Optimal Control for a Mathematical Model of HIV-AIDS with Tuberculosis

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ABSTRACT

In this paper, we have formulated a mathematical model for HIV-AIDS and Tuberculosis. In addition, human population is divided into four states; susceptible state (S), HIV infectious state (I), HIV infectious with tuberculosis state (H) and AIDS state (A). In this study, the epidemic and endemic analyses have also presented along with numerical simulations to verify our model. Meanwhile, we also extended our work to an optimal control problem to investigate control strategy to stop the AIDS outbreak such that it can be further studied for public health interventions.

Keywords: HIV/AIDS, Tuberculosis, Control strategy, Mathematical model, Optimal control theory.

INTRODUCTION

HIV is a virus spread through certain body fluids that attacks the body's immune system, specifically the CD4 cells, often called T cells. Over time, HIV can destroy so many of these cells that the body cannot fight off infections and disease. These special cells help the immune system fight off infections. Untreated, HIV reduces the number of CD4 cells (T cells) in the body. This damage to the immune system makes it harder and harder for the body to fight off infections and some other diseases. Opportunistic infections or cancers take advantage of a very weak immune system and signal that the person has AIDS. AIDS (Acquired Immune Deficiency Syndrome) is a syndrome caused by a virus called HIV (Human Immunodeficiency Virus). The illness alters the immune system, making people much more vulnerable to infections and diseases. This susceptibility worsens as the syndrome progresses. The terms "HIV" and "AIDS" both terms refer to the same disease. However, "HIV" refers to the virus itself, and "AIDS" refers to the late stage of HIV infection (Centers for Disease Control and prevention, 2017). Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs. Tuberculosis is curable and preventable. TB is spread from person to person through the air. About one-quarter of the world's population has latent TB, which means people have been infected by TB bacteria but are not ill with the disease and cannot transmit the disease. However, persons with compromised immune systems, such as people living with

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HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill. When a person develops active TB disease, the symptoms (such as cough, fever, night sweats, or weight loss) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die (WHO, 2017). People living with HIV are 20 to 30 times more likely to develop active TB disease than people without HIV. HIV and TB form a lethal combination, each speeding the other's progress. In 2016 about 0.4 million people died of HIV-associated TB. About 40% of deaths among HIV-positive people were due to TB in 2016. In 2016, there were an estimated 1.4 million new cases of TB amongst people who were HIV-positive, 74% of whom were living in Africa (WHO, 2017).

Many mathematical models have been proposed and analyzed to understand the dynamics of spread of infectious diseases. In order to explore the transmission rules and find effective control strategies for HIV/AIDS. For example, Z.Mukandavire, W.Garira and J.M. Tchuenche proposed a model in 2009. They use the model to study the effects of public health educational campaigns on the spread of HIV/AIDS as a single-strategy approach in HIV prevention. F.Nyabadza, Z.Mukandavire and S.D. Hove-Musekwa proposed a model in 2011. They study a simple deterministic HIV/AIDS model incorporating condom use, sexual partner acquisition, behavior change and treatment as HIV/AIDS control strategies is formulated using a system of ordinary differential equations with the object of applying it to the current South African situation. S. Mushayabasa et al. proposed a model in 2011. They formulate a deterministic model to investigate the effects of socioeconomic status on the transmission dynamics of HIV/AIDS. We also studied a research of Joyce K. Nthiiri, George O. Lawi and Alfred Manyonge in 2015. In this paper, they consider a deterministic model incorporating protection from infection for both tuberculosis (TB) disease and HIV/AIDS.

In this paper, our model helps to lower any complication occurred in the previous model. We studied factors that reduced the number of HIV/AIDS infections. In addition, we will further apply optimal control theory to our model to seek optimal solutions for control strategies. We will first present the HIV/AIDS with Tuberculosis model with control measures incorporated. We will conduct an equilibrium analysis for the epidemic and endemic dynamics of the system when the controls are constants. Then, we will turn to the time-dependent control system and perform an optimal control study for HIV/AIDS with Tuberculosis model. Finally, we give a brief discussion about the main results.

MATERIALS AND METHODS

1. Model formulation

For our model formulation, we let N represents the population of humans. The population is classified into four states: Susceptible (S), HIV infective (I), HIV with Tuberculosis infective (H), and AIDS (A). We let ϕ_1 represents vaccinated rate for HIV and ϕ_2 represents medication rate for TB. Assume that natural birth and natural death rate is μ . b_1, b_2 and b_3 are transmission coefficient of the infectious form HIV people, HIV with TB people and AIDS people respectively. d is the proportional rate of susceptible infected with HIV or HIV with TB. AIDS has progression rate s from HIV with TB. ϵ_1 is the progression rate to HIV with TB form HIV. ϵ_2 is the progression rate to AIDS form HIV. Tuberculosis mortality rate is a . f_1 is the vaccinated rate for HIV. f_2 is the medication rate for TB. For the equations of human populations are;

$$\frac{dS}{dt} = \mu N - \beta_1 SI - \beta_2 HS - \beta_3 AS - \mu S - \phi_1 S \quad (1.1)$$

$$\frac{dI}{dt} = \beta_1 IS + (1-\delta)\beta_2 HS + \beta_3 AS - \varepsilon_1 IH - \varepsilon_2 I - \mu I + \phi_2 H \quad (1.2)$$

$$\frac{dH}{dt} = \varepsilon_1 IH + \delta\beta_2 HS - \sigma H - \mu H - \alpha H - \phi_2 H \quad (1.3)$$

$$\frac{dA}{dt} = \varepsilon_2 I + \sigma H - \mu A \quad (1.4)$$

2. Epidemic analysis

2.1 Disease-free equilibrium

With constant controls and setting $I = H = A = 0,$ the disease-free equilibrium (DFE) of the equation (1.1)-(1,4) is given by

$$\varepsilon_0 = (\frac{\mu N}{\mu + \phi_1}, 0, 0, 0) \cdot \quad (2.1)$$

2.2 Basic reproduction number (R_0)

We start our analysis by determining the basic reproduction number, R_0. R_0 is mathematically defined as the spectral radius of the next-generation matrix. To compute the basic reproduction number, we use the well-known method of van den Driessche and Watmough in 2002 (Van den Dricssche et al., 2002). We have

$$\mathrm{F} = \begin{bmatrix} \beta_1 IS + (1-\delta)\beta_2 HS + \beta_3 AS \\ \delta\beta_2 HS \\ 0 \end{bmatrix} \text{ and } \mathrm{V} = \begin{bmatrix} \varepsilon_1 IH + \varepsilon_2 I + \mu I - \phi_2 H \\ \sigma H + \mu H + \alpha H + \phi_2 H - \varepsilon_1 IH \\ \mu A - \varepsilon_2 I - \sigma H \end{bmatrix} . (2.2.1)$$

Then we have

$$F=\begin{bmatrix}\beta_1 S & (1-\delta)\beta_2 S & \beta_3 S\\ 0 & \delta\beta_2 S & 0\\ 0 & 0 & 0\end{bmatrix} \text{ and } V=\begin{bmatrix}\varepsilon_1 H+\varepsilon_2+\mu & \varepsilon_1 I-\phi_2 & 0\\ -\varepsilon_1 H & \sigma+\mu+\alpha+\phi_2-\varepsilon_1 I & 0\\ -\varepsilon_2 & -\sigma & \mu\end{bmatrix}. \quad (2.2.2)$$

By substituting the disease-free equilibrium point $e_0=(\frac{mN}{m+f_1},0,0,0)$ in the Jacobian matrices (2.2.2), we get

$$F(\varepsilon_0)=\begin{bmatrix}\frac{\beta_1\mu N}{\mu+\phi_1} & \frac{(1-\delta)\beta_2\mu N}{\mu+\phi_1} & \frac{\beta_3\mu N}{\mu+\phi_1}\\ 0 & \frac{\delta\beta_2\mu N}{\mu+\phi_1} & 0\\ 0 & 0 & 0\end{bmatrix} \text{ and } V(\varepsilon_0)=\begin{bmatrix}\varepsilon_2+\mu & -\phi_2 & 0\\ 0 & \sigma+\mu+\alpha+\phi_2 & 0\\ -\varepsilon_2 & -\sigma & \mu\end{bmatrix}. \quad (2.2.3)$$

Therefore, the eigenvalues of the matrix FV^{-1} are

$$\lambda=\left\{\frac{\beta_1\mu N+\beta_3\varepsilon_2 N}{(\mu+\phi_1)(\varepsilon_2+\mu)},\frac{\delta\beta_2\mu N}{(\mu+\phi_1)(\sigma+\mu+\alpha+\phi_2)},0\right\}.$$

By our calculation with parameter values in Table 1, we obtain that $\frac{\beta_1\mu N+\beta_3\varepsilon_2 N}{(\mu+\phi_1)(\varepsilon_2+\mu)}$ is the biggest magnitude of eigenvalues of the matrix FV^{-1}.

Hence, the basic reproduction number is given by $r\left(FV^{-1}\right)$, that is

$$R_0=\frac{b_1 mN+b_3 e_2 N}{(m+f_1)(e_2+m)}. \quad (2.2.4)$$

2.3 Endemic equilibrium

When the disease is present in the population, $I^*\neq 0$, there may be several critical points where $I^*\neq 0$, which are the endemic equilibrium points (EEP) of the model. We obtain the endemic equilibrium point as follows:

$e_0^*=(S^*,I^*,H^*,A^*)$, where $S^*=\frac{mN-(e_2+m-b_1e_2)I^*-b_1mA^*}{b_2}$

and $H^*=\frac{mA^*-e_2I^*}{s}$, such that $b_1=\frac{s+m+a}{s}$ and $b_2=m+f_1$.

2.4 Stability

2.4.1 Stability of disease-free equilibrium point

Theorem1 The disease-free equilibrium of the model is locally asymptotically stable if $R_0<1$, and unstable if $R_0>1$.

To determine the global asymptotic stability of the DFE, the following lemma introduced by Castillo-Chavez et al (Castillo-chavez, C., et al., 2002).

Lemma1 Consider a model system written in the form

$$\frac{dX_1}{dt} = F(X_1, X_2)$$
$$\frac{dX_2}{dt} = G(X_1, X_2), \qquad G(X_1, 0) = 0,$$

where $X_1 \in \mathbb{R}^m$ denotes (its components) the number of uninfected individuals and $X_2 \in \mathbb{R}^m$ denotes (its components) the number of infected individuals including latent, infections, etc.; $X_0 = (X_1^*, 0)$ denotes the disease-free equilibrium of the system. Also assume the conditions (H1) and (H2) below:

(H1) For $dX_1 / dt = F(X_1, 0)$ is globally asymptotically stable;

(H2) $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2)$, $\hat{G}(X_1, X_2) \geq 0$ for

$(X_1, X_2) \in \Omega$, where the Jacobian $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$ is an M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. Then the DFE is globally asymptotically stable.

Theorem2 The DFE of the model (1.1)-(1.4) is globally asymptotically stable.

Proof. We adopt the notations in Lemma1 and verify the conditions (H1) and (H2). In our model, $X_1 = S$, $X_2 = (I, H, A)$ and $X_1^* = \frac{\mu N}{\mu + f_1}$. We note that the system is linear and its solution can be easily found as:

$$\frac{dX_1}{dt} = F(X_1, X_2) = \mu N - b_1 IS - b_2 HS - b_3 AS - \mu S - f_1 S. \qquad (2.4.1)$$

We have

$$\frac{dX_1}{dt} = F(X_1, 0) = \mu N - \mu S - f_1 S.$$

Thus, $S(t) \to \frac{\mu N}{\mu + f_1}$, as $t \to \infty$. Hence, $X_1^* = \frac{\mu N}{\mu + f_1}$ is globally asymptotically stable for the subsystem (2.4.1).

Now, note that

$$G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2) \qquad (2.4.2)$$

where $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$. Substituting into (2.4.2) gives, $\hat{G}(X_1, X_2) = (0,0)^T \geq 0$.

We complete the proof.

2.4.2 Stability of endemic equilibrium point

Next, we proceed to analyze the stability properties of the endemic equilibrium. First, we prove the following result regarding the local stability.

Theorem3 The positive endemic equilibrium e_0^* is locally asymptotically stable if it satisfies the Routh-Hurwitz criterion.

Proof. The Jacobian matrix of the system (1.1) - (1.4) at $x = e_0^*$ is given by

$$J\left(S^*, I^*, H^*, A^*\right) =$$

$$\begin{bmatrix} \beta_1 I^* - \beta_2 H^* - \beta_3 A^* - \mu - \phi_1 & -\beta_1 S^* & -\beta_2 S^* & \beta_3 S^* \\ \beta_1 I^* + (1-\delta)\beta_2 H^* + \beta_3 A^* & \beta_1 S^* - \varepsilon_1 H^* - \varepsilon_2 - \mu & (1-\delta)\beta_2 S^* - \varepsilon_1 I^* + \phi_2 & \beta_3 S^* \\ \delta\beta_2 H^* & \varepsilon_1 H^* & \varepsilon_1 I^* + \delta\beta_2 S^* - \sigma - \mu - \alpha - \phi_2 & 0 \\ 0 & \varepsilon_2 & \sigma & -\mu \end{bmatrix}.$$

The characteristic polynomial of $J\left(e_0^*\right)$ is $\det\left(J\left(e_0^*\right) - \lambda I^*\right) = 0.$

We have $\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0$, where

$a_1 = \alpha + \varepsilon_2 + 4\mu + \phi_1 + \phi_2 + \sigma + \beta_3 A^* + \beta_2 H^* + \varepsilon_1 H^* - \varepsilon_1 I^* - \beta_1 S^* - \delta\beta_2 S^*$,

$$
\begin{aligned}
a_2 &= 6\mu^2 + \varepsilon_2\phi_1 + \varepsilon_2\sigma + 3\mu\phi_1 + 3\mu\phi_2 + \phi_1\phi_2 + 3\mu\sigma + \sigma\phi_1 + \alpha\varepsilon_2 + 3\alpha\mu + \alpha\phi_1 \\
&+3\varepsilon_2\mu + \alpha\beta_3 A^* + \alpha\beta_2 H^* + \alpha\beta_1 I^* + \alpha\varepsilon_1 H^* + \varepsilon_2\beta_2 H^* + 3\mu\beta_3 A^* + \varepsilon_2\beta_1 I^* + \phi_2\beta_3 A^* + \sigma\beta_3 A^* \\
&+3\mu\beta_2 H^* + 3\mu\beta_1 I^* + \phi_2\beta_2 H^* + 3\mu\varepsilon_1 H^* + \phi_2\beta_1 I^* + \sigma\beta_2 H^* + \phi_1\varepsilon_1 H^* + \sigma\beta_1 I^* + \sigma\varepsilon_1 H^* + \varepsilon_1\beta_2 H^{*^2} \\
&+\delta\beta_1\beta_2 S^{*^2} + \varepsilon_1\beta_3 H^* A^* + \varepsilon_1\beta_1 H^* I^* + \varepsilon_1\beta_1 I^* S^* - \varepsilon_1\varepsilon_2 I^* - \alpha\beta_1 S^* - 3\mu\varepsilon_1 I^* - \phi_1\varepsilon_1 I^* - 3\mu\beta_1 S^* \\
&-\phi_1\beta_1 S^* - \phi_2\beta_1 S^* - \sigma\beta_1 S^* - 2\varepsilon_1^2 I^* H^* - \phi_1\beta_1 I^{*^2} - \varepsilon_1\beta_3 A^* I^* - \varepsilon_1\beta_2 H^* I^* - \varepsilon_1\beta_2 H^* S^* - \delta\varepsilon_2\beta_2 S^* \\
&-3\mu\delta\beta_2 S^* - \phi_1\delta\beta_2 S^* - \delta\beta_1\beta_2 H^* S^* - \delta\beta_1\beta_2 I^* S^* - 2\varepsilon_1\delta\beta_2 H^* S^* + \varepsilon_2\beta_3 A^* + \beta_2\varepsilon_1 H^{*^2} - \beta_3\varepsilon_2 S^* \\
&+\beta_2\varepsilon_1 H^{*^2},
\end{aligned}
$$

$$
\begin{aligned}
a_3 &= 4\mu^3 + 3\mu^2\phi_1 3\mu^2\phi_2 + 3\mu^2\sigma + 3\alpha\mu^2 + 3\varepsilon_2\mu^2 + 2\alpha\varepsilon_2\mu + \alpha\beta_3\varepsilon_2 A^* \\
&+\alpha\varepsilon_2\phi_1 + 2\alpha\mu\phi_1 + 2\varepsilon_2\mu\phi_2 + 2\varepsilon_2\mu\phi_2 + \varepsilon_2\phi_1\phi_2 + 2\varepsilon_2\mu\sigma + \varepsilon_2\phi_1\sigma + 2\mu\phi_1\phi_2 + 2\mu\phi\sigma \\
&+3\mu^2\beta_3 A^* + 3\mu^2\beta_2 H^* + 3\mu^2\beta_1 I^* + 3\mu^2\varepsilon_{12}\beta_1 I^* + \alpha\varepsilon_1\phi_1 H^* + \varepsilon_2\phi_2\beta_2 H^* + 2\mu\phi_2\beta_3 A^* + \varepsilon_2\phi_2\beta_1 I^* \\
&+2\mu\beta_1\alpha I^* + 2\mu\alpha\varepsilon_1 H^* + 2\mu\varepsilon_2\beta_2 H^* + 2\mu\varepsilon_2\beta_1 I^* + \alpha\varepsilon_1\phi_1 H^* + \varepsilon_2\phi_2\beta_2 H^* + 2\mu\phi_2\beta_3 A^* + \varepsilon_2\phi_2\beta_1 I^* \\
&+\varepsilon_2\sigma\beta_2 H^* + 2\mu\sigma\beta_3 A^* + \sigma\varepsilon_2\beta_1 I^* + 2\mu\phi_2\beta_2 H^* + 2\mu\phi_2\beta_2 I^* + 2\mu\sigma\beta_2 H^* + 2\mu\phi_1\varepsilon_1 H^* + 2\mu\sigma\beta_1 I^* \\
&+2\mu\sigma\varepsilon_1 H^* + \sigma\phi_1\varepsilon_1 H^* + \alpha\varepsilon_1\beta_2 H^{*^2} + 2\mu\varepsilon_1\beta_2 H^{*^2} + \varepsilon_1\sigma\beta_2 H^{*^2} + 2\mu\delta\beta_1\beta_2 S^{*^2} + \phi_1\delta\beta_1\beta_2 S^{*^2} \\
&+\varepsilon_1\alpha\beta_3 H^* A^* + 2\mu\varepsilon_1\beta_3 H^* A^* + 2\mu\varepsilon_1\beta_1 H^* I^* + \sigma\varepsilon_1\beta_1 H^* I^* + 2\mu\varepsilon_1\beta_1 I^* S^* + \phi_1\varepsilon_1\beta_1 I^* S^* \\
&+2\beta_3\varepsilon_2\mu A^* + \varepsilon_2\phi_2\beta_3 A^* + \varepsilon_2\sigma\beta_3 A^* + \varepsilon_2\delta\beta_2\beta_3 S^{*^2} + \alpha\varepsilon_1\beta_1 H^* I^* + \sigma\varepsilon_1\beta_3 A^* H^* + \varepsilon_1\varepsilon_2\beta_3 I^* S^* \\
&+\sigma\varepsilon_1\beta_3 H^* S^* + \varepsilon_2\delta\beta_2\beta_3 H^* S^* - \varepsilon_2\alpha\beta_3 S^* - 2\mu\varepsilon_2\beta_3 S^* - \phi_1\varepsilon_2\beta_3 S^* - \phi_2\varepsilon_2\beta_3 S^* - \sigma\varepsilon_2\beta_3 S^* \\
&-2\varepsilon_2\beta_3^2 A^* S^* - \varepsilon_1\varepsilon_2\beta_3 A^* I^* - \varepsilon_2\beta_2\beta_3 H^* S^* - 2\varepsilon_2\beta_2\beta_3 I^* S^* - \sigma\delta\beta_2\beta_3 H^* S^* - \varepsilon_2\delta\beta_2\beta_3 A^* S^* \\
&-3\mu^2\varepsilon_1 I^* - 3\mu^2\beta_1 S^* - 2\mu\varepsilon_1\varepsilon_2 I^* - 2\mu\alpha\beta_1 S^* - \phi_1\varepsilon_1\varepsilon_2 I^* - \phi_1\alpha\beta_1 S^* - 2\mu\phi_1\varepsilon_1 I^* \\
&-2\mu\phi_1\beta_1 S^* - 2\mu\phi_2\beta_1 S^* - \phi_1\phi_2\beta_1 S^* - 2\mu\sigma\beta_1 S^* - \phi_1\sigma\beta_1 S^* - 4\mu\varepsilon_1^2 I^* H^* - 2\phi_1\varepsilon_1^2 I^* H^* \\
&-\varepsilon_1\varepsilon_2\beta_1 I^{*^2} - 2\mu\varepsilon_1\beta_1 I^{*^2} - 3\delta\mu^2\beta_2 S^* \varepsilon_1^2\beta_1 H^* I^{*^2} - 2\varepsilon_1^2\beta_2 I^* H^{*^2} - 2\varepsilon_1\beta_2^2 S^* H^{*^2} - 2\delta\beta_1\beta_2^2 H^* S^{*^2} \\
&-\varepsilon_1\varepsilon_2\beta_2 H^* I^* - 2\mu\varepsilon_1\beta_3 I^* A^* - 2\mu\varepsilon_1\beta_2 H^* I^* - 2\mu\varepsilon_1\beta_2 H^* S^* - \phi_1\varepsilon_1\beta_2 H^* S^* - 2\mu\varepsilon_2\delta\beta_2 S^* \\
&-\phi_1\varepsilon_2\delta\beta_2 S^* - 2\mu\phi_1\delta\beta_2 S^* - 2\varepsilon_1^2\beta_3 A^* H^* I^* - 4\mu\varepsilon_1\delta\beta_2 H^* S^* - \sigma\delta\beta_1\beta_2 H^* S^* - 2\phi_1\varepsilon_1\delta\beta_2 H^* S^* \\
&-2\varepsilon_1\beta_2\beta_3 A^* H^* S^* - 2\varepsilon_1\beta_1\beta_2 I^* H^* S^* - \alpha\delta\beta_1\beta_2 S^* H^* - 2\mu\delta\beta_2\beta_3 A^* S^* - \varepsilon_2\delta\beta_1\beta_2 I^* S^* - 2\mu\delta\beta_1\beta_2 H^* S^* \\
&-2\mu\delta\beta_1\beta_2 I^* S^* - 2\phi_2\delta\beta_1\beta_2 H^* S^* - 2\varepsilon_1\delta\beta_2\beta_3 A^* H^* S^* - 2\varepsilon_1\delta\beta_1\beta_2 I^* H^* S^*,
\end{aligned}
$$

$$
\begin{aligned}
a_4 = {} & \phi_2\mu^3 + \sigma\mu^3 + \mu^4 + \phi_1\varepsilon_2\mu^2 + \phi_2\varepsilon_2\mu^2 + \sigma\varepsilon_2\mu^2 + \phi_1\phi_2\mu^2 + \sigma\phi_1\mu^2 + \beta_3\mu^3A^* + \beta_2\mu^3H^* \\
& + \mu^3\beta_1I^* + \mu^3\varepsilon_1H^* + \alpha\mu^2\varepsilon_2 + \phi_1\mu^2\alpha + \alpha\mu\phi_1\varepsilon_2 + \phi_1\phi_2\varepsilon_2\mu + \sigma\phi_1\mu\varepsilon_2 + \mu^2\alpha\beta_3A^* + \mu^2\alpha\beta_2H^* \\
& + \alpha\mu^2\beta_1I^* + \alpha\mu^2\varepsilon_1H^* + \mu^2\varepsilon_2\beta_2H^* + \mu^2\varepsilon_2\beta_1I^* + \phi_2\mu^2\beta_3A^* + \sigma\mu^2\beta_3A^* + \phi_2\mu^2\beta_2H^* + \phi_2\mu^2\beta_1I^* \\
& + \sigma\mu^2\beta_2H^* + \phi_1\mu^2\varepsilon_1H^* + \sigma\mu^2\beta_1I^* + \sigma\mu^2\varepsilon_1H^* + \mu^2\delta\beta_1\beta_2S^{*^2} + \mu\varepsilon_2\alpha\beta_2H^* + \mu\varepsilon_2\alpha\beta_1I^* + \mu^2\varepsilon_2\beta_3A^* \\
& + \mu\phi_1\alpha\varepsilon_1H^* + \mu\phi_2\varepsilon_2\beta_2H^* + \mu\phi_2\varepsilon_2\beta_1I^* + \mu\sigma\varepsilon_2\beta_2H^* + \mu\sigma\varepsilon_2\beta_1I^* + \mu\sigma\phi_1\varepsilon_1H^* + \mu^2\varepsilon_1\beta_3H^*A^* \\
& + \mu^2\varepsilon_1\beta_1H^*I^* + \mu^2\varepsilon_1\beta_1I^*S^* + \mu\alpha\varepsilon_1\beta_2H^{*^2} + \mu\sigma\varepsilon_1\beta_2H^{*^2} + \mu\varepsilon_2\alpha\beta_3A^* + \mu\phi_2\varepsilon_2\beta_3A^* + \mu\sigma\varepsilon_2\beta_3A^* \\
& + \mu\varepsilon_2\delta\beta_2\beta_3S^{*^2} + \phi_1\varepsilon_2\delta\beta_2\beta_3S^{*^2} + 2\varepsilon_2\delta\beta_2\beta_3^2A^*S^{*^2} + \mu\phi_1\delta\beta_1\beta_2S^{*^2} + \mu\varepsilon_1\alpha\beta_3H^*A^* + \mu\alpha\varepsilon_1\beta_1H^*I^* \\
& + 2\varepsilon_2\delta\beta_2^2\beta_3H^*S^{*^2} + \mu\sigma\varepsilon_1\beta_3A^*H^* + \mu\varepsilon_1\varepsilon_2\beta_3S^*I^* + \mu\sigma\varepsilon_1\beta_1I^*H^* + \mu\phi_1\varepsilon_1\beta_1S^*I^* + \phi_1\varepsilon_1\varepsilon_2\beta_3I^*S^* \\
& + \mu\sigma\varepsilon_1\beta_3H^*S^* + \sigma\phi_1\varepsilon_1\beta_3H^*S^* + 2\varepsilon_1\varepsilon_2\beta_3^2I^*A^*S^* + 2\sigma\varepsilon_1\beta_3^2H^*S^*A^* + 2\varepsilon_1\varepsilon_2\beta_1\beta_2S^*I^{*^2} + 2\sigma\varepsilon_1\beta_2\beta_3S^*H^{*^2} \\
& + 2\varepsilon_2\delta\beta_1\beta_2\beta_3I^*S^{*^2} + 2\sigma\delta\beta_1\beta_2\beta_3H^*S^{*^2} + 2\varepsilon_1\varepsilon_2\beta_2\beta_3H^*S^*I^* + 2\sigma\varepsilon_1\beta_1\beta_3H^*S^*I^* + \varepsilon_2\delta\alpha\beta_2\beta_3H^*S^* \\
& + \mu\delta\varepsilon_2\beta_2\beta_3H^*S^* + 2\phi_2\varepsilon_2\delta\beta_2\beta_3H^*S^* - \mu\varepsilon_2\delta\beta_2\beta_3A^*S^* - 2\sigma\varepsilon_1\delta\beta_2\beta_3S^*H^{*^2} - \mu\sigma\delta\beta_2\beta_3H^*S^* \\
& - \mu^2\varepsilon_1\varepsilon_2I^* - \mu^2\alpha\beta_1S^* - \delta\mu^3\beta_2S^* - \phi_1\mu^2\varepsilon_1I^* - \phi_1\mu^2\beta_1S^* - \phi_2\mu^2\beta_1S^* - \sigma\mu^2\beta_1S^* - 2\mu^2\varepsilon_1^2H^*I^* \\
& - \mu^3\varepsilon_1I^* - \mu^3\beta_1S^* - \mu^2\varepsilon_1\beta_1I^{*^2} - \mu\phi_1\varepsilon_1\varepsilon_2I^* - \mu\phi_1\alpha\beta_1S^* - \mu\phi_1\phi_2\beta_1S^* - \mu\phi_1\sigma\beta_1S^* - \mu^2\varepsilon_1\beta_3I^*A^* \\
& - \mu^2\varepsilon_1\beta_2H^*I^* - \mu^2\varepsilon_1\beta_2H^*S^* - 2\mu\phi_1\varepsilon_1^2H^*I^* - \mu\varepsilon_1\varepsilon_2\beta_1I^{*^2} - \mu^2\varepsilon_2\delta\beta_2S^* - \mu^2\phi_1\delta\beta_2S^* - 2\mu\varepsilon_1^2\beta_1H^*I^{*^2} \\
& - 2\mu\varepsilon_1^2\beta_2I^*H^{*^2} - \mu\varepsilon_1\beta_2^2S^*H^{*^2} - \mu\delta\beta_1\beta_2^2H^*S^{*^2} - \delta\mu^2\beta_2\beta_3A^*S^* - 2\sigma\varepsilon_2\beta_1\beta_3I^*S^* - 2\sigma\varepsilon_2\beta_2\beta_3H^*S^* \\
& - \mu\varepsilon_1\varepsilon_2\beta_2H^*I^* - \mu\phi_1\varepsilon_1\beta_2H^*S^* - \mu\phi_1\varepsilon_2\delta\beta_2S^* - 2\mu\varepsilon_1^2\beta_3I^*H^*A^* - \mu^2\delta\beta_2\beta_3A^*S^* - \mu^2\delta\beta_1\beta_2H^*S^* \\
& - \mu^2\delta\beta_1\beta_2I^*S^* - 2\mu^2\varepsilon_1\delta\beta_2H^*S^* - 2\mu\phi_2\delta\beta_1\beta_2H^*S^* - \mu\sigma\delta\beta_1\beta_2H^*S^* - 2\mu\phi_1\varepsilon_1\delta\beta_2H^*S^* \\
& - 2\mu\varepsilon_1\beta_2\beta_3S^*H^*A^* - \mu\alpha\delta\beta_1\beta_2H^*S^* - \mu\varepsilon_2\delta\beta_1\beta_2I^*S^* - 2\mu\varepsilon_1\delta\beta_2\beta_3S^*H^*A^* - 2\mu\varepsilon_1\delta\beta_1\beta_2I^*H^*S^* \\
& - \sigma\phi_1\varepsilon_2\beta_3S^* - 2\varepsilon_2\alpha\beta_3^2A^*S^* - 2\mu\varepsilon_2\beta_3^2A^*S^* - 2\phi_2\varepsilon_2\beta_3^2A^*S^* - 2\sigma\varepsilon_2\beta_3^2A^*S^* - \mu\varepsilon_1\varepsilon_2\beta_3A^*I^* \\
& - 2\varepsilon_2\alpha\beta_2\beta_3H^*S^* - 2\alpha\varepsilon_2\beta_1\beta_3I^*S^* - 2\mu\varepsilon_2\beta_2\beta_3H^*S^* - 2\mu\varepsilon_2\beta_1\beta_3I^*S^* - 2\phi_2\varepsilon_2\beta_2\beta_3H^*S^* \\
& - 2\phi_2\varepsilon_2\beta_1\beta_3I^*S^* - \mu\sigma\varepsilon_2\beta_3S^* - \phi_1\phi_2\varepsilon_2\beta_3S^* - \mu\phi_2\varepsilon_2\beta_3S^* - \mu\phi_1\varepsilon_2\beta_3S^* - \alpha\phi_1\varepsilon_2\beta_3S^* \\
& - \alpha\mu\varepsilon_2\beta_3S^* + \alpha\mu^3 + \varepsilon_2\mu^3 + \phi_1\mu^3.
\end{aligned}
$$

By using Routh-Hurwitz criteria, e_0^* is stable if $a_1 > 0,\ a_3 > 0,\ a_4 > 0$ and $a_1a_2a_3 > a_3^2 + a_1^2a_4$. Furthermore, by substituting $a_1,\ a_2,\ a_3$ and a_4 with all parameters values in Table 1. By our calculation, we obtain that $a_1 = 0.4442$, $a_2 = 3.8202$, $a_3 = 0.1458$ and $a_4 = 0.0013$. In addition, we have $a_1a_2a_3 > a_3^2 + a_1^2a_4$. Therefore e_0^* is locally asymptotically stable. We complete the proof.

3. Optimal control

Now we turn to the more general model with time-dependent controls $f_1(t)$ and $f_2(t)$. We consider the system on a time interval [0, T]. The function $f_1(t)$ and $f_2(t)$ are assumed to be at least Lebesgue measurable on [0,T]. The control set is defined as

$$W = \left\{ \left(f_1(t), f_2(t) \right) \mid 0 \le f_1(t) \le f_{1\max}, 0 \le f_2 \le f_{2\max} \right\}$$

where $f_{1\max}$ and $f_{2\max}$ denotes the upper bounds for the effort of vaccination for HIV and treatment for TB, respectively. The presence of time-dependent controls makes the analysis of our system difficult. In fact, the disease dynamics now depend on the evolution of control. In what follows we perform an optimal control study on this problem. We aim to minimize the total number of infections and the costs of control over the time interval [0, T]; i.e.,

$$\min_{f_{1,2} \in W} \int_0^T \left(I(t) + H(t) + A(t) + c_{11} f_1(t) S(t) + c_{21} f_2(t) H(t) + c_{12} f_1^2(t) + c_{22} f_2^2(t) \right) dt. \tag{3.1}$$

Here, the parameters c_{11}, c_{12}, c_{21} and c_{22} with appropriate units, define the appropriate costs associated with these controls. Quadratic terms are introduced to indicate nonlinear costs potentially arising at high intervention level. The minimization process is subject to the differential equation of our system, which are now referred to as the state equations. Correspondingly, the unknowns I, H and A are now called the state variables, in contrast to the control variables ϕ_1 and ϕ_2. Our goal is to determine the optimal controls $\phi_1^*(t)$ and $\phi_2^*(t)$, so as to minimize the objective functional in (3.1).

Let us first define the adjoint functions $\lambda_S, \lambda_I, \lambda_H$ and λ_A associated with the state equations for S, I, H and A respectively. We then form the Hamiltonian, M, by corresponding state equations, and adding each of these products to the integrand of the objective functional. As a result, we obtain

$$\begin{aligned} M = {} & I(t) + H(t) + A(t) + c_{11} f_1(t) S(t) + c_{12} f_1^2(t) + c_{21} f_2(t) H(t) + c_{22} f_2^2(t) \\ & + \lambda_S(\mu N - b_1 IS - b_2 HS - b_3 AS - \mu S - f_1 S) \\ & + \lambda_I(b_1 IS + (1-\delta) b_2 HS + b_3 AS - \varepsilon_1 IH - \varepsilon_2 I - \mu I + f_2 H) \\ & + \lambda_H(\varepsilon_1 IH + \delta b_2 HS - \sigma H - \mu H - \alpha H - f_2 H) \\ & + \lambda_A(\varepsilon_2 I + \sigma H - \mu A). \end{aligned}$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_S}{dt} = -\frac{\partial M}{\partial S}$, $\frac{d\lambda_I}{dt} = -\frac{\partial M}{\partial I}$, $\frac{d\lambda_H}{dt} = -\frac{\partial M}{\partial H}$, and $\frac{d\lambda_A}{dt} = -\frac{\partial M}{\partial A}$ with final time conditions:

$$\lambda_S(T) = 0, \quad \lambda_I(T) = 0, \quad \lambda_H(T) = 0 \text{ and } \lambda_A(T) = 0.$$

The characterization of the optimal control $\phi_1^*(t)$ and $\phi_2^*(t)$ are based on the conditions $\frac{\partial M}{\partial f_1} = 0$ and $\frac{\partial M}{\partial f_2} = 0$, respectively. Furthermore, the control set $\left(f_1^*, f_2^* \right)$ is characterized by

$$f_1^*(t) = \max\left(0, \min\left(f_1(t), f_{1\max}\right)\right) \text{ and } f_2^*(t) = \max\left(0, \min\left(f_2(t), f_{2\max}\right)\right),$$

where $f_1(t) = \dfrac{\prime_S(S) - c_{11}S(t)}{2c_{12}}$ and $f_2(t) = \dfrac{\prime_H(H) - c_{21}H(t) - \prime_I(H)}{2c_{22}}$.

Due to the presence of both initial conditions (for the state equations) and final time conditions (for the adjoint equations), and the fact that most models of our interest are nonlinear, the optimal control system has to be solved numerically.

4. Numerical simulation

In this study, we show some numerical solutions on the optimal control model. We apply the Euler method to compute the optimality control solution. The simulations were carried out using the following values in Table1. We use Matlab software for the numerical simulations.

Table1 HIV/AIDS with Tuberculosis model parameters.

Parameter	Value	Reference	Parameter	Value	Reference
N	10000	Assumed	ε_1	$5\times10^{-2.5}$	Estimated
μ	0.02	Mukandavire, Z.et al.(2009)	ε_2	0.125	Joyce K.N. et al (2015)
β_1	8×10^{-4}	Estimated	δ	0.3	Estimated
β_2	2.5×10^{-4}	Estimated	σ	0.125	Estimated
β_3	1×10^{-4}	Joyce K.N. et al (2015)	α	0.4	Estimated

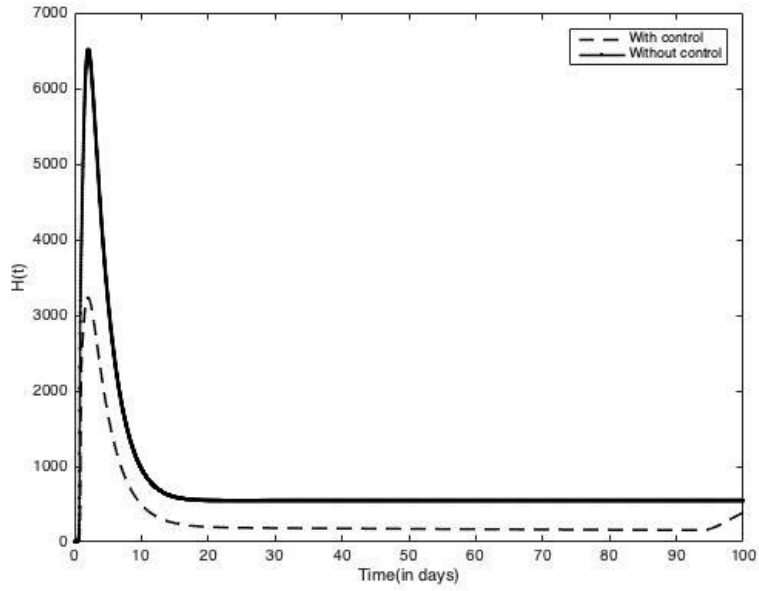

Figure 1: HIV infectious with Tuberculosis population.

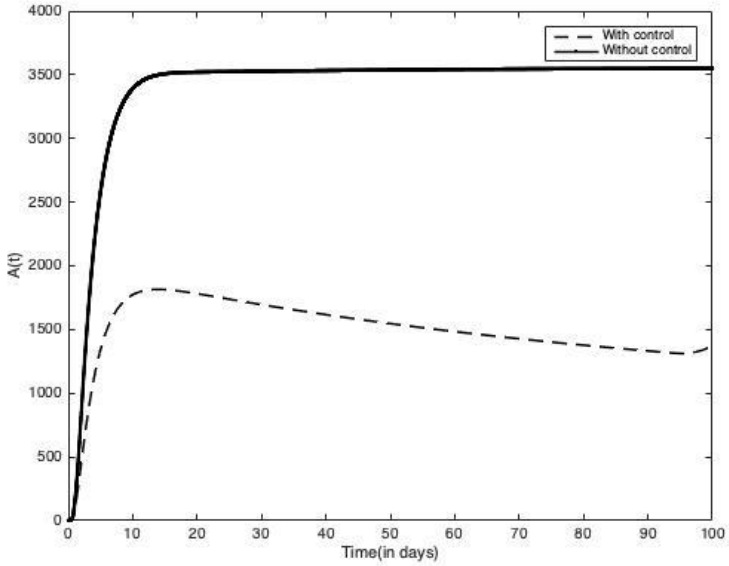

Figure 2: Full-blown AIDS population

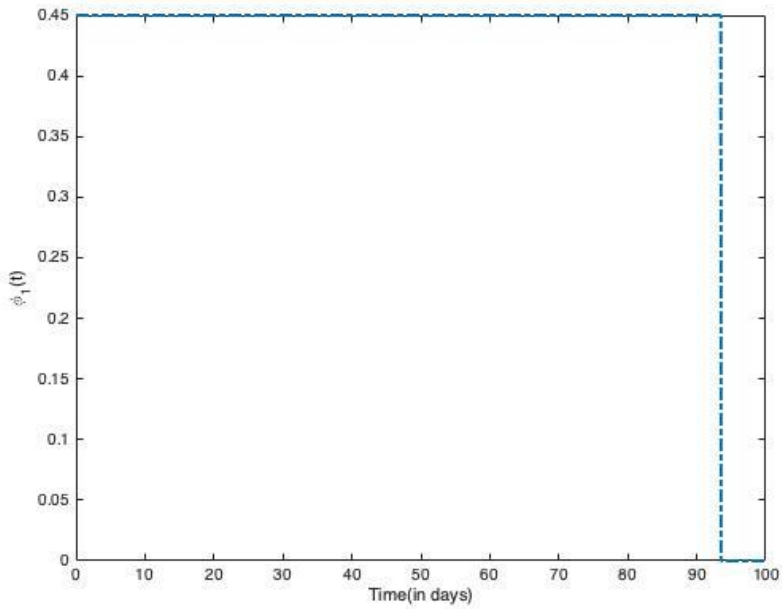

Figure 3: Vaccinated rate for HIV

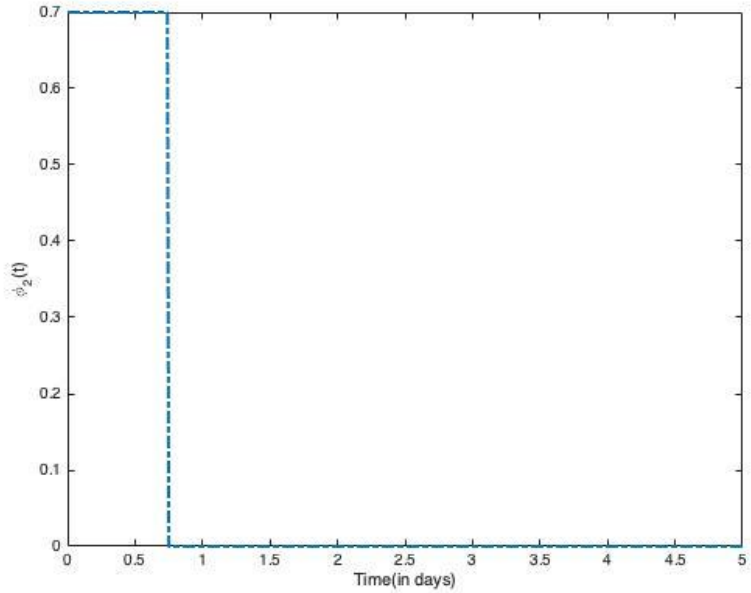

Figure 4: Medication rate for HIV with Tuberculosis

Figure1 and figure 2 shows simulation result of the model with and without the control. The figure shows the infection curves for the model with controls (dashed line) and that without the optimal controls (solid line). It is observed in Figure 1 that the number of HIV infectious with Tuberculosis population remains higher for the controlled problem than for the uncontrolled problem. Similarly, Figure 2 show that the number of full-blown AIDS populations remains higher for the controlled problem than for the uncontrolled problem. That means that the vaccination for HIV and treatment for TB strategies will lead to saving more people from being infected. Furthermore, figure 3 and figure 4 shows strategy guidelines of controls. Figure 3 shows the strategy of f_1 that it has to give f_1 at 45% about 93 days. Figure 4 show the strategy of f_2 that it has to give f_2 at 70% about 0.8 day.

CONCLUSIONS

This study has presented a mathematical model for the control problem of HIV/AIDS. This model has been constructed using both theoretical and numerical methods. In order to observe the effect of rate of medical therapy and the efficiency of medical treatments on the spread control of the disease. The equilibrium analysis has been conducted. The stability of the disease-free equilibrium point and the endemic equilibrium point are controlled by the threshold number (R_0). If R_0 is less than one, then the disease dies out and the disease-free equilibrium is stable. If R_0 is greater than one, then the disease persists and the disease-free equilibrium is unstable. From the numerical results, we found that the vaccination for HIV and treatment for

TB strategies will lead to saving more people from being infected. In conclusion, this work demonstrated the value of optimal control theory as a tool to determine an effective strategy to reduce HIV with TB and AIDS populations.

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