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A MATHEMATICAL SIMULATION AND OPTIMAL CONTROL OF A VIH MODEL WITH DIFFERENT INFECTIOUS LEVEL

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Abstract. In this paper, we consider a mathematical model of propagation HIV disease. We propose a case with three different levels of infection. The model was analyzed using the stability theory of a nonlinear differential equation. We describe the equilibrium point of the model and the basic reproduction number. This equilibrium point is both locally and globally stable under certain conditions. A control problem is formulated, we use an optimal control strategies to reduce the number of deaths and to reduce the spread of HIV. Some results concerning the existence and the characterization of the optimal control will be given. The Pontryagin's maximum principle is used to characterize the optimal control. We obtained an optimality system that we sought to solve numerically by an iterative discrete schema that converges following an appropriate test similar the one related to the forward-backward sweep method. Numerical simulations are given to illustrate the obtained results.

Keywords: VIH model; stability; basic reproduction number; optimal control.

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1. INTRODUCTION

HIV is a virus that exists and spreads in both developed and developing countries, but with a different rate. It is transmitted from person to person in different ways: sexual transmission, sharing of needles by users, intravenous drug use, mother-to-child transmission (vertical transmission), and transmission by blood transfusion contaminated. To slow the spread of HIV there are many strategies include voluntary HIV testing, use of condoms and awareness programs to promote safer sex, circumcision, use of vaginal microbicides and the use of antiretroviral (ARV) drugs. There is no safe and effective vaccine against HIV yet.

HIV is one of the deadly diseases, causing millions of deaths in the word. More than 38 million people worldwide are living with HIV in 2019. At the end of 2019 and according to estimates by the Ministry of Health 21,500 people were living with HIV in Morocco, of which 6,000 (22%) do not yet know their HIV status. On the 850 new HIV infections recorded in Morocco in 2019, 34% were among those aged 15-24. The data also show 300 deaths. In detail, 67% of new infections occur in networks of key populations at higher risk of infection. $70,7\%$ of women are infected by their spouse. Statistics reveal a low prevalence of HIV in Morocco among the general population $(0,08\%)$, $1,7\%$ among "female workers", $5,9\%$ on average among homosexuals, $7,1\%$ on average among people who inject drugs. Three regions account for almost 65% of notifed cases, namely Sous-Massa (25%), Marrakech-Safi (21%) and Casablanca-Settat (20%).

The importance of creating a mathematical model of HIV is to provide an explanation and interpretation of the spread of HIV, given that it is an invisible and contagious virus. Based on this model, we can judge the approved procedures mentioned by many analysts and specialist physicians and pharmacists are sufficient to limit the spread of this virus. Many HIV models have been discussed by several authors [7], [2], [8], [9], [12], [13], [14], [18], [15], [16], [17], [19], [21]. J. Silva [19] has proposed a epidemiological model of HIV/AIDS transmission including Pre-exposure prophylaxis PrEP. In the same context Zhiming Li [12] established a susceptible-exposed in the latent stage-infectious (SEI) mode to sketch the evolution of epidemic. A vivo deterministic model has studied by Purity Ngina and Al [14], they have give a various HIV treatment strategies. Mohammad Shirazian [18] has proposed a mathematical method implemented to formulate guidelines for

clinical testing and monitoring of HIV/AIDS disease.

We proposed a mathematical HIV model that identifies and describes the spread of HIV. Discrete modeling is more realistic because HIV data are collected discreetly, but we rely on a continuous model because it is less complex to treat. In this paper, we formulated a system of HIV disease, assuming three, different and varying infections cases.

Symptoms of HIV/AIDS vary depending on the stage of infection. The first case is the primary infection (acute HIV). However, the amount of virus in your bloodstream (viral load) is very high at the same time. The virus infects a large number of TCD4+ cells and reproduces rapidly. As a result, infection spreads during the initial infection more easily than during the next stage. The second case is the secondary state of infection where the immune system deteriorates. As the virus continues to multiply and destroy immune cells, cells in the body that help fight germs may develop mild infections or chronic signs. The third case is the advanced state of the disease where the immune system breaks down and the individual develops a loss of immunity to many other pathogens. The methods adopted by the Moroccan Ministry of Health in dealing with this dangerous epidemic are good methods and give good results, as the World Health Organization stated that the proportion of people infected with HIV and those infected with AIDS does not exceed 0.003 globally. Thus, we conclude that most people infected with HIV do not develop AIDS. If HIV is not treated, it will turn into AIDS. With AIDS, your immune system is severely damaged. You're more likely to develop opportunistic infections or opportunistic cancers, which usually don't affect people with a healthy immune system.

In this work, we will study an HIV model with its three cases of infection and we assume that the states of the patient can deteriorate and pass from one state to another and we will assume that the state of an infected can also improve and change the infection level, for example from an advanced state to a secondary state or from a secondary state to a primary state.

Optimal control theory is well used as an available and effective option for decision-makers to develop and simulate control strategies, see [7], [1], [4], [11], [18], [19]. We use an optimal control strategy to control the spread of infectious diseases by setting four controls. The first two controls

are introduced to reduce the deterioration of patient's condition and the others controls are considered for improve the patient's condition. The two controls are considered in order to minimize the number of death and infected in critical cases, increase the number of recovered individuals and this with an optimal cost.

The paper is organized as follows: In section 2, the HIV model is described and basic properties are given. Local stability analysis of the HIV disease-free equilibrium is presented in section 3. The analysis of the optimal control strategies is presented, we first show the existence of solutions of the system, after that we will prove the existence of optimal control in section 4. In section 5, we give the numerical method and the simulation results. Finally a conclusion is summarized in section 6.

2. A Mathematical Model and Basic Properties

2.1. Structure of the model. We propose a continuous model SIIQR to describe the interaction within a population where the disease HIV exists. where $S(t), I_1(t), I_2(t), Q(t), R(t)$ are the number of susceptible population, infective population step 1, infective population step 2, infective population under the stone , recovered population,respectively.

We assume that the total size of population $N(t)$ is constant, in the rest of paper i.e,

$$S(t)+I_1(t)+I_2(t)+Q(t)+R(t)=N(t).\ t\geq 0$$

The graphical representation of the proposed model is shown in Figure (1).

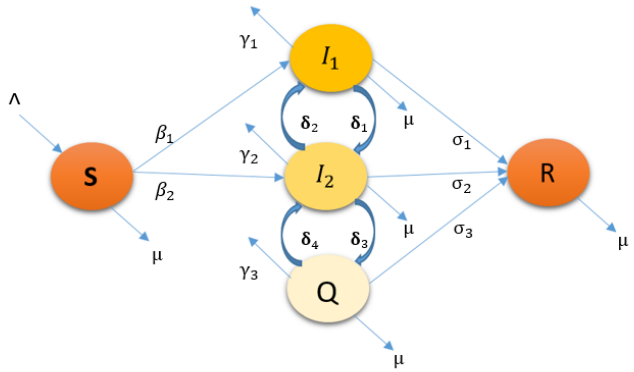


Figure (1): The schematic diagram of the HIV model

We consider the following system of five non-linear differential equations

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - (\beta_1 I_1 + \beta_2 I_2)S \\ \frac{dI_1}{dt} = \beta_1 I_1 S + \delta_2 I_2 - \delta_1 I_1 - \gamma_1 I_1 - \mu I_1 - \sigma_1 I_1 \\ \frac{dI_2}{dt} = \beta_2 I_2 S + \delta_4 Q + \delta_1 I_1 - \gamma_2 I_2 - \delta_2 I_2 - \delta_3 I_2 - \mu I_2 - \sigma_2 I_2 \\ \frac{dQ}{dt} = \delta_3 I_2 - \gamma_3 Q - \delta_4 Q - \mu Q - \sigma_3 Q \\ \frac{dR}{dt} = \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 Q - \mu R \end{cases} \quad (1.1)$$

where $S(0) \geq 0$; $I_1(0) \geq 0$; $I_2(0) \geq 0$; $Q(0) \geq 0$ and $R(0) \geq 0$ are the given initial states.

Where Λ represents new birth rate in susceptible human population, β_1 represents the transmission coefficient from susceptible individuals to infected step 1 and β_2 represents the transmission coefficient from susceptible individuals to infected step 2 $\star$ μ represents the natural death rate in all compartments. δ_1 represents the rate of transmission of infected step 1 to infected step 2. δ_2 represents the rate of transmission of infected step 2 to infected step 1. δ_3 represents the rate of transmission of infected step 2 to infected hospitalized. δ_4 represents the rate of transmission of hospitalized to infected step 2. σ_1,σ_2 and σ_3 represents the transmission coefficient of infected step 1 ,infected step 2 and the hospitalized cases to the recovered cases. γ_1, γ_2 and γ_3 respectively represent the death rate of infected step 1 ,infected step 2 and the hospitalized cases.

For the rest of this paper, we will consider the system (1.1) in its following form

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - (\beta_1 I_1 + \beta_2 I_2)S \\ \frac{dI_1}{dt} = \beta_1 I_1 S + \delta_2 I_2 - m_1 I_1 \\ \frac{dI_2}{dt} = \beta_2 I_2 S + \delta_4 Q + \delta_1 I_1 - m_2 I_2 \\ \frac{dQ}{dt} = \delta_3 I_2 - m_3 Q \\ \frac{dR}{dt} = \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 Q - \mu R \end{cases} \quad (1.2)$$

where

$$\begin{cases} m_1 = \delta_1 + \gamma_1 + \mu + \sigma_1 \\ m_2 = \gamma_2 + \delta_2 + \delta_3 + \mu + \sigma_2 \\ m_3 = \gamma_3 + \delta_4 + \mu + \sigma_3. \end{cases}$$

2.2. Basic properties of the model.

Proposition 1. *The set*

$$\Omega = \{(S,I_1,I_2,Q,R) \in R^5_+, S,I_1,I_2,Q,R > 0 \text{ and } S+I_1+I_2+Q+R < \frac{\Lambda}{\mu}\}$$

is a positively invariant and attracting region for the disease transmission model given by our system with initial conditions.

Proof. *Summing up the five equations in our system and denoting*

$$S(t)+I_1(t)+I_2(t)+Q(t)+R(t) = N(t)$$

we get

$$\begin{aligned} \frac{dN(t)}{dt} = \Lambda - \mu(S+I_1+I_2+Q+R) - \gamma_1 I_1 - \gamma_2 I_2 - \gamma_3 Q &\leq \Lambda - \mu N(t) \\ \frac{dN(t)}{dt} + \mu N(t) &\leq \Lambda \end{aligned}$$

Now integrating both sides of the above inequality and using the theory of differential inequality , we obtain

$$0 < N \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1-e^{-\mu t}).$$

Clearly, $0 < N \leq \frac{\Lambda}{\mu}$ *as* $t \longrightarrow \infty$ *. if* $N(0) \leq \frac{\Lambda}{\mu}$, $N(t) \leq \frac{\Lambda}{\mu}$ $\forall t \geq 0$.*Thus, the set* Ω *is positive invariant,i.e., all initial solutions belong to* Ω *remain in* Ω *for all* $t > 0$.

2.2.1. *Positivity of states.*

Theorem 1. *If* $S(0) \geq 0$, $I_1(0) \geq 0$, $I_2(0) \geq 0$, $Q(0) \geq 0$ *and* $R(0) \geq 0$, *then the solutions of system equation (1.2)* $S(t)$, $I_1(t)$, $I_2(t)$, $Q(t)$ *and* $R(t)$ *are positive for all* $t > 0$.

Proof. *From the first equation of the system (1.2), we have*

$$\begin{aligned} \frac{dS(t)}{dt} &= \Lambda - \mu S(t) - (\beta_1 I_1(t) + \beta_2 I_2(t))S(t) \\ \frac{dS(t)}{dt} &= \Lambda - A(t)S(t) \end{aligned} \tag{1}$$

where

$$A(t) = \mu + (\beta_1 I_1 + \beta_2 I_2)$$

We multiply equation (1) by $exp(\int_0^t A(s)ds)$,we find

$$\frac{dS(t)}{dt}exp(\int_0^t A(s)ds) = (\Lambda - A(t)S(t))exp(\int_0^t A(s)ds)$$

$$\frac{dS(t)}{dt}exp(\int_0^t A(s)ds) + A(t)S(t)exp(\int_0^t A(s)ds) = \Lambda exp(\int_0^t A(s)ds)$$

Therefore

$$\frac{d}{dt}[S(t)exp(\int_0^t A(s)ds)] = \Lambda exp(\int_0^t A(s)ds).$$

Taking integral with respect to s from 0 to t, we get

$$S(t)exp(\int_0^t A(s)ds) - s(0) = \Lambda \int_0^t (exp \int_0^w A(s)ds)dw. \tag{2}$$

Multiplying the equation (2) by $exp(-\int_0^t A(s)ds)$,we get

$$S(t) - s(0)exp(-\int_0^t A(s)ds) = \Lambda exp(-\int_0^t A(s)ds).\int_0^t (\int_0^w A(s)ds)dw$$

then,

$$S(t) = S(0)exp(-\int_0^t A(s)ds) + \Lambda exp(-\int_0^t A(s)ds).\int_0^t (\int_0^w A(s)ds)dw \geq 0.$$

So, the solution S(t) is positive.

Similarly, from the others equations of system (1.2), we have

$$\begin{aligned} I_1(t) \geq I_1(0)exp(-(\beta_1 S(t) - m_1)) &\geq 0 \\ I_2(t) \geq I_2(0)exp(-(\beta_2 S(t) - m_2)) &\geq 0 \\ Q(t) \geq Q(0)exp(m_3) &\geq 0 \\ R(t) \geq R(0)exp(\mu) &\geq 0. \end{aligned}$$

Therefore, we can see that the solutions $S(t); I_1(t); I_2(t); Q(t)$ and $R(t)$ of the system (1.2) are positive for all $t \geq 0$. This completes the proof.

3. Stability Analysis of the Model

3.1. Equilibrium point. Free equilibrium point of the spread dynamic of HIV disease is

$$E_0 = (S, I_1, I_2, Q, R) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$$

3.2. Reproduction number analysis. By using the concepts of next generation matrix and reproduction number presented in [5, 20], we compute the reproduction number of the system (1.2).

$$Where\ F = \begin{pmatrix} \beta_1 I_1 S \\ \beta_2 I_2 S \end{pmatrix}\ and\ V = \begin{pmatrix} \delta_2 I_2 - m_1 I_1 \\ \delta_4 Q + \delta_1 I_1 - m_2 I_2 \end{pmatrix}$$

Suppose f is Jacobian matrix from F and v is Jacobian matrix from V . So, at the free equilibrium disease $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$ obtained :

$$f = \begin{pmatrix} \beta_1 \frac{\Lambda}{\mu} & 0 \\ 0 & \beta_2 \frac{\Lambda}{\mu} \end{pmatrix}\ and\ v = \begin{pmatrix} m_1 & -\gamma_2 \\ -\gamma_1 & m_2 \end{pmatrix}$$

the inverse matrix $v^{-1} = \frac{1}{m_1 m_2 - \gamma_1 \gamma_2} \begin{pmatrix} m_2 & \gamma_2 \\ \gamma_1 & m_1 \end{pmatrix}$ and $\zeta = \frac{1}{m_1 m_2 - \gamma_1 \gamma_2}$

than ,

$$fv^{-1} = \zeta \begin{pmatrix} \beta_1 m_2 & \beta_1 \gamma_2 \\ \beta_2 \gamma_1 & \beta_2 m_1 \end{pmatrix}$$

for,

$$det(fv^{-1} - \lambda I) = \zeta((\beta_1 m_2 - \lambda)(\beta_2 m_1 - \lambda) - (\beta_1 \gamma_2 \beta_2 \gamma_1)) = 0.$$

We obtained R_0 from the absolute biggest of eigenvalues from fv^{-1} so

$$R_0 = \frac{\zeta}{2}((\beta_1 m_2 + \beta_2 m_1) + \sqrt{(\beta_1 m_2 - \beta_2 m_1)^2 + 4\beta_1 \beta_2 \gamma_1 \gamma_2}).$$

$\star$ If $R_0 < 1$ it means that every individual infected can transmit the disease to less than one new patients so that HIV sickness cannot have developed in the population.

$\star$ If $R_0 > 1$ it means that individuals infected can transmit the disease to more than new one patients so that HIV sickness can spreading in the population.

3.3. Local stability analysis of the HIV disease-free equilibrium.

Theorem 2. *the system (1.2) is locally asymptotically stable at the free aquilibrium point* $E_0 = (\frac{\Lambda}{\mu},0,0,0,0)$ *if* $R_0 < 1$ *.Whereas,* $E_0 = (\frac{\Lambda}{\mu},0,0,0,0)$ *is unstable if* $R_0 > 1$.

Proof. *To proof the stability from the free equilibrium of disease* E_0*, we proced to the linearization of system by determining the Jacobian matrix.*

The Jacobian matrix of E_0 *follows:*

$$J_0 = \begin{pmatrix} \beta_1 \frac{\Lambda}{\mu} - m_1 & \gamma_2 \\ \gamma_1 & \beta_2 \frac{\Lambda}{\mu} - m_2 \end{pmatrix}$$

and

$$det(J_0 - \lambda I) = \begin{pmatrix} \beta_1 \frac{\Lambda}{\mu} - m_1 - \lambda & \gamma_2 \\ \gamma_1 & \beta_2 \frac{\Lambda}{\mu} - m_2 - \lambda \end{pmatrix}.$$

Stability at the point of free equilibrium disease can be seen from the value of the eigen at matrix jacobian, if all the parts of the value of real eigen Jacobian matrix are negative.so E_0 *locally asyptotically stable.*

The eigenvalue of the Jacobien matrix are :

$$\lambda_1 = \frac{\frac{\Lambda}{\mu}(\beta_1 + \beta_2) - (m_1 + m_2) - \sqrt{(\frac{\Lambda}{\mu}(\beta_1 - \beta_2) - m_1 + m_2)^2 + 4\gamma_1\gamma_2}}{2}$$
$$\lambda_2 = \frac{\frac{\Lambda}{\mu}(\beta_1 + \beta_2) - (m_1 + m_2) + \sqrt{(\frac{\Lambda}{\mu}(\beta_1 - \beta_2) - m_1 + m_2)^2 + 4\gamma_1\gamma_2}}{2}.$$

If $R_0 < 1$*, then*

$$\frac{\zeta}{2}((\beta_1 m_2 + \beta_2 m_1) + \sqrt{(\beta_1 m_2 - \beta_2 m_1)^2 + 4\beta_1\beta_2\gamma_1\gamma_2}) < 1$$

$\Rightarrow$ $\frac{\zeta}{2}\beta_1 m_2 < 1$, $\frac{\zeta}{2}\beta_2 m_1 < 1$ *and* $\frac{\zeta^2}{4}((\beta_1 m_2 - \beta_2 m_1)^2 + 4\beta_1\beta_2\gamma_1\gamma_2) < 1$.

We have

$$\begin{aligned}
\diamond\ \lambda_1 < 0 \ &\Rightarrow\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)-\sqrt{(\frac{\Lambda}{\mu}(\beta_1-\beta_2)-m_1+m_2)^2+4\gamma_1\gamma_2}<0\\
&\Rightarrow\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)<\sqrt{(\frac{\Lambda}{\mu}(\beta_1-\beta_2)-m_1+m_2)^2+4\gamma_1\gamma_2}\\
&\Rightarrow\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)m_2-(m_1m_2+\gamma_1\gamma_2)>0.
\end{aligned}$$

$$\begin{aligned}
Then, if\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)<0 \ &\Rightarrow\ \lambda_1<0\\
and if\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)>0 \ &\Rightarrow\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-m_1>m_2\\
&\Rightarrow\ 4\frac{\Lambda}{\mu}(\beta_1+\beta_2)m_2-4m_1m_2+4\gamma_1\gamma_2>0.
\end{aligned}$$

So the reality of an eigenvalue λ_1 is negative

$$\begin{aligned}
We have \diamond\ \lambda_2<0 \ &\Leftrightarrow\ \frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)+\sqrt{(\frac{\Lambda}{\mu}(\beta_1-\beta_2)-m_1+m_2)^2+4\gamma_1\gamma_2}<0\\
&\Leftrightarrow\ (\frac{\Lambda}{\mu}(\beta_1-\beta_2)-m_1+m_2)^2+4\gamma_1\gamma_2<((m_1+m_2)-\frac{\Lambda}{\mu}(\beta_1+\beta_2))^2\\
&\Leftrightarrow\ \frac{\Lambda}{\mu}(\beta_2m_1+\beta_1m_2-\frac{\Lambda}{\mu}\beta_1\beta_2)-\frac{\Lambda}{\mu\zeta}<0
\end{aligned}$$

if $\frac{\Lambda}{\mu}(\beta_1+\beta_2)-(m_1+m_2)<0 \Rightarrow \frac{\Lambda}{\mu}(\beta_1+\beta_2)<m_1+m_2$ *and if* $R_0<1$*, then*

$$\begin{aligned}
\frac{\zeta}{2}((\beta_1m_2+\beta_2m_1)+\sqrt{(\beta_1m_2-\beta_2m_1)^2+4\beta_1\beta_2\gamma_1\gamma_2}) &< 1\\
((\beta_1m_2+\beta_2m_1)+\sqrt{(\beta_1m_2-\beta_2m_1)^2+4\beta_1\beta_2\gamma_1\gamma_2}) &< \frac{2}{\zeta}\\
(\beta_1m_2-\beta_2m_1)^2+4\beta_1\beta_2\gamma_1\gamma_2 &< \frac{4}{\zeta^2}-\frac{4}{\zeta}(\beta_1m_2+\beta_2m_1))^2+(\beta_1m_2+\beta_2m_1)^2\\
\beta_1\beta_2(\gamma_1\gamma_2-m_1m_2) &< \frac{1}{\zeta}(\frac{1}{\zeta}-(\beta_1m_2+\beta_2m_1))\\
\frac{\Lambda}{\mu}(\beta_2m_1+\beta_1m_2-\frac{\Lambda}{\mu}\beta_1\beta_2)-\frac{\Lambda}{\mu\zeta} &< 0 \qquad (3)
\end{aligned}$$

It is easy to see that if $R_0<1 \ \Rightarrow\ \lambda_2<0$

3.4. Global stabilty of the HIV disease-free equilibrium. To show that the system (1.2) is globally asymptotically stable, we use the Lyapunov function theory for the HIV disease free equilibrium.

Theorem 3. *The system (1.2) at the free equilibruim* $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$ *is globally asymptotically stable if* $R_0 \leq 1$ *and unstable otherwise.*

Proof. *Let the following Lyapunov function:*

$$V : \Delta \longrightarrow \mathbb{R}$$

$$V(I_1, I_2, Q) = \frac{\Lambda}{\mu}((m_1 - \frac{\Lambda}{\mu}\beta_1)(I_2 + Q) + \delta_1 I_1)$$

where

$$\Delta = \{(I_1, I_2, Q) \in \Omega / I_1 > 0, I_2 > 0, Q > 0\}$$

Then, the time derivative of the Lyapunov function is given by:

$$\begin{aligned}
\frac{dV(I_1, I_2, Q)}{dt} &= \frac{\Lambda}{\mu}((m_1 - \frac{\Lambda}{\mu}\beta_1)(\beta_2 S I_2 + \delta_1 I_1 + \delta_4 Q - m_2 I_2 + \delta_3 I_2 - m_3 Q) + \beta_1 S I_1 + \delta_2 I_2 - m_1 I_1) \\
\frac{dV(I_1, I_2, Q)}{dt} &= \frac{\Lambda}{\mu}(\beta_1 m_2 + \beta_2 m_1 - \frac{\Lambda}{\mu}\beta_1\beta_2 - \frac{1}{\zeta})SI_2 - \frac{\Lambda}{\mu}\delta_1\beta_1(S_0 - S)I_1 - \frac{\Lambda}{\mu}(m_1 - \frac{\Lambda\beta_1}{\mu})(m_3 - \delta_4)Q \\
&- \frac{\Lambda}{\mu}((m_1 - \frac{\Lambda\beta_1}{\mu})(m_2 - \delta_3) + (S(\beta_1 m_2 - \frac{\Lambda}{\mu\zeta}) - \delta_1\delta_2))I_2
\end{aligned}$$

from the equation (3)

$$(\beta_1 m_2 + \beta_2 m_1 - \frac{\Lambda}{\mu}\beta_1\beta_2 - \frac{1}{\zeta}) < 0 \; for \; R_0 < 1$$

than

$$\frac{dV(I_1, I_2, Q)}{dt} < 0 \; for \; (\beta_1 m_2 + \beta_2 m_1 - \frac{\Lambda}{\mu}\beta_1\beta_2 - \frac{1}{\zeta}) < 0.$$

Note $\frac{dV(I_1, I_2, Q)}{dt} = 0$ *if and only if* $I_1 = 0, I_2 = 0$ *and* $Q = 0$. *Hence, by Lasalle's invariance principle,* E_0 *is globally asymptotically stable in* Ω.

4. The Optimal Control Problem

As all we know that the VIH exist from a long time ago. Every day the scientists try and try to find the efficacy treatment, but we still haven't found the medicine yet. So we have to control the VIH to reduce the number of patients. In our paper we will propose the controls u_1 and v_1 are introduced to minimize deterioration of patients condition and u_2 and v_2 to improve the condition of patients.

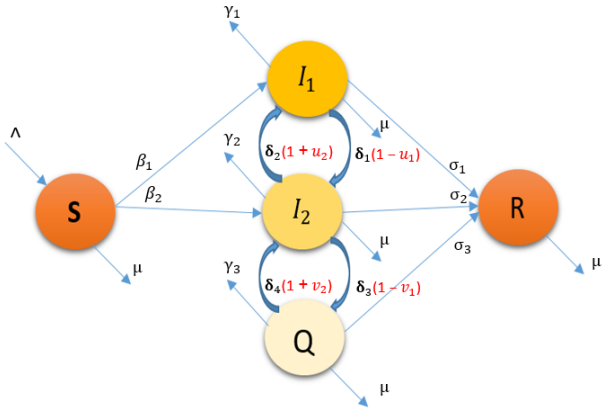


Figure (2): The schematic diagram of the HIV model with the optimal control .

So the mathematical controled system is given by following difference equations and schematically given by figure 2.

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - (\beta_1 I_1 + \beta_2 I_2) S \\ \frac{dI_1}{dt} = \beta_1 I_1 S + (1+u_2)\delta_2 I_2 - (1-u_1)\delta_1 I_1 - \gamma_1 I_1 - \mu I_1 - \sigma_1 I_1 \\ \frac{dI_2}{dt} = \beta_2 I_2 S + (1+v_2)\delta_4 Q + (1-u_1)\delta_1 I_1 - \gamma_2 I_2 - (1+u_2)\delta_2 I_2 - (1-v_1)\delta_3 I_2 - \mu I_2 - \sigma_2 I_2 \\ \frac{dQ}{dt} = (1-v_1)\delta_3 I_2 - \gamma_3 Q - (1+v_2)\delta_4 Q - \mu Q - \sigma_3 Q \\ \frac{dR}{dt} = \sigma_1 I_1 + \sigma_2 I_2 + \sigma_3 Q - \mu R \end{cases} \quad (1.3)$$

and the problem is to minimize the objective functional

$$J(u_1,u_2,v_1,v_2) = AI_1(T) + BI_2(T) + \int_0^T (AI_1(t) + BI_2(t) + \frac{M}{2}u_1^2 + \frac{N}{2}u_2^2 + \frac{K}{2}v_1^2 + \frac{F}{2}v_2^2)dt$$

In other words, we seek the optimal controls u_1^*, u_2^*, v_1^* and v_2^* such that

$$J(u_1^*,u_2^*,v_1^*,v_2^*) = minJ(u_1,u_2,v_1,v_2)\ (u_1,u_2,v_1,v_2) \in \mathscr{U}$$

where U is the set defined by

$$\mathscr{U} = \{\ (u_1,u_2,v_1,v_2) \in [0,1]^4\ /\ 0 \leq u_{1min} \leq u_1 \leq u_{1max} \leq 1,\ 0 \leq u_{2min} \leq u_2 \leq u_{2max} \leq 1,$$
$$0 \leq v_{1min} \leq v_1 \leq v_{1max} \leq 1,\ 0 \leq v_{2min} \leq v_2 \leq v_{2ax} \leq 1\}$$

4.1. The optimal control: Existence. We first show the existence of solutions of the system, after that we will prove the existence of optimal control.

Theorem 4. *Consider the control problem with the system. There are four optimal controls* $(u_1^*,u_2^*,v_1^*,v_2^*) \in U^4$ *such that*

$$J(u_1^*,u_2^*,v_1^*,v_2^*) = min(J(u_1,u_2,v_1,v_2))\ (u_1,u_2,v_1,v_2) \in \mathscr{U}$$

Proof. *We will use Fleming and Rishel* [6] *to proof the existence of the optimal control :*

⋆ *It follows that the set of controls and corresponding state variables is not empty. we will use a simplified version of an existence result.*

⋆ *The control space*

$$U = \{(u_1,u_2,v_1,v_2) \in [0,1]^4\ /\ 0 \leq u_{1min} \leq u_1 \leq u_{1max} \leq 1,\ 0 \leq u_{2min} \leq u_2 \leq u_{2max} \leq 1,$$
$$0 \leq v_{1min} \leq v_1 \leq v_{1max} \leq 1,\ 0 \leq v_{2min} \leq v_2 \leq v_{2max} \leq 1\}$$

is convex and closed by definition

⋆ $J(u_1,u_2,v_1,v_2)$ *is convex in U*

⋆ *All the right-hand sides of equations of system are continuous, bounded above by a sum of bounded control and state, and can be written as a linear function of* u_1, u_2, v_1, *and* v_2 *with coefficients depending on the time and state.*

⋆ *The integrand in the objective functional,*

$$AI_1(t) + BI_2(t) + \frac{M}{2}u_1^2 + \frac{N}{2}u_2^2 + \frac{K}{2}v_1^2 + \frac{F}{2}v_2^2,$$

is clearly convex on $\mathscr{U}$.

$\star$ *It rests to show that there exist constants $\zeta_1, \zeta_2, \zeta_3, \zeta_4, \zeta_5 > 0$ and ζ such that*

$$AI_1(t) + BI_2(t) + \frac{M}{2}u_1^2 + \frac{N}{2}u_2^2 + \frac{K}{2}v_1^2 + \frac{F}{2}v_2^2$$

satisfait

The state variables are being bounded; let $\zeta_1 = inf_{t\in[0,T]}(AI_2(t) + BQ(t))$, $\zeta_2 = M$, $\zeta_3 = N$, $\zeta_4 = K$, $\zeta_5 = F$ and $\zeta = 2$, then, it follows that

$$AI_1(t) + BI_2(t) + \frac{M}{2}u_1^2 + \frac{N}{2}u_2^2 + \frac{K}{2}v_1^2 + \frac{F}{2}v_2^2 \geq \zeta_1 + \zeta_2 \mid u_1 \mid^{\zeta} + \zeta_3 \mid u_2 \mid^{\zeta} + \zeta_4 \mid v_1 \mid^{\zeta} + \zeta_5 \mid v_2 \mid^{\zeta}$$

Then, from Fleming and Rishel, we conclude that there exists an optimal control.

4.2. Characterization of the optimal control. In order to derive the necessary conditions for the optimal control, we apply Pontryagin's maximum principle [3, 10] to the Hamiltonian H at time t defined by

$$H(t) = AI_1(t) + BI_2(t) + \frac{M}{2}u_1^2 + \frac{N}{2}u_2^2 + \frac{K}{2}v_1^2 + \frac{F}{2}v_2^2 + \sum_{i=1}^{5}\lambda_i f_i(S, I_1, I_2, Q, R)$$

where f_i is the right side of the difference equation of the ith state variable

Theorem 5. *Given the optimal controls $u_1^*, u_2^*, v_1^*, v_2^*$ and the solutions S, I_1, I_2, Q , and R of the corresponding state system (1.3), there exists adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4$, and λ_5 satisfying*

$$\begin{aligned}
\lambda_1^{'} &= -\frac{\partial H}{\partial S} = \lambda_1(\mu + (\beta_1 I_1 + \beta_2 I_2)) - \lambda_2\beta_1 I_1 - \lambda_3\beta_2 I_2 \\
\lambda_2^{'} &= -\frac{\partial H}{\partial I_1} = -A + \lambda_1\beta_1 S - \lambda_2(\beta_1 S - (1-u_1)\delta_1 - (\gamma_1 + \mu + \sigma_1)) - \lambda_3(1-u_1)\delta_1 - \lambda_5\sigma_1 \\
\lambda_3^{'} &= -\frac{\partial H}{\partial I_2} = -B + \lambda_1\beta_2 S - \lambda_2(1+u_2)\sigma_2 - \lambda_3(\beta_2 S - (1+u_2)\delta_2 - (1-v_1)\delta_3 - \mu - \sigma_2) \\
&\quad -\lambda_4(1-v_1)\delta_3 - \lambda_5\sigma_2 \\
\lambda_4^{'} &= -\frac{\partial H}{\partial Q} = -\lambda_3(1+v_2)\delta_4 + \lambda_4(\gamma_3 + (1+v_2)\delta_4 + \mu + \sigma_3) - \lambda_5\sigma_3 \\
\lambda_5^{'} &= -\frac{\partial H}{\partial R} = \lambda_5\mu
\end{aligned}$$

With the transversality conditions at time T: $\lambda_1(T)=0, \lambda_2(T)=-A, \lambda_3(T)=-B, \lambda_4(T)=0$ *and* $\lambda_5(T)=0$.

Furthermore, for $t\in[0,T]$*, the optimal controls* u_1^*, u_2^*, v_1^* *and* v_2^* *are given by*

$$u_1^* = min(1, max(0, \frac{(\lambda_3-\lambda_2)\delta_1 I_1}{M}))$$
$$u_2^* = min(1, max(0, \frac{(\lambda_3-\lambda_2)\delta_2 I_2}{N}))$$
$$v_1^* = min(1, max(0, \frac{(\lambda_4-\lambda_3)\delta_3 I_2}{K}))$$
$$v_2^* = min(1, max(0, \frac{(\lambda_4-\lambda_3)\delta_4 Q}{F}))$$

Proof. *The Hamiltonian is defined as follows:*

$$\begin{aligned}
f_1(S,I_1,I_2,Q,R) &= \Lambda-\mu S-(\beta_1 I_1+\beta_2 I_2)S\\
f_2(S,I_1,I_2,Q,R) &= \beta_1 I_1 S+(1+u_2)\delta_2 I_2-(1-u_1)\delta_1 I_1-\gamma_1 I_1-\mu I_1-\sigma_1 I_1\\
f_3(S,I_1,I_2,Q,R) &= \beta_2 I_2 S+(1+v_2)\delta_4 Q+(1-u_1)\delta_1 I_1-\gamma_2 I_2-(1+u_2)\delta_2 I_2-(1-v_1)\delta_3 I_2\\
&\quad -\mu I_2-\sigma_2 I_2\\
f_4(S,I_1,I_2,Q,R) &= (1-v_1)\delta_3 I_2-\gamma_3 Q-(1+v_2)\delta_4 Q-\mu Q-\sigma_3 Q\\
f_5(S,I_1,I_2,Q,R) &= \sigma_1 I_1+\sigma_2 I_2+\sigma_3 Q-\mu R.
\end{aligned}$$

For $t\in[0,T]$*, the adjoint equations and transversality conditions can be obtained by using Pontryagin's maximum principle* [3, 10] *such that*

$$\begin{aligned}
\lambda_1' &= -\frac{\partial H}{\partial S}=\lambda_1(\mu+(\beta_1 I_1+\beta_2 I_2))-\lambda_2\beta_1 I_1-\lambda_3\beta_2 I_2\\
\lambda_2' &= -\frac{\partial H}{\partial I_1}=-A+\lambda_1\beta_1 S-\lambda_2(\beta_1 S-(1-u_1)\delta_1-(\gamma_1+\mu+\sigma_1))-\lambda_3(1-u_1)\delta_1-\lambda_5\sigma_1\\
\lambda_3' &= -\frac{\partial H}{\partial I_2}=-B+\lambda_1\beta_2 S-\lambda_2(1+u_2)\sigma_2-\lambda_3(\beta_2 S-(1+u_2)\delta_2-(1-v_1)\delta_3-\mu-\sigma_2)\\
&\quad -\lambda_4(1-v_1)\delta_3-\lambda_5\sigma_2\\
\lambda_4' &= -\frac{\partial H}{\partial Q}=-\lambda_3(1+v_2)\delta_4+\lambda_4(\gamma_3+(1+v_2)\delta_4+\mu+\sigma_3)-\lambda_5\sigma_3\\
\lambda_4' &= -\frac{\partial H}{\partial R}=\lambda_5\mu
\end{aligned}$$

For, $t \in [0,T]$ the optimal controls u_1^*, u_2^*, v_1^*, and v_2^* can be solved from the optimality condition, $\frac{\partial H}{\partial S} = 0$, $\frac{\partial H}{\partial I_1} = 0$, $\frac{\partial H}{\partial I_2} = 0$, $\frac{\partial H}{\partial Q} = 0$, $\frac{\partial H}{\partial R} = 0$ and to find the optimal controls for $t \in [0,T]$,

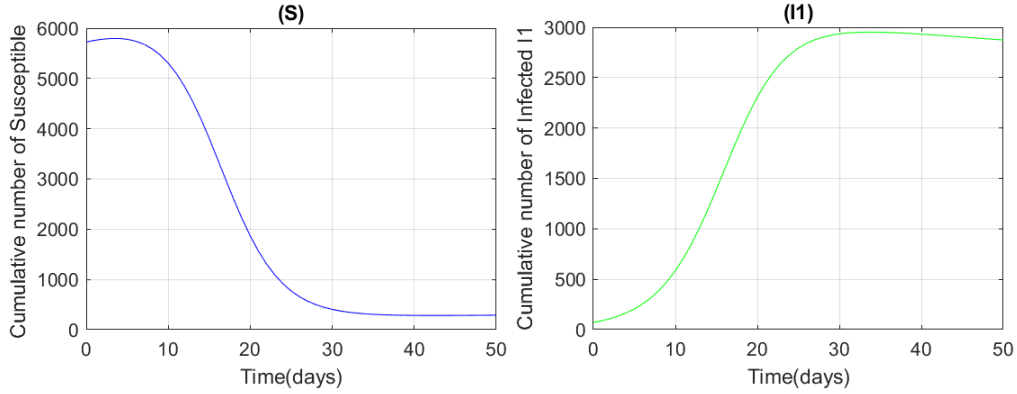
$$\begin{aligned}
\frac{\partial H}{\partial u_1} &= Mu_1 + (\lambda_2 - \lambda_3)\delta_1 I_1 = 0 \\
\frac{\partial H}{\partial u_2} &= Nu_2 + (\lambda_2 - \lambda_3)\delta_2 I_2 = 0 \\
\frac{\partial H}{\partial v_1} &= Kv_1 + (\lambda_3 - \lambda_4)\delta_3 I_2 = 0 \\
\frac{\partial H}{\partial v_2} &= Fv_2 + (\lambda_3 - \lambda_4)\delta_4 Q = 0
\end{aligned}$$

Then, we have $u_1 = \frac{(\lambda_3-\lambda_2)\delta_1 I_1}{M}$,$u_2 = \frac{(\lambda_3-\lambda_2)\delta_2 I_2}{N}$,$v_1 = \frac{(\lambda_4-\lambda_3)\delta_3 I_2}{K}$,$u_1 = \frac{(\lambda_4-\lambda_3)\delta_4 Q}{F}$.
By the bounds in U of the controls, we deduce that u_1^*, u_2^*, v_1^*, and v_2^* are given the form in the theorem.

5. Numerical Simulations

To validate the analytical results established in previous section, we conduct the numerical simulation by taking an example. The system (1.1) is simulated by fixing the default values of the parameters as $\Lambda = 70$, $\beta_1 = 0.0000405$, $\beta_2 = 0.0000483$, $\gamma_1 = 0.01$, $\gamma_2 = \gamma_3 = 0.02$, $\delta_1 = 9.2274e-03$ $\delta_2 = 8.0037e-03$, $\delta_3 = 2.8595e-03$, $\delta_4 = 1.8595e-03$, $\sigma_1 = 0, \sigma_2 = 0$, $\sigma_3 = 0$. All simulations are performed using Matlab. The initial values are taken as $S = 5726$, $I_1 = 70$, $I_2 = 40$, $Q = 10$ and $R = 0$.

Population size without control



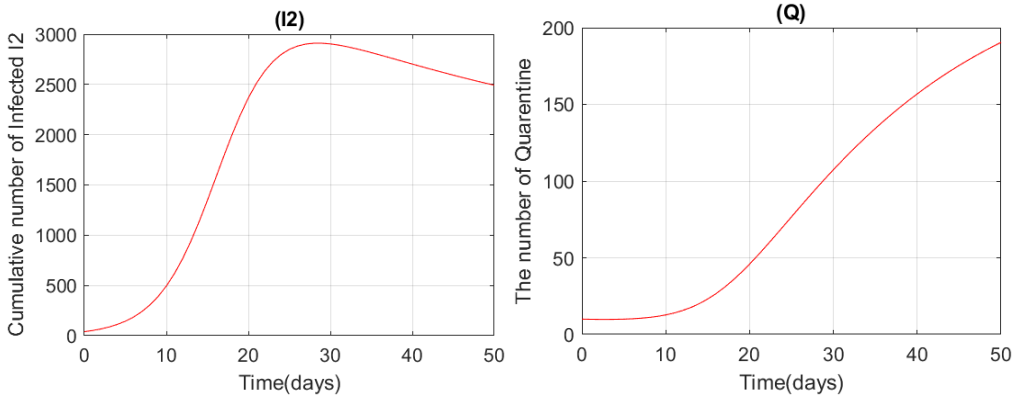


Figure 1: Simulation results of the HIV model without controls. Described the evolution of the states S, I_1, I_2, Q and R without controlfrom day 1 to day 50.

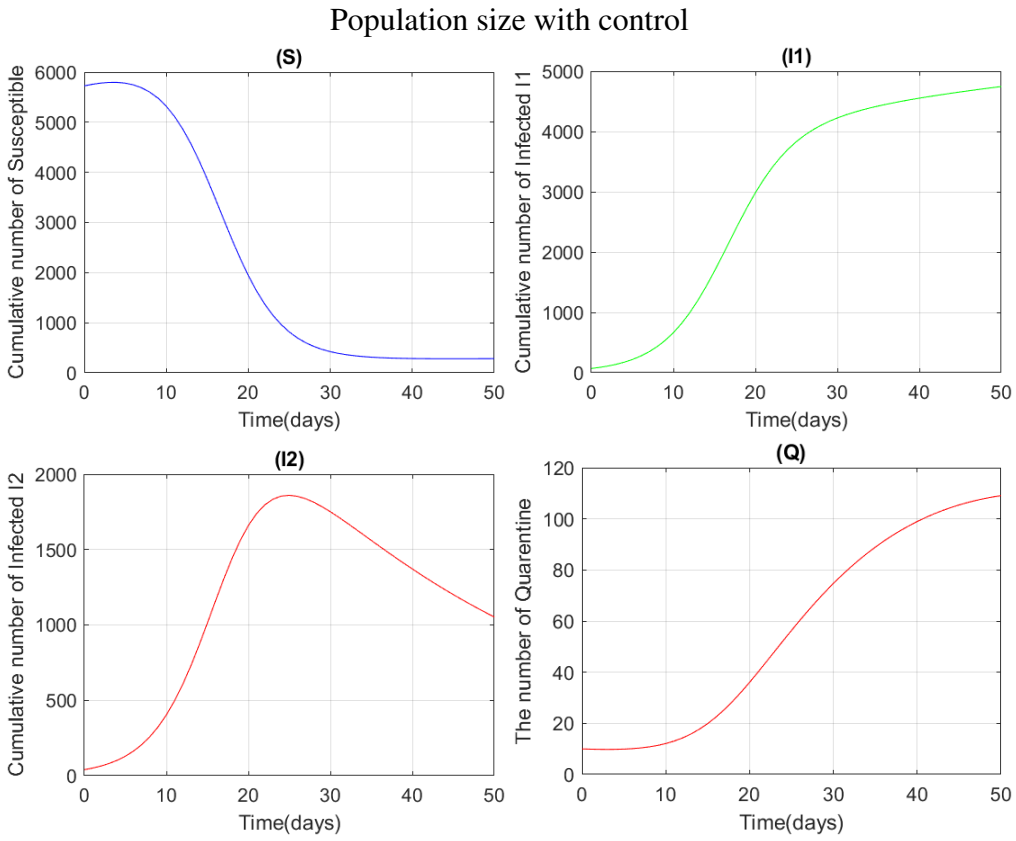


Figure 2: Simulation results of the HIV model with the controls u_1, v_1, u_2 and v_2. Described the evolution of the states S, I_1, I_2, Q and R with control from day 1 to day 50.

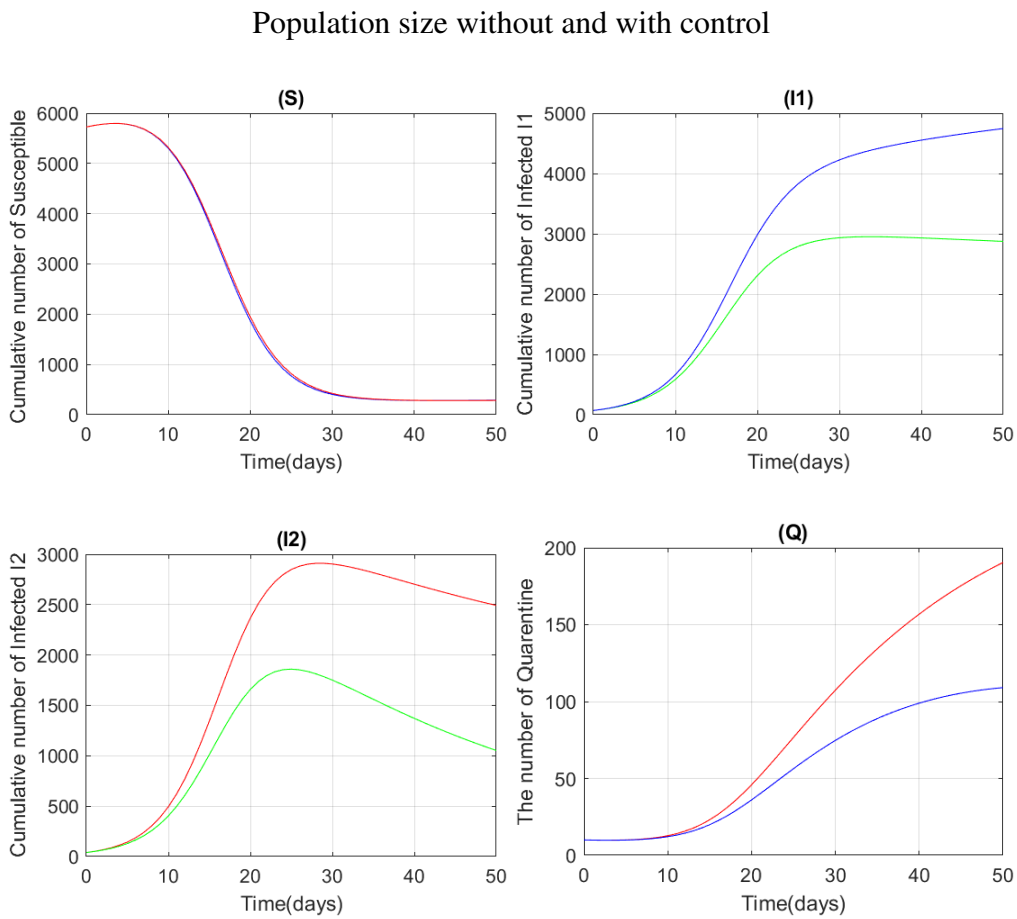


Figure 3: Simulation results of the HIV model without and with controls u_1, v_1, u_2 and v_2. Described the evolution of the states S, I_1, I_2, Q and R with control from day 1 to day 50.

From the Figure 3, we can notice very well the difference between the number of cases at each level S, I_1, I_2, Q and R, before and after the optimal control that we applied.

For the patients in the first level, the difference starts from day 10 until we reach day 50 with 4800 cases without control and 2900 with the optimal control, this is a difference of about 1900 cases. As for the patients in the second level we see that after day 10 the difference begins to increase until day 25 as the number of cases was 2950 without control and 1870 with control, then on day 50 we find 2600 cases without control and 1050 with control, this is a difference of about 1550 cases. And for the patients under the stone we observe that the difference began to widen from the day 15 until it reaches on the day 50 to 190 cases without control and 110 cases with the control,

this is a difference of about 80 cases. Starting from the three levels, we find that the control gave a big difference in the decrease in the number of cases.

6. Conclusion

In this paper, we consider a HIV mathematical model with three different levels of infection. We suppose the stats of infected can be deteriorate and also can be improved from one state to another state. The stability of equilibrium point are discussed, the optimal control has been considered and four controls have been introduced representing the effort to reduce the displacement of infection states. The Pontrygin's maximum principale is used to characterize the optimal control. A comparison between individual with optimal control and no control is presented. A numerical simulation has been given to demonstrate the use of the obtained results.

Conflict of Interests

The author(s) declare that there is no conflict of interests.

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