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SIGNIFICANT PARAMETERS IN THE HIV/AIDS TRANSMISSION AND CONTROL OPTIMAL PROBLEM

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Abstract. This article studies how to figure out important parameters in the HIV/AIDS model using sensitivity analysis. The parameters that arise in the basic-reproduction number (R_0) are calculated to get the sensitivity index. We get two significant parameters, Ω and β_2, the recruitment rate of uneducated subpopulation and transmission rate from uneducated individual to infected individual taking ARV, respectively. These parameters give a higher contribution to the transmission of HIV. Furthermore, we conduct the problem of optimal control on the mathematical model of the spread of HIV/AIDS to minimize HIV-infected individuals. We propose two controls, public education and ARV treatment. We establish the existence of an optimal control pair. The Pontryagin minimum principle is used to obtain the best conditions to control the disease transmission. Numerical simulations were conducted to get the results of the analysis. The results show that a combination of public education and ARV treatment helps to control the spread of HIV disease and to get the minimum cost related to the realization of controls.

1. Introduction

HIV (Human Immunodeficiency Virus) caused a disease of the immune system called AIDS (Acquired Immune Deficiency Syndrome) [2],[6]-[9],[21]. The AIDS epidemic has become a global health problem (including in Indonesia) because AIDS can lead to mortality/death [3],[14]-[16]. HIV is transmitted through contaminated blood transfusions, unsafe sex or sex with multiple partners, contaminated syringes, and from mother to child [1],[5],[20]. Since 1980, the AIDS epidemic has killed more than

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30 million people. It has become a worldwide issue. In 2010, there were 34 million individuals suffering HIV, and about 1.8 million individuals deaths were caused by AIDS.

WHO states that education and treatment are two important steps that must be taken to prevent epidemics and control infectious diseases [6],[10]. Biomedical is applied as prevention, such as early identification and medications. It can help reduce the number of new infections [10]. The treatments given to the infected individual resulted in more individuals surviving with HIV than no treatment.

Human behavior in the spread and control of the disease is also important. Changes in people's behavior towards prevention efforts, for example, public education, significantly affect the dynamics of the epidemic [10]. Therefore, the WHO supplies education on how dangerous this disease is and supplies controls. An antiretroviral is applied as a treatment to the HIV/AIDS model [8][24].

Mathematical modeling of epidemiological problems has become increasingly important in the management and control of epidemics. Epidemiological mathematical models are typically in the form of nonlinear ordinary differential equations (NODEs), it can be challenging to overcome NODEs analytically in most circumstances [23]. Mathematical models give valuable information about disease transmission dynamics and insights for deciding control strategies. Recently, mathematical models have been developed to respond to different infectious diseases. SIR is the basic model, as a basic framework for further research in epidemic modelling. The original model by Kermack-Mckendrick attracted epidemiologists to study the dynamics of epidemic transmission. Various modifications have been developed to accommodate distinct aspects of the epidemic.

In [22] was shown that the effect of public education was much more effective to reduce the number of infected individuals. The method that was used to solve the control problem was the Pontryagin minimum principle. Furthermore, in [12],[21] investigated HIV disease control in a human population by education and treatment. The study found that combining these controls could help minimize the spread of disease and control costs.

In this study, we use sensitivity analysis to evaluate crucial parameters in the HIV/AIDS formula. Understanding how the state variable changes in response to small changes in the initial data, parameters (or constant lags) appearing in the model, and control functions can provide insights into the model's behavior and aid in the modeling process. Sensitivity analysis can help simplify complex models by identifying the factors and parameters that influence the system's key behavior. As a result, any simplified model must include it. For example, if it is evident that a certain parameter has no effect on the solution, it may be possible to eliminate it from the modeling process at some stage, according to [25]. The greater the relative sensitivity, the more essential the model input parameter [26]. The sensitivity index will be used to determine parameters that appear in the basic reproduction number. The sensitivity index will be computed using the Next Generation Matrix after citing [4],[18],[19]. We can determine which parameters contribute significantly to HIV transmission using the sensitivity index. This information may aid in the control of HIV transmission.

Furthermore, we propose an optimal control problem to minimize the HIV-infected sub-populations. We propose two controls in the model, public education and ARV treatment as control strategies to minimize HIV/AIDS-infected individuals and costs related to the control strategies. We use the Pontryagin minimum principle to find the best conditions to control disease transmission. For numerical simulations, we also apply the back-and-forward sweep method.

2. HIV/AIDS Transmission Formula

The HIV/AIDS formula with an educated subpopulation is adopted from [6]. The population is divided into seven subpopulations are $S(t)$, $E(t)$, $I_1(t)$, $I_2(t)$, $T(t)$, $A(t)$ and $R(t)$. $S(t)$ is susceptible/un-educated subpopulation, $E(t)$ is educated subpopulation, $I_1(t)$ is HIV positive subpopulation taking ARV, $I_2(t)$ is HIV infected subpopulation not taking ARV, $A(t)$ is full-blown AIDS subpopulation not taking treatment, $T(t)$ is subpopulation with ARV, and $R(t)$ is subpopulations who change unhealth sexual habits.

The number of susceptible people S grows with the rate of recruitment Ω and drops as a result of interactions with I_1 and I_2. This subpopulation is declining due to the natural death rate d and HIV/AIDS education at the rate η. Uneducated people modify their habits with the rate μ becomes educated people decrease susceptible persons. As a result, the dynamic of uninformed or susceptible individuals is provided by

$$\frac{dS}{dt} = \Omega - \beta_1 S I_1 - \beta_2 S I_2 - (\eta + \mu + d)S.$$

The number of educated people (E) increases as susceptible people get education at a rate of η. The natural death rate d decreases the quantity of educated people (E). The following is the dynamic of educated people.

$$\frac{dE}{dt} = \eta S - dE.$$

The number of HIV-positive people on ARV (I_1) increases as a result of meets with those without education (S), with a transmission rate of β_1. A successful therapy causes an increase in I_1 at the rate of α_1. The number of patients with HIV who are taking ARV (I_1) on the other hand is decreasing due to the natural death rate d. Individuals with HIV who are on ARV (I_1) will have the worst health, necessitating medical therapy at a k_1 rate. The dynamic of HIV patients taking ARV (I_1) is provided by

$$\frac{dI_1}{dt} = \beta_1 S I_1 + \alpha_1 T - (k_1 + d)I_1.$$

Following that, interactions with illiterate people (S) increase the number of people with HIV who are not taking ARV (I_2), with a transmission rate of β_2. The natural death rate d, on the other hand, reduces the number of people with HIV who do not take ARV (I_2). Individuals with HIV who do not use ARV (I_2) have the worst health and develop full-blown AIDS (A) at a rate of k_2, necessitating medical treatment at a rate of k_3. The dynamic of HIV patients who do not take ARV (I_2) is provided by

$$\frac{dI_2}{dt} = \beta_2 S I_2 - (k_2 + k_3 + d)I_2.$$

The number of people receiving ARV treatment (T) rises in tandem with the progression rates of people with HIV who are using ARV (I_1) and those who are not taking ARV (I_2) and then obtain treatment. In turn, successful therapy adds to a

drop in T at a rate of α_1, then (T) individuals become the I_1 individuals. Treatment failure causes a T decline at a rate of α_2, T individuals become the A individuals. It means that those receiving therapy will develop full-blown AIDS (A). Both the natural death rate d and the disease-related death rate for treatment individuals δ_2 contribute to the decrease in treatment individuals. The dynamic of individuals receiving ARV treatment (T) is shown.

$$\frac{dT}{dt} = k_1 I_1 + k_3 I_2 - (\alpha_1 + \alpha_2 + \delta_2 + d)T.$$

The number of individuals with AIDS who do not receive any therapy (full-blown AIDS) (A) rises in lockstep with the progression rate of people with HIV who do not take ARV (I_2) and treatment failure at a rate of α_2. The disease-related death rate α_1 for AIDS (A) patients, on the other hand, and the natural death rate d both contribute to the declining number of AIDS (A) patients. The dynamic of people who are not receiving ARV treatment (A) is provided by

$$\frac{dA}{dt} = k_2 I_2 + \alpha_2 T - (\delta_1 + d)A.$$

The final equation is the rate change of R individuals, susceptible individuals (S) who adopt and maintain safe sexual habits for the rest of their lives at the rate of μ. At the natural death rate d, this class decreases. The recovered individual R dynamics is provided by

$$\frac{dR}{dt} = \mu S - dR.$$

TABLE 1. Parameter description [6]

Symbol	Description	Value
Ω	The rate of recruitment	0.55
μ	The rate of S to R	0.03
β_1	Transmission rate from S to I_1	0.0023
β_2	Transmission rate from S to I_2	0.0033
d	The human natural death rate	0.0196
η	Education rate	0.01
k_1	Rate of progression from I_1 to T	0.0498
k_2	Rate of progression from I_2 to A	0.008
k_3	Rate of progression from I_2 to T	0.05
α_1	Fraction of successful treatment	0.02
α_2	Fraction of failure of treatment	0.05
δ_1	Death rate related to disease for AIDS individuals	0.0909
δ_2	Death rate related to disease for Treatment individuals	0.0667

Furthermore, a SEI_1I_2TAR model is presented in a non-linear system of differential equations as follows.

$$
\begin{aligned}
\frac{dS}{dt} &= \Omega - \beta_1 S I_1 - \beta_2 S I_2 - (\eta + \mu + d)\, S, \\
\frac{dE}{dt} &= \eta S - dE, \\
\frac{dI_1}{dt} &= \beta_1 S I_1 + \alpha_1 T - (k_1 + d)\, I_1, \\
\frac{dI_2}{dt} &= \beta_2 S I_2 - (k_2 + k_3 + d)\, I_2, \\
\frac{dT}{dt} &= k_1 I_1 + k_3 I_2 - (\alpha_1 + \alpha_2 + \delta_2 + d)\, T, \\
\frac{dA}{dt} &= k_2 I_2 + \alpha_2 T - (\delta_1 + d)\, A, \\
\frac{dR}{dt} &= \mu S - dR.
\end{aligned}
\tag{2.1}
$$

Table 1 describes the parameters in Eq. (2.1). Eq. (2.1) contains two equilibrium points: free-infection equilibrium and endemic equilibrium. A constant solution to a differential equation is an equilibrium point. Simply setting the left side of Eq. (2.1) to zero gave an equilibrium point. The equilibrium point for free-infection is

$$\begin{aligned} E^0 &= (S^0, E^0, I_1^0, I_2^0, T^0, A^0, R^0), \\ &= \left(\frac{\Omega}{\eta+\mu+d}, \frac{\eta\Omega}{d\,(\eta+\mu+d)}, 0, 0, 0, 0, \frac{\mu\Omega}{d\,(\eta+\mu+d)} \right). \end{aligned} \tag{2.2}$$

This condition states that there is no HIV infection in a population. The second equilibrium point is called an endemic equilibrium point $E^* = (S^*, E^*, {I_1}^*, {I_2}^*, T^*, A^*, R^*)$ can be written as follows

$$\begin{aligned} S^* &= \frac{c}{\beta_2}, \\ E^* &= \frac{\eta c}{\beta_2 d}, \\ {I_1}^* &= \frac{ac\alpha_1 k_3 (R_0 - 1)}{c\beta_1\alpha_1 k_3 I_1 + c\,(\beta_2 be - \alpha_1\beta_2 k_1 - e\beta_1 c)}, \\ {I_2}^* &= \frac{(\beta_2 be - \alpha_1\beta_2 k_1 - e\beta_1 c)\,{I_1}^*}{\alpha_1\beta_2 k_3}, \\ T^* &= \frac{(\beta_2 b - \beta_1 c)\,{I_1}^*}{\alpha_1\beta_2}, \\ A^* &= \frac{(k_2\,(\beta_2 be - \alpha_1\beta_2 k_1 - e\beta_1 c) + \alpha_2 k_3\,(\beta_2 be - e\beta_1 c))\,{I_1}^*}{f\alpha_1\beta_2 k_3}, \\ R^* &= \frac{\mu c}{\beta_2 d}, \end{aligned} \tag{2.3}$$

where $a = \eta + \mu + d$, $b = k_1 + d$, $c = k_2 + k_3 + d$, $e = \alpha_1 + \alpha_2 + \delta_2 + d$, and $f = \delta_1 + d$. In the numerical simulation, the solution of Eq. (2.1) will be shown to converge to the equilibrium points.

The basic-reproductive number of Eq. (2.1) can be found using the method called Next Generation Matrix [11]. The basic reproduction numbers provide the threshold of infected individuals in the model, whether they are present or die out. The Next Generation Matrix method's constituent components are only infected population groups. ${x_i}' = ({I_1}', {I_2}')^T$ is defined so that the system (2.1) can be written as

$$\begin{pmatrix} x_1' \\ x_2' \end{pmatrix} = \begin{pmatrix} F_1 \\ F_2 \end{pmatrix} - \begin{pmatrix} V_1 \\ V_2 \end{pmatrix},$$

where

$$F = \begin{pmatrix} F_1 \\ F_2 \end{pmatrix} = \begin{pmatrix} \beta_1 S I_1 \\ \beta_2 S I_2 \end{pmatrix},$$

and

$$V = \begin{pmatrix} V_1 \\ V_2 \end{pmatrix} = \begin{pmatrix} bI_1 - \alpha_1 T \\ cI_2 \end{pmatrix}.$$

The Next Generation Matrix is obtained as follows

$$R = \left(DF\left(E^0\right)\right)\left(DV(E^0)\right)^{-1} = \begin{pmatrix} \frac{\beta_1 S^0}{b} & 0 \\ 0 & \frac{\beta_1 S^0}{b} \end{pmatrix},$$

where $DF(E^0)$ and $DV(E^0)$ is partial derivative of matrix F and V respectively, after substituting the free-disease equilibrium point E^0 to them. The basic reproduction number (R_0) is obtained from the spectral radius of the R or the largest modulus of the eigenvalues of the matrix R. The basic-reproduction number (R_0) is

$$R_0 = \frac{\beta_2 \Omega}{(\eta + \mu + d)(k_2 + k_3 + d)}. \tag{2.4}$$

There are seven parameters that contribute to the spread of HIV/AIDS. We will investigate which parameters give a significant contribution to the model through the sensitivity analysis in the next section.

3. Sensitivity Analysis

To decide the parameter that has the most significant contribution to HIV/AIDS transmission, we conduct an analysis of sensitivity. First, we should calculate the sensitivity index of each parameter in basic reproduction number (R_0). This can help to determine proper control that is suitable to prevent the epidemic [18]. The sensitivity analysis is the method introduced by [4]. We use the parameter values

described in Table 1. We gained a sensitivity index as follows.

$$C_{\beta_2}^{R_0} = \frac{\partial R_0}{\partial \beta_2} \times \frac{\beta_2}{R_0} = 1,$$

$$C_{\Omega}^{R_0} = \frac{\partial R_0}{\partial \Omega} \times \frac{\Omega}{R_0} = 1,$$

$$C_{\eta}^{R_0} = \frac{\partial R_0}{\partial \eta} \times \frac{\eta}{R_0} = -\frac{\eta}{\eta + \mu + d} = -0.6685,$$

$$C_{\mu}^{R_0} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\mu}{\eta + \mu + d} = -0.2005,$$

$$C_{d}^{R_0} = \frac{\partial R_0}{\partial d} \times \frac{d}{R_0} = -\frac{d\,(k_2 + k_3 + 2d + \eta + \mu)}{(k_2 + k_3 + d)\,(\eta + \mu + d)} = -0.3836,$$

$$C_{k_2}^{R_0} = \frac{\partial R_0}{\partial k_2} \times \frac{k_2}{R_0} = -\frac{k_2}{k_2 + k_3 + d} = -0.1031,$$

$$C_{k_3}^{R_0} = \frac{\partial R_0}{\partial k_3} \times \frac{k_3}{R_0} = -\frac{k_3}{k_2 + k_3 + d} = -0.6443,$$

where sensitivity index values have positive and negative signs. Parameters with positive index are Ω and β_2. It means that R_0 will increase when the value of parameters is increased. This can cause HIV transmission to increase, and vice versa. In Table 2, we order the sensitivity index from the most sensitive parameter to the less sensitive parameter. It is worth noting that the higher the relative sensitivity, the more essential the model's input parameter [26].

Furthermore, we design control strategies consisting of education and ARV treatment to the model and solve it by using the Pontryagin minimum principle in the next section.

TABLE 2. Order of sensitivity index values of parameters.

No	Parameter	Sensitivity index
1	Ω	1
2	β_2	1
3	η	-0.6685
4	k_3	-0.6443
5	d	-0.3836
6	μ	-0.2005
7	k_2	-0.1031

4. Optimal Control Problem

The problem of optimal control of the HIV/AIDS model is developed from the SEI_1I_2TAR model. We add two-control variables in the model, public education ($u_1(t)$) given to the susceptible/un-educated individual (S) and ARV treatment ($u_2(t)$) given to full-blown AIDS (I_2) such that we have

$$\begin{aligned}
\frac{dS}{dt} &= \Omega - \beta_1 S I_1 - \beta_2 S I_2 - (u_1 + \mu + d)\, S, \\
\frac{dE}{dt} &= u_1 S - dE, \\
\frac{dI_1}{dt} &= \beta_1 S I_1 + \alpha_1 T - (k_1 + d)\, I_1 + u_2 I_2, \\
\frac{dI_2}{dt} &= \beta_2 S I_2 - (k_2 + k_3 + d)\, I_2 - u_2 I_2, \\
\frac{dT}{dt} &= k_1 I_1 + k_3 I_2 - (\alpha_1 + \alpha_2 + \delta_2 + d)\, T, \\
\frac{dA}{dt} &= k_2 I_2 + \alpha_2 T - (\delta_1 + d)\, A, \\
\frac{dR}{dt} &= \mu S - dR.
\end{aligned} \tag{4.1}$$

In this problem, ARV treatment is the function of time where previously it is a constant value in the SEI_1I_2TAR model. The optimal control study aims to minimize the number of I_2 and the cost associated with controlling. The objective function is

$$J(u_1, u_2) = \int_0^{t_f} (w_1 u_1^2 + w_2 u_2^2 + w_3 I_2) dt, \tag{4.2}$$

with constraints in the form of a system of Eq. (4.1). The term $w_1u_1^2 + w_2u_2^2$ is the cost associated with public education and ARV treatment, respectively. w_3 is a positive weight to balance the load while w_3I_2 represents the infection cost and t_f is the final time. Optimal controls $u_1^*(t)$ and $u_2^*(t)$ that fulfil the objective function must satisfy

$$J(u_1^*, u_2^*) = \min_{(u_1, u_2 \in U)} J(u_1, u_2),$$

with $U = \{(u_1, u_2) | 0 \leq u_i \leq 1, i = 1, 2, t \in [t_0, t_f]\}$.

We use the Existence Theorem in [27] and [28] to show the existence of the best solution of (4.1).

Invariant region. If the initial value of the system's solution is positive, it must necessarily stay positive for all $t > 0$.

Theorem 4.1. *All possible sets of system* (4.1) *are confined by the region* $D = \{(S, E, I_1, I_2, A, T, R) \in \Re^7 : S + E + I_1 + I_2 + A + T + R \leq \Omega/d\}$.

Proof. From system equation (4.1),

$$\dot{N} = \dot{S} + \dot{E} + \dot{I}_1 + \dot{I}_2 + \dot{A} + \dot{T} + \dot{R} = \Omega - dN(t) - \delta_1 A - \delta_2 T,$$

indicates that

$$\dot{N} \leq \Omega - dN(t),$$

as a result of which

$$N \leq \Omega/d + N(0)e^{-dt},$$

where $N(0)$ is the total subpopulation's beginning value. Then

$$\lim_{t\to\infty} \sup N(t) \leq \Omega/d,$$

we get $S + E + I_1 + I_2 + A + T + R \leq \Omega/d$ as a result. The area denoted by the set $D = \{(S, E, I_1, I_2, A, T, R) \in \Re^7 : S + E + I_1 + I_2 + A + T + R \leq \Omega/d\}$, which is a positivity invariant set for the system (4.1), is obtained for the study of the model (4.1). It is necessary to take into account the dynamics of system (4.1) on non-negative solutions of the set D.

We concur that the supersolutions of the system are

$$\dot{S} = \Omega,$$

$$\dot{E} = u_1,$$

$$\dot{I}_1 = \beta_1 S I_1 + \alpha_1 T + u_2 I_2,$$

$$\dot{I}_2 = \beta_2 S I_2,$$

$$\dot{A} = k_2 I_2 + \alpha_2 T,$$

$$\dot{T} = k_1 I_1 + k_3 I_2,$$

$$\dot{R} = \mu S,$$

which have a finite time interval, and sub-solutions are zero. □

Existence of optimal control.

Theorem 4.2. *Given the objective functional in* (4.1)*, there exists an optimal control* $u_i(t) * inU$*,* $i = 1, 2$ *such that the equation* (4.1) *meets the conditions listed below.*

(1) *The state variables (*$S(t)$*,* $I_1(t)$*,* $I_2(t)$*,* $A(t)$*,* $T(t)$*, and* $R(t)$*, as well as the control set* U*, are not empty.*
(2) U *is a convex and closed control set.*
(3) *The right-hand side of the state system* (4.1) *is limited above by a linear function made up of state and control variables.*
(4) *The objective functional's integrand in* (4.2) *is convex on* U *and is constrained below by* $-v_2 + v_1 u_i^2$*, where* $v_1, v_2 > 0$*.*

Proof.

1. Employing Theorems (4.1) and (4.2), we can show that the system (4.1) has bounded coefficients and solutions on the finite time range $0 < t < \infty$. To demonstrate the existence of the system's solution (4.1), [27] and [28] can be cited.

2. By definition, the control set U is closed and convex.

3. The system's right-hand side (4.1) must be continuous. The denominators of all fractions on the system's right side are all positive entities. We let $\vec{G}(t, \vec{x})$ be the system's right hand side (4.1) without a control variable.

$$\vec{F}(t, \vec{x}) = \vec{G}(t, \vec{x}) + \begin{bmatrix} \Omega - u_1 S & u_1 S & u_2 I_2 & -u_2 I_2 & 0 & 0 & 0 \end{bmatrix}^T,$$

with $\vec{x} = \begin{bmatrix} S & E & I_1 & I_2 & A & T & R \end{bmatrix}^T$. Using the boundedness of the solutions, we get

$$|\vec{F}(t, \vec{x})| \leq \left| \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_1 S & 0 & 0 & \alpha_1 & 0 \\ 0 & 0 & 0 & \beta_2 S & 0 & 0 & 0 \\ 0 & 0 & k_1 & k_3 & 0 & & 0 \\ 0 & 0 & 0 & k_2 & 0 & \alpha_2 & 0 \\ \mu & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} S \\ E \\ I_1 \\ I_2 \\ A \\ T \\ R \end{bmatrix} \right| + \left| \begin{bmatrix} \Omega \\ u_1 S \\ u_2 I_2 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \right| \leq v_1(|\vec{x}| + |\vec{u}|),$$

where v_1 is determined by the system's coefficients. As a result, the sum of the state and control variables bounds the right side of the state equation from above.

4. The functional J's integrand $h(u_i)$ is convex on U. When the following condition is met, the function $h(u_i)$ is convex in the interval $u_i \epsilon [0,1], i = 1,2$.

$$h(\theta u_1 + (1-\theta)u_2) \leq \theta h(u_1) + (1-\theta)h(u_2). \tag{4.3}$$

For an arbitrary $u_1, u_2 \epsilon [0,1]$ with a given function

$$h(u_i) = w_1 u_1^2 + w_2 u_2^2 + w_3 I_2 + w_4 A,$$

It is comparable to writing the left side of equation (4.3) as follows.

$$h(\theta u_1 + (1-\theta)u_2) = (w_1 + w_2)(\theta u_1 + (1-\theta)u_2)^2 + w_3 I_2 + w_4 A, \tag{4.4}$$

and the right hand side of equation (4.3) is

$$\theta h(u_1) + (1-\theta)h(u_2) = (w_1 + w_2)(\theta u_1^2 + (1-\theta)u_2^2) + w_3 I_2 + w_4 A. \tag{4.5}$$

By substituting equations (4.4) and (4.5) into (4.3), it yields

$$(\theta u_1 + (1-\theta)u_2)^2 \leq (\theta u_1^2 + (1-\theta)u_2^2). \tag{4.6}$$

We may express the equation of the left-hand side of (4.6) using simple algebra as follows.

$$(\theta u_1 + (1-\theta)u_2)^2 = ((u_1 - u_2)\theta)^2 + u_2^2 - 2u_2^2\theta(1 - u_1/u_2), \tag{4.7}$$

and the right-hand side of (4.6) as follows

$$(\theta u_1^2 + (1-\theta)u_2^2) = \theta u_1^2 + u_2^2 - \theta u_2^2.$$

By choosing, $\theta \epsilon [0,1]$, and u_1, $u_2 \epsilon [0,1]$, we agree $((u_1 - u_2)\theta)^2 \leq \theta u_1^2$ and obviously $-2u_2^2\theta(1 - u_1/u_2) \leq (-\theta u_2^2)$, hence equation (4.7) can be written as

$$\begin{aligned}(\theta u_1 + (1-\theta)u_2)^2 &= ((u_1 - u_2)\theta)^2 + u_2^2 - 2u_2^2\theta(1 - u_1/u_2) \\ &\leq \theta u_1^2 + u_2^2 - \theta u_2^2, = \theta u_1^2 + (1-\theta)u_2^2. \end{aligned} \tag{4.8}$$

We can deduce from equation (4.8) that the integrand $h(u_i)$ of functional J is convex on U.

Following that, we shall show that the integrand $h(u_i)$ of functional J is bounded below by $-v_2 + v_1 u_i^2$ for $v_1, v_2 > 0$, $i = 1, 2, 3, 4$, and $\vec{u} = u_1, u_2$. If $v_1 > \epsilon/2$, and remember that I_2 and A are bounded in the interval $[0, 1]$, we obtain

$$I_2 + A + \frac{\epsilon}{2}\bar{u}^2 \geq \frac{\epsilon}{2}\bar{u}^2 \geq -v_2 + \frac{\epsilon}{2}u_i^2,$$

which we can show that the functional J integrand $h(u_i)$ is constrained from below by $-v_2 + v_1 u_i 2$.

Finally, we conclude that the system can be controlled optimally.

□

Necessary optimality conditions. The Minimum Pontryagin Principle is used to determine the best possible control in the system (4.1) as necessary conditions. The Hamilton function is defined as follows.

$$H = f\left(t, \vec{x}, \vec{u}\right) + \sum_{i=1}^{7} \lambda_i g_i\left(t, \vec{x}, \vec{u}\right),$$

where λ_i is the co-state or adjoint variables, and g_i is the right-hand side of Eq. (4.1). The Hamiltonian function is written as follows

$$\begin{aligned} H &= w_1 u_1^2 + w_2 u_2^2 + w_3 I_2 + \lambda_1\left(\Omega - \beta_1 S I_1 - \beta_2 S I_2\right) - \lambda_1\left(u + \mu + d\right) S \\ &\quad + \lambda_2\left(u_1 S - dE\right) + \lambda_3\left(\beta_1 S I_1 + \alpha_1 T - \left(k_1 + d\right) I_1 + u_2 I_2\right) \\ &\quad + \lambda_4\left(\beta_2 S I_2 - \left(k_2 + k_3 + d\right) I_2 - u_2 I_2\right) + \lambda_5\left(k_1 I_1 + k_3 I_2 - \left(\alpha_1 + \alpha_2 + \delta_2 + d\right) T\right) \\ &\quad + \lambda_6\left(k_2 I_2 + \alpha_2 T - \left(\delta_1 + d\right) A\right) + \lambda_7\left(\mu S - dR\right). \end{aligned}$$

The optimal system is obtained when the Hamiltonian function satisfies the conditions as follows:

$$
\begin{aligned}
\frac{dS}{dt} &= \tfrac{\partial H}{\partial \lambda_1} &&= \Omega - \beta_1 S I_1 - \beta_2 S I_2 - (u_1 + \mu + d)\, S, \\
\frac{dE}{dt} &= \tfrac{\partial H}{\partial \lambda_2} &&= u_1 S - dE, \\
\frac{dI_1}{dt} &= \tfrac{\partial H}{\partial \lambda_3} &&= \beta_1 S I_1 + \alpha_1 T - (k_1 + d)\, I_1 + u_2 I_2, \\
\frac{dI_2}{dt} &= \tfrac{\partial H}{\partial \lambda_4} &&= \beta_2 S I_2 - (k_2 + k_3 + d)\, I_2 - u_2 I_2, \\
\frac{dT}{dt} &= \tfrac{\partial H}{\partial \lambda_5} &&= k_1 I_1 + k_3 I_2 - (\alpha_1 + \alpha_2 + \delta_2 + d)\, T, \\
\frac{dA}{dt} &= \tfrac{\partial H}{\partial \lambda_6} &&= k_2 I_2 + \alpha_2 T - (\delta_1 + d)\, A, \\
\frac{dR}{dt} &= \tfrac{\partial H}{\partial \lambda_7} &&= \mu S - dR.
\end{aligned}
\tag{4.9}
$$

with the initial condition is $S(0) \geq 0, E(0) \geq 0, I1(0) \geq 0, I2(0) \geq 0, A(0) \geq 0, T(0) \geq 0$ and $R(0) \geq 0$. Eq. (4.9) is called a state equation. Next, co-state equations are obtained as follows

$$
\begin{aligned}
\frac{d\lambda_1}{dt} = \frac{\partial H}{\partial S} &= \lambda_1 \left(\beta_1 I_1 + \beta_2 I_2 + u_1 + \mu + d\right) - \lambda_2 u_1 - \lambda_3 \beta_1 I_1 - \lambda_4 \beta_2 I_2 - \lambda_7 \mu, \\
\frac{d\lambda_2}{dt} &= \frac{\partial H}{\partial E} = \lambda_2 d, \\
\frac{d\lambda_3}{dt} &= \frac{\partial H}{\partial I_1} = \left(\lambda_1 - \lambda_3\right) \beta_1 S + \lambda_3 \left(k_1 + d\right) - \lambda_5 k_1, \\
\frac{d\lambda_4}{dt} = \frac{\partial H}{\partial I_2} &= \left(\lambda_1 - \lambda_4\right) \beta_2 S + \left(\lambda_4 - \lambda_3\right) u_2 + \lambda_4 \left(k_2 + k_3 + d\right) - \lambda_5 k_3 - \lambda_6 k_2 - w_3, \\
\frac{d\lambda_5}{dt} &= \frac{\partial H}{\partial T} = \lambda_5 \left(\alpha_1 + \alpha_2 + \delta_2 + d\right) - \lambda_3 \alpha_1 - \lambda_6 \alpha_2, \\
\frac{d\lambda_6}{dt} &= \frac{\partial H}{\partial A} = \lambda_6 \left(\delta_1 + d\right), \\
\frac{d\lambda_7}{dt} &= \frac{\partial H}{\partial R} = \lambda_7 d.
\end{aligned}
\tag{4.10}
$$

with transversal conditions $\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = \lambda_7(t_f) = 0$. The stationary condition is $\partial H/\partial u_i = 0,\ i = 1, 2$. From stationery

condition, we obtain the optimal control u_1^* and u_2^* as follows

$$u_1^* = \max\left\{0, min\left(\frac{(\lambda_1 - \lambda_2)\, S^*}{2w_1}, 1\right)\right\},$$
$$u_2^* = \max\left\{0, \min\left(\frac{(\lambda_4 - \lambda_3)\, I_2^*}{2w_2}, 1\right)\right\}. \tag{4.11}$$

Next, we derive the second derivatives of the Hamiltonian equation with respect to u_1 and u_2, $\frac{\partial^2 H}{\partial u_1^2} = 2w_1 > 0$ and $\frac{\partial^2 H}{\partial u_1^2} = 2w_2 > 0$. Hence, we are sure that this is a minimization problem. Finally, the numerical solution of the optimal system is obtained by substituting Eq. (4.11) into Eq. (4.9) and (4.11). An interpretation of the control strategies is given in Section 5.

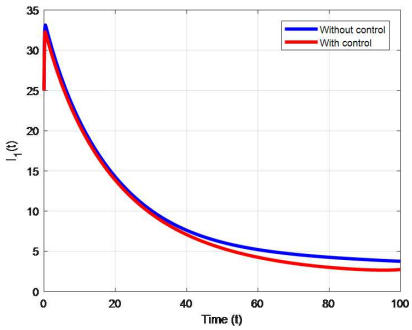
5. Numerical Simulation

Using the backward-and-forward sweep method, we numerically solve the optimal control problem. The co-state variables are approximated using the same technique as the state variables, but with a backward step, using the Runge-Kutta method $O(h^4)$ to approach the state variables. Applying the strategy involves citing [13] and [19]. Three strategies are also created by us for the model.

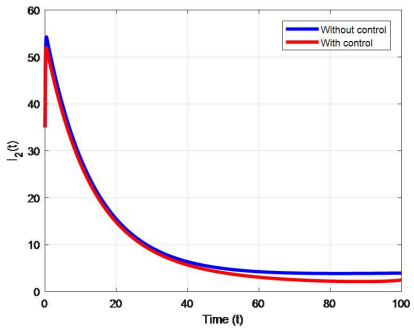
- Strategy I: Public education (u_1) is given to the susceptible/un-educated individual (S).
- Strategy II: ARV Treatment (u_2) is given to full-blown AIDS (I_2).
- Strategy III: Combination of public education (u_1) and ARV treatment (u_2).

We use time interval $t \in [0, 100]$, and the weights in the objective function J in Eq. (4.2) are $w_1 = 0.4, w_2 = 0.01$, and $w_3 = 1$, respectively. The parameter values are presented in Table 2, and the initial value is (S, E, I_1, I_2, T, A, R) = (30, 10, 25, 35, 20, 16, 50). The public education (u_1) is considered to increase the objective function J and ignore the control (u_2) by setting it to zero. Figure 1 shows that public education (u_1) decreases I_1 and I_2. However, the contribution of public education (u_1) is not enough to decrease the individual in I_1 and I_2.

The second strategy is used by applying the ARV treatment (u_2) to the objective function J, while the public education (u_1) is set to zero. As shown in Figure 1, the obtained results show a fairly significant difference in (I_1, I_2) with control against

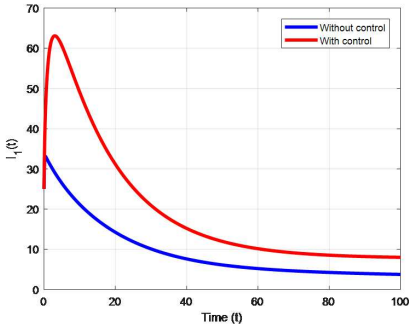


(A) HIV-positive subpopulation taking ARV

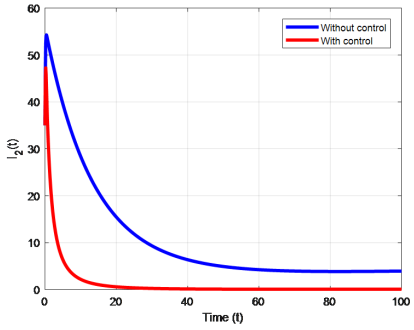


(B) HIV-positive subpopulation not taking ARV

FIGURE 1. Strategy I: The effect of public education (u_1) on the spread of HIV/AIDS.



(A) HIV-positive subpopulation taking ARV

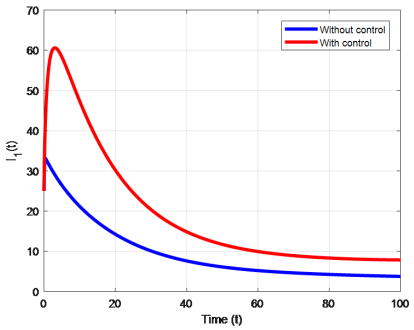


(B) HIV-positive subpopulation not taking ARV

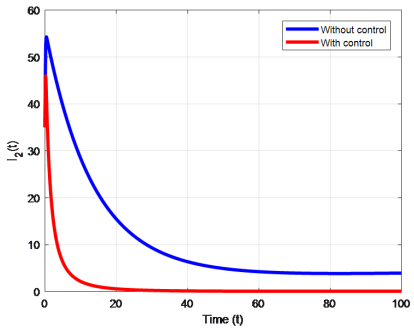
FIGURE 2. Strategy II: The effect of ARV treatment (u_2) on the spread of HIV/AIDS.

(I_1, I_2) without control. Furthermore, Figure 2a shows that the HIV-positive subpopulation taking ARV increases due to controls, and the opposite result can be seen from cases without control. Figure 2b shows that the HIV-positive subpopulation not taking ARV decreases to zero when the ARV treatment is applied.

The final strategy is a combination between public education (u_1) and ARV treatment (u_2). The result shows that the combination of two controls successfully decreases (I_1, I_2). We can see in Figure 3.



(A) HIV-positive subpopulation taking ARV



(B) HIV-positive subpopulation not taking ARV

FIGURE 3. Strategy II: The combination of public health education (u_1) and ARV treatment (u_2).

TABLE 3. The difference in the value of the objective function

Strategy I	Strategy II	Strategy III
955.1174	134.9174	131.9753

Table 3 shows that the combination of the two controls gives the minimum value of the objective function. It means the cost related to the control is minimum when we apply the combination of two controls

6. CONCLOUSION

We investigated the sensitivity analysis and optimal control of a non-linear deterministic SEI_1I_2TAR HIV/AIDS model in this study. The model comprises two equilibrium points: free-disease equilibrium and endemic equilibrium. The sensitivity index is generated using the characteristics that derive from the fundamental reproduction number (R_0). We obtain two significant factors with larger and positive values, Ω and β_2, which represent the recruitment rate of the ignorant subpopulation and the transmission rate from the uneducated subpopulation to the infection-taking ARV, respectively. These characteristics have a greater impact on HIV transmission.

Since the endemic, we have been working on the problem of optimum control on the mathematical model of HIV/AIDS propagation in order to reduce the number of HIV-infected people. In the model, we propose two controls: public education (u_1)

and ARV therapy (u_2). We demonstrate the existence of optimal control, and the results show that the system can be optimally controlled. Furthermore, the Pontryagin minimum concept is used as necessary requirements to find the best possible model control. The numerical findings of three solutions reveal that a combination of education (u_1) and ARV treatment (u_2) successfully controls the spread of HIV disease and the expense associated with control.

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