# Optimal Control of HIV-1 Spread in Combination with Nutritional Status and ARV-Treatment

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***Abstract*—HIV-1 is a virulent virus, it has the ability to easily spread the virus. This study aims to optimally control the spread of the HIV-1 virus with SIPA (Susceptible-Infection-PreAIDS-AIDS) model by using nutritional status and ARV-treatment. Assessment of nutritional status is carried out on people with HIV/AIDS (ODHA). The results showed that the control in the form of nutritional status and ARV-treatment was able to reduce the infected subpopulation. Routine assessment of nutritional status can form balanced nutrition for ODHA. ARV-treatment works by reducing the amount of HIV viral load, so that HIV infection cannot cause disorders of the immune system.**

***Index Terms*—optimal control, HIV-1, nutritional status, ARV-treatment.**

## I. Introduction

MATHEMATICAL modeling is the application of science developed from real phenomena [1]. With the modeling, we can perform stability analysis on a system. It is then possible to develop mathematical models by performing optimal control. In modeling, optimal control can be used to develop continuous dynamic systems. With optimal control, disease spread can be modeled and optimized. The simple model of disease modeling is SIR, which consists of the Susceptible-Infection-Recover subpopulation. Disease modeling has developed following a real ongoing phenomenon.

HIV (Human-Immunodeficiency Virus) is a virus that can cause decreased immunity and can form antibodies. Saha et al studied the HIV/AIDS Model using Pre-exposure prophylaxis (PrEP), the study showed that PrEP reduced the number of HIV infections in the population [2]. The spread of HIV has been researched by Vicentin, et al. The study included two classes of antiretroviral treatment, namely reserve transcriptase inhibitor (RTI) and protease inhibitor (PI) [3]. A nonlinear HIV/AIDS dynamics model based on HIV-infected populations is presented by Dutta et al. As a result, they divide the HIV-infected population into tested and untested sections [4]. Apenteng et al. observed the impact of migration on HIV and AIDS spread. As migrants migrate, the HIV infection rate increases by approximately 12 percentage points [5]. Other studies related to HIV/AIDS model were established by Wu et al. The study identified a model based on the three-age structure, spatial diffusion, viral load-dependent infection, and conversion rate to examine the global dynamic behavior of HIV/AIDS transmission [6]. The analysis of the S-I-P-A model in the case of the spread of HIV/AIDS shows that there is a very significant effect the difference between the number of the AIDS population when free of disease and during endemic conditions [7].

The spread of the HIV virus is still a global problem in Indonesia. Therefore, it is necessary to anticipate the spread of the virus by using optimal control. Research conducted by Akudibillah et al regarding optimal treatment to reduce the prevalence of HIV/AIDS [8]. Further research on the mathematical model of HIV/AIDS transmission with awareness effect by applying optimal control in the form of prevention, campaign, and treatment of Anti-retroviral Therapy (ART) observed by Odinsyah et al [9]. Control of HIV/AIDS with education campaigns and ARV as a control variable was shown to be able to help reduce the number of individuals in the stage of infection have been studied [10]. Marsudi et al used to control the spread of HIV by using prevention methods in the form of human education, screening, and treatment of infected humans disscude. The study showed the level of interaction susceptible to unconscious HIV infection was the most sensitive parameters on the number of successful reproduction [11]. The mathematical model of HIV virus type-1 (HIV-1) with contact rates was studied by Jan et al. The study showed that treatment control was able to reduce concentration levels virus cells [12].

Based on viral load (the amount of HIV virus in the blood), HIV is divided into two, namely HIV-1 and HIV-2. HIV-1 has a viral load greater than HIV-2. HIV-1, a virulent virus, is more easily transmitted and is responsible for most of the virus spread in the world [13]. Without treatment, the HIV-1 virus can replicate and cause AIDS, the last stage of HIV infection that occurs when the body's immune system weakens. This study aims to control the spread of HIV-1 through nutritional status and ARV-treatment. Assessment of nutritional status is carried out on people with HIV/AIDS (ODHA). Routine assessment of nutritional status (weight and changes in body weight, height, body mass index or arm circumference, and symptoms of disease) can form balanced nutrition for ODHA. It is expected that the results of this study will provide guidance to policymakers in determining how to make optimal use of the nutritional status of ODHA and allocate ARV-treatment.

## II. Mathematical Model

This model of HIV-1 spread comprises four compartments: Susceptible population $S(t)$, Infection population $I(t)$, Pre-AIDS population $P(t)$, and AIDS population $A(t)$. Infected

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individuals can be classified as Pre-AIDS or AIDS. It is assumed that people who are infected with AIDS are weak and unhealthy. Compartment diagram of HIV-1 spread is shown in Figure 1.

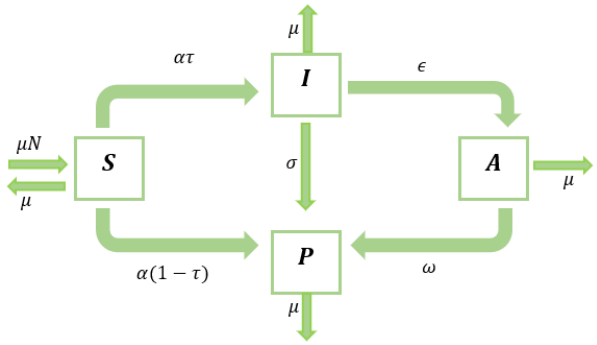


Fig. 1. SIPA Model Compartment Diagram

from Figure 1, the following equation is obtained [7].

$$\begin{aligned}\frac{dS}{dt} &= \mu N - \frac{\alpha\tau IS}{N} + \frac{\alpha(1-\tau)IS}{N} + \mu S\\ \frac{dI}{dt} &= \frac{\alpha\tau IS}{N} - (\sigma+\epsilon+\mu)I\\ \frac{dP}{dt} &= \frac{\alpha(1-\tau)IS}{N} + \sigma I + (\omega+\mu)P\\ \frac{dA}{dt} &= \epsilon I + \omega P - \mu A \end{aligned} \tag{1}$$

This study used the SIPA model with controls based on nutritional status and ARV-treatment. The purpose of nutritional status control is to provide information on how infected people maintain balanced nutrition. The next control effort is ARV-treatment. As a result of ARV treatment, the number of infected populations is minimized. Controls in the form of nutritional status ($u_1$) and ARV-treatment ($u_2$) against (1), were obtained.

$$\begin{aligned}\frac{dS}{dt} &= \mu N - \frac{u_1\alpha\tau IS}{N} + \frac{u_1\alpha(1-\tau)IS}{N} + \mu S\\ \frac{dI}{dt} &= \frac{u_1\alpha\tau IS}{N} - (\sigma+\epsilon+\mu+u_2)I\\ \frac{dP}{dt} &= \frac{u_1\alpha(1-\tau)IS}{N} + \sigma I + (\omega+\mu)P + u_2 I\\ \frac{dA}{dt} &= \epsilon I + \omega P - \mu A \end{aligned} \tag{2}$$

Descriptions
with the following objective function.

$$J(u_1,u_2) = \int_0^T I + Au_1^2 + Bu_2^2 dt$$

for optimal control $u_1^*$ and $u_2^*$, then

$$J(u_1^*,u_2^*) = min\{J(u_1,u_2)|u_1,u_2 \in U\} \tag{3}$$

with $U = \{(u_1,u_2)|0 \le u_1 \le 1, 0 \le u_2 \le 1\}$.

$S$ : Susceptible population number
$I$ : Infection population number
$P$ : Pre-AIDS population number
$A$ : AIDS population number
$N$ : Human population-rate
$\mu$ : Birth and death rate
$\alpha$ : Rate of HIV spread from susceptible to infection
$\tau$ : The probability of the population being infected but not already in Pre-AIDS
$\sigma$ : The rate at which HIV-infected individuals develop pre-AIDS
$\epsilon$ : HIV infection rates and the rate of AIDS directly entering the population
$\omega$ : The rate of AIDS sufferers in the pre-AIDS population

Halmitonian function in the spread of HIV-1 as follows.

$$H = I + Au_1^2 + Bu_2^2 + \sum_i^4 \lambda_i f_i$$

then, we get

$$\begin{aligned} H &= I + Au_1^2 + Bu_2^2\\ &+ \lambda_1\left(\mu N - \frac{u_1\alpha\tau IS}{N} + \frac{u_1\alpha(1-\tau)IS}{N} + \mu S\right)\\ &+ \lambda_2\left(\frac{u_1\alpha\tau IS}{N} - (\sigma+\epsilon+\mu+u_2)I\right)\\ &+ \lambda_3\left(\frac{u_1\alpha(1-\tau)IS}{N} + \sigma I + (\omega+\mu)P + u_2 I\right)\\ &+ \lambda_4(\epsilon I + \omega P - \mu A) \end{aligned}$$

According to Pontryagin's minimum principle, the Halmitonian function can be solved optimally if it satisfies the three conditions, namely stationary, state equation, and costate equation, given as follows.

**1** Stationary

The optimal control $u_1$ and $u_2$, is said to be stationary if the first derivative of the Halmitonian function with respect to $u_1$ and $u_2$ is equal to zero [14].

$$\frac{\delta H}{\delta u_1} = 0$$

and

$$\frac{\delta H}{\delta u_2} = 0$$

then the optimal control value is obtained as follows.

$$u_1^* = min\left\{max\left(0, \frac{\alpha SI}{2AN}\left((\lambda_1-\lambda_3)+(\lambda_3-\lambda_2)\tau\right)\right), 1\right\}$$

$$u_2^* = min\left\{max\left(0, \frac{\lambda_2-\lambda_3}{2B}\right), 1\right\}$$

**2** State Equation

The state equation is used to solve the optimal control

as the constraint equation as follows.

$$\begin{aligned}
\frac{dH}{d\lambda_1} &= \frac{dS}{dt} \\
&= \mu N - \left(\frac{\alpha\tau u_1}{N} I + \frac{\alpha(1-\tau)}{N} u_1 I + \mu\right) S \\
\frac{dH}{d\lambda_2} &= \frac{dI}{dt} \\
&= \left(\frac{\alpha\tau u_1}{N}\right) IS - (\sigma + \epsilon + \mu + u_2) I \\
\frac{dH}{d\lambda_3} &= \frac{dP}{dt} \\
&= \left(\frac{\alpha(1-\tau)u_1}{N}\right) IS - (\omega + \mu) P + u_2 I \\
\frac{dH}{d\lambda_4} &= \frac{dA}{dt} \\
&= \epsilon I + \omega P - \mu A
\end{aligned}$$

with initial condition $S(0) = S_0, I(0) = I_0, P(0) = P_0$ dan $A(0) = A_0$.

**3** Costate Equation

The costate equation in the form of a negative value of the Halmitonian function derived from the state variables is given as follows.

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{dH}{dS} \\
&= \lambda_1 \left(\frac{\alpha\tau u_1}{N} I + \frac{\alpha(1-\tau)u_1}{N} I + \mu\right) \\
&- \lambda_2 \left(\frac{\alpha\tau u_1}{N} I\right) \\
&- \lambda_3 \left(\frac{\alpha(1-\tau)u_1}{N} I\right)
\end{aligned}$$

$$\begin{aligned}
\frac{d\lambda_2}{dt} &= -\frac{dH}{dI} \\
&= \lambda_1 \left(\frac{\alpha\tau u_1}{N} S + \frac{\alpha(1-\tau)u_1}{N} S\right) \\
&- \lambda_2 \left(\frac{\alpha\tau u_1}{N} S - (\sigma + \epsilon + \mu + u_2)\right) \\
&- \lambda_3 \left(\frac{\alpha(1-\tau)u_1}{N} S + \sigma + u_2\right) \\
&- \lambda_4 \epsilon
\end{aligned}$$

$$\begin{aligned}
\frac{d\lambda_3}{dt} &= \frac{dH}{dP} \\
&= \lambda_3 (\omega + \mu) - \lambda_4 \omega
\end{aligned}$$

$$\begin{aligned}
\frac{d\lambda_4}{dt} &= \frac{dH}{dA} \\
&= \mu
\end{aligned}$$

with the transverse condition
$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = \lambda_4(T) = 0$.

## III. Results and Discussion

In this section, we have discussed optimal control variables that minimize the total cost. We shall perform numerical simulations to validate our analytical findings, and then find the minimal cost for implementing two control strategies. The optimal control model for the spread of HIV-1 with nutritional status and ARV-treatment was solved numerically using Runge-Kutta. This study uses the initial conditions $S_0 = 0.70, I_0 = 0.15$, $P_0 = 0.1$, and $A_0 = 0.05$.

TABLE I
Values of Parameters

| Parameters | Parameter-Values | References |
|---|---|---|
| $N$ | 10000 | [7] |
| $\mu$ | 0.0001 | Assumed |
| $\tau$ | 0.0000092 | [7] |
| $\epsilon$ | 0.000525 | [7] |
| $\sigma$ | 0.12351 | [7] |
| $\alpha$ | 0.0054 | [15] |
| $\omega$ | 0.3787 | [15] |

The control system (2) and (3) can be solved numerically using the parameter values in Table 1 and the calculated population size after a fixed final time $t_f = 25$ years. The weights used in this study are $A = 10$ and $B = 15$. Figure 2 shows that after the control there was an increase in the healthy subpopulation up to $t = 25$. This is due to the effect of additional control in the form of nutritional status in vulnerable subpopulations.

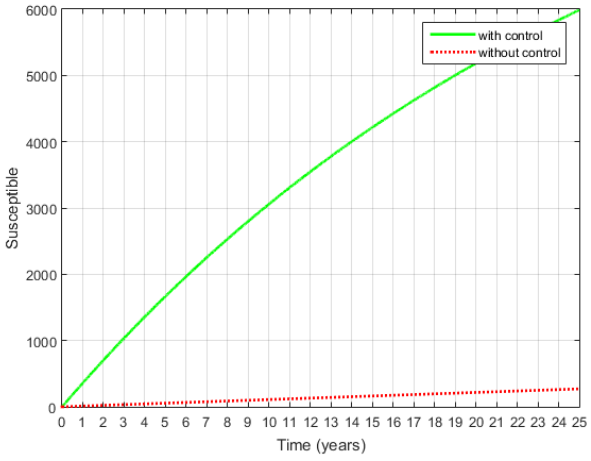


Fig. 2. Effects of Controls $u_1$ and $u_2$ on S

Controls in the form of nutritional status and ARV-treatment were used to reduce the number of infected subpopulations. Figure 3 shows that the infected subpopulation after being given control decreased until it reached 0 at the time of $t = 0.9$ to $t = 25$. This means showing the success of optimal control in the spread model of HIV-1.

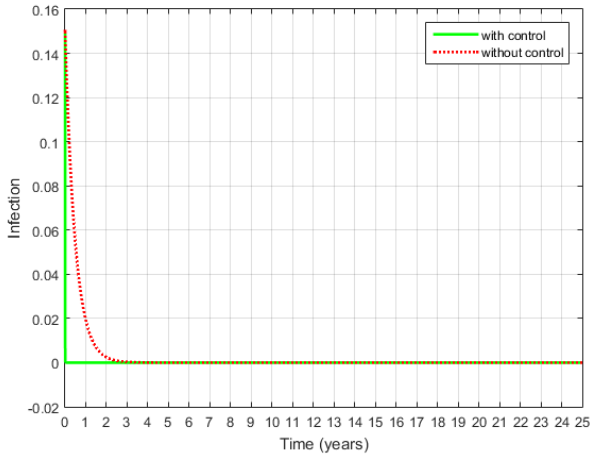


Fig. 3. Effects of Controls $u_1$ and $u_2$ on I

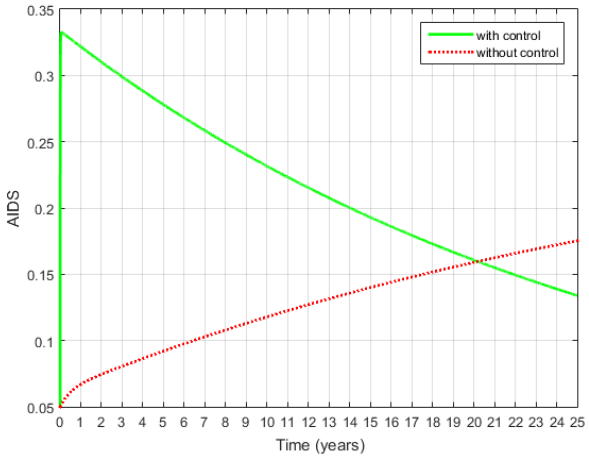


Fig. 5. Effects of Controls $u_1$ and $u_2$ on A

Subpopulation growth in Pre-AIDS and AIDS after being given control respectively is shown in Figure 3 and Figure 4. Figure 3 shows that Pre-AIDS has increased from $t = 0$ to $t = 0.5$. Then the graph of Pre-AIDS at $t = 0.5$ has decreased to $t = 25$. This is due to the control of nutritional status in the infected subpopulation.

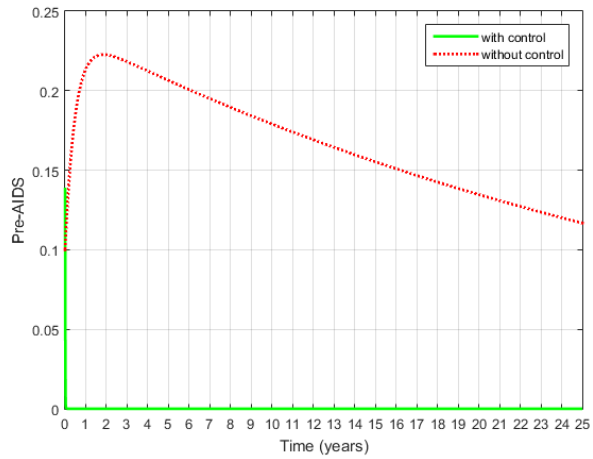


Fig. 4. Effects of Controls $u_1$ and $u_2$ on P

On the other hand, Figure 4 shows that the AIDS graph has decreased from $t = 0$ to $t = 25$. With the addition of controls, the AIDS subpopulation decreased from $t = 20$ to $t = 25$. Nutritional status and ARV-treatment applied to infected subpopulations were able to reduce the number of Pre-AIDS and AIDS populations.

The nutritional balance of HIV-infected patients helps balance the immune system, malnutrition, and effects of the disease. The nutritional status of people living with HIV (ODHA) should be assessed regularly by assessing their weight and changes in body weight, height, body mass index or arm circumference, as well as by looking at their symptoms of disease.

Control with nutritional status shown in Figure 6. From Figure 6 it can be seen that nutritional support can delay the

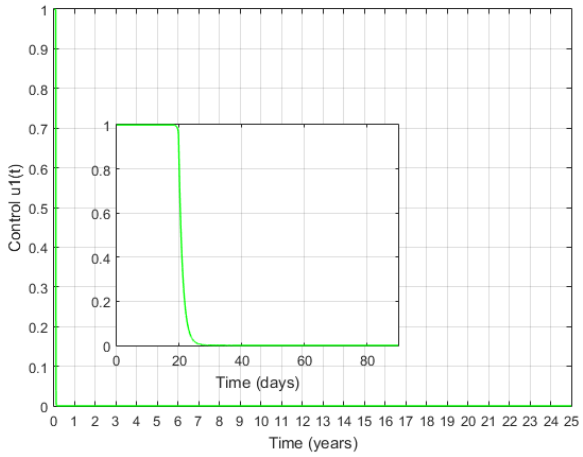


Fig. 6. Nutritional Status Control

development of AIDS and can improve the quality and length of life of ODHA. ODHA patients should pay more attention to the intake of nutrients consumed in order to meet their body's needs so that unwanted weight loss can be prevented. The addition of control of nutritional status is shown in Figure 6. It can be seen in the figure, the control given at the beginning of $t$ is 1 , then it decreases sharply until when $t = 0.9$ to $t = 23$ is no longer given control of nutritional status.

Control with ARV-treatment shown in Figure 7 is given at the maximum level, namely 1, until $t = 0.03$, then decreases to $t = 0.1$. At the time $t = 18$ was not given ARV-treatment. ARV-treatment works by reducing the amount of HIV viral load, so that HIV infection cannot cause disorders of the immune system.

This research is focused on controlling the infected subpopulation. The numerical results show that by applying control in the form of nutritional status and ARV-treatment, it can reduce the infected subpopulation, including the Pre-AIDS and AIDS subpopulations.

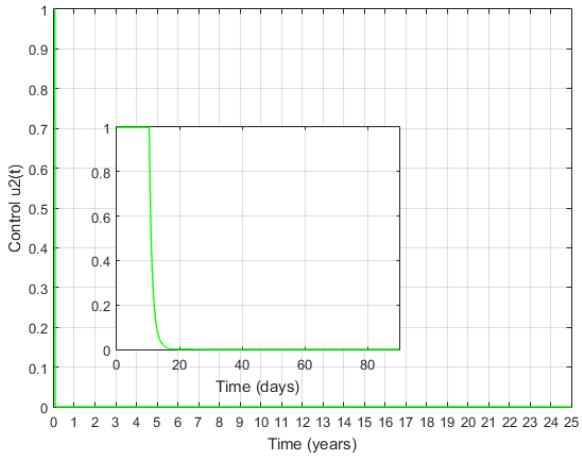


Fig. 7. ARV-treatment Control

## IV. Conclusions

We controlled the SIPA model to assess the effect of nutritional status and ARV-treatment on the spread of HIV in the population. The nutritional balance of HIV-infected patients helps balance the immune system, malnutrition, and effects of the disease. Assessment of nutritional status is carried out on people with HIV/AIDS (ODHA). ARV-treatment works by reducing the amount of HIV viral load, so that HIV infection cannot cause disorders of the immune system. Analysis showed that nutritional status and ARV-treatment reduced disease transmission.

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