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# Impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives

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## ABSTRACT

In this paper, we study the impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives on the transmission dynamics of the disease in a homogeneous population with constant immigration of susceptibles incorporating use of condom, screening of unaware infectives and treatment of the infected. Initially we consider constant controls and thereafter treat control measures as time dependent control parameters. In the constant controls case, we calculate the basic reproduction number and investigate the existence and stability of equilibria. The model is found to exhibit transcritical bifurcation. For the time dependent controls, we formulate the appropriate optimal control problem and investigate the necessary conditions for the disease control in order to determine the role of unaware infectives in the spread of HIV/AIDS. We observed that unawareness by infectives has a great cost impact on the community. We further investigate the impact of combinations of the strategies in the control of HIV/AIDS. Carrying out cost-effectiveness analysis, we found that the most cost-effective strategy is the combination of all the control strategies.

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## 1. Introduction

Infection with the human immunodeficiency virus (HIV) is almost very dangerous and fatal if left untreated and uncontrolled. Globally, HIV is now the major cause of years of potential lives lost and the most common cause of death attributed to many infectious diseases. Just in 2005 alone, 3.1 million people died from AIDS (acquired immunodeficiency syndrome) globally, while 4.9 million people became infected with HIV, resulting into 40.3 million the number of people living with the virus across the world (UNAIDS 2005).

After 25 years of the discovery of HIV, controlling the spread of the disease has proved very difficult. The difficulties arise from lack of adequate medical facilities and personnel and unwillingness of people to strictly adhere to preventive measures. The other major challenge is that in most part of Sub-Sahara Africa, Europe and Asia, many persons who are infected are not even aware of the infection, this is partly due to illiteracy, scarcity of medical equipments and other factors. In addition, some who are aware of their infection do not always take necessary precautions deliberately when engaging in sexual interactions [1,2]. The present mode of controlling the disease include, abstinence, use of condom, treatment of infectives and blood screening. It is important to note that to effectively control the spread of HIV, the susceptible individuals must be protected from being infected and the already infected individuals must be adequately informed of available measures to ensure that they do not spread the disease any further. However, at present there is no cure for the disease and hence examining various strategies for controlling the spread of HIV/AIDS in order to minimize the disease prevalence is very important.

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This work is motivated by the large number of cases of unaware infectives reported worldwide, which has now become a global concern. For example in France, it was found that roughly 40,000 of the estimated 106,000–134,000 HIV infected people throughout the entire country remain unaware of their infection [3]. Findings from a survey carried out by US Centers for Disease Control and Prevention in 2008 on HIV among men who have sex with other men, indicated that among the 8153 men tested, about 1562 tested positive for HIV and of these 680 were unaware of their infection, amounting to about 44% of the infected cases. The study further revealed that the proportion of those who were unaware of their infection was highest among blacks and lowest among whites and this also decreased with increased education and income [1]. Also, the United Kingdom Health Protection Agency report that over 22,000 people were unaware that they have HIV virus (BBC health news, 26 November 2010). According to the Taipei Times report 2004, 90% of the Chinese HIV-AIDS cases were unaware of their infection status. Despite the effort, the total number of people tested for HIV globally remain low with an estimated 90% of people who are HIV infected worldwide are aware of their status [4].

The challenge posed by the number of cases of unaware infectives calls for urgent need for a better understanding of the important parameters in the disease transmission, and to develop an effective and optimal strategies for prevention and control of the spread of HIV/AIDS disease.

Mathematical modelling over the years have been useful in analysing various diseases dynamics, such as HIV/AIDS, Malaria and Tuberculosis and also play an important role in the better understanding of epidemiological patterns for disease control. Anderson et al. [5] presented a simple mathematical HIV transmission model to investigate the effects of various factors on the overall pattern of the AIDS epidemic. Nikolaos et al. [6] proposed a detailed analysis of a dynamical model to describe pathogenesis of HIV infection. Christopher and Jorge [7] derived a simple two-dimensional SIS (susceptible-infected-susceptible) model with vaccination and multiple endemic states. Guihua and Zhen [8], studied the global dynamics of an SEIR (susceptible-exposed-infected-recovered) epidemic model in which latent and immune states were infective. In [9], a mathematical model was proposed to study the effect of screening of unaware infectives on the spread of HIV infection.

Karrakchou et al. [10] investigated the fundamental role of chemotherapy treatment in controlling the virus reproduction in an HIV patient, while Adams et al. [11] derived HIV therapeutic strategies by formulating and analyzing an optimal control problem using two types of dynamic treatments. Gul et al. [12] studied the stability and optimal vaccination of an SIR epidemic model. Mukandavire et al. [13] proposed a system of discrete time delay equations to model the effects of public health educational campaigns on HIV/AIDS transmission. The authors in [14] studied the impact of chemo-therapy on optimal control of malaria disease with infected immigrants. For optimal control applied in other epidemic models, we refer the reader to [15–18].

Having pointed out that the screening of unaware infectives has substantial effect on the spread of AIDS [9], it is, therefore, desirable to promote the voluntary or random screening by targeting especially the high risk groups. After being detected, the individual may be motivated to change their behavior and to take preventive measures like condom use so that the risk of spreading the infection is reduced. To the best of our knowledge, very little attention has been paid to models addressing this aspect which may be helpful in reducing the spread of the disease.

The model we consider in this paper is an improved model of [9] by the inclusion of time dependent control parameters (use of condom, screening of unaware infectives and treatment of infectives) and with the assumption that the AIDS individuals can also transmit the disease recklessly. In this study we analyze and apply optimal control to the improved model to determine the possible impacts of condom use, optimal screening of unaware infectives and treatment of infectives on the spread of HIV. We carry out detailed qualitative optimal control analysis of the resulting model and find the necessary conditions for optimal control of the disease using Pontryagin's maximum principle in order to determine optimal strategies for controlling the spread of the disease.

Our main goal are: firstly to investigate the model under the assumption that the control measures are constants (condom use, screening of unaware infectives and treatment of infectives) and secondly, set up an optimal control problem relative to the model. In order to do this, we use the following control parameters, use of condom ( $u_1$ ), screening of unaware infectives ( $\theta$ ) and treatment of HIV individuals ( $\pi$ ) as time dependent variables.

The organization of the paper is as follows. In Section 2, we derive a model consisting of ordinary differential equations that describes the dynamics of HIV/AIDS and the underlying assumptions. Sections 3 and 4 are devoted to the mathematical analysis of the HIV models under constant control measures. In Section 5, we use Pontryagin's maximum principle to investigate analysis of control strategies and to determine the necessary conditions for the optimal control of the disease. In Sections 6, we show and discuss the simulation results. Section 7 is devoted to the cost-effectiveness analysis of the controls and our conclusions are presented in Section 8.

## 2. Model formulation

The model sub-divides the total human population at time  $t$ , denoted by  $N(t)$ , into the following sub-populations of susceptible individuals  $S(t)$ , infective individuals who do not know that they are infected  $I_1(t)$ , HIV positive individuals that know that they are infected  $I_2(t)$  and that of the AIDS population  $A(t)$ . So that

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t).$$

The susceptibles are individuals that have not contracted the infection but may be infected through the sexual contacts with both types of infectives. The unaware infected population are individuals that have contracted the infection but are not

aware of their infection. The infected population who are aware of their status comprise of individuals that have contracted the virus and are known to be infected after being detected by a screening method (i.e. by way of medical screening or otherwise). We use standard incidence to model the disease transmission.

Here  $\beta_i (i = 1, 2, 3)$  are the probabilities for susceptible individuals with unaware infectives, infectives that are already aware of their status and AIDS individuals respectively. Control  $u_1 \in [0, 1]$  is the successful use of condom by susceptibles to protect themselves. The term  $\theta$  measures the rate at which unaware infectives are detected by a screening method to become aware infectives, the term  $\pi$  measures the progression rate at which the already aware infective individuals on treatment move to the  $A$  class in each time period. Here,  $\delta$  is the rate by which both types of infectives not on treatment develop AIDS ( $\pi < \delta$ ).  $\mu$  is the natural mortality rate unrelated to HIV/AIDS disease and  $\alpha$  is the AIDS related death rate. It is assumed that the rate of contact of susceptibles with AIDS individuals is much less than aware infectives which in turn is much less than that with unaware infectives ( $\beta_3 \ll \beta_2 \ll \beta_1$ ). This is so because on becoming aware of their infection, the infected persons may choose to use preventive measures and change their behavior and thus may contribute little in spreading the infection. However, in some cases the aware infectives may also contribute to spreading of infection due to lack of taking necessary precautions or the decreased fear of the disease. We assume also the  $A$  class is less sexually active.

The resulting system of equations is as shown below:

$$\begin{cases} \frac{dS}{dt} = Q_0 - \beta_m S - \mu S, \\ \frac{dI_1}{dt} = \beta_m S - (\theta + \delta + \mu) I_1, \\ \frac{dI_2}{dt} = \theta I_1 - (\delta + \mu + \pi) I_2, \\ \frac{dA}{dt} = \delta I_1 + \delta I_2 + \pi I_2 - (\alpha + \mu) A. \end{cases} \quad (1)$$

Here,

$$\beta_m = \frac{(1 - u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N}. \quad (2)$$

The terms  $c_i (i = 1, 2, 3)$  are the number of sexual partners of susceptible individuals with unaware infectives, aware infectives and the AIDS individuals respectively in each time period.

### 3. Mathematical analysis of the HIV/AIDS model

#### 3.1. Positivity and boundedness of solutions

For the HIV/AIDS transmission model (1) to be epidemiologically meaningful, it is important to prove that all solutions with non-negative initial data will remain non-negative for all time.

**Theorem 1.** If  $S(0), I_1(0), I_2(0), A(0)$  are non negative, then so are  $S(t), I_1(t), I_2(t)$  and  $A(t)$  for all time  $t > 0$ . Moreover,

$$\limsup_{t \rightarrow \infty} N(t) \leq \frac{Q_0}{\mu}. \quad (3)$$

Furthermore, if  $N(0) \leq \frac{Q_0}{\mu}$ , then  $N(t) \leq \frac{Q_0}{\mu}$ .

The proof is omitted for simplicity. The feasible region for system (1) is therefore given by

$$\mathcal{D} = \mathcal{D}_1 \subset \mathbb{R}_+^4, \quad (4)$$

where,

$$\mathcal{D}_1 = \left\{ (S, I_1, I_2, A) \in \mathbb{R}_+^4 : S + I_1 + I_2 + A \leq \frac{Q_0}{\mu} \right\}, \quad (5)$$

$\mathcal{D}$  is positively invariant, see [9].

#### 3.2. Stability of the disease-free equilibrium (DFE)

The disease-free equilibrium (DFE) of the HIV/AIDS model (1) exists only when  $u_1$  and  $\theta$  are constant, it is given by,

$$\mathcal{E}_0 = \left( \frac{Q_0}{\mu}, 0, 0, 0 \right).$$

The basic reproduction number of the model with condom use and screening of unaware infective individuals (1), is given by

$$R = \frac{(1 - u_1)((\alpha + \mu)(\pi + \delta + \mu)c_1\beta_1 + \theta(\alpha + \mu)c_2\beta_2 + ((\pi + \delta)(\delta + \theta) + \delta\mu)c_3\beta_3)}{(\alpha + \mu)(\pi + \delta + \mu)(\delta + \theta + \mu)}, \quad (6)$$

while the basic reproduction number of the model without condom use and screening of unaware infective individuals is then given by

$$R_0 = \frac{(\alpha + \mu)(\pi + \delta + \mu)c_1\beta_1 + (\pi + \delta + \mu)\delta c_3\beta_3}{(\alpha + \mu)(\pi + \delta + \mu)(\delta + \mu)}, \quad (7)$$

We use Theorem 2 of [19] to established the following result.

**Proposition 1.** The DFE of the HIV/AIDS model 1, is locally asymptotically stable if  $R < 1$ , and unstable if  $R > 1$ .

The basic reproduction number  $R$  measures the average number of new infections generated by a single infected individual in a completely susceptible population. Thus, Proposition 1 implies that the disease can be eliminated from the community when  $R < 1$ . Next we calculate the endemic steady states.

### 3.3. Existence of endemic equilibrium

**Proof.** Solving the HIV/AIDS model equation in-terms of  $\beta_m^*$ , we calculate the endemic equilibrium point and obtain,

$$\begin{cases} S^* = \frac{Q_0}{\beta_m^* + \mu}, \\ I_1^* = \frac{Q_0\beta_m^*}{(\delta + \theta + \mu)(\beta_m^* + \mu)}, \\ I_2^* = \frac{Q_0\theta\beta_m^*}{(\delta + \theta + \mu)(\pi + \delta + \mu)(\beta_m^* + \mu)}, \\ A^* = \frac{Q_0\beta_m^*((\pi + \delta)(\delta + \theta) + \delta\mu)}{(\alpha + \mu)(\delta + \theta + \mu)(\pi + \delta + \mu)(\beta_m^* + \mu)}, \\ N^* = \frac{Q_0 - \alpha A^*}{\mu}. \end{cases} \quad (8)$$

By solving system (1) at the equilibrium we obtain  $\beta_m^* = 0$  (which corresponds to the DFE) or

$$B_1\beta_m^* + B_0 = 0, \quad (9)$$

where

$$\begin{aligned} B_1 &= (\delta + \alpha + \mu)(\theta + \delta + \mu) + \pi(\alpha + \delta + \theta + \mu), \\ B_0 &= (\alpha + \mu)(\pi + \delta + \mu)(\delta + \theta + \mu)(1 - R). \end{aligned} \quad (10)$$

Clearly,  $B_1 > 0$  and  $B_0 \geq 0$  whenever  $R < 1$  or  $\theta > \theta^*$ , so that  $\beta_m^* = \frac{-B_0}{B_1} \leq 0$ . Therefore the HIV/AIDS model has no endemic equilibrium whenever  $\theta > \theta^*$  where the critical screening coverage

$$\theta^* = \frac{(\pi + \delta + \mu)((1 - u_1)c_3\delta\beta_3 + (\alpha + \mu)(1 - u_1)c_1\beta_1 - (\alpha + \mu)(\delta + \mu))}{(1 - u_1)((\alpha + \mu)c_2\beta_2 + (\pi + \delta)c_3\beta_3) - (\alpha + \mu)(\pi + \delta + \mu)}. \quad \square$$

**Proposition 2.** The HIV model has a unique endemic equilibrium if and only if  $R > 1$ .

The above result suggests the impossibility of backward bifurcation in the HIV/AIDS model, since no endemic equilibrium exists when  $R < 1$  or  $\theta > \theta^*$ .

## 4. Modified HIV/AIDS model

We now modify the model (1) by sub-dividing the total human population at time  $t$ , denoted by  $N_1(t)$ , into the following sub-populations of susceptible individuals  $S(t)$ , unaware infective individuals  $I_1(t)$ , Screened and already aware infective individuals who are not yet on treatment  $I_2(t)$  and HIV positive individuals who are on treatment  $H(t)$  and that of the AIDS population  $A(t)$ . So that

$$N_1(t) = S(t) + I_1(t) + I_2(t) + H(t) + A(t).$$

The resulting system of equations is the following,

$$\begin{cases} \frac{dS}{dt} = Q_0 - \beta_H S - \mu S, \\ \frac{dI_1}{dt} = \beta_H S - (\theta + \delta + \mu)I_1, \\ \frac{dI_2}{dt} = \theta I_1 - (\delta + \mu + \pi)I_2, \\ \frac{dH}{dt} = \pi I_2 - (\sigma\delta + \mu)H, \\ \frac{dA}{dt} = \delta I_1 + \delta I_2 + \sigma\delta H - (\alpha + \mu)A. \end{cases} \quad (11)$$

Here,

$$\beta_H = \frac{(1 - u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{N_1}, \quad (12)$$

where  $\beta_h$  is the per capita contact rates for susceptible individuals with HIV positive individuals on treatment and  $c_h$  are the number of sexual partners with HIV positive individuals on treatment. Here  $\sigma\delta$  is the rate of progression of HIV positive individuals on treatment to AIDS population, where  $\sigma$  is the modification parameter due to treatment.

#### 4.1. Stability of the disease-free equilibrium (DFE) of the modified model

The disease-free equilibrium (DFE) of the HIV/AIDS model (11) also exists only when  $u_1$  and  $\theta$  are constant, it is given by,

$$\mathcal{E}_0 = \left( \frac{Q_0}{\mu}, 0, 0, 0, 0 \right).$$

The basic reproduction number of the model (11) with condom use and screening of unaware infective individuals, is given by  $\mathcal{E}_0$  established by using the linear stability of the next generation operator method [19] on the system (11). The matrices  $F$  and  $V$ , for the new infection terms and the remaining transfer terms, are, respectively given by

$$F = (1 - u_1) \begin{pmatrix} \frac{\beta_1 c_1}{N_1} & \frac{\beta_2 c_2}{N_1} & \frac{\beta_h c_h}{N_1} & \frac{\beta_3 c_3}{N_1} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} (\theta + \delta + \mu) & 0 & 0 & 0 \\ -\theta & (\delta + \mu + \pi) & 0 & 0 \\ -\pi & 0 & (\sigma\delta + \mu) & 0 \\ -\delta & -\delta & -\sigma\delta & (\alpha + \mu) \end{pmatrix},$$

It follows that the reproduction number of the HIV/AIDS system (11), denoted by  $\mathcal{R}_H$ , is given by

$$\mathcal{R}_H = \frac{(1 - u_1)(\Omega + \delta((\theta + \delta + \mu)(\delta\sigma + \mu) + \pi(\mu + (\delta + \theta)\sigma))c_3\beta_3 + \pi\theta(\alpha + \mu)c_h\beta_h)}{(\alpha + \mu)(\pi + \delta + \mu)(\delta + \theta + \mu)(\mu + \delta\sigma)},$$

$$\Omega = (\alpha + \mu)(\pi + \delta + \mu)(\mu + \delta\sigma)c_1\beta_1 + \theta(\alpha + \mu)(\mu + \delta\sigma)c_2\beta_2, \quad (13)$$

while the basic reproduction number of the model without condom use and screening of unaware infective individuals is then given by

$$\mathcal{R}_{0h} = \frac{((\alpha + \mu)(\pi + \delta + \mu)(\mu + \delta\sigma)c_1\beta_1 + \delta((\delta + \mu)(\delta\sigma + \mu) + \pi(\mu + \delta\sigma))c_3\beta_3)}{(\alpha + \mu)(\pi + \delta + \mu)(\delta + \mu)(\mu + \delta\sigma)}. \quad (14)$$

We use Theorem 2 of [19] to establish the following result. The critical condom use coverage  $u_1^0$  that would be required to contain HIV/AIDS can be calculated by setting  $\mathcal{R}_H = 1$ , we obtain,

$$u_1^0 = 1 - \frac{1}{\mathcal{R}_{0h}}.$$

$\mathcal{R}_H \geq 1$ , if and only if  $u_1 \leq u_1^0$ . Hence when  $u_1 < u_1^0$ , then the disease will persist, but when  $u_1 > u_1^0$ , the disease may be eradicated if DFE is globally asymptotically stable.

**Proposition 3.** The DFE of the modified HIV/AIDS model (11), is locally asymptotically stable if  $\mathcal{R}_H < 1$ , and unstable if  $\mathcal{R}_H > 1$ .

Thus, the Proposition 3 also implies that the disease can be eliminated from the community when  $\mathcal{R}_H < 1$ . Next we calculate the endemic steady states of the modified model.

#### 4.2. Existence of endemic equilibrium

**Proof.** Solving the HIV/AIDS model equation in-terms of  $\beta_H^*$ , we calculate the endemic equilibrium point and obtain,

$$\begin{cases} S^* = \frac{Q_0}{\beta_H^* + \mu}, \\ I_1^* = \frac{Q_0 \beta_H^*}{(\delta + \theta + \mu)(\beta_H^* + \mu)}, \\ I_2^* = \frac{Q_0 \theta \beta_H^*}{(\delta + \theta + \mu)(\pi + \delta + \mu)(\beta_H^* + \mu)}, \\ H^* = \frac{Q_0 \theta \pi \beta_H^*}{(\delta + \theta + \mu)(\pi + \delta + \mu)(\beta_H^* + \mu)(\mu + \delta\sigma)}, \\ A^* = \frac{Q_0 \delta \beta_H^* ((\delta + \theta + \mu)(\delta\sigma + \mu) + \pi(\mu + (\delta + \theta)\sigma))}{(\alpha + \mu)(\delta + \theta + \mu)(\pi + \delta + \mu)(\beta_H^* + \mu)(\mu + \delta\sigma)}, \\ N_1^* = \frac{Q_0 - \alpha A^*}{\mu}. \end{cases} \quad (15)$$

By solving system (11) at the equilibrium we obtain  $\beta_H^* = 0$  (which corresponds to the DFE) or

$$P_1 \beta_H^* + P_0 = 0, \quad (16)$$

where

$$\begin{aligned} P_1 &= (\delta + \alpha + \mu)(\theta + \delta + \mu)(\mu + \delta\sigma) + \pi((\delta + \theta + \mu)(\mu + \delta\sigma) + \alpha(\theta + \mu + \delta\sigma)), \\ P_0 &= (\alpha + \mu)(\pi + \delta + \mu)(\delta + \theta + \mu)(\mu + \delta\sigma)(1 - R_H). \end{aligned} \quad (17)$$

Clearly,  $P_1 > 0$  and  $P_0 \geq 0$  whenever  $R_H < 1$  or  $\theta > \theta_h^*$ , so that  $\beta_H^* = \frac{-P_0}{P_1} \leq 0$ . Therefore the modified HIV/AIDS model has no endemic equilibrium whenever  $\theta > \theta_h^*$  where the critical screening coverage

$$\theta_h^* = \frac{(\pi + \delta + \mu)(\mu + \delta\sigma)((1 - u_1)c_3\delta\beta_3 + (\alpha + \mu)(1 - u_1)c_1\beta_1 - (\alpha + \mu)(\delta + \mu))}{(1 - u_1)((\alpha + \mu)(\mu + \delta\sigma)c_2\beta_2 + \delta(\mu + (\pi + \delta)\sigma)c_3\beta_3 + \pi(\alpha + \mu)c_h\beta_h) - \chi},$$

where  $\chi = (\alpha + \mu)(\pi + \delta + \mu)(\mu + \delta\sigma)$ .  $\square$

**Theorem 2.** The DFE is locally asymptotically stable if  $R_H < 1$  and unstable if  $R_H > 1$

**Proof.** We evaluate the Jacobian matrix of the model at the disease-free equilibrium and we obtain

$$J_s = \begin{pmatrix} -G - \mu & 0 & 0 & J_1 & J_2 \\ G & -B + J_3 & J_4 & -J_1 & -J_2 \\ 0 & \theta & -C & 0 & 0 \\ 0 & 0 & \pi & -D & 0 \\ 0 & \delta & \delta & \delta\sigma & -E \end{pmatrix},$$

where

$$B = \theta + \delta + \mu, \quad C = \delta + \pi + \mu, \quad D = \sigma\delta + \mu, \quad E = \alpha + \mu,$$

$$G = \frac{(N^* - S^*)(1 - u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2},$$

$$J_1 = -\frac{Sc_h\beta_h(1 - u_1)}{N} + \frac{S(1 - u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2},$$

$$J_2 = -\frac{Sc_3\beta_3(1 - u_1)}{N} + \frac{S(1 - u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2},$$

$$J_3 = -\frac{Sc_1\beta_1(1 - u_1)}{N} + \frac{S(1 - u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2},$$

$$J_4 = -\frac{Sc_2\beta_2(1 - u_1)}{N} + \frac{S(1 - u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}.$$

Then, the local stability of the DFE is determined by the eigenvalues of the matrix

$$J_s = \begin{pmatrix} -\mu & 0 & 0 & -c_h\beta_h(1 - u_1) & -c_3\beta_3(1 - u_1) \\ 0 & -B + c_1\beta_1(1 - u_1) & c_2\beta_2(1 - u_1) & c_h\beta_h(1 - u_1) & c_3\beta_3(1 - u_1) \\ 0 & \theta & -C & 0 & 0 \\ 0 & 0 & \pi & -D & 0 \\ 0 & \delta & \delta & \delta\sigma & -E \end{pmatrix},$$

It is clear that the first column has diagonal entry, so, this diagonal entry  $-\mu$  is an eigenvalue. Hence, removing this column and the row corresponding to it, the Jacobian matrix ( $J_s$ ) is then reduced to the following:

$$J_{as} = \begin{pmatrix} -B + c_1\beta_1(1 - u_1) & c_2\beta_2(1 - u_1) & c_h\beta_h(1 - u_1) & c_3\beta_3(1 - u_1) \\ \theta & -C & 0 & 0 \\ 0 & \pi & -D & 0 \\ \delta & \delta & \delta\sigma & -E \end{pmatrix},$$

We therefore calculate the eigenvalues of the reduced matrix. Solving the eigenvalues of  $J_{as}$ , requires that

$$\det(J_{as} - \Lambda) = 0,$$

which leads to the following characteristic polynomial,

$$\Lambda^4 + a_1\Lambda^3 + a_2\Lambda^2 + a_3\Lambda + a_4 = 0.$$

Here,

$$\begin{aligned} a_1 &= (B + C + D + E) - (1 - u_1)c_1\beta_1, \\ a_2 &= BC + BD + CD + (B + C + D)E - (1 - u_1)((C + D + E)c_1\beta_1 + \theta c_2\beta_2 + \delta c_3\beta_3), \\ a_3 &= BCD + CDE + BE(D + C) - (1 - u_1)((DE + C(D + E))c_1\beta_1 + (D + E)\theta c_2\beta_2 + \delta(C + D + \theta)c_3\beta_3 + \pi\theta c_h\beta_h), \\ a_4 &= BCDE - (1 - u_1)(CDEc_1\beta_1 + DE\theta c_2\beta_2 + \delta(D(C + \theta) + \pi\theta\sigma)c_3\beta_3 + E\pi\theta c_h\beta_h) = BCDE(1 - R_H). \end{aligned} \quad (18)$$

By applying the Routh–Hurwitz stability conditions, we establish the following for the polynomial;  $a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0$  and

$$H_1 = a_1 > 0, \quad H_2 = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix} > 0, \quad H_3 = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & a_4 & a_3 \end{vmatrix} > 0,$$

$$H_4 = \begin{vmatrix} a_1 & 1 & 0 & 0 \\ a_3 & a_2 & a_1 & 1 \\ 0 & a_4 & a_3 & a_2 \\ 0 & 0 & 0 & 0 \end{vmatrix} > 0.$$

The steady state is stable (that is,  $Re < 0$ ) for all  $\lambda$  if and only if  $\det H_j \geq 0$  for  $j = 1, 2, 3, 4$ . Furthermore, we only need to prove that  $H_2 > 0, H_3 > 0, H_4 > 0$ .

$$H_2 = a_1a_2 - a_3, \quad H_3 = a_3(a_1a_2 - a_3) - a_1a_4 \quad \text{and} \quad H_4 = a_4H_3$$

Using Mathematica 5.0, we found that

$$\begin{aligned} H_2 &= (C + D)(C + E)(D + E) + B^2(C + D + E) + B(C + D + E)^2 + c_1\beta_1(1 - u_1)^2((C + D + E)c_1\beta_1 + \theta c_2\beta_2 + \delta c_3\beta_3) \\ &\quad - (1 - u_1)((2B + C + D + E)(C + D + E)c_1\beta_1 + \theta(B + C)c_2\beta_2 + \delta(B + E - \theta)c_3\beta_3 - \pi\theta c_h\beta_h) \\ H_3 &= a_3H_2 - a_1a_4 \\ H_4 &= a_4H_3. \end{aligned} \quad (19)$$

Consequently, having that  $H_2 > 0, H_3 > 0$  and  $H_4 > 0$ , shows that the eigenvalues of the Jacobian matrix,  $J_{as}$ , are all having negative real parts whenever  $R_H < 1$ . But if  $R_H > 1$ , clearly we can see that  $a_4 < 0$ . Moreover, having  $a_1 > 0, a_2 > 0, a_3 > 0$  and  $a_4 > 0$  shows that not all the roots of the polynomial will have a negative real part. This means that whenever  $R_H > 1$ , the disease-free equilibrium point is unstable, that is, it is not stable.  $\square$

**Proposition 4.** The modified HIV model has a unique endemic equilibrium if and only if  $R_H > 1$ .

The above result suggests the impossibility of backward bifurcation in the HIV/AIDS model, since no endemic equilibrium exists when  $R_H < 1$  or  $\theta > \theta_h^*$ .

We now investigate the global stability property of the endemic equilibrium of the modified HIV/AIDS model for the case when there is no disease induced death.

#### 4.3. Global stability of the endemic equilibrium of the HIV/AIDS model for $\alpha = 0$

Considering the model (11) with  $\alpha = 0$ , we get

$$\begin{cases} \frac{dS}{dt} = Q_0 - \beta_H S - \mu S, \\ \frac{dI_1}{dt} = \beta_H S - (\theta + \delta + \mu)I_1, \\ \frac{dI_2}{dt} = \theta I_1 - (\delta + \mu + \pi)I_2, \\ \frac{dH}{dt} = \pi I_2 - (\sigma\delta + \mu)H, \\ \frac{dA}{dt} = \delta I_1 + \delta I_2 + \sigma\delta H - \mu A. \end{cases} \quad (20)$$

It is obvious from (15) that there is no change in the endemic equilibrium. Let,

$$\mathcal{D}_2 = \{(S, I_1, I_2, H, A) \in \mathbb{R}_+^5 : I_1 = I_2 = H = A = 0\}, \quad \text{and} \quad R_{h1} = R_h|_{\alpha=0}. \quad (21)$$

We claim then the following



**Theorem 3.** The endemic equilibrium of the HIV model (20) with  $\alpha = 0$  is globally asymptotically stable (GAS) in  $\mathcal{D}_1 \setminus \mathcal{D}_2$  whenever  $R_{h1} > 1$ .

**Proof.** It can be shown, as for the case of Proposition 2, that the unique endemic equilibrium for this special case exists only if  $R_{h1} > 1$ . Further,  $N_1 = \frac{Q_0}{\mu}$  as  $t \rightarrow \infty$ . Thus, using  $S = \frac{Q_0}{\mu} - I_1 - I_2 - H - A$  and substituting in (20) gives the following limiting system

$$\begin{cases} \frac{dI_1}{dt} = \beta_H \left( \frac{Q_0}{\mu} - I_1 - I_2 - H - A \right) - (\theta + \delta + \mu)I_1, \\ \frac{dI_2}{dt} = \theta I_1 - (\delta + \mu + \pi)I_2, \\ \frac{dH}{dt} = \pi I_2 - (\sigma\delta + \mu)H, \\ \frac{dA}{dt} = \delta I_1 + \delta I_2 + \sigma\delta H - \mu A. \end{cases} \quad (22)$$

Using the Dulac's multiplier  $\frac{1}{I_1 A}$  (see [20]), it follows that

$$\begin{aligned} & \frac{\partial}{\partial A} \left[ \frac{\delta}{I_2 H A} + \frac{\delta}{I_1 H A} + \frac{\delta\sigma}{I_1 I_2 A} - \frac{\mu}{I_1 I_2 H} \right] + \frac{\partial}{\partial I_1} \left[ \frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{I_1 I_2 H A Q_0 / \mu} \left( \frac{Q_0}{\mu} - I_1 - I_2 - H - A \right) - \frac{(\theta + \delta + \mu)}{I_2 H A} \right] \\ &= -\frac{Q_0 A H + \delta I_2 H}{I_2^2 H^2 A^2} - \frac{\delta I_H}{I_1^2 H^2 A^2} - \frac{\delta\sigma I_1 I_2}{I_1^2 I_2^2 A^2} - \frac{c_1 \beta_1 \mu}{Q_0 I_2 H A} - \frac{c_2 \beta_2}{I_1^2 A H} \left( 1 - \frac{(I_2 + H + A)}{Q_0 / \mu} \right) - \frac{c_3 \beta_3}{I_1^2 I_2 H} \left( 1 - \frac{(I_2 + H + A)}{Q_0 / \mu} \right) \\ & - \frac{c_h \beta_h}{I_1^2 I_2 A} \left( 1 - \frac{(I_2 + H + A)}{Q_0 / \mu} \right) < 0 \text{ since } (I_2 + H + A) < Q_0 / \mu \text{ in } \mathcal{D}_1. \end{aligned} \quad (23)$$

Hence, by Dulac's criterion, there are no periodic orbits in  $\mathcal{D}_1 \setminus \mathcal{D}_2$ . Since  $\mathcal{D}_1$  is positively invariant, and the endemic equilibrium exists whenever  $R_{h1} > 1$ , then it follows from the Poincaré–Bendixon Theorem [21] that all solutions of the limiting system originating in  $\mathcal{D}_1$  remain in  $\mathcal{D}_1$  for all  $t$ . Further, the absence of periodic orbits in  $\mathcal{D}_1$  implies that the unique endemic equilibrium of the special case of the HIV/AIDS model is GAS whenever  $R_{h1} > 1$ .  $\square$

The HIV/AIDS model has a locally-asymptotically stable disease-free equilibrium whenever  $R_h \leq 1$ , and a unique endemic equilibrium whenever  $R_h > 1$ . The unique endemic equilibrium is globally-asymptotically stable for the case  $\alpha = 0$  if  $R_{h1} > 1$ . In Fig. (1) we show the contour plot of the reproductive number  $R_h$  as a function of  $\theta$  and  $\pi$  when there is condom use and the case without condom use.

In the next section, we apply the optimal control method using Pontryagin's Maximum Principle to determine the necessary conditions for the optimal control of screening of unaware infectives and use of condom on the spread of HIV.

## 5. Analysis of optimal control

From the previous section, we show that effective control of the disease may be too costly when constant controls are considered as it requires treatment at higher levels for all time. For effective control to be achievable in a finite time, we need to consider time dependent controls. When the control is time dependent the disease free equilibrium no longer exists (see [18]). We then proceed by applying Pontryagin's maximum principle to determine the conditions for effective control in finite time. We introduce into the model (11), condom use ( $u_1$ ), screening of unaware infectives ( $u_2$ ) and treatment of infectives ( $u_3$ ) as time dependent controls to curtail the spread of HIV/AIDS. The model (11) becomes

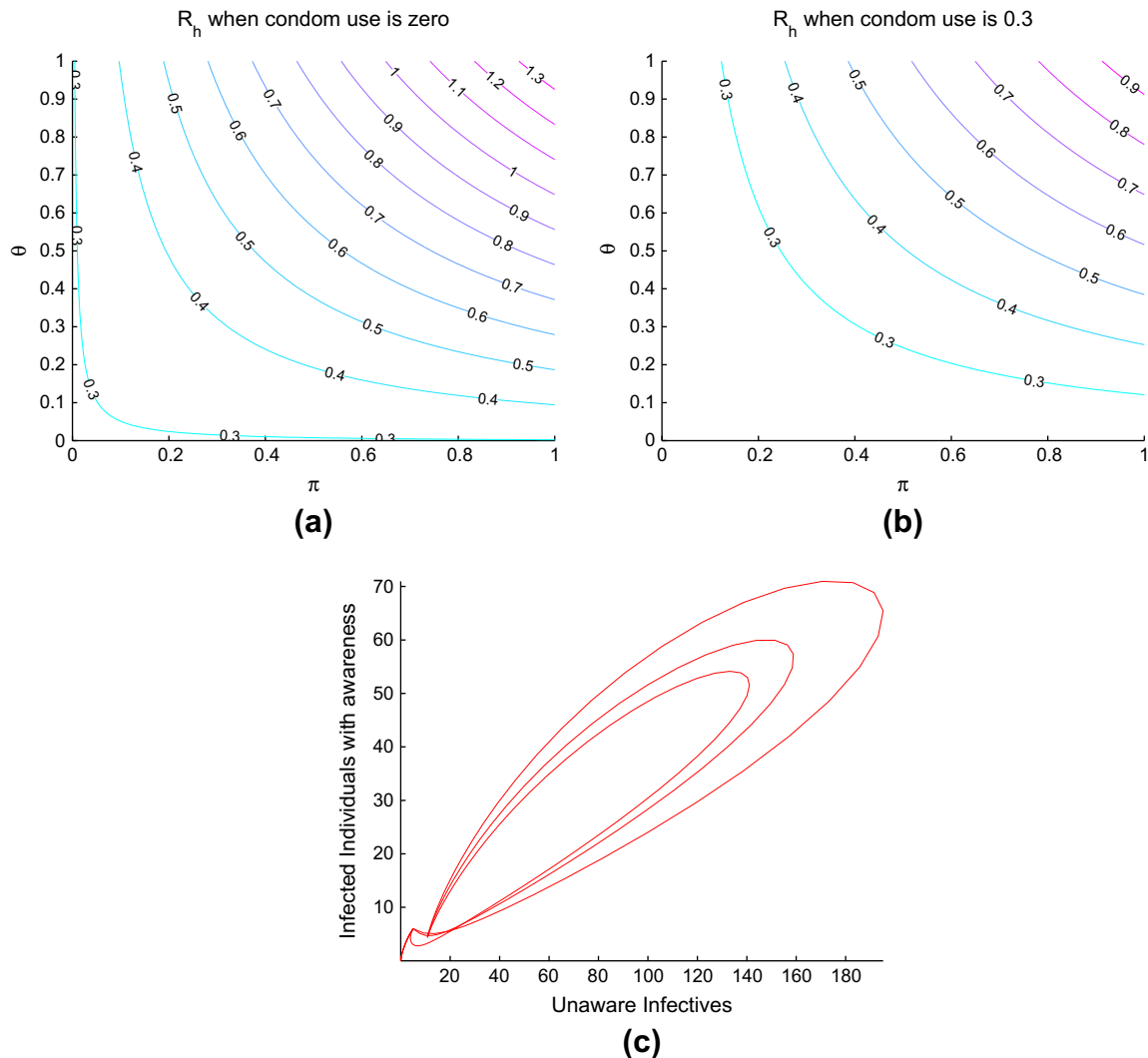
$$\begin{cases} \frac{dS}{dt} = Q_0 - \beta_H S - \mu S, \\ \frac{dI_1}{dt} = \beta_H S - (u_2 \theta + \delta + \mu)I_1, \\ \frac{dI_2}{dt} = u_2 \theta I_1 - (\delta + \mu + u_3 \pi)I_2, \\ \frac{dH}{dt} = u_3 \pi I_2 - (\sigma\delta + \mu)H, \\ \frac{dA}{dt} = \delta I_1 + \delta I_2 + \sigma\delta H - (\alpha + \mu)A. \end{cases} \quad (24)$$

Here,

$$\beta_H = \frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{N_1}, \quad (25)$$

where  $0 \leq u_1 \leq 1$ , is the condom use control,  $0 \leq u_2 \leq 1$  is the control on screening of unaware infectives and  $0 \leq u_3 \leq 1$ , is the control on treatment of infectives. To investigate the optimal level of efforts that would be needed to control the disease, we give the objective functional  $J$ , which is to minimize the number of unaware infectives and the cost of applying the control  $u_1, u_2$  and  $u_3$ .

$$J = \min_{u_1, u_2, u_3} \int_0^{t_f} (aI_1 + b_1 u_1^2 + b_2 u_2^2 + b_3 u_3^2) dt, \quad (26)$$



**Fig. 1.** Simulation of the model (11) showing a contour plot of reproduction number  $R_h$  as a function of  $\theta$  and  $\pi$  at steady state. Parameter values used are as given in Table 1. In Fig. 1(a) the contour plot when  $u_1$  is set to zero and (b) when  $u_1 = 0.3$ . In Figure 1(c) the projected  $I_1 - I_2$  phase plane of the phase space.

where  $a, b_1, b_2$  and  $b_3$  are positive weights. The terms  $b_1 u_1^2, b_2 u_2^2$  and  $b_3 u_3^2$  are the costs associated with condom use, screening of unaware infectives and treatment of infectives respectively. We choose a quadratic cost on the controls, in keeping with what is in other literature on control of epidemic [11,15,16,22,17]. With the given objective function  $J(u_1, u_2, u_3)$ , our goal is to minimize the number of unaware infectives ( $I_1$ ), while minimizing the cost of controls  $u_1(t), u_2(t)$  and  $u_3(t)$ . We thus seek an optimal control triple  $u_1^*, u_2^*$  and  $u_3^*$  such that

$$J(u_1^*, u_2^*, u_3^*) = \min \{J(u_1, u_2, u_3) | u_1, u_2, u_3 \in \mathcal{U}\}. \quad (27)$$

Here  $\mathcal{U} = \{(u_1, u_2, u_3) \text{ such that } u_1, u_2, u_3 \text{ measurable with } 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1 \text{ and } 0 \leq u_3 \leq 1 \text{ for } t \in [0, t_f]\}$  is the control set. The necessary conditions that an optimal control problem must satisfy come from Pontryagin's maximum principle [23]. This principle converts (24)–(26) into a problem of minimizing pointwise a Hamiltonian  $H_{pm}$ , with respect to  $u_1, u_2$  and  $u_3$

$$\begin{aligned} H_{pm} = & aI_1 + b_1 u_1^2 + b_2 u_2^2 + b_3 u_3^2 + \lambda_5 \left\{ Q_0 - (1 - u_1) \left( \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N} \right) - \mu S \right\} \\ & + \lambda_{I_1} \left\{ (1 - u_1) \left( \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N} \right) - (u_2 \theta + \delta + \mu) I_1 \right\} + \lambda_{I_2} \{ u_2 \theta I_1 - (\delta + \mu + u_3 \pi) I_2 \} \\ & + \lambda_H \{ u_3 \pi I_2 - (\delta \sigma + \mu) H \} + \lambda_A \{ \delta I_1 + \delta I_2 + \delta \sigma H - (\alpha + \mu) A \} \end{aligned} \quad (28)$$

where  $\lambda_S, \lambda_{I_1}, \lambda_{I_2}, \lambda_H$  and  $\lambda_A$  are adjoint variables or co-state variables. By applying Pontryagin's maximum principle [23] and the existence result for optimal control from [24], we obtain

**Proposition 5.** For the optimal control triple  $u_1^*, u_2^*$  and  $u_3^*$  that minimizes  $J(u_1, u_2, u_3)$  over  $\mathcal{U}$ , then there exist adjoint variables  $\lambda_S, \lambda_{I_1}, \lambda_{I_2}, \lambda_H, \lambda_A$  satisfying

$$\begin{aligned} -\frac{d\lambda_S}{dt} &= (1-u_1) \left( \frac{\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H}{N} - \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N^2} \right) (\lambda_S - \lambda_{I_1}) + \mu \lambda_S - \frac{d\lambda_{I_1}}{dt} \\ &= -a + (1-u_1) \left( \frac{\beta_1 c_1 S}{N} - \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N^2} \right) (\lambda_S - \lambda_{I_1}) + (u_2 \theta + \delta + \mu) \lambda_{I_1} - u_2 \theta \lambda_{I_2} - \delta \lambda_A \\ &\quad - \frac{d\lambda_{I_2}}{dt} \\ &= (1-u_1) \left( \frac{\beta_2 c_2 S}{N} - \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N^2} \right) (\lambda_S - \lambda_{I_1}) + (\delta + \mu + u_3 \pi) \lambda_{I_2} - u_3 \pi \lambda_H - \delta \lambda_A \\ &\quad - \frac{d\lambda_H}{dt} \\ &= (1-u_1) \left( \frac{\beta_h c_h S}{N} - \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N^2} \right) (\lambda_S - \lambda_{I_1}) + (\sigma \delta + \mu) \lambda_H - \sigma \delta \lambda_A - \frac{d\lambda_A}{dt} \\ &= (1-u_1) \left( \frac{\beta_3 c_3 S}{N} - \frac{\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h S H}{N^2} \right) (\lambda_S - \lambda_{I_1}) + (\alpha + \mu) \lambda_A \end{aligned} \quad (29)$$

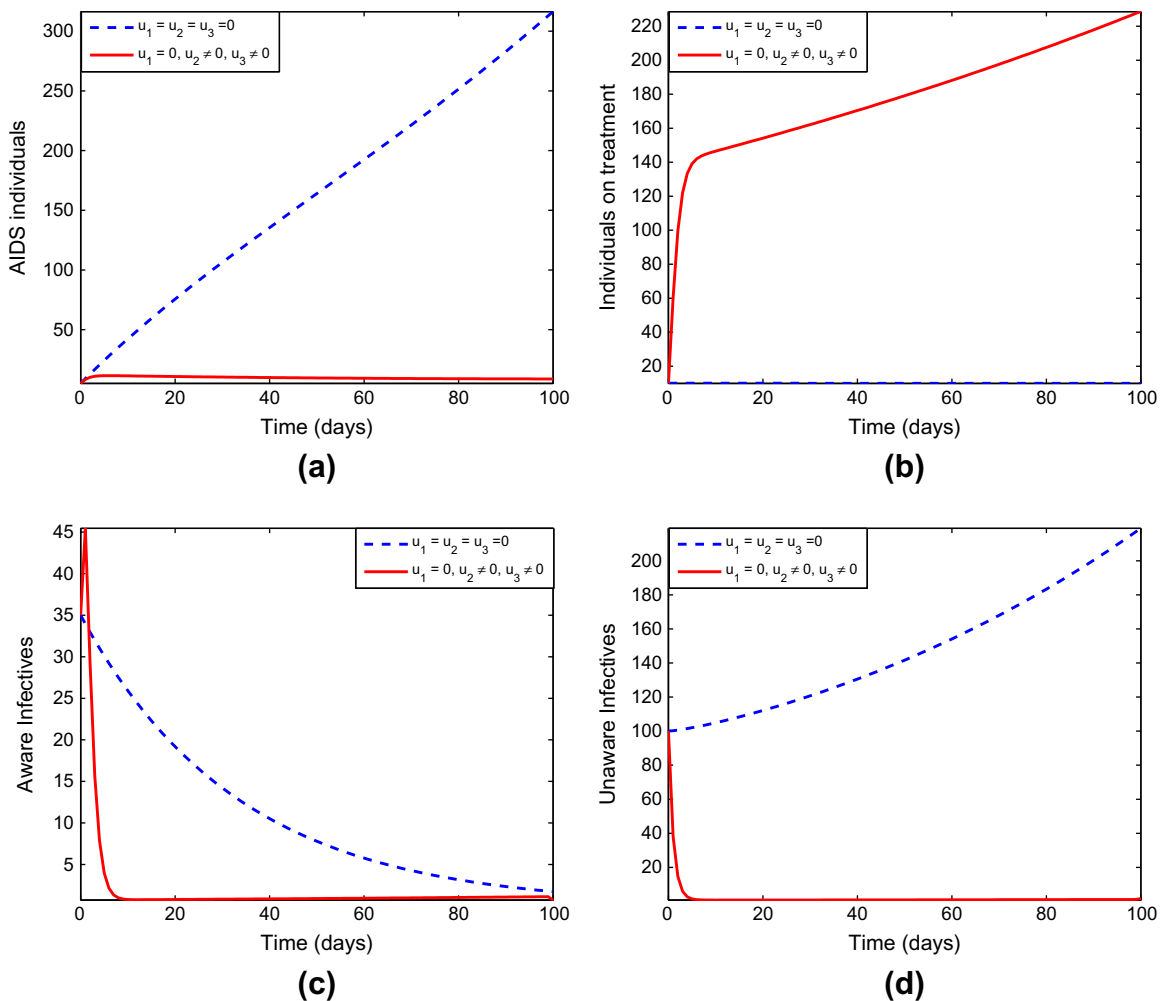


Fig. 2. Simulations of the model showing the effect of treatment control ( $u_3$ ) and screening control ( $u_2$ ) the spread of HIV/AIDS.

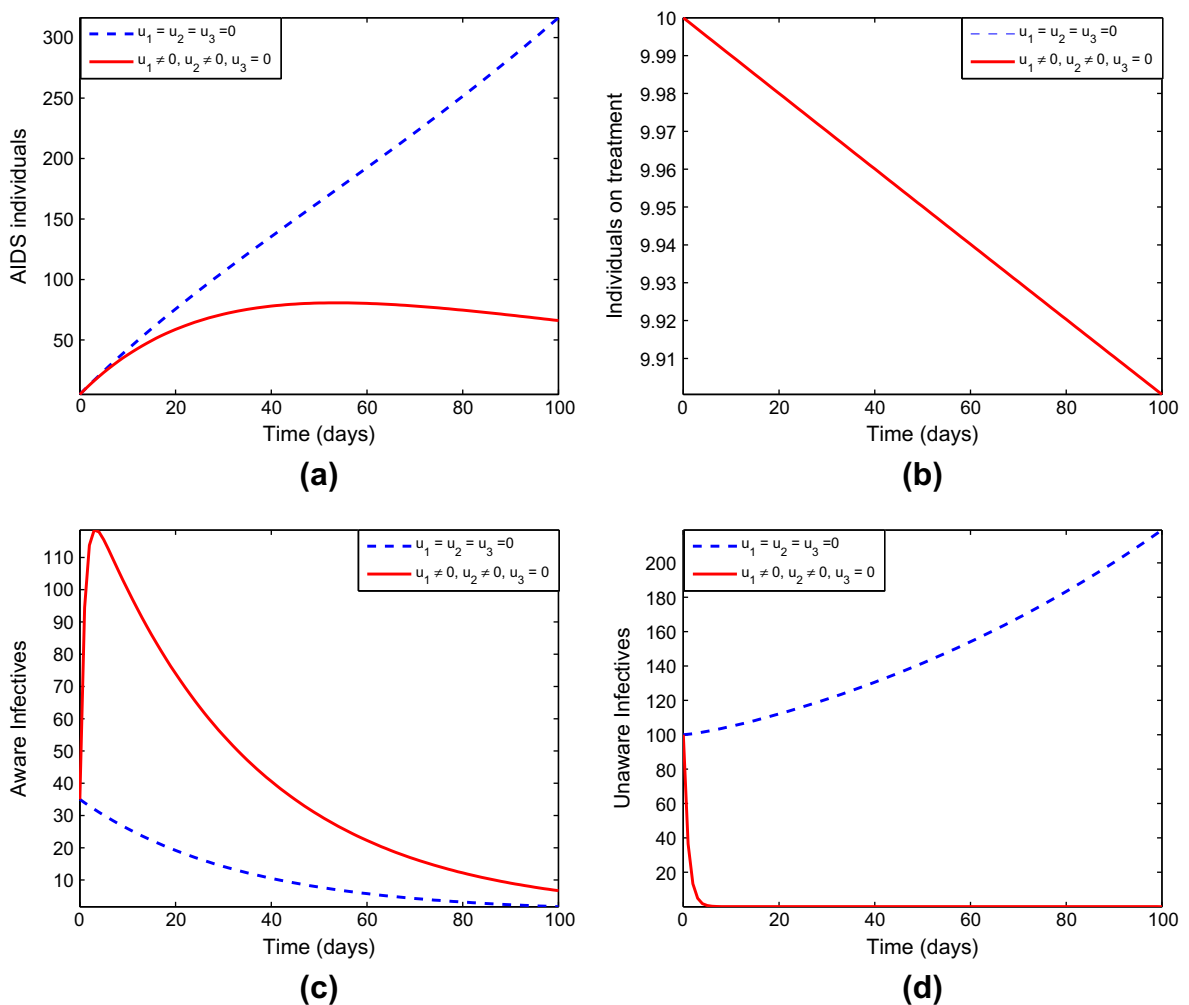
and with transversality conditions

$$\lambda_S(t_f) = \lambda_{I_1}(t_f) = \lambda_{I_2}(t_f) = \lambda_H(t_f) = \lambda_A(t_f), \quad (30)$$

$$\begin{aligned} u_1^* &= \max \left\{ 0, \min \left( 1, \frac{(\lambda_{I_1} - \lambda_S)(\beta_1 c_1 S I_1 + \beta_2 c_2 S I_2 + \beta_3 c_3 S A + \beta_h c_h H S)}{2 b_1 N_1} \right) \right\} \\ u_2^* &= \max \left\{ 0, \min \left( 1, \frac{\theta(\lambda_{I_1} - \lambda_{I_2}) I_1}{2 b_2} \right) \right\} \\ u_3^* &= \max \left\{ 0, \min \left( 1, \frac{\pi(\lambda_{I_2} - \lambda_H) I_2}{2 b_3} \right) \right\} \end{aligned} \quad (31)$$

**Proof.** Corollary 4.1 of [24] gives the existence of an optimal control due to the convexity of the integrand of  $J$  with respect to  $u_1, u_2$  and  $u_3$ , *a priori* boundedness of the state solutions, and the *Lipschitz* property of the state system with respect to the state variables. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control.

Due to the *a priori* boundedness of the state system, adjoint system and the resulting *Lipschitz* structure of the ODEs, we obtain the uniqueness of the optimal control for small  $t_f$ . The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (29) and (30) with characterization (31). There is a restriction on the length of the

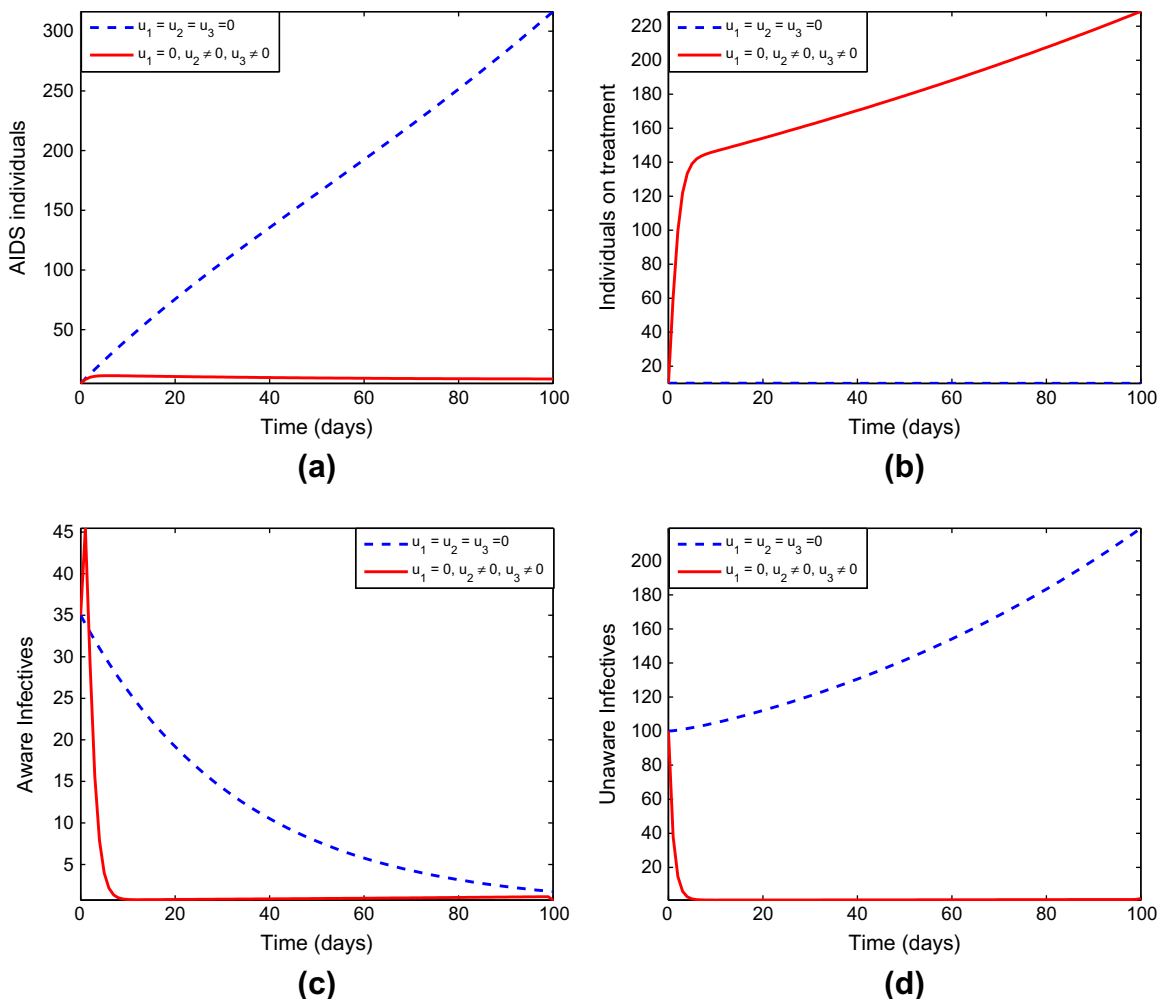


**Fig. 3.** Simulations of the model showing the effect of condom use control ( $u_1$ ) and screening of infectives ( $u_2$ ) on the spread of HIV/AIDS.

time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length of time is due to the opposite time orientations of (29) and (30); the state problem has initial values whereas the adjoint problem has final values. This restriction is very common in control problems (see [15,16,22,17,14]).  $\square$

## 6. Numerical results and discussions

In this section, we examine the modified deterministic HIV/AIDS model and study the effects of condom use, screening of unaware infectives and treatments on the transmission dynamics of the disease. We carry out numerical simulations and discuss results. The optimal control set is obtained by solving the optimality system, consisting of the state and adjoint systems. An iterative scheme is used for solving the optimality system. We start to solve the state equations with a guess for the controls over the simulated time using the fourth order Runge–Kutta scheme. Because of the transversality conditions (30), the adjoint equations are solved by a backward fourth order Runge–Kutta scheme using the current iterations' solutions of the state equation. Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (31). This process is repeated and iterations are stopped if the values of the unknowns at the previous iteration are very close to the ones at the present iteration [25]. We investigate and compare numerical results in the following scenario (i) when control efforts on screening of unaware infectives ( $u_2$ ) and treatment ( $u_3$ ) are optimized while the control on condom use ( $u_1$ ) is set to zero (ii) when control efforts on screening of unaware infectives ( $u_2$ ) and condom use ( $u_1$ ) are optimized while treatment control ( $u_3$ ) is set to zero (iii) when control efforts on treatment ( $u_3$ ) and condom use ( $u_1$ ) are optimized while the control on screening of unaware infectives ( $u_2$ ) is set to zero (iv) when all controls are optimized.



**Fig. 4.** Simulations of the model showing the effects of treatment ( $u_3$ ) and condom use ( $u_1$ ) on the spread of HIV/AIDS.

We assume that the weight factor,  $b_1$ , associated with control  $u_1$  is lower than  $b_2$  and  $b_3$  which are associated with controls  $u_2$  and  $u_3$ . This assumption is based on the facts that the cost associated with  $u_2$  will include the cost of screening and the cost associated with treatment,  $u_3$ , will include the cost of drugs, medical examinations and hospitalization. We have chosen the same set of the weight factors,  $a = 800$ ,  $b_1 = 35$ ,  $b_2 = 55$  and  $b_3 = 75$  with initial state variables  $S(0) = 800$ ,  $I_1(0) = 40$ ,  $I_2(0) = 45$ ,  $H(0) = 30$ ,  $A(0) = 0$  to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS in a population.

### 6.1. Optimal screening of unaware infectives ( $u_2$ ) and treatment ( $u_3$ ) only

With this strategy, the screening control ( $u_2$ ) and the treatment control ( $u_3$ ) on are both used to optimize the objective function ( $J$ ) while the condom use control ( $u_1$ ) is set to zero. In Fig. 2, we observe that this control strategy results in a significant decrease in the number of unaware infectives ( $I_1$ ) and AIDS ( $A$ ) compared with the case without control. The total averted cases of unaware infectives and AIDS are 6100 and 7900 respectively. Also this control strategy results in a significant increase in the number of HIV positive individuals on treatment which stabilizes at 250. The control profile is shown in Fig. 6(a), control  $u_2$  is at the upper bound for 98 days before dropping to the lower bound at the final time and the control  $u_3$  remain at the upper bound till the final time.

### 6.2. Optimal screening of unaware infectives ( $u_2$ ) and condom use ( $u_1$ ) only

With this strategy, the screening control ( $u_2$ ) and condom use control ( $u_1$ ) on are both used to optimize the objective function ( $J$ ) while treatment control ( $u_3$ ) is set to zero. In Fig. 3, we observe that this control strategy also results in a significant

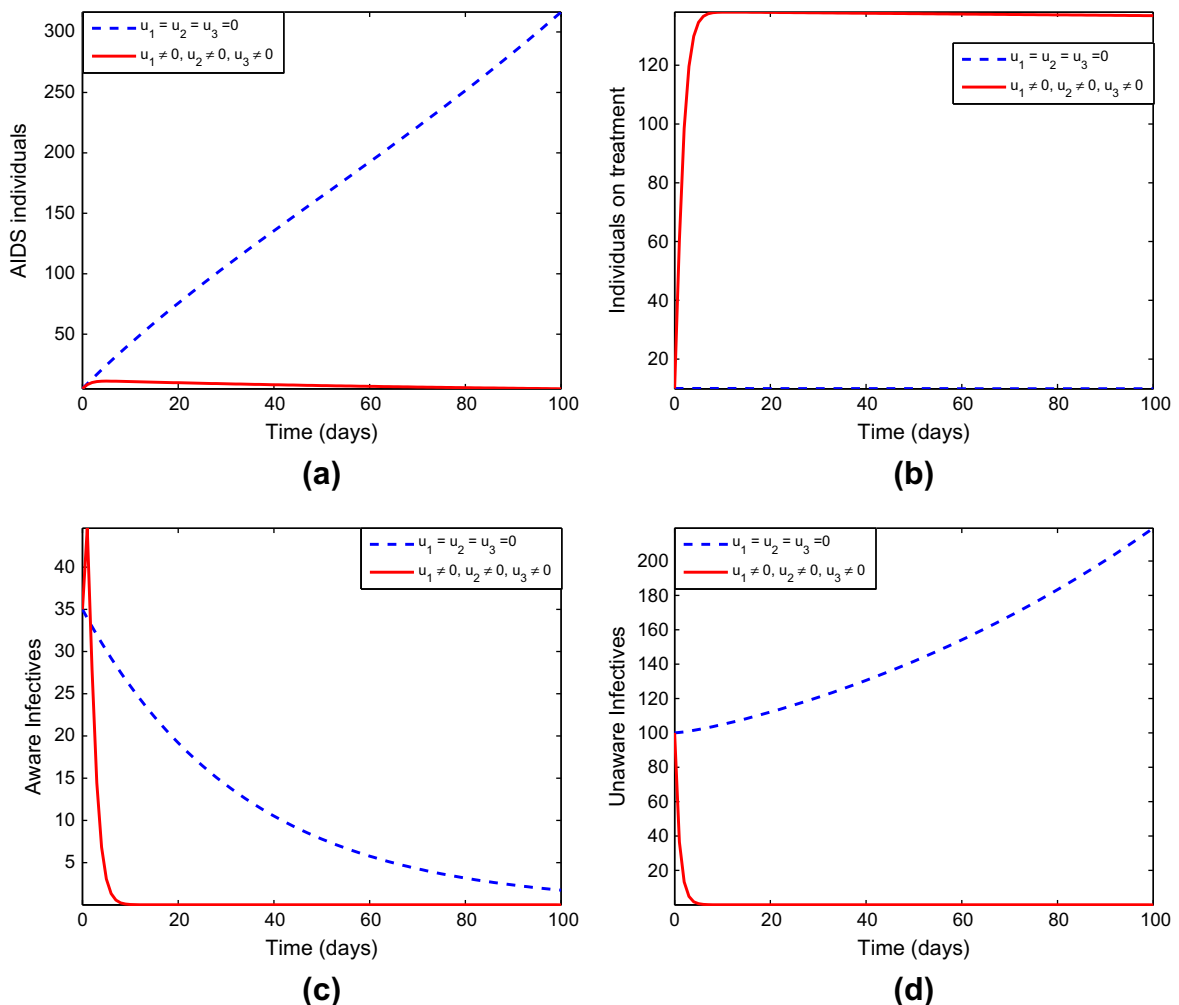


Fig. 5. Simulations of the model showing the effects of all controls on spread of HIV/AIDS.

decrease in the number of unaware infectives ( $I_1$ ) and AIDS ( $A$ ) compared with the case without control. Here, the total averted cases of unaware infectives and AIDS are 6100 and 7800 respectively. The control profile is shown in Fig. 6(b), control  $u_2$  is at the upper bound for 18 days before dropping to the lower bound at the final time and the control  $u_1$  remain at the upper bound till the final time.

### 6.3. Optimal condom use ( $u_1$ ) and treatment ( $u_3$ ) only

With this strategy, the control on treatment ( $u_3$ ) and the condom use control ( $u_1$ ) are both used to optimize the objective function ( $J$ ) while screening control ( $u_2$ ) is set to zero. In Fig. 4, we observe that this control strategy results in a significant increase in the number of HIV positive individuals on treatment ( $H$ ) which stabilizes at 45 and a significant reduction in the number of AIDS ( $A$ ). The control profile is shown in Fig. 6(c), control  $u_1$  is at the upper bound till the final time and the control  $u_3$  is also maintained at the upper bound till the final time.

### 6.4. Optimal condom use ( $u_1$ ), screening of unaware infectives ( $u_2$ ) and treatment ( $u_3$ )

With this strategy, the condom use control ( $u_1$ ), screening control ( $u_2$ ) and the treatment control ( $u_3$ ) are all used to optimize the objective function ( $J$ ). In Fig. 5, we observe that this control strategy results in a significant increase in the number of HIV positive individuals on treatment ( $H$ ) which stabilizes at 140 and a significant reduction in the number of AIDS ( $A$ ). The control profile is shown in Fig. 6(d), controls  $u_1$  and  $u_3$  are at the upper bound till the final time and the control  $u_2$  dropped gradually from the upper bound to the lower bound after 18 days.

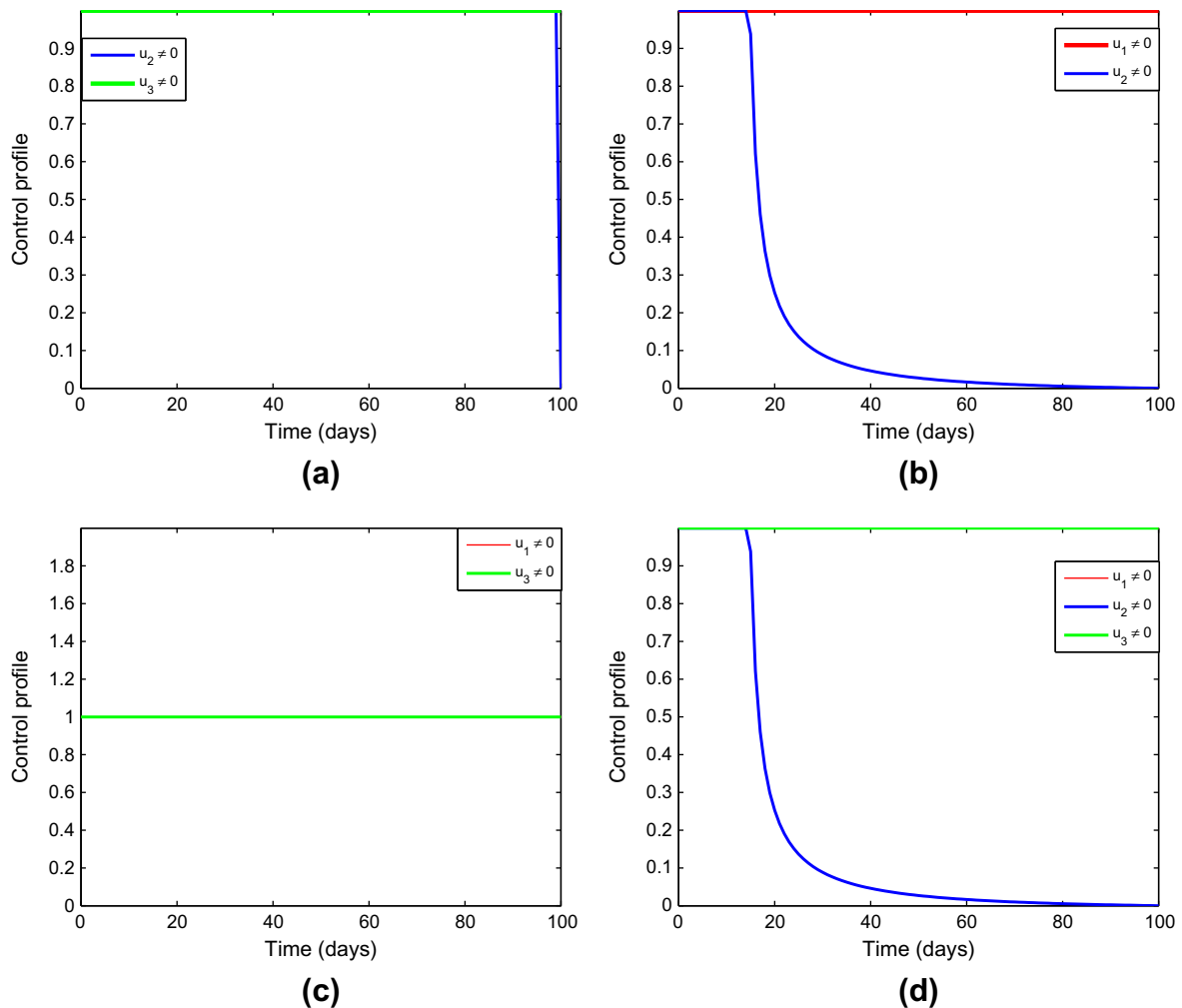
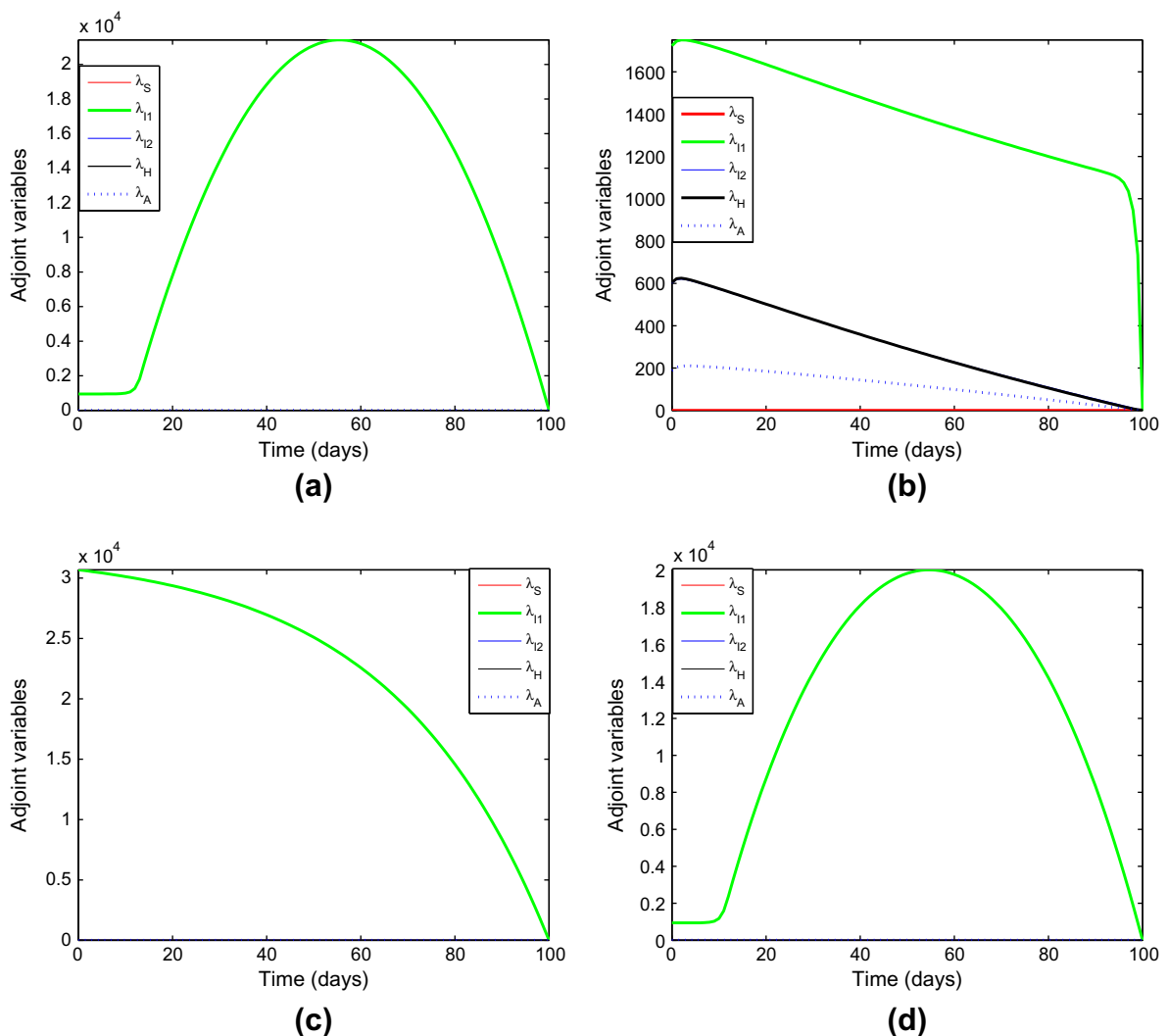


Fig. 6. Simulations of the model showing the control profiles of the intervention strategies.

In Fig. 7, we show the simulations of the effect of the controls strategies on adjoint variables. We observed that, in all the control strategies the shadow prices of the unaware infectives has highest impact on the economy. The shadow prices of the unaware infectives are also very high in all the cases compared with others. Fig. 8 shows that the number of sexual partners of susceptible individuals with unaware infectives has higher impact on the AIDS individuals in the absence of all controls. However, when all controls are used, the number of sexual partners of the susceptible individuals does not have a significant effect on the total number of AIDS individuals.

## 7. Cost effectiveness analysis

To determine the most cost effective strategy to use to control the disease (combination of screening and condom use only, treatment and condom use only, combination of screening and treatment only, and combination of screening, treatment and condom use), we use cost effectiveness analysis. To achieve this purpose we need to compare the differences between the costs and health outcomes of these interventions. This is done by calculating the incremental cost-effectiveness ratio (ICER) which is generally described as the additional cost per additional health outcome. When comparing two or more competing intervention strategies incrementally, one intervention should be compared with the next-less-effective alternative. The ICER numerator includes the differences in intervention costs, averted disease costs, costs of prevented cases and



**Fig. 7.** Simulations of the model showing the effect of control measures on adjoint variables (shadow price) of the spread of HIV/AIDS. (a), all controls are optimized, in (b), only controls  $u_2$  and  $u_3$  are optimized and (c), only controls  $u_1$  and  $u_3$  are optimized while (d), only controls  $u_1$  and  $u_2$  are optimized.



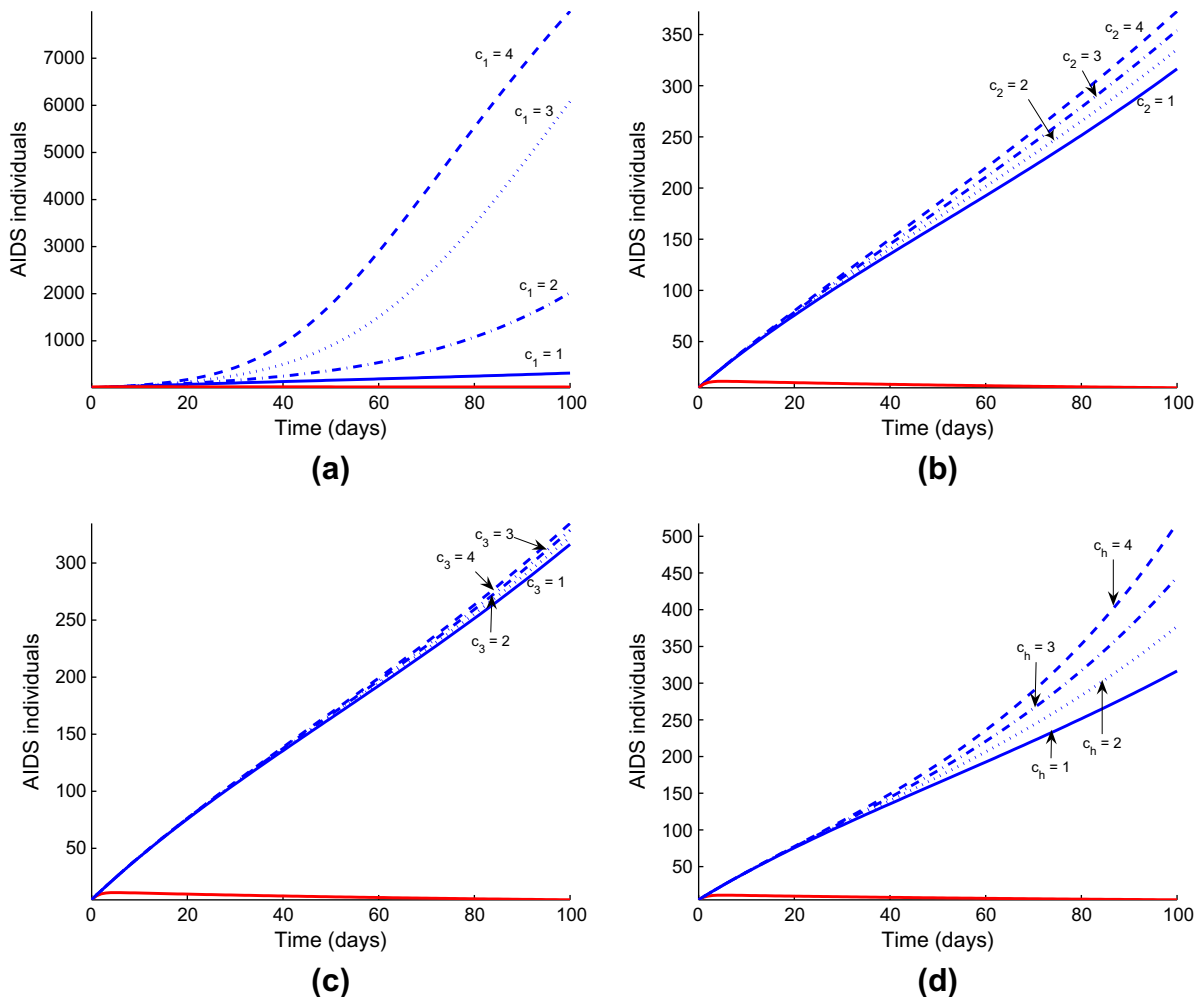
averted productivity losses if applicable. The ICER denominator is the differences in health outcomes (e.g. total number of infections averted, number of susceptibility cases prevented).

We rank the strategies in increasing order of effectiveness, namely combination of screening and condom use only (strategy A), treatment and condom use only (strategy B), combination of screening and treatment only (strategy C) and combination of screening, treatment and condom use (strategy D) based on the model simulation results.

The difference between the total infectious individuals without control and the total infectious individuals with control was used to determine the “total number of infections averted” used in the table of cost-effectiveness analysis

Strategy	Total infection averted	Total cost (\$)
Strategy A	622230	\$149,310
Strategy B	626760	\$87,691,000

$$\begin{aligned} \text{ICER(A)} &= \frac{149,310}{622230} = 0.2400 \\ \text{ICER(B)} &= \frac{87,691,000 - 149,310}{626760 - 622230} = 19324.88 \end{aligned} \quad (32)$$



**Fig. 8.** Simulations model showing the effects of the number of sexual partners ( $c_1$ ), ( $c_2$ ), ( $c_3$ ) and ( $c_4$ ) on the spread of AIDS. The red line shows the impact when there is optimal control of use of condom, screening of unaware infectives and treatment.

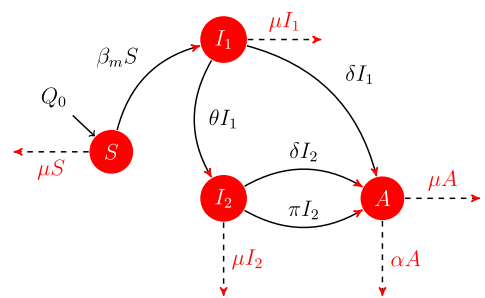


Diagram 1. Flow diagram for HIV/AIDS disease transmission model.

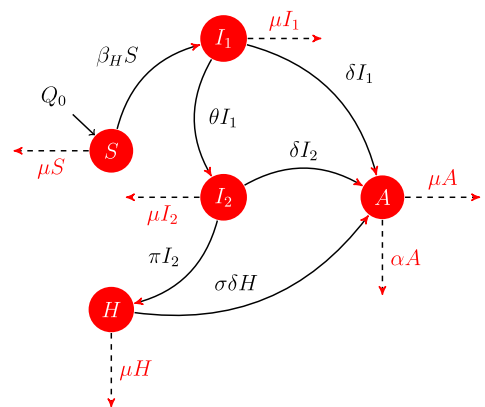


Diagram 2. Flow diagram for the modify HIV/AIDS disease transmission model.

The comparison between ICER (A) and ICER (B) shows a cost saving of 0.2400 for strategy A over strategy B. The ICER for strategy A indicates the strategy B is “strongly dominated”. That is, strategy B is more costly and less effective than strategy A. Therefore, strategy B, the strongly dominated is excluded from the set of alternatives so that it does not consume limited resources.

We exclude strategy B and compare strategies A and C. From the numerical results we have

Strategy	Total infection averted	Total cost (\$)
Strategy A	622230	\$ 149,310
Strategy C	627800	\$ 507,980

Table 1  
Description of variables and parameters of the HIV/AIDS model (24).

Baseline parameter	Description	Estimated value	Ref.
$\beta_1$	Probability of susceptible individuals with unaware infective	0.20	Assumed
$\beta_2$	Probability of susceptible individuals with aware infectives	0.15	[9]
$\beta_3$	Probability of susceptible individuals with AIDS	0.12	[9]
$\beta_h$	Probability of susceptible individuals with infectives on treatment	0.15	Assumed
$\mu$	Natural mortality	0.02	[9]
$\alpha$	AIDS induced death rate	1	[9]
$Q_0$	Immigration rate	2000	[9]
$\delta$	Rate of development to AIDS	0.1	[9]
$\sigma$	Treatment modification impact on progression to AIDS	0.002	Assumed
$\theta$	Rate of screening of unaware infectives	0.02	Assumed
$\pi$	Rate of treatment	0.6	Assumed

This leads to the following values for the ICER,

$$\begin{aligned} \text{ICER}(A) &= \frac{149310}{622230} = 0.2400 \\ \text{ICER}(C) &= \frac{507980 - 149310}{627800 - 622230} = 64.39 \end{aligned} \quad (33)$$

The comparison between ICER (A) and ICER (C) shows a cost saving of 0.2400 for strategy A over strategy C. Similarly, the ICER for strategy A indicates the strategy C is “strongly dominated”. That is, strategy C is more costly and less effective than strategy A. Therefore, strategy C, the strongly dominated is excluded and compare strategies A and D. From the numerical results we have

This leads to the following values for the ICER,

$$\begin{aligned} \text{ICER}(A) &= \frac{149310}{622230} = 0.2400 \\ \text{ICER}(D) &= \frac{148680 - 149310}{628190 - 622230} = -0.106 \end{aligned} \quad (34)$$

The comparison between ICER (A) and ICER (D) shows a cost saving of 0.106 for strategy D over strategy A. The negative ICER for strategy D indicates the strategy A is “strongly dominated”. That is, strategy A is more costly and less effective than strategy D. Therefore, strategy A, the strongly dominated is excluded.

With this result, we therefore conclude that strategy D (combination of screening  $u_2$  with treatment  $u_3$  and condom use  $u_1$ ) is the most cost-effective of all the strategies for HIV/AIDS disease control considered.

## 8. Conclusion

In this paper, we performed optimal control analysis for HIV/AIDS model. We derived and analyzed the conditions for optimal control of the disease with effective use of condoms, treatment regime and screening of infectives. We conclude that the successful screening of unaware infectives has a significant impact in reducing the endemicity of HIV/AIDS. This may be as a result of awareness by infectives who also took necessary precautionary measures not to spread the disease. Control programs that follow these strategies can effectively reduce the spread of HIV/AIDS in a population. Also, from the numerical results it is very clear that the impact and cost of unaware infectives in the community is very high. See Figs. 1, 2 Table 1.

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## References

- [1] Centers for Disease Control and Prevention, Prevalence and awareness of HIV infection among men who have sex with men – 21 cities, United States 2008, Morbidity and Mortality weekly report, vol 59, no 37, 2010.
- [2] J. Brannstrom, B. Akerlund, M. Arneborn, A. Blaxhult, J. Giesecke, Unaware infection in HIV cases, *Int. J. ZSTD AIDS* 16 (10) (2005) 702–706.
- [3] Y. Yazdanpanah, C.E. Sloan, C. Charlois-ou, S. Le Vu, C. Semaille, D. Costagliola, J. Pillonel, A. Poullie, O. Scemama, S. Deuffic-Burban, E. Losina, R.P. Walensky, K.A. Freedberg, A.D. Paltiel, Routine HIV screening in France: clinical impact and cost-effectiveness, *J. PLoS ONE* 5 (10) (2010) e13132. <[www.plosone.org](http://www.plosone.org)>.
- [4] M.J. Waxman, S. Kimaiyo, N. Ongaro, K.K. Wools-Kaloustian, T.P. Flanigan, E.J. Carter, Initial outcomes of an emergency department rapid HIV testing program in Western Kenya, *AIDS Patient Care STDS* 21 (12) (2007) 981–986.
- [5] R.M. Anderson, G.F. Medly, R.M. May, A.M. Johnson A.M., A preliminary study of the transmission dynamics of the Human Immunodeficiency Virus (HIV), the causative agent of AIDS, *IMA J. Math. Appl. Med. Biol.* 3 (1986) 229–263.
- [6] I.S. Nikolaos, K. Dietz, D. Schenzle, Analysis of a model for the pathogenesis of AIDS, *Math. Biosci.* 145 (1997) 27–46.
- [7] M.K. Christopher, X.V. Jorge, A simple vaccination model with multiple endemic states, *Math. Biosci.* 164 (2000) 183–201.
- [8] L. Guihua, J. Zhen, Global stability of a SEIR epidemic model with infectious force in latent, infected and immune period, *Chaos Soliton Fract* 25 (5) (2005) 1177–1184.
- [9] A. Tripathi, R. Naresh, D. Sharma, Modelling the effect of screening of unaware infectives on the spread of HIV infection, *Appl. Math. Comput.* 184 (2007) 1053–1068.
- [10] Karrakchou, M. Rachik, S. Gourari, Optimal control and infectiology: application to an HIV/ AIDS model, *Appl. Math. Comput.* 177 (2006) 807–818.
- [11] B.M. Adams, H.T. Banks, Kwon Hee-Dae, T.T. Hien T, Dynamic multidrug therapies for HIV: Optimal and STI control approaches, *Mathematical Biosciences and Engineering*, vol 1 and 2, (2004) 223–241.
- [12] Z. Gul, H.K. Yong, H.J. I, Stability analysis and optimal vaccination of an SIR epidemic model, *BioSystems* 93 (2008) 240–249.
- [13] Z. Mukandavire, W. Garira, J.M. Tchuente, Modelling effects of public health educational campaigns on HIV/AIDS transmission dynamics, *Appl. Math. Model.* 33 (2009) 2084–2095.
- [14] O.D. Makinde, K.O. Okosun, Impact of chemo-therapy on optimal control of malaria disease with infected immigrants, *BioSystems* 104 (1) (2011) 32–41, <http://dx.doi.org/10.1016/j.biosystems.2010.12.010>.
- [15] J.A.M. Felipe de Souza, A.L.C. Marco, T. Yoneyama, Optimal control theory applied to the anti-viral treatment of AIDS, In: *Proceedings of the 39th Conference on Decision and Control (CDC' 2000)*, Sydney, Australia, December 2000.
- [16] H.R. Joshi, Optimal control of an HIV immunology model, *Optim. Control Appl. Math.* 23 (2002) 199–213.
- [17] S.M. Lenhart, J. Yong, Optimal control for degenerate parabolic equations with logistic growth, *Preprint Institute for Mathematics and Application*, 1997.

- [18] K.O. Okosun, R. Ouifki, N. Marcus, Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity, *BioSystems* 106 (2011) 136–145, <http://dx.doi.org/10.1016/j.biosystems.2011.07.006>.
- [19] V.P. Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180 (2002) 29–48.
- [20] Z. Mukandavire, A.B. Gumel, W. Garira, J.M. Tchuente, Mathematical analysis of a model for HIV-Malaria co-infection, *Math. Biosci. Eng.* 6 (2009) 333–362.
- [21] L. Perko, *Differential equations and dynamical systems*, Text in Applied Mathematics, 7, Springer, Berlin, 2000.
- [22] D. Kirschner, S. Lenhart, S. Serbin, Optimal control of the chemotherapy of HIV, *J. Math. Biol.* 35 (1997) 775–792.
- [23] L.S. Pontryagin, V.G. Boltyanskii, R.V. Gamkrelidze, E.F. Mishchenko, *The Mathematical Theory of Optimal Processes*, Wiley, New York, 1962.
- [24] W.H. Fleming, R.W. Rishel, *Deterministic and Stochastic Optimal Control*, Springer Verlag, New York, 1975.
- [25] S. Lenhart, J.T. Workman, *Optimal Control Applied to Biological Models*, Chapman and Hall, 2007.