Optimal Control of an HIV Model with Condom Education and Therapy

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Abstract: In this paper, we propose and analyze an optimal control problem to asses the effectiveness of control measures on the spread of HIV. We formulate and analyze a deterministic mathematical model with use of condom education and antiretroviral therapy as control variables using optimal control theory and Pontryagin's maximal principle. We formulated the appropriate optimal control problem and investigate the necessary conditions for the disease control in order to determine the role of asymptomatic infectives, pre-AIDS, and full-down AIDS in the spread of HIV. We further investigate the impact of combinations of the strategies in the control of HIV infection. The combination of antiretroviral therapy on pre-AIDS and full-blown AIDS shows a significant difference in the number of the infected individuals in the asymptomatic stage, infected individuals in the pre-AIDS class, and infected individuals in full-blown AIDS class.

1 INTRODUCTION

The model to be considered in this paper is an extension of the model proposed by Marsudi *et. al.* (2017) in which the effect of antiretroviral therapy at full-blown AIDS group is considered by the inclusion of model validation and applying optimal control theory to study and analyze the dynamics of HIV model. The stability analysis and optimal control of an epidemic model with vaccination and treatment have discussed by Sharma and Samanta (2015). Marsudi *et. al.* (2018) used the optimal control to examine the role of educational campaigns and antiretroviral therapy in controlling the spread of HIV dynamics. Okosun *et. al.* (2013) studied the impact of treatment of HIV/AIDS and screening of unaware infectives on optimal control of HIV/AIDS.

Many mathematical models of HIV/AIDS transmission dynamics have been developed including those with optimal control (Joshi, 2002; Lenhart and Workman, 2002; Marsudi *et. al.*, 2017; Yusuf and Benyah, 2011). The main objective of this paper is to develop a mathematical model for human interaction, this will be done with the aim of using three optimal control strategies: condom education, antiretroviral therapy for pre-AIDS and full-blown AIDS at different rates on the spread of the disease.

In section 2, we show the mathematical model for the HIV model that will be studied in this paper. Sections 3 is presented to the optimal control problem formulation. In this section, we use Pontryagin's maximum principle to analyze the control strategies and to determine the necessary conditions for the optimal control of the HIV infection. In Section 4, we presented the numerical simulations of the model in order to interpret the results of the dynamics and the conclusion is presented in Section

2 MATHEMATICAL MODEL

Following the model proposed by Marsudi *et. al.* (2017), the total population (N) is divided into six categories: susceptible (S), susceptible who receive condom education (E), infected in the asymptomatic stage (I), infected in pre-AIDS class (P), full-blown AIDS class (A), and pre-AIDS and full-blown AIDS who receive antiretroviral therapy (T).

The model is built according to the following main assumptions:

(i) The rate of transmission is directly proportional to the susceptibles individuals and also to the ratio

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between the members of the infected population (I and P) to the total population.

(ii) Asymptomatic infectives and pre-AIDS class can infect susceptibles class at different rates β_1 and β_2 respectively where $\beta_1 < \beta_2$).

(iii) Susceptible individuals who receive condom educations at the rate u_1 $(0 \le u_1 \le 1)$.

(iv) Only pre-AIDS and full blown AIDS can be treated with antiretroviral therapy at different rates u_2 and u_3 respectively $(0 \le u_i \le 1, i = 2, 3)$.

(v) Asymptomatic infectives only move to pre-AIDS at different rates σ_1 and pre-AIDS class will move to full-blown AIDS at different rates σ_2.

(vi) Natural death rate μ, the death rate due to full-blown AIDS and pre-AIDS who receive antiretroviral therapy at different rates α_1 and α_2 respectively $(\alpha_1 > \alpha_2)$.

(vii) The recruitment rate Λ and condom education efficacy on the S class is $\delta (0 \le \delta \le 1)$.

The population is homogeneously mixed and each susceptible individual has an equal chance of acquiring HIV infection when contacting asymptomatic infective individuals or pre-AIDS individuals.

The population dynamics is given by the following set of ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{(\beta_1 I + \beta_2 P)S}{N} - (u_1 + \mu)S \\
\frac{dE}{dt} &= u_1 S - \frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{N} - \mu E \\
\frac{dI}{dt} &= \frac{(\beta_1 I + \beta_2 P)S}{N} + \frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{N} - (\sigma_1 + \mu)I \\
\frac{dP}{dt} &= \sigma_1 I - (\sigma_2 + u_2 + \mu)P \\
\frac{dT}{dt} &= u_2 P + u_3 A - (\alpha_2 + \mu)T \\
\frac{dA}{dt} &= \sigma_2 P - (\alpha_1 + u_3 + \mu)A
\end{aligned} \tag{1}$$

with initial conditions

$$\begin{aligned}
&S(0) = S_0, E(0) = E_0, I(0) = I_0, P(0) = P_0, \\
&T(0) = T_0, A(0) = A_0.
\end{aligned} \tag{2}$$

The effective reproduction number R_e, for system (1) is given

$$R_e = \frac{\beta_1\big((1-\delta)u_1 + \mu\big)}{(u_1 + \mu)(\sigma_1 + \mu)} + \frac{\beta_2 \sigma_1[(1-\delta)u_1 + \mu]}{(u_1 + \mu)(\sigma_1 + \mu)(\sigma_2 + u_2 + \mu)}. \tag{3}$$

3 OPTIMAL CONTROL PROBLEM

We search the optimal strategies for implementing condom education and antiretroviral therapy use on a finite time T. Our goal is to minimize the number of cases in asymptomatic class I, pre-AIDS class P, full-blown AIDS class, and the costs required to control HIV by these three control measures. The objective function considered takes the form

$$J(u_1, u_2, u_3) = \int_0^T [b_1 I + b_2 P + b_3 A + \tfrac{1}{2}(w_1 u_1^2 + w_2 u_2^2 + +w_3 u_3^2)]\, dt \tag{4}$$

where T stands for the final time to control HIV. The constants $w_i, i = 1,2,3$ are measure of the relative cost of the interventions associated with the control u_1, u_2, and u_3, respectively, and the constant $b_i, i = 1,2,3$ are the weight constant for the class I, P, and A.

We seek an optimal control triple (u_1^*, u_2^*, u_3^*) such that

$$J(u_1^*, u_2^*, u_3^*) = \min \left\{ J(u_1, u_2, u_3) \,\middle|\, u_1, u_2, u_3 \in U \right\} \tag{5}$$

where $U = \left\{ (u_1, u_2, u_3) \,\middle|\, 0 \le u_i \le 1, i = 1,2,3, \ \forall t \in [0, T] \right\}$ is the control set.

The optimal control must satisfy the necessary conditions that are formulated by Pontryagin's maximum principle7]. This principle transforms the system of equations (1) and (4) into the problem of minimizing point-wise a Hamiltonian (H), with respect to $u_1(t), u_2(t), u_3(t)$ as

$$\begin{aligned}
H = {} & b_1 I + b_2 P + b_3 A + \tfrac{1}{2}(w_1 u_1^2 + w_2 u_2^2 + w_3 u_3^2) \\
& + \lambda_1 \left[\Lambda - \frac{(\beta_1 I + \beta_2 P)S}{N} - u_1 S - \mu S \right] \\
& + \lambda_2 \left[u_1 S - \frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{N} - \mu E \right] \\
& + \lambda_3 \left[\frac{(\beta_1 I + \beta_2 P)S}{N} + \frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{N} - (\sigma_1 + \mu)I \right] \\
& + \lambda_4 [\sigma_1 I - (\sigma_2 + u_2 + \mu)P] + \lambda_5 [u_2 P + u_3 A - (\alpha_2 + \mu)T] \\
& + \lambda_6 [\sigma_2 P - (\alpha_1 + u_3 + \mu)A].
\end{aligned} \tag{6}$$

where $\lambda_i, i = 1, 2, 3, 4, 5, 6$ are the adjoint variables associated by S, E, I, P, T, A. We differentiate Hamiltonian (6) with respect to states S, E, I, P, T, and A, respectively, and then the adjoint system can be written as

$$\frac{d\lambda_1}{dt}=-\frac{\partial H}{\partial S}=(\lambda_1-\lambda_3)\left[\frac{\beta_1 I+\beta_2 P}{N}-\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right] +(\lambda_3-\lambda_2)\left[\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right]+(\lambda_1-\lambda_2)u_1+\lambda_1\mu \quad (7)$$

$$\frac{d\lambda_2}{dt}=-\frac{\partial H}{\partial E}=(\lambda_2-\lambda_3)\left[\frac{(1-\delta)(\beta_1 I+\beta_2 P)}{N}-\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right] +(\lambda_3-\lambda_1)\left[\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right]+\lambda_2\mu \quad (8)$$

$$\frac{d\lambda_3}{dt}=-\frac{\partial H}{\partial I}=-b_1+(\lambda_1-\lambda_3)\left[\frac{\beta_1 S}{N}-\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right] +(\lambda_2-\lambda_3)\left[\frac{(1-\delta)\beta_1 E}{N}-\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right] +(\lambda_3-\lambda_4)\sigma_1+\lambda_3\mu \quad (9)$$

$$\frac{d\lambda_4}{dt}=-\frac{\partial H}{\partial P}=-b_2+(\lambda_1-\lambda_3)\left[\frac{\beta_2 S}{N}-\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right] +(\lambda_2-\lambda_3)\left[\frac{(1-\delta)\beta_2 E}{N}-\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right] +(\lambda_4-\lambda_6)\sigma_2\ (\lambda_4-\lambda_5)u_2-\lambda_4\mu \quad (10)$$

$$\frac{d\lambda_5}{dt}=-\frac{\partial H}{\partial T}=(\lambda_3-\lambda_1)\left[\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right] +(\lambda_3-\lambda_2)\left[\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right]+\lambda_5(\alpha_2+\mu) \quad (11)$$

$$\frac{d\lambda_6}{dt}=-\frac{\partial H}{\partial A}=-b_3+(\lambda_3-\lambda_1)\left[\frac{(\beta_1 I+\beta_2 P)S}{N^2}\right] +(\lambda_3-\lambda_2)\left[\frac{(1-\delta)(\beta_1 I+\beta_2 P)E}{N^2}\right]+(\lambda_6-\lambda_5)u_3 +\lambda_6(\alpha_1+\mu). \quad (12)$$

The optimal control pair (u_1^*, u_2^*, u_3^*) that solves the control problem is the pair of the time-dependent functions that minimizes *H*. We solved the equation $\frac{\partial H}{\partial u_i}=0$ at u_i^*, for $i=1, 2, 3$ and obtained:

$$u_1^c=\frac{(\lambda_1-\lambda_2)S^*}{w_1} \qquad u_2^c=\frac{(\lambda_4-\lambda_5)P^*}{w_2} \qquad .u_3^c=\frac{(\lambda_6-\lambda_5)A^*}{w_3}. \quad (13)$$

We can now impose the bounds $0 \le u_i \le 1$, $i = 2, 3$, on the controls to get

$$u_1^*=\max\{0, \min(u_1^c, 1)\}, \quad u_2^*=\max\{0, \min(u_2^c, 1)\}, \quad u_3^*=\max\{0, \min(u_3^c, 1)\} \quad (14)$$

and

$$\frac{\partial^2 H}{\partial u_1^2}=w_1>0, \frac{\partial^2 H}{\partial u_2^2}=w_2>0, \frac{\partial^2 H}{\partial u_3^2}=w_3>0. \quad (15)$$

4 NUMERICAL RESULTS

In this section, we give some numerical results of the system (1), using parameter values from Marsudi *et. al*. (2018b),

$$\Lambda=33638, \beta_1=0.1422, \beta_2=0.711, \alpha_1=0.0909, \alpha_2=0.0667, \delta=0.3, \sigma_1=0.198, \sigma_2=0.4621, \text{ and } \mu=0.0139. \quad (16)$$

and initial conditions

$$S(0)=957263, E(0)=959, I(0)=67, P(0)=34, T(0)=996, A(0)=89. \quad (17)$$

The solution of the optimal control problem was obtained by solving the optimality system of state and adjoint system through Forward-Backward Sweep method Lenhart and Workman (2002). The adjoint system (7-12) were solved by fourth–order Runge-Kutta scheme using the forward solution of the state equations. We used the weight at the final time, $b_1=b_2=b_3=1, w_1=50, w_2=20$ and $w_3=2$ for Simulation of HIV model with optimal control.

4.1 Strategy A: Control with Combination of Antiretroviral Therapy of Pre-AIDS and Full-blown AIDS

In this strategy, we applied antiretroviral therapy control u_2 and antiretroviral therapy control u_3 are used to optimize the objective function while we set condom education is set to zero. In Figure 1(a), (b), and (c), we observe the control strategies with combination of antiretroviral therapy of Pre-AIDS and full-blown AIDS results in decreasing the numbers of infected in the asymptomatic stage *I*, infected in pre-AIDS *P*, and infected in full-blown AIDS respectively, but not go to zero. Therefore, this strategy is not 100% effective in eradicating the disease in the specified period of time.

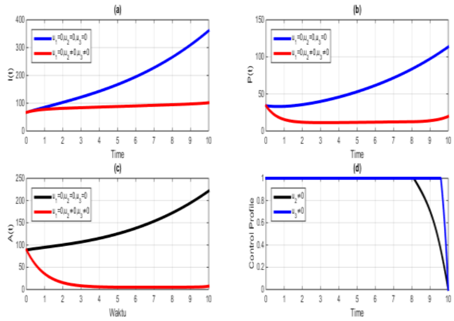

Figure 1: Simulation optimal control with antiretroviral therapy on pre-AIDS class and full-blown AIDS group

Figure 1(d) shows the controll profile for antiretroviral therapy of pre-AIDS class (u_2) is at the upper bound for about $t = 8.11$ before dropping to lower bound while the control profile for antiretroviral therapy of full-blown AIDS (u_3) is at the upper bound until about $t = 9.59$ before gradually decreasing to lower bound.

4.2 Strategy B: Control with Combination of Condom Education and Antiretroviral Therapy of Full-blown AIDS

Figure 2 show the simulation of the model where both control condom education (u_1) in susceptible and the antiretroviral therapy of full-blown AIDS group (u_3) are optimized. The numerical results shows that the infected individuals in the asymptomatic stage and infected individuals in pre-AIDS class increases (Figure 2(a) and 2(b)) while infected individuals in full-blown AIDS group decrease and then starts to increase because of a lack of antiretroviral therapy (Figure 2(c)). As a result, the use combination of condom education and antiretroviral therapy might not be sufficient to eradicate the burden of the infection of HIV.

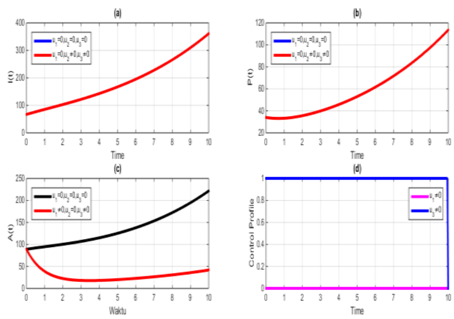

Figure 2: Simulation optimal control with condom education on susceptible and full-blown AIDS

Figure 2(d) shows the control profile of antiretroviral therapy (u_3) in which the control u_3 as at the upper bound for about $t = 9.95$ before dropping to the lower bound at the final time while the control profile of condom education at the lower bound from the beginning to the end of the intervention.

4.3 Strategy C: Control with Combination of Condom Education and Antiretroviral Therapy of Pre-AIDS

With this strategy, the condom education and antiretroviral therapy are used to optimize the objective function while controlling antiretroviral therapy of full-blown AIDS class is set to zero. In Figure 3(a)-(c) we observe that this control strategy show a significant decrease in the number of the infected individuals in the asymptomatic stage, infected individuals in the pre-AIDS class, and infected individuals in full-blown AIDS group compared with the case without control.

The control profile is shown in Fig. 3(d), control antiretroviral therapy of full-blown AIDS group (u_3) is at the upper bound for about $t = 8.33$ before dropping to lower bound while control condom education (u_1) to be at the lower bound.

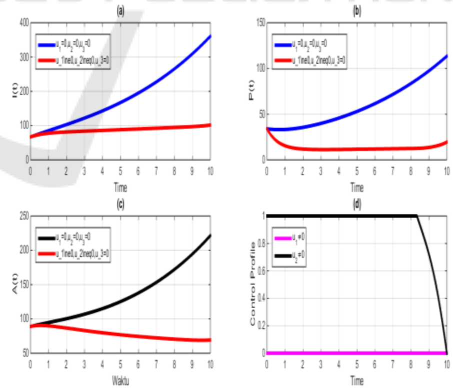

Figure 3: Simulation optimal control with condom education and pre-AIDS class.

4.4 Strategy D: Control with Combination of Condom Education, Antiretroviral Therapy of Pre-AIDS, and Full-blown AIDS

In this strategy, the combination of three controls condom education, antiretroviral therapy of pre-

AIDS and full-blown AIDS are used to optimize the objective function and then analysed its impact in infected individuals. Figure 4(a)-(c) shows the impact of with and without control application in the model. The significant difference is observed in the number of the infected individuals in the asymptomatic stage, infected individuals in the pre-AIDS class, and infected individuals in full-blown AIDS group.

Figure 4(d) showns the the controll profile for antiretroviral therapy of pre-AIDS class (u_2) is at the upper bound for about $t = 8.11$ before dropping to lower bound while the control profile for antiretroviral therapy of full-blown AIDS (u_3) is at the upper bound until about $t = 9.59$ before gradually decreasing to lower bound.

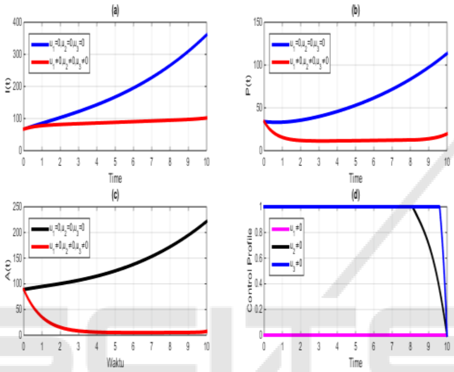

Figure 4: Simulation optimal control with condom education, antiretroviral therapy on pre-AIDS and full-blown AIDS

5 CONCLUSIONS

In this paper, a deterministic model with optimal control for HIV was derived and analyzed to examine the effect of condom education, antiretroviral therapy on pre-AIDS and full-blown AIDS on the dynamics of HIV. The Pontryagin's maximum principle used to derive and analyze the necessary conditions for optimal control strategies such as condom education (u_1), antiretroviral therapy on pre-AIDS (u_2), and antiretroviral therapy on full-blown AIDS (u_1) for minimizing the spread of HIV. Numerically, the model was analyzed. Graphically, strategies A, C, and D shows a significant difference in the number of the infected individuals in the asymptomatic stage, infected individuals in pre-AIDS class, and infected individuals in full-blown AIDS group while strategy B it's not positive impact observed in the infected individuals in the asymptomatic stage and infected individuals in pre-AIDS class.

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