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Application of Optimal Control Strategies for the Spread of HIV in a Population

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ABSTRACT

This paper presents an application of optimal control theory to assess the effectiveness of control measures on the spread of HIV in a population. This paper formulates and analyzes a deterministic mathematical model with use of condom, screening and therapy as control variables using optimal control theory and Pontryagin's Maximum Principle. It formulates 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 using of condom, screening of unaware infective and antiretroviral therapy are used as the control items. The optimality system is derived and solved numerically.

Keyword: Optimal control; HIV; unaware infective; Pontryagin's maximum principle.

INTRODUCTION

HIV (Human Immunodeficiency) and AIDS (Acquired Immune Deficiency Syndrome) is one of the health problems. Currently, the development effectiveness of screening control and antiretroviral therapy have not been adequate despite increased coverage. Many aspects of the response is not yet known, for example, the phenomenon of the spread of the HIV epidemic. The number of cases of unaware infective very urgent and need to know the important parameters in the spread and develop optimal strategies and effective way to prevent and control the spread of HIV/AIDS.

Mathematical models have been used to help understand the transmission dynamics of HIV infections, for example Anderson (2001) presented a theoretical framework for transmission of HIV/AIDS with screening of unaware infectives. Modelling the effect of screening of unaware infectives and treatment on the spread of HIV infection (Tripathi *et al*., 2007 and Safiel *et al*., 2012). Marsudi *et al*. (2014, 2016) studied the impact of educational campaign, screening and HIV Therapy on the Dynamics of Spread of HIV. On the other hand, optimal control theory has been applied extensively in HIV model, for example Joshi *et al*. (2006) showed how optimal control theory can be applied to find an optimal vaccination strategy that will minimize the size of the infectious population as well as the cost of vaccination. Okosun *et al.* (2013) used optimal control approach to determine impact of screening of unaware infectives and treatment of HIV/AIDS.

The model we consider in this paper was developed from Marsudi *et al*. (2014) by adding the condom use control, the control on screening of unaware infectives and the control on antiretroviral therapy as a time dependent control parameters. Our objective functional balances the effect of minimizing the number of unaware infectives in the spread of HIV/AIDS and minimizing the cost of implementing the control.

The paper is organized as follows: In section two describes material and methods. Section three describes results and discussions that contains mathematical model, the optimal control problem and numerical simulations. Finally, the conclusion are summarized in section four.

MATERIAL AND METHODS

This paper considers the HIV model used in Marsudi *et al.* (2014). The population (N) is divided into five subclass: susceptible individuals or HIV negative (S), unaware infective individuals or HIV positive who do not know they are infected (I1), screened infective individuals or HIV positive who know they are infected after a screening method (I2), therapy infective or HIV positive and accept HIV therapy after being screened (T), and AIDS patient or full blown AIDS (A). We assume that an individual can be infected only through the sexual contacts with third types of infective. This model is governed by the following nonlinear system of differential equations.

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - \lambda S - \mu S \\
\frac{dI_1}{dt} &= \lambda S - (\theta + \sigma_1 + \mu) I_1 \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \sigma_2 + \mu) I_2 \\
\frac{dT}{dt} &= \delta I_2 - (\sigma + \mu) T \\
\frac{dA}{dt} &= \sigma_1 I_1 + \sigma_2 I_2 + \sigma T - (\gamma + \mu) A
\end{aligned}
\qquad (1)
$$

Where:

$\lambda = \dfrac{c_1\beta_1 I_1 + c_2\beta_2 I_2 + c_3\beta_3 T}{N}$ and

$N = S + I_1 + I_2 + T + A.$

The definitions of above model parameters are listed in Table 1.

The model considered in this paper is an improved model (1) by the inclusion of time dependent control parameters (use of condoms, screening of unaware infectives and antiretroviral therapy). This paper analyzed and applied optimal to the improved model to determine the impact of condom use, optimal screening of unaware infectives and antiretroviral therapy of HIV on the spread of HIV with the following steps:

(1) Describing proposed model and we estimate the model stated initial conditions and parameter values.
(2) Formulating an optimal control problem subject to the model dynamics, characterize the optimal controls, and constitute its optimality using Pontryagin's Maximum Principle.
(3) Solving the resulting optimality system numerically using a fourth order iterative Runge-Kutta scheme (forward-backward sweep method).

RESULT AND DISCUSSION

1. Mathematical Model.

This paper introduces into the model (1), condom use (u1), screening of unaware infectives (u2) andantiretroviral therapy (u3) as time dependent control to reduce the spread of HIV/AIDS. The model (1) becomes.

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - (1-u_1)\lambda S - \mu S \\
\frac{dI_1}{dt} &= (1-u_1)\lambda S - (u_2\theta + \sigma_1 + \mu) I_1 \\
\frac{dI_2}{dt} &= u_2\theta I_1 - (u_3\delta + \sigma_2 + \mu) I_2 \\
\frac{dT}{dt} &= u_3\delta I_2 - (\sigma + \mu) T \\
\frac{dA}{dt} &= \sigma_1 I_1 + \sigma_2 I_2 + \sigma T - (\gamma + \mu) A
\end{aligned}
\qquad (2)
$$

Where:

$S(0) = S_0, I_1(0) = I_{10}, I_2(0) = I_{20}, T(0) = T_0, A(0) = A_0$ are given. Here, the condom use control is bounded $(0 \le u_1 \le 1)$ the control on screening of unaware infective is bounded $(0 \le u_2 \le 1)$ and the control on antiretroviral therapy is bounded $(0 \le u_3 \le 1)$.

The description of parameters of HIV/AIDS model (2), together with the baseline values used in numerical analysis, are given in Table 1.

Table 1. Description of variables and parameters of HIV/AIDS model (2).

Parameter	Description	Values	Sources
β_1	probability of susceptible individuals with unaware infectives	0.86	Safiel *et al*. [3]
β_2	probability of susceptible individuals with screened infectives	0.15	Tripathi *et al*. [1]
β_3	probability of susceptible individuals with therapy infectives	0.10	Safiel *et al*. [3]
θ	rate of screening of unaware infectives	0.6	
δ	rate of therapy of infectives	0.99	Safiel *et al*. [3]
σ_1	the rate at which unaware infectives develop full blown AIDS	0.20	Safiel *et al*. [3]
σ_2	the rate at which screened infectives develop full blown AIDS	0.01	Safiel *et al*. [3]
σ	the rate at which therapy infectives develop full blown AIDS.	0.001	Safiel *et al*. [3]
μ	natural mortality rate	0.1	Safiel *et al*. [3]
γ	AIDS related death rate	1	Tripathi *et al*. [1]
c_1	average number of sexual partners per unit time for unaware infectives	3	Safiel *et al*. [3]
c_2	average number of sexual partners per unit time for screened infectives	2	Safiel *et al*. [3]
c_3	average number of sexual partners per unit time for therapy of infective	1	Safiel *et al*. [3]
Λ	the recruitment rate into the susceptible class	700	Assumed

2. The Optimal Control Problems

The problem is to minimize the number of unaware infectives and the cost of applying the control on the objective functional

$$J(u_1, u_2, u_3) = \min_{u_1, u_2, u_3} \int_0^{t_f} [w_1 I_1 + \tfrac{1}{2}(w_2 u_1^2 + w_3 u_2^2 + w_4 u_3^2)]\, dt \qquad (3)$$

subject to the system of equations (2) with appropriate state initial conditions, and t_f is the final time, while the control set U is defined as:

$$U = \{(u_1, u_2, u_3) \mid 0 \le u_1 \le 1, 0 \le u_2 \le 1, 0 \le u_3 \le 1 \text{ for } t \in t_f\} \quad (4)$$

where w_1, w_2, w_3 and w_4 are positive weights. The weight constants, w_1, is the relative measure of the importance of reducing the unaware infectives on the spread of HIV/AIDS, while w_2, w_3 and w_4 are the relative measures of the cost or effort required to implement each of the associated controls. Our target is to minimize the objective functional defined in equation (3) by minimizing the number of the unaware infectives. In other words, this paper was seeking optimal control triple u_1^*, u_2^* and u_3^* such that:

$$J(u_1^*, u_2^*, u_3^*) = \min\{J(u_1, u_2, u_3) \mid u_1, u_2, u_3 \in U\}. \quad (5)$$

Pontryagin's Maximum Principle (Lenhart and Workman, 2007) provides necessary conditions for an optimal control problem. This principle converts (1), (3), and (5) into a problem of minimizing a Hamiltonian pointwisely with respect to u_1, u_2 and u_3

$$\begin{aligned} H &= f(\mathrm{x},u,t) - \sum_{\mathrm{i}} \lambda_i g_i(\mathrm{x},u,t) \\ &= w_1 I_1 + \tfrac{1}{2}(w_2 u_1^2 + w_3 u_2^2 + w_4 u_3^2) \\ &\quad + \lambda_S \left[\Lambda - (1-u_1)\frac{(c_1\beta_1 I_1 + c_2\beta_2 I_2 + c_3\beta_3 T)S}{S + I_1 + I_2 + T + A} + \mu S \right] \\ &\quad + \lambda_{I_1} \left[(1-u_1)\frac{(c_1\beta_1 I_1 + c_2\beta_2 I_2 + c_3\beta_3 T)S}{S + I_1 + I_2 + T + A} - (u_2\theta + \sigma_1 + \mu)I_1 \right] \\ &\quad + \lambda_{I_2} \left[u_2\theta I_1 - (u_3\delta + \sigma_2 + \mu)I_2 \right] \\ &\quad + \lambda_T \left[u_3\delta I_2 - (\sigma + \mu)T \right] \\ &\quad + \lambda_A \left[\sigma_1 I_1 + \sigma_2 I_2 + \sigma T - (\gamma + \mu)A \right] \end{aligned} \quad (6)$$

where $\lambda_S, \lambda_{I_1}, \lambda_{I_2}, \lambda_T$ and λ_A are adjoint (co-state) variables. By applying Pontryagin's Maximum Principle and the existence result for the optimal control from (Fleming and Rishel, 1975), we obtain the following theorem.

Theorem 1. There exists an optimal control u_1^*, u_2^* and u_3^* and corresponding solution $S^*(t), I_1^*(t), I_2^*(t), T^*(t)$ and $A^*(t)$, that minimizes $J(u_1, u_2, u_3)$ over u_1, u_2 and u_3. Then, there exists adjoint functions $\lambda_S, \lambda_{I_1}, \lambda_{I_2}, \lambda_T$ and λ_A satisfying the equations:

$$\begin{aligned} \frac{d\lambda_S}{dt} &= (\lambda_S - \lambda_{I_1}) \left[\frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)}{S^* + I_1^* + I_2^* + T^* + A^*} - \frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{(S^* + I_1^* + I_2^* + T^* + A^*)^2} \right] \\ &\quad - \lambda_S \mu \\ \frac{d\lambda_{I_1}}{dt} &= -w_1 + (\lambda_S - \lambda_{I_1}) \left[\frac{(1-u_1)c_1\beta_1 S^*}{S^* + I_1^* + I_2^* + T^* + A^*} - \frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{(S^* + I_1^* + I_2^* + T^* + A^*)^2} \right] \\ &\quad + (\lambda_{I_1} - \lambda_{I_2})u_2\theta + (\lambda_{I_1} - \lambda_A)\sigma_1 + \lambda_{I_1}\mu. \end{aligned} \quad (7)$$

$$
\begin{aligned}
\frac{d\lambda_{I_2}}{dt} &= (\lambda_S - \lambda_{I_1})\left[\frac{(1-u_1)c_2\beta_2 S^*}{S^*+I_1^*+I_2^*+T^*+A^*} - \frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{(S^*+I_1^*+I_2^*+T^*+A^*)^2}\right] \\
&\quad + (\lambda_{I_1} - \lambda_T)u_3\theta + (\lambda_{I_2^*} - \lambda_{A^*})\sigma_2 + \lambda_{I_2^*}\mu. \\
\frac{d\lambda_T}{dt} &= (\lambda_S - \lambda_{I_1})\left[\frac{(1-u_1)c_3\beta_3 S^*}{S^*+I_1^*+I_2^*+T^*+A^*} - \frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{(S^*+I_1^*+I_2^*+T^*+A^*)^2}\right] \\
&\quad + (\lambda_T - \lambda_A)\sigma + \lambda_T\mu. \\
\frac{d\lambda_A}{dt} &= (\lambda_{I_1} - \lambda_S)\left[\frac{(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{(S^*+I_1^*+I_2^*+T^*+A^*)^2}\right] + \lambda_A(\gamma+\mu).
\end{aligned} \tag{7}
$$

and transversalisty conditions:

$$
\lambda_S(t_f) = \lambda_{I_1}(t_f) = \lambda_{I_2}(t_f) = \lambda_T(t_f) = \lambda_A(t_f) = 0. \tag{8}
$$

with the optimal control is given by

$$
\begin{aligned}
u_1^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_1} - \lambda_S)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{w_2(S^*+I_1^*+I_2^*+T^*+A^*)}\right)\right\} \\
u_2^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_1} - \lambda_{I_2})\theta I_1^*}{w_3}\right)\right\} \\
u_3^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_2} - \lambda_T)\delta I_2^*}{w_4}\right)\right\}.
\end{aligned} \tag{9}
$$

Proof.

Due to the convexity of integrand of $J(u_1,u_2,u_3)$ with respect to u_1, u_2 and u_3, a prior boundedness of the state solutions, and the Lipschitz property of the state system with the respect to the state variables. The existence of an optimal control has been given by Fleming and Rishel (1975). The adjoint equations and transversality conditions can be obtained by using Pontryagin's Maximum Principle such that:

$$
\begin{aligned}
\frac{d\lambda_S}{dt} &= -\frac{\partial H}{\partial S}, \quad \lambda_S(t_f) = 0, \\
\frac{d\lambda_{I_1}}{dt} &= -\frac{\partial H}{\partial I_1}, \quad \lambda_{I_1}(t_f) = 0, \\
\frac{d\lambda_{I_2}}{dt} &= -\frac{\partial H}{\partial I_2}, \quad \lambda_{I_2}(t_f) = 0, \\
\frac{d\lambda_T}{dt} &= -\frac{\partial H}{\partial T}, \quad \lambda_T(t_f) = 0, \\
\frac{d\lambda_A}{dt} &= -\frac{\partial H}{\partial A}, \quad \lambda_A(t_f) = 0.
\end{aligned} \tag{10}
$$

The Hamiltonian is maximized with respect to the controls at the optimal control $u^* = (u_1^*, u_2^*, u_3^*)$, thus we differentiate *H* with respect to u_1, u_2 and u_3 on *U*, respectively, to obtain:

$$\begin{aligned}
\frac{\partial H}{\partial u_1} &= w_2 u_1 + (\lambda_S - \lambda_{I_1})\left[\frac{(c_1\beta_1 I_1 + c_2\beta_2 I_2 + c_3\beta_3 T)S}{S + I_1 + I_2 + T + A}\right] = 0 \quad \text{at } u_1 = u_1^*,\\
\frac{\partial H}{\partial u_2} &= w_3 u_2 + (\lambda_{I_2} - \lambda_{I_1})\theta I_1 = 0 \quad \text{at } u_2 = u_2^*,\\
\frac{\partial H}{\partial u_3} &= w_4 u_3 + (\lambda_T - \lambda_{I_2})\delta I_2 = 0. \quad \text{at } u_3 = u_3^*.
\end{aligned} \tag{11}$$

Hence, solving for u_1^*, u_2^* and u_3^* on the interior sets gives:

$$\begin{aligned}
u_1^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_1} - \lambda_S)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 T^*)S^*}{w_2(S^* + I_1^* + I_2^* + T^* + A^*)}\right)\right\}\\
u_2^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_1} - \lambda_{I_2})\theta I_1^*}{w_3}\right)\right\}\\
u_3^* &= \max\left\{0, \min\left(1, \frac{(\lambda_{I_2} - \lambda_T)\delta I_2^*}{w_4}\right)\right\}.
\end{aligned} \tag{12}$$

3. Numerical Simulations.

The optimal control system thus, is a coupled forward state equation and a backward adjoint equation, along with the regular control. This problem, being nonlinear and coupled in nature, needs to be solved using concurrent and iterative numerical procedures. In this paper, the optimal strategy is simulated by solving the state and adjoint systems and the transversality conditions based on Runge-Kutta fourth order scheme. This method solves the state equations with an initial guess for u_1, u_2 and u_3 forward in time, after which it solves the adjoint equations backward in time, and then the controls are updated using equations (12). This computational procedure is done iteratively until a convergence is attained. Details on the forward-backward sweep procedure are given in Lenhart and Workman (2007).

The numerical simulations are carried out using Matlab. The parameter values we used are given in Table 1. The cost coefficients w_1=200, w_2=35, w_3=55, and w_4=75 and the initial conditions is taken to be *S*(0)= 25.000.000, I_1(0)= 200.000, I_2(0)= 25.000, *T*(0)= 5000, and *A*(0)= 2000. Using model parameter values shown in Table 1 is obtained the effective reproduction numbers, R_{ef} = 3.1035. Because $R_{ef} > 1$, the HIV infection will persist in population.

Figure 1 (a)-(b) shows the comparison between the numbers of unaware infectives (I_1) with and without control. In Figure 1 (a), we observe that in presence of control efforts on condom use (u_1), screening of unaware infectives (u_2) and the antiretroviral therapy (u_3) results in a significant decrease in the number of unaware invectives compared with the case without control. The numbers of unaware infectives initially increases rapidly then reaches the maximum number of I_1 would be 6.737x10^5 (*t*=4.4) in the case without control and 2408 (*t*=0) with control (Figure 1(b). From the point of maximum value is then starts to decreases then reaches at the final time t_f = 20 (years) is 716.6 in the case without control and 7.04x10^{-7} with control. It is nearly 99.99% of the effectiveness of the combinations of the strategies in the control HIV.

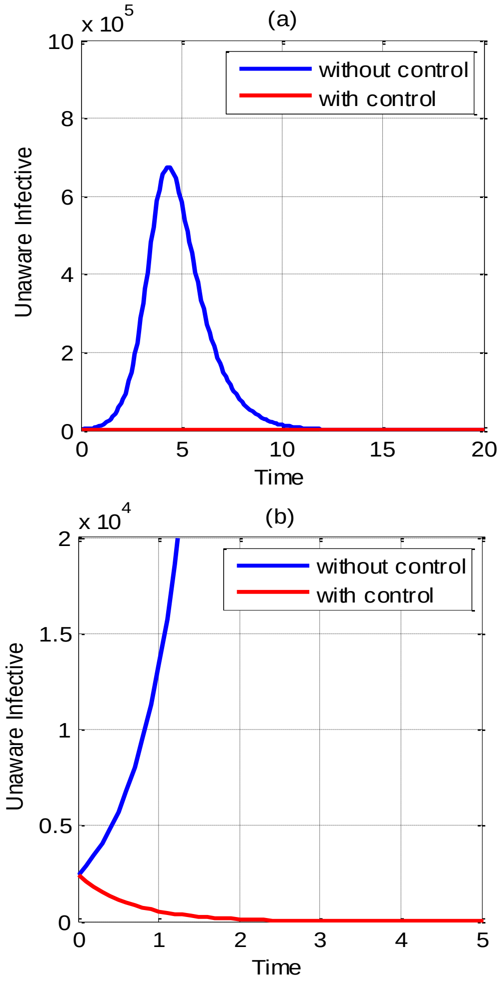

Figure 1. The comparison between the number of unaware infectives with and without control.

Similarly, the comparison between the numbers of AIDS patient (A) with and without control is shown in Figure 2. From Figure 2, we know that the optimal control can make the AIDS patient far more than that without control, which show that the HIV has been effectively controlled based on our optimal control strategy. The numbers of unaware infectives initially increases rapidly then reaches the maximum number of A is 4.059x10^5 (t = 5.1) in the case without control and 1130 (t = 0.3) with control (Figure 2b). It reaches 531 at the end of this control against 1.835 in the absence of control, i.e. a reduction of 529.165 cases.

Finally, the control profile of the combination of the three kinds of the control strategies is shown in Figure 3. The control of condom use (u_1) is at the upper bound till the final time (Figure 3-a), the screening control (u_2) never reached the upper limit dropped gradually from the upper bound to the lower bound after t = 5.5 (Figure 3-b) and the antiretroviral therapy control (u_3) is at 1.455x10^{-11} at the beginning of the period then increases rapidly reaches the maximum at 4.366x10^{-11} and then decreases gradually while oscillating up to 9.095x10^{-13} and to zero at the final time.

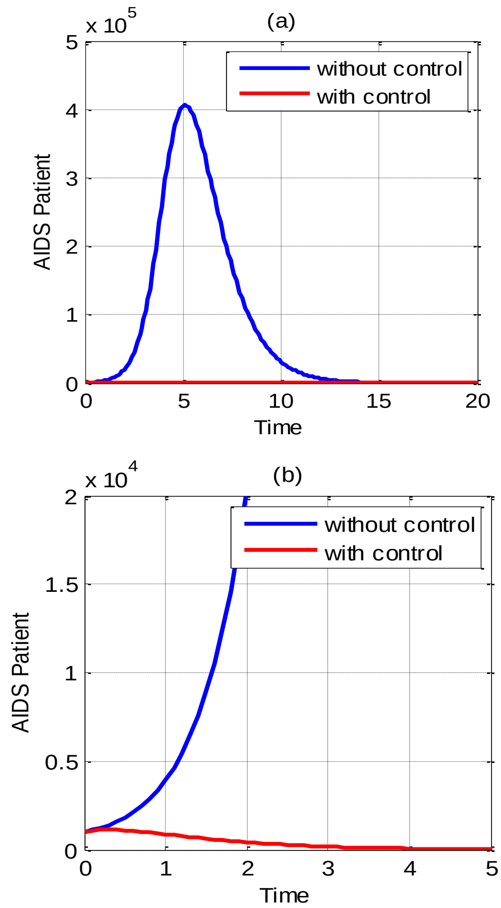

Figure 2. The comparison between the number of HIV patient with and without control.

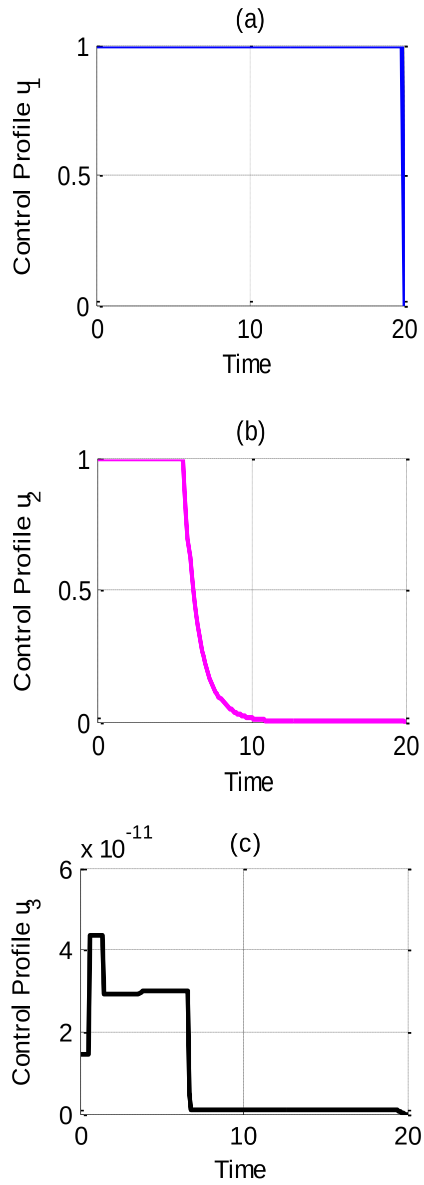

Figure 3. The optimal control profiles of u_1, u_2, and u_3.

CONCLUSION

This paper presented a deterministic model for controlling the impact of condom use, screening of unaware infectives and antiretroviral therapy of HIV on the spread of HIV in a population. It formulates an optimal control problem subject to the model dynamics, investigates the necessary conditions for the disease control in order to determine the role of unaware infectives in the spread of HIV and proves the uniqueness of the optimal control using Pontryagin's Maximum Principle.

The numerical simulations of both the systems i.e. with control and without control, shows that this strategy helps to reduce the number of unaware infectives and the number of AIDS patient greatly. The results obtained shows also that the effectiveness of the combinations of condom use, screening of unaware infectives and antiretroviral therapy in the control HIV can reach 99.99%.

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