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Optimal strategy for controlling the spread of HIV dynamics with educational campaigns and antiretroviral therapy

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Abstract. A deterministic mathematical model with educational campaigns and ARV (Anti Retro Viral) therapy as control variables are formulated and analyzed using optimal control theory (the Pontryagin's Maximum Principle). We formulate the appropriate optimal control problem and investigate the necessary conditions for the disease control in order to determine the role of the asymptomatic stage and pre-AIDS stage of HIV infection and in the spread of HIV using of educational campaigns and antiretroviral therapy are used as the control items. The numerical simulation of both the systems i.e. with control and without control, shows that the combination of the two strategies helps to reduce a significant difference in the number of individuals in the asymptomatic stage of HIV infection, the number of individuals in pre-AIDS stage, and the number of individuals with full-blown AIDS.

1. Introduction

Mathematical representation and analysis of infectious diseases have been central to infectious disease epidemiology. Mathematical models have been used to help understand the transmission dynamics of HIV infections. Sensitivity analysis allows to investigate how uncertainty in the input variables affect the model outputs and which input variables tend to drive variation in the outputs. Reference [1] assess qualitatively of the role of public health education program on HIV transmission dynamics. Reference [5, 10] presented modelling the effect of screening of unaware infective and treatment on the spread of HIV infection. The impact of educational campaign, screening and HIV therapy on the dynamics of spread of HIV has been investigated by [5] and [7] studied sensitivity analysis of the parameters of an HIV/AIDS model with condom campaign and antiretroviral therapy.

Other Modelling tool plays a big role in epidemiology by providing a concrete mechanism for understanding spreads of the disease and suggesting effective control measure [2, 4]. Optimal control theory is one area of mathematics that is used extensively in the control of the spread of infectious diseases [3, 4, 6, 8, 11]. Reference [3] used two examples to illustrate the concept of optimal control in two different diseases model (to find an optimal vaccination strategy and to determine a drug treatment strategy).

Modelling tool plays a big role in epidemiology by providing a concrete mechanism for understanding spreads of the disease and suggesting effective control measure [2, 4, 12]. Optimal control theory is one area of mathematics that is used extensively in the control of the spread of infectious diseases [3, 4, 6, 8, 11]. Reference [3] used two examples to illustrate the concept of optimal control in two different diseases model (to find an optimal vaccination strategy and to determine a drug treatment strategy).

In this study the model in [7] by the inclusion of time dependent control parameters. We formulate an optimal control problem with our objective functional balances the effect of minimizing the number of individuals in the asymptomatic stage of HIV infection, the number of individuals in pre-AIDS stage, and the number of individuals with full-blown AIDS in the spread of HIV/AIDS and minimizing the cost of implementing the control.

2. Mathematical Model

In this paper, we consider the HIV/AIDS model used in [7] by the inclusion of time dependent control (educational campaign (u_1) and antiretroviral therapy (u_2)). We divided the sexually active population $N(t)$ into six subpopulations, namely, susceptible individuals $S(t)$, susceptible individuals who receive condom campaigns $E(t)$, infected individuals in the asymptomatic stage of HIV infection $I(t)$, infected individuals in pre-AIDS stage but not receiving antiretroviral therapy $P(t)$, individuals with full-blown AIDS but not receiving antiretroviral therapy $A(t)$, and pre-AIDS individuals who are receiving antiretroviral therapy $T(t)$. The population dynamics is given by the following set of ordinary differential equations:

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

with initial conditions

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

Since the model monitors changes in the human population, the variables and the parameters are assumed to be positive for all $t \geq 0$. We can shows that all feasible solutions are uniformly bounded in positively invariant set $\Gamma = \left\{(S,E,I,P,T,A) \in \mathbb{R}_+^6 \mid N \leq \Lambda/\mu\right\}$. Since the model monitors changes in the human population, the variables and the parameters are assumed to be positive for all $t \geq 0$. We can shows that all feasible solutions are uniformly bounded in positively invariant set $\Gamma = \left\{(S,E,I,P,T,A) \in \mathbb{R}_+^6 \mid N \leq \Lambda/\mu\right\}$. The disease-free equilibrium (DFE) and the effective reproduction number of the system (1), given by [7],

$$E_0 = \left(\frac{\Lambda}{u_1 + \mu}, \frac{u_1 \Lambda}{\mu(u_1 + \mu)}, 0, 0, 0, 0\right). \tag{3}$$

$$R_e = \frac{\beta_1((1-\delta)u_1 + \mu)}{(u_1 + \mu)(\sigma_1 + \mu)} + \frac{\beta_2 \sigma_1((1-\delta)u_1 + \mu)}{(u_1 + \mu)(\sigma_1 + \mu)(\sigma_2 + u_2 + \mu)}. \tag{4}$$

The effective reproduction number shows the average number of new infections caused by a single HIV infected individual in a population which educational campaign and therapy programs is used to control strategies.

3. Analysis of Optimal Control

We apply control theory as a mathematical tool to make decision involving complex biological situations ([2]). To investigate the optimal level of efforts that would be needed to control the disease,

the control educational campaign (u_1) and antiretroviral therapy (u_2) are minimized subject to the system of equations (1) and formulate the objective functional as

$$J(u_1,u_2)=\min_{u_1,u_2}\int_0^{t_f}[w_1I+w_2P+w_3A+\tfrac{1}{2}(w_4u_1^2+w_5u_2^2)]\,dt \tag{5}$$

where w_1, w_2, w_3, w_4 and w_5 are the relative weights and help to balance each term in the integrand so that any of the terms do not dominate. t_f is the final time. Our aim is to minimize the objective function $J(u_1,u_2)$ given in (5) so that infected individuals in the asymptomatic stage $I(t)$, infected individuals in pre-AIDS stage $P(t)$, infected individuals with full-blown AIDS $A(t)$, and the cost of applying the control u_1 and u_2 can be minimized. So, we seek a set of optimal controls u_1^* and u_2^* such that

$$J(u_1^*,u_2^*)=\min\left\{J(u_1,u_2)\,\middle|\,u_1,u_2\in U\right\} \tag{6}$$

where $U=\left\{(u_1,u_2)\,\middle|\,0\le u_1\le 1,0\le u_2\le 1 \text{ for } t\in t_f\right\}$.

The necessary conditions that an optimal control problem must satisfy come from Pontryagin's Maximum Principle [9]. This principle converts the system of equations (1) and (5) into a problem of minimizing point-wise a Hamiltonian H, with respect to u_1 and u_2 as

$$\begin{aligned}H=\;&w_1I+w_2P+w_3A+\tfrac{1}{2}(w_4u_1^2+w_5u_2^2)+\lambda_S\left[\Lambda-\frac{(\beta_1I+\beta_2P)S}{S+E+I+P+T+A}-u_1S-\mu S\right]\\&+\lambda_E\left[u_1S-\frac{(1-\delta)(\beta_1I+\beta_2P)E}{S+E+I+P+T+A}-\mu E\right]+\lambda_I\left[\frac{(\beta_1I+\beta_2P)S}{S+E+I+P+T+A}+\frac{(1-\delta)(\beta_1I+\beta_2P)E}{S+E+I+P+T+A}-(\sigma_1+\mu)I\right]\\&+\lambda_P[\sigma_1I-(\sigma_2+u_2+\mu)P]+\lambda_T[u_2P-(\sigma+\mu)T]+\lambda_A[\sigma_2P+\sigma T-(\alpha+\mu)A].\end{aligned} \tag{7}$$

where $\lambda_S,\lambda_E,\lambda_I,\lambda_P,\lambda_T$ and λ_A are the adjoint variables. The adjoint differential equations are given by

$$\begin{aligned}\frac{d\lambda_S}{dt}&=-\frac{\partial H}{\partial S}=(\lambda_S-\lambda_I)\left[\frac{\beta_1I+\beta_2P}{S+E+I+P+T+A}-\frac{(\beta_1I+\beta_2P)S}{(S+E+I+P+T+A)^2}\right]\\&\quad+(\lambda_I-\lambda_E)\left[\frac{(1-\delta)(\beta_1I+\beta_2P)E}{(S+E+I+P+T+A)^2}\right]+(\lambda_S-\lambda_E)u_1-\lambda_S\mu\\\frac{d\lambda_E}{dt}&=-\frac{\partial H}{\partial E}=(\lambda_E-\lambda_I)\left[\frac{(1-\delta)(\beta_1I+\beta_2P)}{S+E+I+P+T+A}-\frac{(1-\delta)(\beta_1I+\beta_2P)}{(S+E+I+P+T+A)^2}\right]\\&\quad+(\lambda_I-\lambda_S)\left[\frac{(\beta_1I+\beta_2P)S}{(S+E+I+P+T+A)^2}\right]+\lambda_E\mu\\\frac{d\lambda_I}{dt}&=-\frac{\partial H}{\partial I}=-w_1+(\lambda_S-\lambda_I)\left[\frac{\beta_1S}{S+E+I+P+T+A}-\frac{(\beta_1I+\beta_2P)S}{(S+E+I+P+T+A)^2}\right]\\&\quad+(\lambda_E-\lambda_I)\left[\frac{(1-\delta)\beta_1E}{S+E+P+T+A}+\frac{(1-\delta)(\beta_1I+\beta_2P)E}{(S+E+P+T+A)^2}\right]+(\lambda_I-\lambda_P)\sigma_1+\lambda_I\mu.\\\frac{d\lambda_P}{dt}&=-\frac{\partial H}{\partial P}=-w_2+(\lambda_S-\lambda_I)\left[\frac{\beta_2S}{S+E+I+P+T+A}-\frac{(\beta_1I+\beta_2P)S}{(S+E+I+P+T+A)^2}\right]\\&\quad+(\lambda_E-\lambda_I)\left[\frac{(1-\delta)\beta_2E}{S+E+P+T+A}+\frac{(1-\delta)(\beta_1I+\beta_2P)E}{(S+E+P+T+A)^2}\right]+(\lambda_P-\lambda_A)\sigma_2\\&\quad+(\lambda_P-\lambda_T)u_2-\lambda_P\mu\end{aligned} \tag{8}$$

$$\frac{d\lambda_T}{dt} = -\frac{\partial H}{\partial T} = (\lambda_I - \lambda_S)\left[\frac{(\beta_1 I + \beta_2 P)S}{(S+E+I+P+T+A)^2}\right] + (\lambda_I - \lambda_E)\left[\frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{(S+E+P+T+A)^2}\right] + (\lambda_T - \lambda_A)\sigma + \lambda_T \mu$$

$$\frac{d\lambda_A}{dt} = -\frac{\partial H}{\partial A} = -w_3 + (\lambda_I - \lambda_S)\left[\frac{(\beta_1 I + \beta_2 P)S}{(S+E+I+P+T+A)^2}\right] + (\lambda_I - \lambda_E)\left[\frac{(1-\delta)(\beta_1 I + \beta_2 P)E}{(S+E+P+T+A)^2}\right] + \lambda_A(\alpha + \mu).$$

The transversality conditions are

$$\lambda_S(t_f) = 0, \lambda_E(t_f) = 0, \lambda_I(t_f) = 0, \lambda_P(t_f) = 0, \lambda_T(t_f) = 0, \text{ and } \lambda_A(t_f) = 0. \tag{8}$$

By the optimality condition, we have

$$\begin{aligned} \frac{\partial H}{\partial u_1} &= w_4 u_1 - \lambda_S S + \lambda_E S = 0 \quad \text{at} \quad u_1 = u_1^* \\ \frac{\partial H}{\partial u_2} &= w_5 u_2 - \lambda_P P + \lambda_T P = 0 \quad \text{at} \quad u_2 = u_2^* \end{aligned} \tag{9}$$

Hence solving for u_1^* and u_2^* we get

$$\begin{aligned} u_1^* &= \frac{(\lambda_S - \lambda_E)S^*}{w_4} \\ u_2^* &= \frac{(\lambda_P - \lambda_T)P^*}{w_5}. \end{aligned} \tag{10}$$

We can now impose the bounds $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$ on the controls to get

$$\begin{aligned} u_1^* &= \max\left\{0, \min\left(1, \frac{(\lambda_S - \lambda_E)S^*}{w_4}\right)\right\}, \\ u_2^* &= \max\left\{0, \min\left(1, \frac{(\lambda_P - \lambda_T)P^*}{w_5}\right)\right\}. \end{aligned} \tag{11}$$

4. Numerical Results

In this section, we simulated our model (1) are carried out using the set of parameters values given in Table 1.

Table 1. Parameter values for the model

Parameter	Values	Sources
β_1	0.86	[10]
β_2	0.5	Estimated
σ_1	0.198	[11]
σ_2	0.4621	[11]
σ	0.0001	[10]
δ	0.615	Estimated
μ	0.0196	[11]
α	0.0909	[11]
u_1	[0, 1]	Estimated
u_2	[0, 1]	Estimated
Λ	700	Estimated

Assume the weights at final time are being kept fixed as,

$$w_1 = 10, w_2 = 10, w_3 = 50, w_4 = 200 \text{ and } w_5 = 1000 \quad (12)$$

and the initial conditions is below

$$S(0) = 25.000.000,\ I_1(0) = 200.000, I_2(0) = 25000, T(0) = 5000 \text{ and } A(0) = 2000 \quad (13)$$

to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS in a population. Using model parameter values shown in Table 1 is obtained the effective reproduction numbers , $R_e = 1.746$. Because $R_e > 1$, the HIV/AIDS infection still exists within the population.

The results in Figure 1(a)-(c) show a significant difference in the numbers of HIV-positive individuals in the asymptomatic stage of HIV infection (I), the number of HIV-positive individuals in pre-AIDS stage but not receiving antiretroviral therapy (P), and the number of individuals with full-blown AIDS but not receiving antiretroviral therapy (A), with optimal strategy compared to the numbers in the case without control.

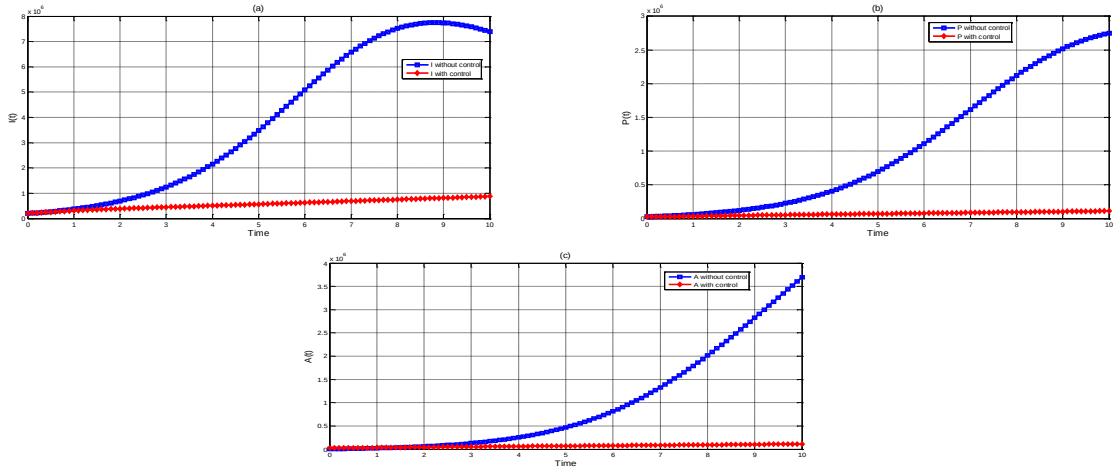

Figure 1. The effect of educational campaigns control (u_1) and antiretroviral therapy (u_2) on the spread of HIV/AIDS

The control profile of the combination of the two kinds of the control strategies is shown in Figure 2. The control of educational campaigns u_1 is at the upper bound before dropped slowly to the lower bound in the final time (t_f=10) while the antiretroviral therapy control u_2 is at the upper bound then decreases gradually to zero at the final time.

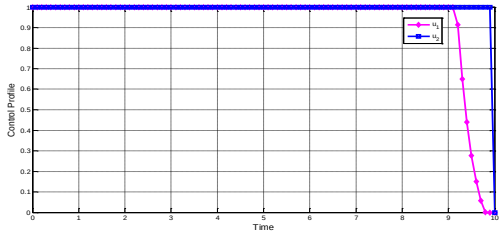

Figure 2. The optimal control profiles of u_1 and u_2

5. Conclusion

In paper, a deterministic model for assess effect of educational campaign on susceptible and antiretroviral therapy on pre-AIDS infections. We proved the existence and uniqueness of the optimal control and characterized the controls using Pontryagin's Maximum Principle. The numerical simulation of both the systems i.e. with control and without control, shows that the combination of the two strategies helps to reduce a significant difference in the number of infected individuals in the

asymptomatic stage of HIV infection, the number of individuals in pre-AIDS stage, and the number of individuals with full-blown AIDS.

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