_3), \\[2mm]
\dfrac{\partial Y_4}{\partial t} = \theta_4 \Delta Y_4 - \mu Y_4 + r(u_1^* Y_0 + S^* \tilde{u}_1), \\[2mm]
\dfrac{\partial Y_j}{\partial \vartheta} = 0, \ on \ (0, \tau) \times \partial\Omega, \ j = 0, 1, 2, 3, \\[2mm]
Y_j(0, x) = 0, \ in \ \Omega, \ j = 0, 1, 2, 3.
\end{cases}
\tag{4.35}
$$

Proof. By the same methods in Theorem 4.3, we have that system (4.35) admits a strong solution. In the next, we show that Y_j^κ, $j = 0, 1, 2, 3$ are all bounded in $L^2(\Omega_T)$ uniformly in regard to κ and

$$
\lim_{\kappa \to 0} ||S^\kappa - S^*||_{L^2(\Omega_T)} = 0, \ \lim_{\kappa \to 0} ||I_i^\kappa - I_i^*||_{L^2(\Omega_T)} = 0, \ i = 1, 2, 3. \lim_{\kappa \to 0} ||P^\kappa - P^*||_{L^2(\Omega_T)} = 0,
$$

For this purpose, let

$$
\mathbf{U}^\kappa = \begin{pmatrix} -rS^\kappa \tilde{u}_1 \\ \eta_2 I_2^\kappa \tilde{u}_2 \\ \eta_3 I_3^\kappa \tilde{u}_3 - \eta_2 I_2^\kappa \tilde{u}_2 \\ -\eta_3 I_3^\kappa \tilde{u}_3 r S^\kappa \tilde{u}_1 \end{pmatrix}, \ \mathbf{U}^* = \begin{pmatrix} -rS^* \tilde{u}_1 \\ \eta_2 I_2^* \tilde{u}_2 \\ \eta_3 I_3^* \tilde{u}_3 - \eta_2 I_2^* \tilde{u}_2 \\ -\eta_3 I_3^* \tilde{u}_3 r S^* \tilde{u}_1 \end{pmatrix}, \tag{4.36}
$$

$$
\mathbf{T}^\kappa = \begin{pmatrix} -\left(\sum_{i=1}^3 \beta_i I_i^\kappa + \mu + ru_1^*\right) & -\beta_1 S^* & -\beta_2 S^* & -\beta_3 S^* & 0 \\ \sum_{i=1}^3 \beta_i I_i^\kappa & \beta_1 S^* - \mu - \alpha_1 & \eta_2 u_2^* & 0 & 0 \\ 0 & \alpha_1 & -(\alpha_2 + \mu + \eta_2 u_2^*) & \eta_3 u_3^* & 0 \\ 0 & 0 & \alpha_2 & -(\mu + d + \eta_3 u_3^*) & 0 \\ ru_1^* & 0 & 0 & 0 & \mu \end{pmatrix}, \tag{4.37}
$$

$$
\mathbf{T}^* = \begin{pmatrix} -\left(\sum_{i=1}^3 \beta_i I_i^* + \mu + ru_1^*\right) & -\beta_1 S^* & -\beta_2 S^* & -\beta_3 S^* & 0 \\ \sum_{i=1}^3 \beta_i I_i^* & \beta_1 S^* - \mu - \alpha_1 & \eta_2 u_2^* & 0 & 0 \\ 0 & \alpha_1 & -(\alpha_2 + \mu + \eta_2 u_2^*) & \eta_3 u_3^* & 0 \\ 0 & 0 & \alpha_2 & -(\mu + d + \eta_3 u_3^*) & 0 \\ ru_1^* & 0 & 0 & 0 & \mu \end{pmatrix}. \tag{4.38}
$$

Then we can rewrite system (4.34) as follows

$$\begin{cases} \dfrac{\partial Y^\kappa}{\partial t} = \mathbf{A}Y^\kappa(t) + \mathbf{T}^\kappa(t)Y^\kappa(t) + \mathbf{U}^\kappa(t), \ in \ \Omega_T, \\ Y^\kappa(0) = 0, \ in \ \Omega. \end{cases} \tag{4.39}$$

We suppose that $\mathbf{A}$ generates semigroup $\{S(t) : t \geqslant 0\}$. Then we have the following expression of $Y^\kappa(t)$ from [43]

$$Y^\kappa(t) = \int_0^t S(t-s)\mathbf{T}^\kappa(s)Y^\kappa(s)ds + \int_0^t S(t-s)\mathbf{U}^\kappa(s)ds, \ t \in [0,\tau]. \tag{4.40}$$

From Lemmas 4.5, 4.6 and Theorem 4.3, the uniformly boundedness of the elements of $\mathbf{U}$ in (4.36) and $\mathbf{T}$ in (4.37) in regard to t holds. Hence, we can choose positive constants B_1 and B_2 such that

$$||Y^\kappa||_{L^2(\Omega)} \leqslant B_1 + B_2 \int_0^t ||Y^\kappa(s)||_{L^2(\Omega)}ds, \ t \in [0,\tau].$$

It follows from Gronwall inequality that Y^κ is bounded in $L^2(\Omega)$. Then we have $||S^\kappa - S||_{L^2(\Omega_T)} = \kappa||S^\kappa||_{L^2(\Omega_T)} \to 0$, $||P^\kappa - P||_{L^2(\Omega_T)} = \kappa||P^\kappa||_{L^2(\Omega_T)} \to 0$, $||I_i^\kappa - I_i||_{L^2(\Omega_T)} = \kappa||I_i^\kappa||_{L^2(\Omega_T)} \to 0$ as $\kappa \to 0$, $i = 1,2,3$. In the next, we show that $Y^\kappa \to Y$, in $L^2(\Omega_T)$. System (4.35) can be rewritten as

$$\begin{cases} \dfrac{\partial Y}{\partial t} = \mathbf{A}Y(t) + \mathbf{T}^*(t)Y(t) + \mathbf{U}^*(t), \ in \ \Omega_T, \\ Y(0) = 0, \ in \ \Omega. \end{cases} \tag{4.41}$$

Then we have the following expression of the solution of system (4.41)

$$Y(t) = \int_0^t S(t-s)\mathbf{T}^*(s)Y(s)ds + \int_0^t S(t-s)\mathbf{U}^*(s)ds, \ t \in [0,\tau]. \tag{4.42}$$

Combination of (4.40) and (4.42), yields

$$Y^\kappa(t) - Y^\kappa(t) = \int_0^t S(t-s)(\mathbf{T}^\kappa Y^\kappa - \mathbf{T}^*Y)(s)ds, \ t \in [0,\tau].$$

Considering that the elements for $\mathbf{T}^\kappa(t)$ are all uniformly bounded and converge to the elements of $\mathbf{T}^*(t)$ in $L^2(\Omega_T)$, respectively. Thus, we can deduce that $Y^\kappa \to Y$ in $L^2(\Omega_T)$ by applying the Gronwall inequality. $\qquad\square$

Theorem 4.8. *Assume that Theorem 4.3 conditions remain hold. If* $(S^*, I_1^*, I_2^*, I_3^*, u^*)$ *is an optimal control pair of the optimal control problem (4.9)-(4.13) and* $(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3, \hat{P})$ *is the solution to system (4.31), then*

$$\int_{\Omega_T} (r\hat{S}S^* + \omega_1)(\hat{u}_1 - u_1^*)(t,x)dxdt + \sum_{k=2}^3 \int_{\Omega_T} (\eta_k \hat{I}_k I_k^* + \omega_k)(\hat{u}_k - u_k^*)dxdt$$

$$\geqslant -\sum_{i=1}^3 \int_\Omega \rho_i(x)(\hat{u}_i - u_i^*)(T,x)dx. \tag{4.43}$$

Moreover, if $\rho_i(x) \equiv 0$ in Ω, $i = 1, 2, 3$, then we have

$$u_1^* = \begin{cases} 1, & in \ \left\{ (t,x) \in \Omega : (rS^*\hat{S} + \omega_1)(t,x) \leqslant 0 \right\}, \\ 0, & in \ \left\{ (t,x) \in \Omega : (rS^*\hat{S} + \omega_1)(t,x) > 0 \right\}, \end{cases} \tag{4.44}$$

$$u_k^*|_{(k=2,3)} = \begin{cases} 1, & in \ \left\{ (t,x) \in \Omega : (\eta_k I_k^* \hat{I}_k + \omega_k)(t,x) \leqslant 0 \right\}, \\ 0, & in \ \left\{ (t,x) \in \Omega : (\eta_k I_k^* \hat{I}_k + \omega_k)(t,x) > 0 \right\}, \end{cases} \tag{4.45}$$

Proof. Suppose that $(S^*, I_1^*, I_2^*, I_3^*, P^*, u^*)$ is an optimal control pair, the control cost function $\mathscr{J}(S, I_1, I_2, I_3, u)$, which is given by (4.12). Hence

$$\mathscr{J}(S^*, I_1^*, I_2^*, I_3^*, u^*) \leqslant \mathscr{J}(S^\kappa, I_1^\kappa, I_2^\kappa, I_3^\kappa, u^\kappa), \ \forall \ \kappa > 0. \tag{4.46}$$

That is to say

$$\int_{\Omega_T} \left[c_0(S^\kappa - S^*) + \sum_{i=1}^{3} c_i(I_i^\kappa - I_i^*) + \sum_{i=1}^{3} \kappa\omega_i\tilde{u}_i \right] (t,x)dtdx$$

$$+ \int_{\Omega} \left[\zeta_0(S^\kappa - S^*) + \sum_{i=1}^{3} \zeta(I_i^\kappa - I_i^*) + \sum_{i=1}^{3} \kappa\rho_i\tilde{u}_i \right] (\tau,x)dx \tag{4.47}$$

$$\geqslant 0.$$

Dividing both sides of inequality (4.47) by κ, yields

$$\int_{\Omega_T} \left(c_0 Y_0^\kappa + \sum_{i=1}^{3} c_i Y_i^\kappa + \sum_{i=1}^{3} \omega_i\tilde{u}_i \right) (t,x)dtdx + \int_{\Omega} \left(\zeta_0 Y_0^\kappa + \sum_{i=1}^{3} \zeta_i Y_i^\kappa + \sum_{i=1}^{3} \rho_i\tilde{u}_i \right) (T,x)dx \geqslant 0. \tag{4.48}$$

Furthermore, if follows from Lemma 4.7 that

$$Y_0^\kappa \to Y_0, \ Y_1^\kappa \to Y_1, \ Y_2^\kappa \to Y_2, \ Y_3^\kappa \to Y_3, \ \in \ L^2(\Omega_T), \ as \ \kappa \to 0,$$
$$Y_0^\kappa \to Y_0, \ Y_1^\kappa \to Y_1, \ Y_2^\kappa \to Y_2, \ Y_3^\kappa \to Y_3, \ in \ L^1(\Omega_T), \ as \ \kappa \to 0,$$
$$Y_0^\kappa(\tau) \to Y_0(\tau), \ Y_1^\kappa(\tau) \to Y_1(\tau), \ Y_2^\kappa(\tau) \to Y_2(\tau), \ Y_3^\kappa(\tau) \to Y_3(\tau), \ in \ L^1(\Omega_T), \ as \ \kappa \to 0.$$

Then we can obtain the following results from (4.48) by sending $\kappa \to 0$

$$\int_{\Omega_T} \left(c_0 Y_0 + \sum_{i=1}^{3} c_i Y_i + \sum_{i=1}^{3} \omega_i\tilde{u}_i \right) (t,x)dtdx + \int_{\Omega} \left(\zeta_0 Y_0 + \sum_{i=1}^{3} \zeta_i Y_i + \sum_{i=1}^{3} \rho_i\tilde{u}_i \right) (\tau,x)dx \geqslant 0. \tag{4.49}$$

From system (4.31) and (4.35), we can obtain that

$$\frac{\partial \hat{S}}{\partial t} Y_0 + \frac{\partial Y_0}{\partial t} \hat{S} + \sum_{i=1}^{3} \left(\frac{\partial \hat{I}_i}{\partial t} Y_i + \frac{\partial Y_i}{\partial t} \hat{I}_i \right)$$

$$= \theta_0 \left(\Delta Y_0 \hat{S} - \Delta\hat{S} Y_0 \right) + \sum_{i=1}^{3} \theta_i \left(\Delta Y_i \hat{I}_i - \Delta\hat{I}_i Y_i \right) + \sum_{i=1}^{3} c_i Y_i - rS^*\hat{S}\tilde{u}_1 - \sum_{k=2}^{3} \eta_k I_k^* \hat{I}_k \tilde{u}_k. \tag{4.50}$$

Recalling the initial boundary conditions of $(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3)$ and integrating (4.50) over Ω_T, we have the result by the Green formula as follows

$$
\int_\Omega \left(Y_0\hat{S} + \sum_{i=1}^3 Y_i\hat{I}_i \right)(\tau, x)dx = \int_{\Omega_T} \sum_{i=1}^3 ciY_i(t, x)dxdt - r\int_{\Omega_T} S^*\hat{S}\tilde{u}_1dxdt
$$
$$
- \int_{\Omega_T} \sum_{k=2}^3 \eta_k\hat{I}_kI_k^*\tilde{u}_kdxdt. \tag{4.51}
$$

Further, from the last equation of system (4.31) and (4.51), yields

$$
\int_\Omega \left(\zeta_0Y_0 + \sum_{i=1}^3 \zeta_iY_i \right)(\tau, x)dx + \int_{\Omega_T} \sum_{i=1}^3 c_iY_i(t, x)dxdt
$$
$$
= r\int_{\Omega_T} S^*\hat{S}\tilde{u}_1dxdt + \int_{\Omega_T} \sum_{k=2}^3 \eta_k\hat{I}_kI_k^*\tilde{u}_kdxdt. \tag{4.52}
$$

Then by (4.49), yields

$$
\int_{\Omega_T} rS^*\hat{S}\tilde{u}_1dxdt + \int_{\Omega_T} \sum_{k=2}^3 \eta_iI_k^*\hat{I}_k\tilde{u}_kdxdt \geqslant -\int_{\Omega_T} \sum_{i=1}^3 (\omega_i\tilde{u}_i)(t, x)dxdt - \int_\Omega \sum_{i=1}^3 (\rho_i\tilde{u}_i)(\tau, x)dx.
$$

On the basis of $\tilde{u} = (\tilde{u}_1, \tilde{u}_2, \tilde{u}_3) \in L^2(\Omega_T)$ is arbitrary, we can set $\tilde{u}_i = \hat{u}_i - u_i^*$, $\forall \hat{u}_i \in \mathscr{U}$, $i = 1, 2, 3$. Then the inequality (4.43) in Theorem 4.8 is obtained. This completes the proof.   □

We study numerically the optimal control problem (4.13) in the next section.

5   Numerical simulations

5.1   Estimation of the model parameters and initial values

In this subsection, we mainly focus on the estimation of model (1.1)-(1.3) parameters and initial values. The mean values of the some parameters in model (1.1)-(1.3) are taken as in Table 2, we set $b(x)$ as constant $b > 0$, where $b = r, \alpha_1, \alpha_2, \eta_2, \eta_3, \mu, d$. We choose $r = 0.01$, $\alpha_1 = 0.33$, $\alpha_2 = 0.34$, $\eta_2 = 0.57$, $\eta_3 = 0.32$ are taken from the literature [9] in Table 2. The natural death rate $\mu = 0.0246$ and AID-related death rate $d = 0.7114$ are taken from the literature [45] in Table 2.

From [44], we can assume that $\Lambda = 830,000$. From the HIV/AID reported case in 2018 [46], we can obtain the new HIV/AIDS cases through homosexual transmission is 34,358 (25.5% of the total new reported cases), where 35.8% of the case under ART treatment [47]. Hence, we assume that $I_{10}(x) = 34,358 \times (1 - 25.8\%) = 22,058$, $I_{20}(x) = 10,000$, $I_{30}(x) = 2,300$. Meanwhile, let $S_0(x) = 20$ million, $P_0(x) = 20$ million $\times 20\% = 4$ million. Similar with the form is given by literature [22], we choose $\beta_1(x) = 1.2 \times 10^{-7}, \beta_2(x) = 1.8 \times 10^{-7}(1 + 0.5\cos(2x)), \beta_3(x) = 6.3 \times 10^{-8}(1 + 0.5\cos(2x))$. We set $\Omega =$

$[0, 1]$ for simplification. The diffusion coefficients of the MSM in different compartments can be set to $\theta_0 = 0.008, \theta_1 = 0.002, \theta_2 = 0.001, \theta_3 = 0.003, \theta_4 = 0.006$.
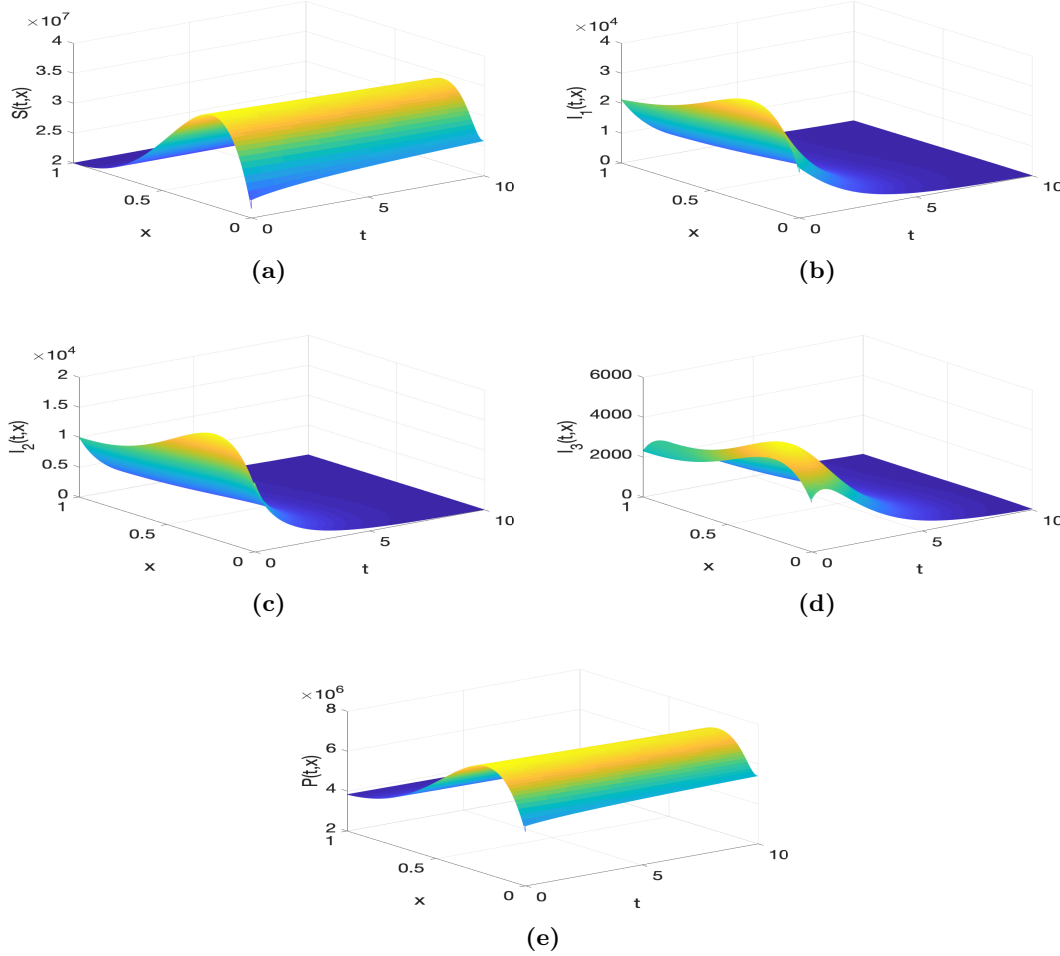

Figure 1. The solution surface to system (1.1)-(1.3) when $R_0 < 1$, on $\Omega_T = [0, 10] \times [0, 1]$.

5.2 Dynamical behaviors of system (1.1)-(1.3)

In this subsection, we first choose $\beta_1(x) = 1.2 \times 10^{-8}, \beta_2(x) = 1.4 \times 10^{-8}(1+0.5\cos(2x)), \beta_3(x) = 1.3 \times 10^{-8}(1 + 0.5\cos(2x))$ and obtain $R_0 \approx 0.942 < 1$. From Figure 1, we can see that the solution of system (1.1-1.3) approaches the disease-free equilibrium as $t \to \infty$. This result is lines in with Theorem 3.2, i.e. E_0 is g.a.s if $R_0 < 1$. When we choose $\beta_1(x) = 1.2 \times 10^{-8}, \beta_2(x) = 3.8 \times 10^{-8}(1+0.5\cos(2x)), \beta_3(x) = 3 \times 10^{-8}(1+0.5\cos(2x))$ and obtain $R_0 \approx 1.209 > 1$. Figure 2 shows that the disease will be present in the MSM group.
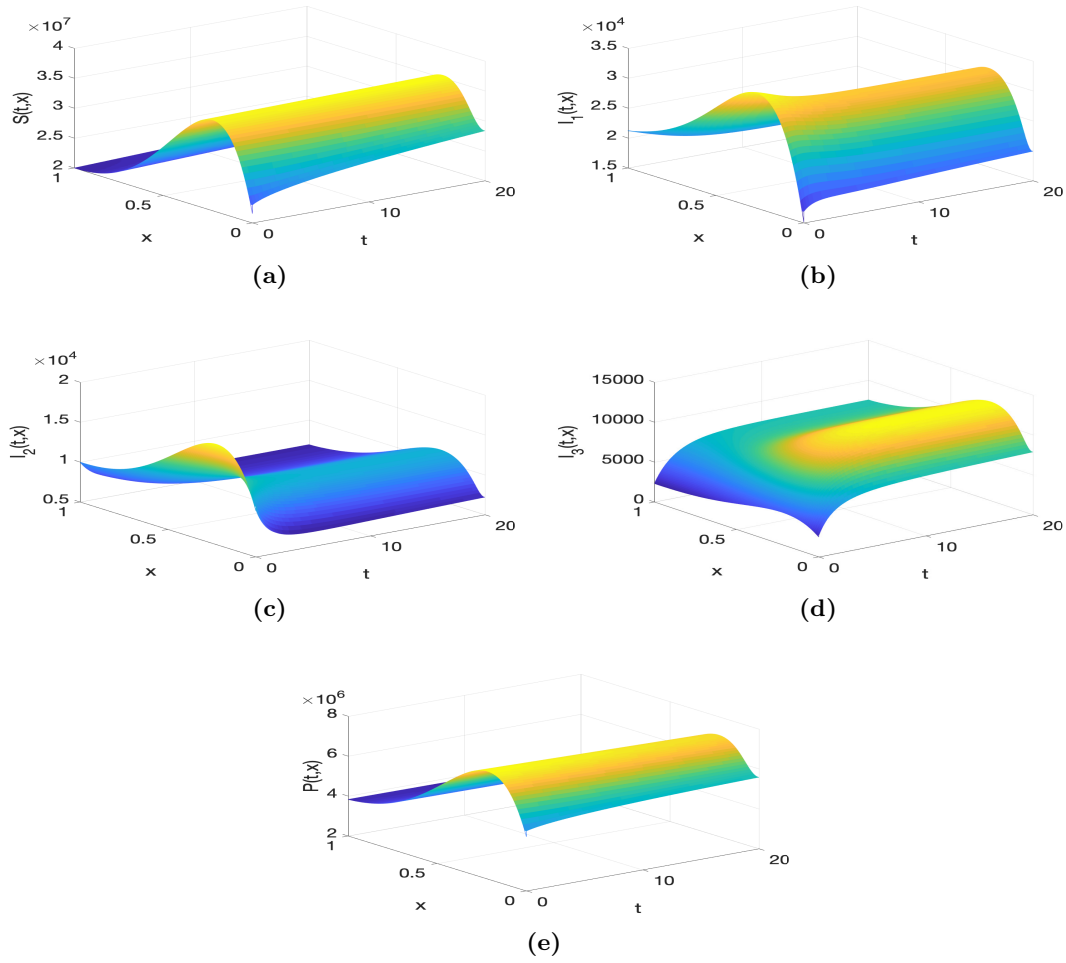
Figure 2. The solution surface to system (1.1)-(1.3) when $R_0 > 1$, on $\Omega_T = [0, 10] \times [0, 1]$.
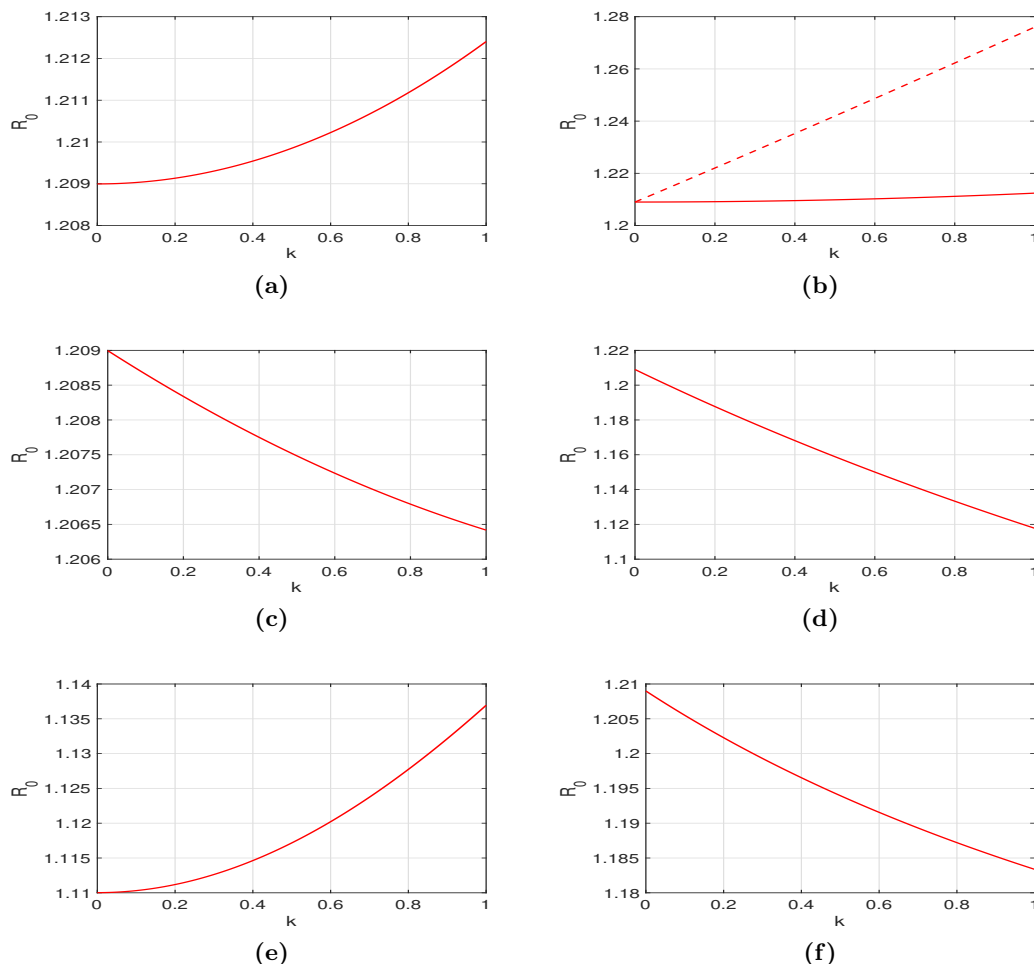
Figure 3. The influence of the spatial heterogeneity on R_0. (a) $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\sin(2x))$. (b) $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\sin(2x))$ and $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\cos(2x))$. (c) $\mu(x) = 0.0246 \times (1 + k\sin(2x))$. (d) $r(x) = 0.01 \times (1 + k\sin(2x))$. (e) $\beta_2(x) = 3.8 \times 10^{-8}(1 + k\sin(2x))$. (f) $d(x) = 0.7114 \times (1 + k\sin(2x))$. Other parameters as their means value in Table 2.

Obviously, we know that an increase in R_0 will increase the risk of HIV transmission among MSM group. Hence, we now study the effect of the heterogenous parameters on R_0, which denotes the key threshold value of the disease transmission. In Figure 3 (a) and (e), we can see that R_0 increases as parameter k increases when we set $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\sin(2x))$ and $\beta_2(x) = 3.8 \times 10^{-8}(1 + k\sin(2x))$, respectively. Furthermore, R_0 in the case of $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\sin(x))$ (red dotted line in Figure 3 (b)) is larger than R_0 in the case of $\beta_1(x) = 1.2 \times 10^{-8}(1 + k\sin(2x))$ (red solid line in Figure 3 (b)). It is revealed that choosing the average the infection the infection ability of HIV will underestimate the risk of HIV transmission. Set $d(x) = 0.7114 \times (1 + k\sin(2x))$ and other parameters are fixed as their values in Table 2. Then k increases will lead to R_0 decreases (see Figure 3 (f)). In Figure 3 (c), the influence of the heterogeneity of $\mu(x)$ on HIV infections risk R_0 can be obtained similarly. Moreover, from Figure 3 (d), it is

indicated that R_0 decreases as k increases, which implies that increasing the coverage of PrEP will effectively reduce the risk of HIV transmission among MSM group.

5.3 Application to the optimal control among MSM in China

In this subsection, we mainly focus on the optimal control of the reaction-diffusion model (4.9)-(4.10) with PrEP and ART treatment. Studies have shown that taking PrEP drug on time and in quantities according to doctor's instructions can effectively prevent HIV transmission through unprotected sexual behaviors. In fact, Gilead's Truvada (PrEP drugs) costs 6,500 (3,675-8,963) USD (United States Dollar) per person each year through the health care system, and private purchases may be more expensive [47]. For private purchases DTG (Dolutegravir) drugs, it almost costs 3,394 USD per HIV infected individual each year [47]. For the sake of simplicity, we choose the mean value of $c_k(x), \zeta_k(x), \ k = 0, 1, 2, 3$ [26, 27], and $\omega_i, \ i = 1, 2, 3$ in cost functional in (4.12) as follows:

$$c_0 = 1, \ c_1 = 1, \ c_2 = 1, \ c_3 = 1.2, \ \zeta_0 = 0.1, \ \zeta_1 = 0.02, \ \zeta_2 = 0.04, \ \zeta_3 = 0.02,$$
$$\omega_1 = 6500, \ \omega_2 = 3394, \ \omega_3 = 3394.$$

We now solve the optimal control problem proposed in (4.13) for $\rho_i(x, \tau) = 0, \ i = 1, 2, 3$, $\tau = 1$ year. It is easy to see from Figure 4 that the optimal controls u_i^* $(i = 1, 2, 3)$ are all of the Bang-Bang form. From Figure 5, it is revealed that the strategy associated with controls leads to a significant decrease on the number of HIV infected individuals at various stages among MSM. The corresponding cost of optimal control (u_1^*, u_2^*, u_3^*) is 1.582 billion USD (see Case 2 in Table 3 and Table 4), which is significantly less than the predicted costs in [47]. In fact, the authors in this paper estimate the total spending on PrEP would be 29.6 (22.2-37.1) billion USD over the period from 2018 to 2037 if 20% MSM initiated daily oral Truvada for usage period of 5 years per person, namely, PrEP treatment costs an average of 1.48 billion USD per year.
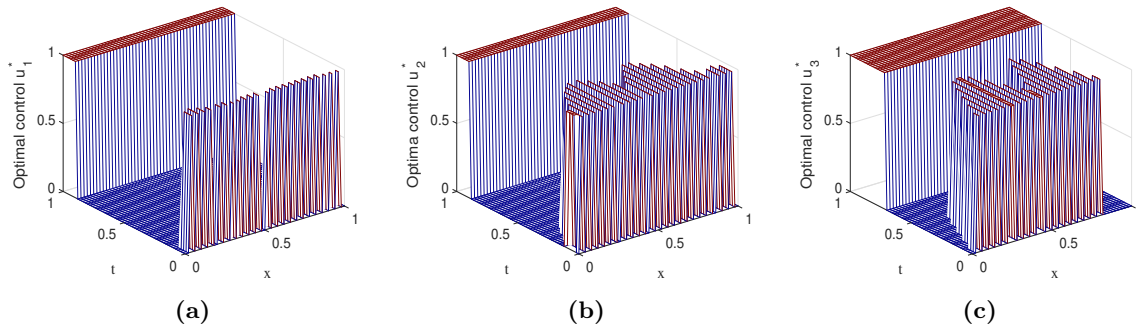

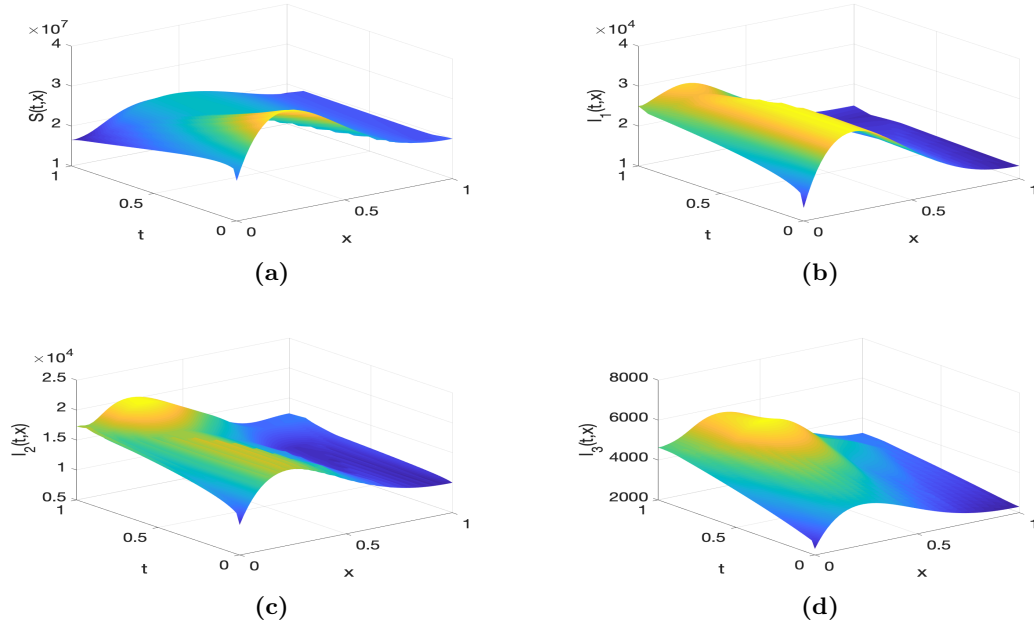**Figure 4.** (a) the surface of u_1^*; (b) the surface of u_2^*; (c) the surface of u_3^*.

Figure 5. The solution surface to controlled equations (4.9)-(4.10) on $\Omega_T = [0,1] \times [0,1]$.

5.3.1 The impact of diffusive coefficients on the optimal control strategy for HIV/AIDS among MSM
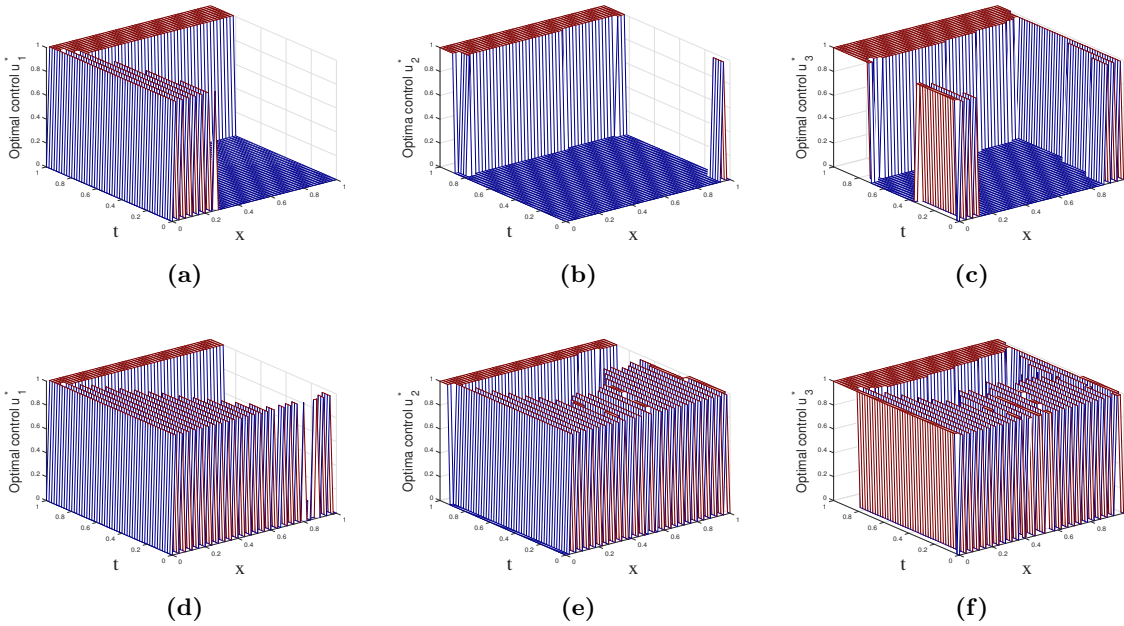

Figure 6. (a)-(c): The optimal control for $\theta_1 = 0.001, \theta_2 = 0.001, \theta_3 = 0.001$. (d)-(f): The optimal control for $\theta_1 = 0.008, \theta_2 = 0.007, \theta_3 = 0.009$.

From the standpoint of epidemiology, it is very meaningful to study whether the diffusion coefficients affect the optimal control strategy. For this purpose, we choose three cases of the diffusive coefficient pairs $(\theta_1, \theta_2, \theta_3)$ in Table 3. From Figures 6 (a)-(f) and Table 3, it can be seen that the strength and cost of the optimal control strategies (u_1^*, u_2^*, u_3^*) increased by the diffusive coefficients, which range from 1.338 to 1.845 billion USD. This indicates that the diffusion of infected individuals is one of the key factors in controlling HIV transmission within the MSM group on account of HIV carriers do not need to be hospitalized to receive ART treatment.

Case	Case 1	Case 2	Case 3
$(\theta_1, \theta_2, \theta_3)$	(0.001,0.001,0.001)	(0.002,0.001,0.003)	(0.008,0.007,0.009)
$\mathscr{J}(u_1^*, u_2^*, u_3^*)$	1.338 billion USD	1.582 billion USD	1.845 billion USD

Table 3. The value of cost functional $\mathscr{J}(u_1^*, u_2^*, u_3^*)$ with respect to the diffusion coefficients $(\theta_1, \theta_2, \theta_3)$.

5.3.2 The impact of initial values on the optimal control strategy for HIV/AIDS among MSM

(a)   (b)   (c)

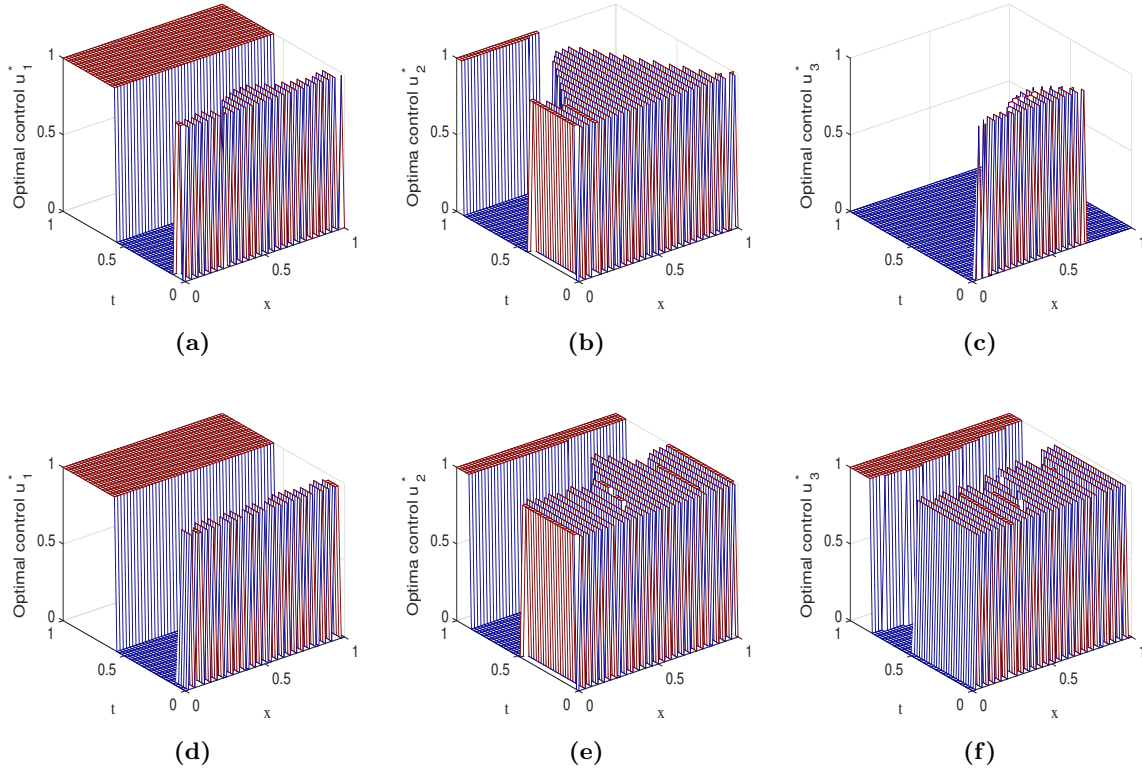(d)   (e)   (f)

Figure 7. (a)-(c): The optimal control for $I_1(0) = 1500, I_2(0) = 800, I_3(0) = 500$. (d)-(f): The optimal control for $I_1(0) = 24000, I_2(0) = 20000, I_3(0) = 13000$.

Although the initial values do not affect the global behaviors of system (1.1-1.3), we are still interested in the effect of initial values on the optimal control strategy for HIV transmission among MSM. For this purpose, we choose three cases of $(I_1(0), i_2(0), i_3(0))$ in Table 4. It can be seen that the strength and cost of the optimal control are increased by the initial values in Figures 7 (a)-(f), which range from 0.874 to 2.645 billion USD. This indicates that the increasing number of HIV infected individuals among MSM will increase the difficulty and effect of the optimal control. Based on the fact of the number of HIV infections among MSM group in China has increased year by year in the past decade, this means that the earlier the PrEP intervention and prevention of HIV transmission among MSM, the lower cost and the less difficulty of the optimal control, thereby increasing the efficiency of optimal control for HIV transmission among MSM group.

Case	Case 1	Case 2	Case 3
$(I_1(0), I_2(0), I_3(0))$	(8000, 4000, 600)	(22,058,10,000, 2,300)	(44000, 20000,13000)
$\mathscr{J}(u_1^*, u_2^*, u_3^*)$	0.717 billion USD	1.582 billion USD	2.645 billion USD

Table 4. The value of cost functional $\mathscr{J}(u_1^*, u_2^*, u_3^*)$ with respect to the initial values $(I_1(0), I_2(0), I_3(0))$.

5.3.3 The impact of the cost of PrEP therapy on the optimal control strategy for HIV/AIDS among MSM

(a)　　　　　　　　(b)　　　　　　　　(c)
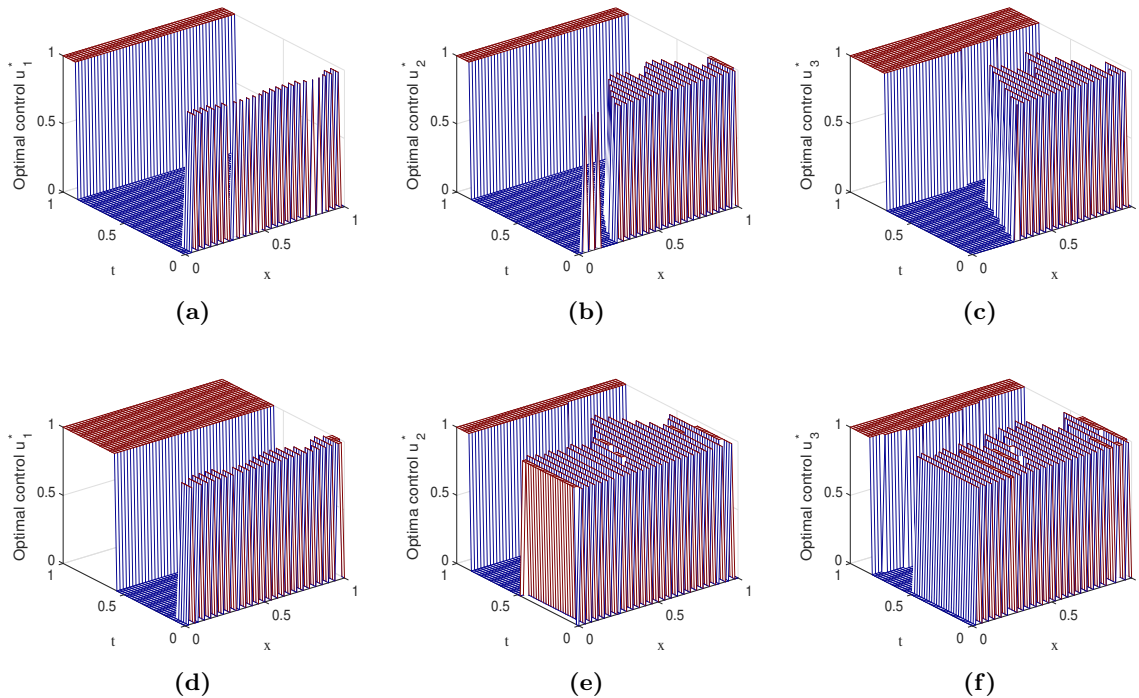
(d)　　　　　　　　(e)　　　　　　　　(f)

Figure 8. (a)-(c): The optimal control for $\omega_1 = 3675$. (d)-(f): The optimal control for $\omega_1 = 8963$.

From the data mentioned in [47], we know that the cost of Gilead's Truvada range from 3,675 USD to 8,963 USD. Hence, in this subsection, we devote to discussing the effect of the cost of the PrEP drug on the optimal control strategy for HIV transmission among MSM. For this purpose, we choose three cases of the initial values ω_1 in Table 5. It can be seen that the strength and cost of the optimal control strategy are increased by the cost of the PrEP drug in Figure 8 (a)-(f), which range from 1.061 to 2.142 billion USD in Table 5. This indicates that high drug prices pose a big challenge to the promotion of PrEP treatment among the MSM group. In fact, this also brings great intervention costs to the national public medical system. Therefore, in order to better play the role of PrEP drugs in preventing the spread of HIV among MSM group in China, the cost of PrEP drug needs to be reduced so that most people can pay for PrEP drug treatment.

Case	Case 1	Case 2	Case 3
ω_1	3,675	6,500	8,963
$\mathscr{J}(u_1^*, u_2^*, u_3^*)$	1.061 billion USD	1.582 billion USD	2.142 billion USD

Table 5. The value of cost functional $\mathscr{J}(u_1^*, u_2^*, u_3^*)$ with respect to the cost ω_1 of PrEP therapy.

6 Conclusion

In this paper, we formulate a realistic HIV/AIDS epidemic model with spatial diffusion to study the combination effect of PrEP and ART on HIV infections among MSM group in heterogenous environment. We derive the basic reproduction number R_0 and demonstrated as a threshold parameters for the dynamical behaviors of the model: the disease dies out when $R_0 < 1$ and presents when $R_0 > 1$ in MSM group.

On the basis of PrEP and ART have substantial advantages in controlling HIV infections among MSM group, we establish an optimal control strategy for the model with positive constant diffusion coefficients. The purpose of the optimal control is minimize the total number of MSM susceptible population and HIV infected population, the cost of PrEP intervention and ART treatment for MSM group. By virtue of minimal sequence techniques and the methods of convex perturbation, we show the existence and the first order necessary optimality conditions of the optimal treatment strategies, respectively. Furthermore, it is worth mentioning that we give the Bang-Bang form for optimal treatment strategies in the case of $\rho_i(\tau, x) = 0, \ i = 1, 2, 3$.

Finally, on the basis of the MSM group data in China, we conduct some numerical simulations to reinforce the analytical results. More specifically, by analyzing the influence of diffusion coefficients on the optimal control, we found that the increase in the diffusion coefficients of MSM group increases the density of maximum control (see Figure 6), and it also increase the cost of control (see Table 3). This implies that spatial diffusion cannot be ignored during intervention for HIV transmissions among MSM group. We are also interested in whether the initial data of HIV infections among MSM group affects the optimal control strategies. By analyzing the influence of initial values on the optimal control (see Figure 7, Table 4) and considering a practical situation, the numbers of HIV

infections among MSM group increase year by year in China. Our works suggest: (1) it will be help to improve control efficacies and reduce its cost if the PrEP intervention and ART treatment measures for MSM group are taken as early as possible; (2) in order to better play the role of PrEP drugs in preventing the spread of HIV among MSM group in China, the price of PrEP drug needs to be reduced so that most people among MSM group can pay for PrEP drug treatment. From the view of practical, the model established in our paper can be applied to comprehend and control the transmission of the disease among MSM in China, which can help the department of health to implement preventive intervention for HIV infections among MSM group.

References

[1] M.V. Barbarossa, G. Rost (2015) Immuno-epidemiology of a population structured by immune status: a mathematical study of waning immunity and immune system boosting. J. Math. Biol. 71: 1737-1770

[2] H. Zhao, P. Wu, S. Ruan (2020) Dynamic analysis and optimal control of a three-age-class HIV/AIDS epidemic model in China. Discrete Cont. Dyn. Syst. Series B. 25: 3491-3521

[3] HIV-Causal Collaboration (2010) The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. AIDS 24: 123

[4] M. May, R. Wood, L. Myer, P. Taffe, A. Rauch, M. Battegay (2009) Matthias Egger for the Cape Town AIDS Cohort and the Swiss HIV Cohort Study, CD4 t-cell declines by ethnicity in untreated HIV-1 infected patients in South Africa and switzerland. J. Infect. Dis. 200:1729

[5] H. Wang, R. Xu, Z. Wang, H. Chen (2014) Global dynamics of a class of HIV-1 infection models with latently infected cells. Nonlinear Anal. Model. Control. 20:21-37

[6] I. Hosseini, F.M. Gabhann (2012) Multi-Scale Modeling of HIV Infection in vitro and APOBEC3G-Based Anti-Retroviral Therapy. PloS Comput. Biol. 8: e1002371

[7] P. Wu, H. Zhao (2020) Dynamics of an HIV Infection Model with Two Infection Routes and Evolutionary Competition between Two Viral Strains. Appl. Math. Model. 84: 240-264

[8] WHO (2010) Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach 2010 Revision. World Health Organization

[9] S.M. Rahman, K.N. Vaidya, X. Zou (2016) Impact of early treatment programs on HIV epidemics: An immunity-based mathematical model. Math. Biosci.280: 38-49

[10] A. Ishaku, A.M. Gazali, S.A. Abdullahi, N. Hussaini (2020) Analysis and optimal control of an HIV model based on CD4 count. J. Math. Biol. 81:209-241

[11] M. Shen, Y. Xiao, L. Rong (2016) Global stability of an infection-age structured HIV-1 model linking within-host and between-host dynamics. Math. Biosci.263: 37-50

[12] P. Narat, J.E. William, et al (2016) Effect of pre-exposure prophylaxis and combination HIV prevention for men who have sex with men in the UK: a mathematical modelling study. Lancet HIV 3: 94-104

[13] CDC (2014) Pre-Exposure Prophylaxis (PrEP). https://www.cdc.gov/hiv/risk/prep/index.html

[14] WHO (215) Policy brief on oral pre-exposure prophylaxis of HIV infection (PrEP), Geneva. http://www.who.int/hiv/pub/prep/policy-brief-prep-2015/en/,

[15] J.M. Baeten (2018) Amplifying the Population Health Benefits of PrEP for HIV Prevention. J. Infect. Dis. 1059-1511

[16] S. M. Rahman, N. K. Vaidya, X. Zou (2014) Impact of Tenofovir gel as a PrEP on HIV infection: A mathematical model. J. Theoret. Biol. 347: 151-159

[17] G. Akudibillah, A. Pandey, J. Medlocy (2017) Maximizing the benefits of ART and PrEP in resource- limited settings. Epidemiol. Infect. 145: 942-956

[18] C. J. Silva, F. M. Torres (2017) Modeling and Optimal Control of HIV/AIDS Prevention through PrEP. arXiv preprint arXiv:1703.06446, 2017.

[19] S. B. Kim, M. Yoon, et al. (2014) Mathematical Modeling of HIV Prevention Measures Including Pre-Exposure Prophylaxis on HIV Incidence in South Korea. PLoS ONE 9:e90080

[20] M.A. Pinto, R.M. Carvalho (2018) The impact of pre-exposure prophylaxis (PrEP) and screening on the dynamics of HIV. J. Comput. Appl. Math 339: 231-244

[21] X. Lai, X. Zou (2016) A reaction diffusion system modeling virus dynamics and CTLS response with chemotaxis. Discrete. Contin. Dyn. Syst-Series B 21: 2567-2585

[22] X. Ren, Y. Tian, L. Liu, X. Liu (2018) A reaction–diffusion within-host HIV model with cell-to-cell transmission. J. Math. Biol. 76: 1831-1872

[23] Y. Gao, J. Wang, (2020) Threshold dynamics of a delayed nonlocal reaction-diffusion HIV infection model with both cell-free and cell-to-cell transmissions, J. Math. Anal. Appl. 488: 124047.

[24] M. Shen, Y. Xiao, L. Rong, et al. (2018) The cost-effectiveness of oral HIV pre-exposure prophylaxis and early antiretroviral therapy in the presence of drug resistance among men who have sex with men in San Francisco. BMC Medicine 16:58

[25] H. Xiang, B. Liu (2015) Solving the inverse problem of an SIS epidemic reaction–diffusion model by optimal control methods. Comput. Math. Appl. 70: 805-819

[26] M. Zhou, H. Xiang, Z. Li (2019) Optimal control strategies for a reaction–diffusion epidemic system. Nonlinear. Anal.: RWA 46:446-464

[27] H. Xiang, B. Liu, Z. Fang (2018) Optimal control strategies for a new ecosystem governed by reaction–diffusion equations. J. Math. Anal. Appl. 467: 270-291

[28] X.-B. Zhang, G. Wang, H. Zhu (2020) Optimal control of a diffusive eco-epidemiological predator–prey model. Int. J. Biomath. 2050065: 1-22

[29] F. Dai, B. Liu (2020) Global solvability and optimal control to a haptotaxis cancer invasion model with two cancer cell species. Appl. Math. Opt. DOI: https://doi.org/10.1007/s00245-020-09712-0

[30] Y. Lou, X. Q. Zhao (2011) A reaction-diffusion malaria model with incubation period in the vector population. J. Math. Biol. 62:543-568

[31] H. L. Smith (1995) Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems, mathematical surveys and monographs, vol 41. American Mathematical Society

[32] R. H. Martin, H. L. Smith (1990) Abstract functional–differential equations and reaction–diffusion systems. Trans Am Math Soc 321:1-44

[33] M. G. Krein and M. A. Rutman Linear operators leaving invariant a cone in a Banach space. Amer. Math. Soc. Transl, New York

[34] Partial differential equations of mathematical physics and integral equations. R. B. Guenther, J. W. Lee (1996) Dover Publications Inc (corrected reprint of the 1988 original), Mineola

[35] J. Wu (1996) Theory and applications of partial functional-differential equations. Applied Mathematical Sciences, vol 119. Springer, New York

[36] J. K. Hale (1988) Asymptotic behavior of dissipative systems, mathematical surveys and monographs, vol 25. American Mathematical Society

[37] W. Wang, X. Zhao (2010) Basic reproduction numbers for reaction-diffusion epidemic models. SIAM J. Appl. Dyn. Syst. 11:1652-1673

[38] L. E. Fraenkel (2010) An introduction to maximum principles and symmetry in elliptic problems. Cambridge University Press, Cambridge

[39] H. L. Smith, X. Zhao (2000) Robust persistence for semi-dynamical systems. In: Proceedings of the third world congress of nonlinear analysts, part 9 (Catania, 2000) 47:6169-6179

[40] A. Pazy (1983) Semigroups of linear operators and applications to partial differential equations, in: Applied Mathematical Science. Springer-Verlag, Berlin, Heidelberg, New York

[41] J. P. Raymond, F. Troltzsch (2000) Second order sufficient optimality conditions for nonlinear parabolic control problems with state constraints. Discrete Contin. Dyn. Syst.6:431-450

[42] S. Zheng (2004) Nonlinear evolution equations. CRC Press

[43] J. L. Lions(1971) Optimal Control of System Governed By Partial Differential Equations. Springer, Berlin

[44] P. Wu, H. Zhao (2021) Mathematical analysis of an age-structured HIV/AIDS epidemic model with HAART and spatial diffusion. Nonlinear Anal. RWA 60: 103289

[45] T. Zhang and Y. Zhou (2016) Mathematical model of transmission dynamics of human immune-deficiency virus: A case study for Yunnan, China. Appl. Math. Model. 40:4859-4875

[46] China CDC (2018) Statistics on the number of HIV infections, incidences, deaths and transmission routes in 2018, China. http://www.chinabaogao.com

[47] L. Zhang, P. Peng, et al. (2019) Modelling the epidemiological impact and cost effectiveness of PrEP for HIV transmission in MSM in China. AIDS and Behavior 23: 523-533