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Optimal Control Strategy on the Transmission Dynamics of Herpes Simplex Virus-II (HSV-II)

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Abstract: In this paper, optimal control theory is applied to Herpes Simplex Virus-II transmission model given by a system of non-linear ordinary differential equations. Optimal control strategy was employed to study the level of effort needed to control the transmission dynamics of HSV-II diseases using three controls; prevention, screening and treatment control strategies. The necessary conditions for the existence of the optimal controls was established using Pontryagin's Maximum Principle. Optimal control system was performed with help of Runge-Kutta forward-backward sweep numerical approximation method. Finally, numerical simulations reveal that a combination of prevention, screening and treatment is the most effective strategy to eradicate the disease from the community.

Keywords: Mathematical model; Numerical solution; Optimal control; Stability.

1. INTRODUCTION

Herpes is caused by Herpes simplex virus (HSV)[1]. There are two types of herpes namely Herpes Simplex Type-I (HSV-I) and Herpes Simplex Type-II (HSV-II). HSV-I is predominantly orally transmitted and it causes orolabial herpes (i.e. cold sores). On the other hand, HSV-II is one of the most common sexually transmitted infections worldwide and it cause genital herpes. The majority of HSV-II infections are transmitted by persons who are unaware that they have the infection or who are asymptomatic when transmission occurs [2]. Worldwide, an estimated 19.2 million new HSV-II infections occurred among adults and adolescents aged 15-49 years in 2012 with the highest rates among younger age groups. HSV-II is a lifelong infection and the estimated global HSV-II prevalence of 11.3% translates into an estimated 417 million people with the infection in 2012. The prevalence of HSV-II is highest in the WHO African Region (31.5%), followed by the Region of the Americas (14.4%) [3].

Several mathematical models have been developed and analyzed to control the transmission dynamics of HSV [4]. Some of them formulated a deterministic model to describe the dynamics of the disease that helped them to propose disease control mechanism and also described the transmission dynamics of the diseases [5, 6]. In [7], a mathematical model for the spread of HSV-II was proposed and analyzed by incorporating all the relevant biological details and poor treatment adherence. The study demonstrates that though time dependent control will be effective on controlling new HSV-II cases it may not be sustainable for certain time intervals.

Recently, Luis Almonte-Vega [8] developed and analyzed a mathematical model to study the transmission and control of HSV-II among the U.S. population between the ages of 15–49 when there are options to treat individuals in different stages of their pathogenicity. Also, this work are to studied the effect on HSV-II transmission dynamics and evaluated and compared the cost-effectiveness of treating HSV-II infections in both constitutional and non-constitutional stages (new strategy) against the current conventional treatment protocol for treating patients in the non-constitutional stage (current strategy).The results distinguished model parameter regimes where each of the two treatment strategies can optimize the available resources and consequently gives the long-term reduced cost associated with each treatment and incidence. Studies such as [9, 10] constructed a mathematical model of HSV-II for vaccination and developed a vaccine against HSV-II to reduce the infection from the community. Many of these models were described by systems of ordinary differential equations and formulated under reasonable assumptions. But in their studies, none of them considered optimal control strategies to control the disease. Therefore, the aim of this work is to study the effect of incorporating three optimal control strategies; prevention, screening and treatment in the transmission dynamics of HSV-II model formulated in [11].

2. MODEL ASSUMPTION AND DESCRIPTION

The total population, represented by $N(t)$, is divided into six sub-population compartments with respect to their disease status in the system. Those are:

- Susceptible individuals (S) are those who are not infected by the disease pathogen but there is a possibility to be infectious.
- Exposed individuals (E) are individuals who are already infected but are not yet infectious.
- Asymptomatic individuals (A) are individuals those who are both infected and infectious but do not show any symptoms of the disease.
- Symptomatic individuals (I) are individuals those who are infectious and who fully developed disease symptoms.
- Herpes Simplex Virus-II individuals (H) are individuals with HSV-II diseases.
- Recovered individuals (R) are individuals who recovered from the diseases.

Thus, the total population becomes $N(t) = S(t) + E(t) + A(t) + I(t) + H(t) + R(t)$. The model in [11] assumed that susceptible population is increased by the recruitment of individuals into the population at a rate Π. Individuals from susceptible class move to exposed sub class with per capita rate η of becoming infectious. Exposed individuals may progress to the symptomatic infectious with probability p, and to asymptomatic infectious with probability $(1-p)$. Asymptomatic individuals are typically assumed to be infectious at a reduced transmission rate qA. The susceptible individuals are infected by asymptomatic or symptomatically infected individuals with a force of infection $\Lambda = \frac{\beta[I+qA]}{N}$ where β is the contact rate and q is the transmission coefficient for the asymptomatic individuals. Some of the asymptomatic and symptomatic individual's progress to Herpes simplex virus-II at a rate φ and ϕ respectively and others recover naturally through body immune system at a rate γ and α respectively. The HSV -II is treated at a rate δ and move to recovery class. Individuals will die due to disease after reaching the full blown HSV-II stage by the rate ξ. The recovered individuals may lose immunity and return to the susceptible individuals at a rate ω. In all compartments, μ is the natural mortality rate of individuals.

The model in [11] is thus governed by the following system of non-linear ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \Lambda S - \mu S + \omega R,\\
\frac{dE}{dt} &= \Lambda S - (\eta + \mu)E,\\
\frac{dA}{dt} &= (1-p)\eta E - (\varphi + \gamma + \mu)A,\\
\frac{dI}{dt} &= p\eta E - (\phi + \alpha + \mu)I,\\
\frac{dH}{dt} &= \varphi A + \phi I - (\delta + \mu + \xi)H,\\
\frac{dR}{dt} &= \gamma A + \alpha I + \delta H - (\omega + \mu)R.
\end{aligned} \tag{1}$$

The non-negative initial conditions of the system of model Equation (1) are denoted by $S(0) \geq 0,\ E(0) > 0,\ A(0) > 0, I(0) > 0,\ H(0) > 0,\ R(0) > 0$. Furthermore, the wellpossedness of the model Equation (1), implies invariant region, existence and uniqueness of the solution of model equation was determined clearly and briefly in the existing model [11].

3. EQUILIBRIUM POINT

In order to understand the transmission dynamics of the model, it is necessary to determine equilibrium points of the solution region. An equilibrium solution is a steady state solution of the model Equation (1) in the sense that if the system begins at such a state, it will remain there for all times. In other words, the population sizes remain unchanged and thus the rate of change for each population vanishes [12]. The model equations have two equilibrium points, disease free equilibrium point and endemic equilibrium points.

Disease free equilibrium points are steady state solutions where there is no disease in the population. To find the disease free equilibrium, we equated the right hand sides of model Equation (1) to zero, evaluating it at $E = I = A = H = R = 0$ and solving the equations, we get:

$$\mathrm{E}_0 = \{S^0,\ E^0,\ A^0,\ I^0,\ H^0,\ R^0\} = \left\{\left(\frac{\Pi}{\mu}\right),\ 0,\ 0\ \ 0,\ 0,\ 0\right\}.$$

while the endemic equilibrium point E_1 is a steady state solution where there is a disease in the population. The endemic equilibrium point is obtained by setting right hand sides of the model Equation (1) to zero. Then solving for state variables we get:

$$\mathrm{E}_1 = (S^*,\ E^*,\ A^*,\ \ I^*,\ \ H^*,\ R^*).$$

where

$$S^* = \frac{[abcde\Pi]}{[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]]},$$

$$E^* = \frac{[bcde\Pi\Lambda^*]}{[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]]},$$

$$A^* = \frac{[cde\Pi\eta\Lambda^*(1-p)]}{[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]]},$$

$$I^* = \frac{[bdep\Pi\eta\Lambda^*]}{\left[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]\right]},$$
$$H^* = \frac{[\Pi\eta\Lambda^*[\varphi c(1-p) + \phi bp]]}{\left[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]\right]},$$
$$R^* = \frac{[\Pi\eta\Lambda^*[\mathrm{dc}\gamma(1-p) + \alpha\mathrm{bd}p + \delta\varphi c(1-p) + \delta\phi\mathrm{b}p]]}{\left[abcde(\Lambda^* + \mu) + \Lambda^*\eta\omega[cf(1-p) - gbp]\right]}.$$

Here $a = (\eta + \mu), b = (\varphi + \gamma + \mu), c = (\phi + \alpha + \mu), d = (\delta + \mu), e = (\omega + \mu)$ and $\Lambda^* = \frac{\beta[I+qA]}{N}$.

4. REPRODUCTION NUMBER

The basic reproduction number denoted by $\Re_0$ and is defined as the expected number of people getting secondary infection among the whole susceptible population. It is determined using the next generation matrix and defined as the largest eigenvalue of the next generation matrix. The formulation of this matrix involves classification of all compartments of the model into two classes: infected and non-infected compartments [13]. This number determines the potential for the spread of disease within a population. When $\Re_0 < 1$, each infected individual produces on average less than one new infected individual so that the disease is expected to die out. On the other hand if $\Re_0 > 1$, then each individual produces more than one new infected individual so that the disease is expected to continue spreading in the population. This means that the threshold quantity for eradicating the disease is to reduce the value of $\Re_0$ to less than one.

Then by the principle of next-generation matrix, we obtained

$$f_i = \begin{bmatrix} \beta(I + qA)S/N \\ 0 \\ 0 \\ 0 \end{bmatrix} \text{ and } v_i = \begin{bmatrix} (\eta + \mu)E \\ -(1-p)\eta E + (\varphi + \gamma + \mu)A \\ -p\eta E + (\phi + \alpha + \mu)I \\ -\varphi A - \phi I + (\delta + \mu + \xi)H \end{bmatrix}.$$

The Jacobian matrices of f_i and v_i evaluated at Disease Free Equilibrium (DFE) are given by F and V, respectively, such that

$$F = \begin{bmatrix} 0 & \beta q & \beta & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} a & 0 & 0 & 0 \\ -(1-p)\eta & b & 0 & 0 \\ -p\eta & 0 & c & 0 \\ 0 & -\varphi & -\phi & d \end{bmatrix}$$

It can be verified that the matrix V is non-singular as its determinant $det[V] = abcd$ is non-zero and after some algebraic computations its inverse matrix is constructed as

$$V^{-1} = \begin{bmatrix} [1/a] & 0 & 0 & 0 \\ [(1-p)\eta/ab] & [1/b] & 0 & 0 \\ [p\eta/ac] & 0 & [1/c] & 0 \\ [-(\phi bp\eta + c\varphi(1-p)\eta)/abcd] & [\varphi/bd] & [\phi/cd] & [1/d] \end{bmatrix}.$$

The product of the matrices F and V^{-1} can be computed as:

$$FV^{-1} == \begin{bmatrix} [(\eta\beta qc(1-p) + \beta p\eta b)/abc] & [\beta q/b] & [\beta/c] & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

Now it is possible to calculate the eigenvalue to determine the basic reproduction number $\Re_0$ by taking the spectral radius of the matrix FV^{-1}. Thus, the eigenvalues are computed by evaluating $det[FV^{-1} - \psi I] = 0$ or equivalently solving

$$\begin{vmatrix} [(\eta\beta qc(1-p) + \beta p\eta b)/abc] - \psi & [\beta q/b] & [\beta/c] & 0 \\ 0 & -\psi & 0 & 0 \\ 0 & 0 & -\psi & 0 \\ 0 & 0 & 0 & -\psi \end{vmatrix} = 0.$$

Thus, after some algebraic computations the basic reproduction number of the model is:

$$\Re_0 = \frac{\beta\eta[qc(1-p)+pb]}{[abc]}.$$

The stability of an equilibrium point determines whether or not, the solutions nearby the equilibrium point remains nearby, gets closer or get further away. Thus, both local and global stability of the disease free equilibrium and endemic equilibrium point of the model equation was established using basic reproduction number in [11].

5. OPTIMAL CONTROL PROBLEM FORMULATION AND ANALYSIS

Model Equation (1) is extended by introducing control function; $u_1(t)$ represents prevention control strategy (preventing susceptible individuals from exposing to the diseases), $u_2(t)$ represents screening individuals by effectively using a pap test to reduce transmission dynamics of the disease and $u_3(t)$ represents the treatments of infectious individuals. Time is specified and is relatively short and is given by $t \in [0, T]$, T is the terminal time.

The corresponding state system for the model Equation (1) is given as follows:

$$\begin{cases} \frac{dS(t)}{dt} = \Pi + \omega R - (1-u_1)\Lambda S - \mu S, \\ \frac{dE(t)}{dt} = (1-u_1)\Lambda S - (1-u_2)\eta E - \mu E, \\ \frac{dA(t)}{dt} = (1-u_2)(1-p)\eta E - (1-u_3)\varphi A - (u_3+\gamma)A - \mu A, \\ \frac{dI(t)}{dt} = (1-u_2)p\eta E - (1-u_3)\phi I - (u_3+\alpha) - \mu I, \\ \frac{dH(t)}{dt} = (1-u_3)\varphi A + (1-u_3)\phi I - (u_3+\delta)H - (\mu+\xi)H, \\ \frac{dR(t)}{dt} = (u_3+\gamma)A + (u_3+\alpha)I + (u_3+\delta)H - (\omega+\mu)R. \end{cases} \tag{2}$$

With a bounded Lebesgue measurable control set is represented as

$$\Omega = \left\{ \left(u_1(t), u_2(t), u_3(t)\right) \in \left(L^{\infty}(0,T)\right)^3 : 0 \le u_i(t) \le 1-\epsilon, \forall_t \in [0,T] \right\}.$$

The controls are bounded between 0 and 1. When the controls vanish, it means no extra measures are implemented for the reduction of the disease. When the controls take the maximum value 1, it means that the intervention is 100% perfectly implemented which is not true in reality and thus we assumed $u_i \le 1-\epsilon,\ i = 1,2,3$ where $\epsilon \ll 1$ denotes a positive real number.

The optimal control problem (Equation (2)) is to minimize the objective functional

$$J(u) = \int_0^T [g(\phi, u)]dt = \int_0^T \left[M_1 E + M_2 A + M_3 I + M_4 H + \frac{w_1 u_1^2}{2} + \frac{w_2 u_2^2}{2} + \frac{w_3 u_3^2}{2}\right] dt \to min. \tag{3}$$

where M_i and w_j for $i = 1,2,3,4$ and $j = 1,2,3$ are positive weights. The constants w_1, w_2 and w_3 measures the cost of effort required for the implementation of each of the three control measures adopted while M_1, M_2, M_3 and M_4 measures the relative importance of reducing the associated classes on the spread of the disease. The goal is to determine an optimal control u_1^*, u_2^* and u_3^* such that:

$$J(u_1^*, u_2^*, u_3^*) = min\{J(u_1, u_2, u_3) : u_1, u_2, u_3 \in \Omega\} \tag{4}$$

5.1. Existence of an Optimal Controls

Theorem 1: Given $J(u_1, u_2, u_3)$ subject to Equation (2) with $(S_0, E_0, A_0, I_0, H_0, R_0) \ge (0,0,0,0,0,0)$, then there exists an optimal control u^* and corresponding $(S^*, E^*, A^*, I^*, H^*, R^*)$, that minimizes $J(u)$ over Ω. The proof is based on the following assumptions and by Fleming and Rishel's [14, 15, 16] theorem.

a) The set of controls and corresponding state variable is nonempty.
b) The measurable control set is convex and closed.
c) All the right hand sides of the state system is continuous, bounded above by a sum of bounded control and state, and can be written as a linear function of u with coefficients depending on time and state.
d) The integrand $g(\phi, u)$ of the objective functional is convex.
e) There exist constants $c_1, c_2, c_3, c_4 \ge 0$ and $\tau^* \ge 1$ such that the integrand of the objective functional satisfies $g(\phi, u) \ge c_1 + c_2|u_1|^{\tau} + c_3|u_2|^{\tau} + c_4|u_3|^{\tau}$.

Proof:

a) Ω is a nonempty set of measurable functions on $0 \le T$ with values in real numbers $\mathbb{R}$. The system Equation (2) has bounded coefficients and hence any solutions are bounded on $[0, T]$. The corresponding solutions for Equation (2) exists.
b) Assume that $u_1, u_2, u_3 \in \Omega$ such that $\| u_i \| \le 1-\epsilon, i = 1,2,3$. Now, let us take any controls $u_1, u_2 \in \Omega$ and $\Gamma \in [0,1]$, then $0 \le \Gamma u_1 + (1-\Gamma)u_2$. Additionally, we observe that $\| \Gamma u_1 \| \le \Gamma \| u_1 \| \le \Gamma$ and $\| (1-\Gamma)u_2 \| \le (1-\Gamma) \| u_2 \| \le (1-\Gamma)$.Then for any $\Gamma \in [0,1]$,

$$\begin{aligned} &\| \Gamma u_1 + (1-\Gamma)u_2 \|, \\ \leq &\| \Gamma u_1 \| + \| (1-\Gamma)u_2 \|, \\ \leq &\Gamma \| u_1 \| + (1-\Gamma) \| u_2 \|, \\ \leq &\Gamma + (1-\Gamma) = 1. \end{aligned}$$

Hence, $0 \leq \Gamma u_1 + (1-\Gamma)u_2 \leq 1$, for all $u_1, u_2 \in \Omega$ and $\Gamma \in [0,1]$. Therefore, the control space $\Omega = \{u = (u_1, u_2, u_3), 0 \leq u_i \leq 1 - \epsilon, i = 1,2,3\}$ and $t \in [0,T]$ is convex and closed by definition.

c) By definition, each right hand side of system Equation (2) is continuous. All variables S, E, A, I, H, R and u_i are bounded on $[0,T]$. To prove the boundedness we use the method in [17], and the super-solutions of Equation (2) is written as:

$$\begin{cases} \frac{dS(t)}{dt} = \Pi + \omega\bar{R}, \\ \frac{dE(t)}{dt} = (1-u_1)\Lambda\bar{S}, \\ \frac{dA(t)}{dt} = (1-u_2)(1-p)\eta\bar{E}, \\ \frac{dI(t)}{dt} = (1-u_2)p\eta\bar{E}, \\ \frac{dH(t)}{dt} = (1-u_3)\varphi\bar{A} + (1-u_3)\phi\bar{I}, \\ \frac{dR(t)}{dt} = (u_3+\gamma)\bar{A} + (u_3+\alpha)\bar{I} + (u_3+\delta)\bar{H}. \end{cases} \tag{5}$$

are bounded on a finite time interval. Equation (5) can be written as:

$$\phi = \begin{bmatrix} \bar{S} \\ \bar{E} \\ \bar{A} \\ \bar{I} \\ \bar{H} \\ \bar{R} \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & \omega \\ (1-u_1)\Lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & (1-u_2)(1-p)\eta & 0 & 0 & 0 & 0 \\ 0 & (1-u_2)p\eta & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-u_3)\varphi & (1-u_3)\phi & 0 & 0 \\ 0 & 0 & (u_3+\gamma) & (u_3+\alpha) & (u_3+\delta) & 0 \end{bmatrix} \begin{bmatrix} \bar{S} \\ \bar{E} \\ \bar{A} \\ \bar{I} \\ \bar{H} \\ \bar{R} \end{bmatrix} + \begin{bmatrix} \Pi \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}. \tag{6}$$

d) The system is linear in finite time with bounded coefficients, then the super-solutions $\bar{S}, \bar{E}, \bar{A}, \bar{I}, \bar{H}$ and $\bar{R}$ are uniformly bounded. Since the solution to each state equation is bounded, we see that,

$$|f(t, \phi, u)| \leq K|\phi| + M|u| + N.$$

where K depends on the coefficients of the system. Thus, the assumption holds.

e) The integrand in the objective functional, which is a cost function $g(\phi, u)$ is an affine function. Recall that any affine function is a convex and the sum of a convex function is a convex. Therefore, $g(\phi, u)$ is convex on U.

f) Assume that there exists constants $c_1, c_2, c_3, c_4 \geq 0$ and $\tau^* \geq 1$ such that $g(\phi, u)$ satisfies $g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|^\tau + c_4|u_3|^\tau + c_5|u_4|^\tau$. Thus, the state variables are being bounded.

Let $c_1 = \inf_{t\in[0,T]}[M_1E + M_2A + M_3I + M_4H], c_2 = \frac{w_1}{2}, c_3 = \frac{w_2}{2}, c_4 = \frac{w_3}{2}$ and $\tau = 2$ then it follows that $g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|^\tau + c_4|u_3|^\tau$. Thus, this assumption is justified.

Therefore, the optimal control exists.

5.2. Characterization of an Optimal Control

In order to determine the necessary conditions for the optimal control the Pontryagin's maximum principle [18, 19] is used. To apply this, we need to convert the optimal control problem into a problem of minimizing point wise a Hamiltonian, H, with respect to u. The Hamiltonian associated to our problem is:

$$\begin{aligned} H(\phi, u, \lambda) = M_1E + M_2A + M_3I + M_4H + \frac{w_1u_1^2}{2} + \frac{w_2u_2^2}{2} + \frac{w_3u_3^2}{2} + +\lambda_1[\Pi + \omega R - (1-u_1)\Lambda S - \mu S] + \\ \lambda_2[(1-u_1)\Lambda S - (1-u_2)\eta E - \mu E] + \lambda_3[(1-u_2)(1-p)\eta E - (1-u_3)\varphi A - (u_3+\gamma)A - \mu A] + \lambda_4[(1-u_2)p\eta E - \\ (1-u_3)\phi I - (u_3+\alpha)I - \mu I] + \lambda_5[(1-u_3)\varphi A + (1-u_3)\phi I - (u_3+\delta)H - (\mu+\xi)H] + \lambda_6[(u_3+\gamma)A + (u_3+\alpha)I + \\ (u_3+\delta)H - (\omega+\mu)R] \end{aligned} \tag{7}$$

Based on [20], if the control u^* and the corresponding state ϕ^* are an optimal couple, necessarily there exists a non trivial adjoint vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6)$ satisfying the following equality

$$\begin{cases} \frac{d\phi}{dt} = \frac{\partial H(\phi,u,\lambda)}{\partial \lambda}, \\ \frac{d\lambda}{dt} = -\frac{\partial H(\phi,u,\lambda)}{\partial \phi}, \\ \frac{\partial H(\phi,u,\lambda)}{\partial u} = 0. \end{cases} \tag{8}$$

which gives after derivation

$$\begin{cases} u_i^* = 0, \quad if \quad \frac{\partial H}{\partial u_i} < 0, \\ 0 \le u_i^* \le 1, \quad if \quad \frac{\partial H}{\partial u_i} = 0, \\ u_i^* = 1, \quad if \quad \frac{\partial H}{\partial u_i} > 0. \end{cases} \tag{9}$$

Now we apply the necessary conditions to the Hamilton function, *H*.

Theorem: 2 Given an optimal control u^* and a solution to the corresponding state Equation (2), ϕ, then there exist an adjoint vector λ and this satisfies the following adjoint equation:

$$\begin{cases} \frac{d\lambda_1}{dt} = \lambda_1[(1-u_1)\Lambda + \mu] - \lambda_2(1-u_1)\Lambda, \\ \frac{d\lambda_2}{dt} = -M_1 + \lambda_2[(1-u_2)\eta + \mu] - \lambda_3(1-u_2)(1-p)\eta - \lambda_4(1-u_2)p\eta, \\ \frac{d\lambda_3}{dt} = -M_2 + \lambda_1[(1-u_1)\frac{\beta q S}{N} - \lambda_2(1-u_1)\frac{\beta q S}{N} + \lambda_3[(1-u_3)\varphi + (u_3+\gamma) + \mu] - \lambda_5(1-u_3)\varphi \\ -\lambda_6(u_3+\gamma), \\ \frac{d\lambda_4}{dt} = -M_3 + \lambda_1[(1-u_1)\frac{\beta S}{N}] - \lambda_2[(1-u_1)\frac{\beta S}{N}] + \lambda_4[(1-u_3)\phi + (u_3+\alpha) + \mu] - \lambda_5(1-u_3)\phi \\ -\lambda_6(u_3+\alpha), \\ \frac{d\lambda_5}{dt} = -M_4 + \lambda_5[(u_3+\delta) + (\mu+\xi)] - \lambda_6(u_3+\delta), \\ \frac{d\lambda_6}{dt} = \lambda_6(\omega+\mu) - \lambda_1\omega\,, \\ \lambda_i(T) = 0, i = 1,2,3,4,5,6. \end{cases} \tag{10}$$

$\lambda_i(T) = 0$ is the transversality condition. Moreover, the optimal control u^* is given by

$$\begin{cases} u_1^* = \min\left\{\max\left\{\frac{(\lambda_2-\lambda_1)\Lambda S}{w_1}, 0\right\}, 1\right\}, \\ u_2^* = \min\left\{\max\left\{\frac{(\lambda_3(1-p)+\lambda_4 p-\lambda_2)\eta E}{w_2}, 0\right\}, 1\right\}, \\ u_3^* = \min\left\{\max\left\{\frac{\lambda_3(A-\varphi A)+\lambda_4(I-\phi I)+\lambda_5(\varphi A+\phi I+H)-\lambda_6(A+I+H)}{w_3}, 0\right\}, 1\right\}. \end{cases} \tag{11}$$

Proof: The adjoint equation is obtained by differentiating the Hamiltonian Equation (7) with respect to $\phi = (S, E, A, I, H, R)$. That is $\frac{d\lambda}{dt} = -\frac{\partial H(\phi,u,\lambda)}{\partial \phi}$. Assuming that the final states $S(T), E(T), A(T), I(T), H(T), R(T)$ are free we get the transversality conditions $\lambda(T) = 0$. The optimal controls u are found from the optimality conditions and using the property of the control space Ω. The optimality condition of the Hamiltonian gives $\frac{\partial H}{\partial u} = 0$. That is

$$\begin{cases} \frac{\partial H}{\partial u_1} = 0 \Rightarrow u_1^* = \frac{(\lambda_2-\lambda_1)\Lambda S}{w_1}, \\ \frac{\partial H}{\partial u_2} = 0 \Rightarrow u_2^* = \frac{(\lambda_3(1-p)+\lambda_4 p-\lambda_2)\eta E}{w_2}, \\ \frac{\partial H}{\partial u_3} = 0 \Rightarrow u_3^* = \frac{\lambda_3(A-\varphi A)+\lambda_4(I-\phi I)+\lambda_5(\varphi A+\phi I+H)-\lambda_6(A+I+H)}{w_3}. \end{cases} \tag{12}$$

and using the property of the control space Ω, the controls are given as

$$\begin{cases} u_1^* = 0, & if \quad (\lambda_2-\lambda_1)\Lambda S < 0, \\ u_1^*, & if \quad 0 \le (\lambda_2-\lambda_1)\Lambda S \le w_1, \\ 1, & if \quad (\lambda_2-\lambda_1)\Lambda S > w_1. \end{cases}$$

$$\begin{cases} u_2^* = 0, & if \quad (\lambda_3(1-p)+\lambda_4 p-\lambda_2)\eta E < 0, \\ u_2^*, & if \quad 0 \le (\lambda_3(1-p)+\lambda_4 p-\lambda_2)\eta E \le w_2, \\ 1, & if (\lambda_3(1-p)+\lambda_4 p-\lambda_2)\eta E > w_2. \end{cases} \tag{13}$$

$$\begin{cases} u_3^* = 0, & if \quad (\lambda_3(A-\varphi A)+\lambda_4(I-\phi I)+\lambda_5(\varphi A+\phi I+H)-\lambda_6(A+I+H)) < 0, \\ u_3^*, & if \quad 0 \le \left(\lambda_3(A-\varphi A)+\lambda_4(I-\phi I)+\lambda_5(\varphi A+\phi I+H)-\lambda_6(A+I+H)\right) \le w_3, \\ 1, & if \left(\lambda_3(A-\varphi A)+\lambda_4(I-\phi I)+\lambda_5(\varphi A+\phi I+H)-\lambda_6(A+I+H)\right) > w_3. \end{cases}$$

5.3. The Optimality System

The optimality system consists of the state system in Equation (2) with its initial conditions coupled with the adjoint system (Equation (10)) with its transversality conditions together with the characterization of the optimal controls. It is written as follows:

$$\begin{cases} \frac{dS(t)}{dt} = \Pi + \omega R - (1-u_1)\Lambda S - \mu S, \\ \frac{dE(t)}{dt} = (1-u_1)\Lambda S - (1-u_2)\eta E - \mu E, \\ \frac{dA(t)}{dt} = (1-u_2)(1-p)\eta E - (1-u_3)\varphi A - (u_3+\gamma)A - \mu A, \\ \frac{dI(t)}{dt} = (1-u_2)p\eta E - (1-u_3)\phi I - (u_3+\alpha) - \mu I, \\ \frac{dH(t)}{dt} = (1-u_3)\varphi A + (1-u_3)\phi I - (u_3+\delta)H - (\mu+\xi)H, \\ \frac{dR(t)}{dt} = (u_3+\gamma)A + (u_3+\alpha)I + (u_3+\delta)H - (\omega+\mu)R, \\ \frac{d\lambda_1}{dt} = \lambda_1[(1-u_1)\Lambda+\mu] - \lambda_2(1-u_1)\Lambda, \\ \frac{d\lambda_2}{dt} = -M_1 + \lambda_2[(1-u_2)\eta+\mu] - \lambda_3(1-u_2)(1-p)\eta - \lambda_4(1-u_2)p\eta, \\ \frac{d\lambda_3}{dt} = -M_2 + \lambda_1[(1-u_1)\frac{\beta qS}{N} - \lambda_2(1-u_1)\frac{\beta qS}{N} + \lambda_3[(1-u_3)\varphi + (u_3+\gamma)+\mu] - \lambda_5(1-u_3)\varphi \\ -\lambda_6(u_3+\gamma), \\ \frac{d\lambda_4}{dt} = -M_3 + \lambda_1[(1-u_1)\frac{\beta S}{N}] - \lambda_2[(1-u_1)\frac{\beta S}{N}] + \lambda_4[(1-u_3)\phi + (u_3+\alpha)+\mu] - \lambda_5(1-u_3)\phi \\ -\lambda_6(u_3+\alpha), \\ \frac{d\lambda_5}{dt} = -M_4 + \lambda_5[(u_3+\delta)+(\mu+\xi)] - \lambda_6(u_3+\delta), \\ \frac{d\lambda_6}{dt} = \lambda_6(\omega+\mu) - \lambda_1\omega. \end{cases} \tag{14}$$

where $\Lambda = \frac{\beta(I+qA)}{N}, \lambda_i(T) = 0, i = 1,2,3,4,5,6.$

5.4. Uniqueness of the Optimality System

In order to successively discuss uniqueness of the optimality system, we notice that the adjoint system is also linear in λ_i for $i = 1,2,3,4,5,6$ with bounded coefficients. Thus, there exists a $M > 0$ such that $|\lambda_i(t)| < M$ for $i = 1,2,3,4,5,6$ on $[0,T]$.

Theorem 3. For T sufficiently small the solution to the optimality system is unique [21].

6. NUMERICAL SIMULATION

In this section, first we discuss the numerical simulation of the autonomous system Equation (1). The values of parameters are either taken from literature or assumed on the basis of reality. Using the initial conditions $S(0) = 600, E(0) = 350, A(0) = 300, I(0) = 250, H(0) = 150, R(0) = 200$ and also coefficients of the state and controls that we used are $M_1 = 5, M_2 = 5, M_3 = 2, M_4 = 2, w_1 = 0.8, w_2 = 0.7, w_3 = 0.6$ a simulation study is conducted. Table 1 further shows the values used in this study, and taken from [4]. Finally, an optimal control strategy is designed and discussed using different control strategies.To solve the optimal controls and states, we use the Runge-Kutta numerical method using MATLAB program.

Table 1. Parameter values [4]

Parameter	Value	Parameter	Value
Π	0.0015	ξ	0.001
β	0.68	ϕ	0.004
μ	0.002	φ	0.003
γ	0.058	q	0.004
α	0.089	ω	0.09
η	0.006	δ	0.078
p	0.048		

6.1. Simulation of the Autonomous

Numerical simulations of the model Equation (1) show that the disease-free equilibrium is globally stable for some parameter values. In particular, Figure 1 shows all solution trajectories starting with different initial points are converges to the disease-free equilibrium as time goes to infinity for $R_0 < 1$. On the other hand, the endemic equilibrium is globally stable for $R_0 > 1$ (Figure 2). Figures 3 and 4 show that Equation (1) starting from different initial points converges to disease free equilibrium point. This confirmed that, in the long time limit, it asymptotically approaches to positive equilibrium point.

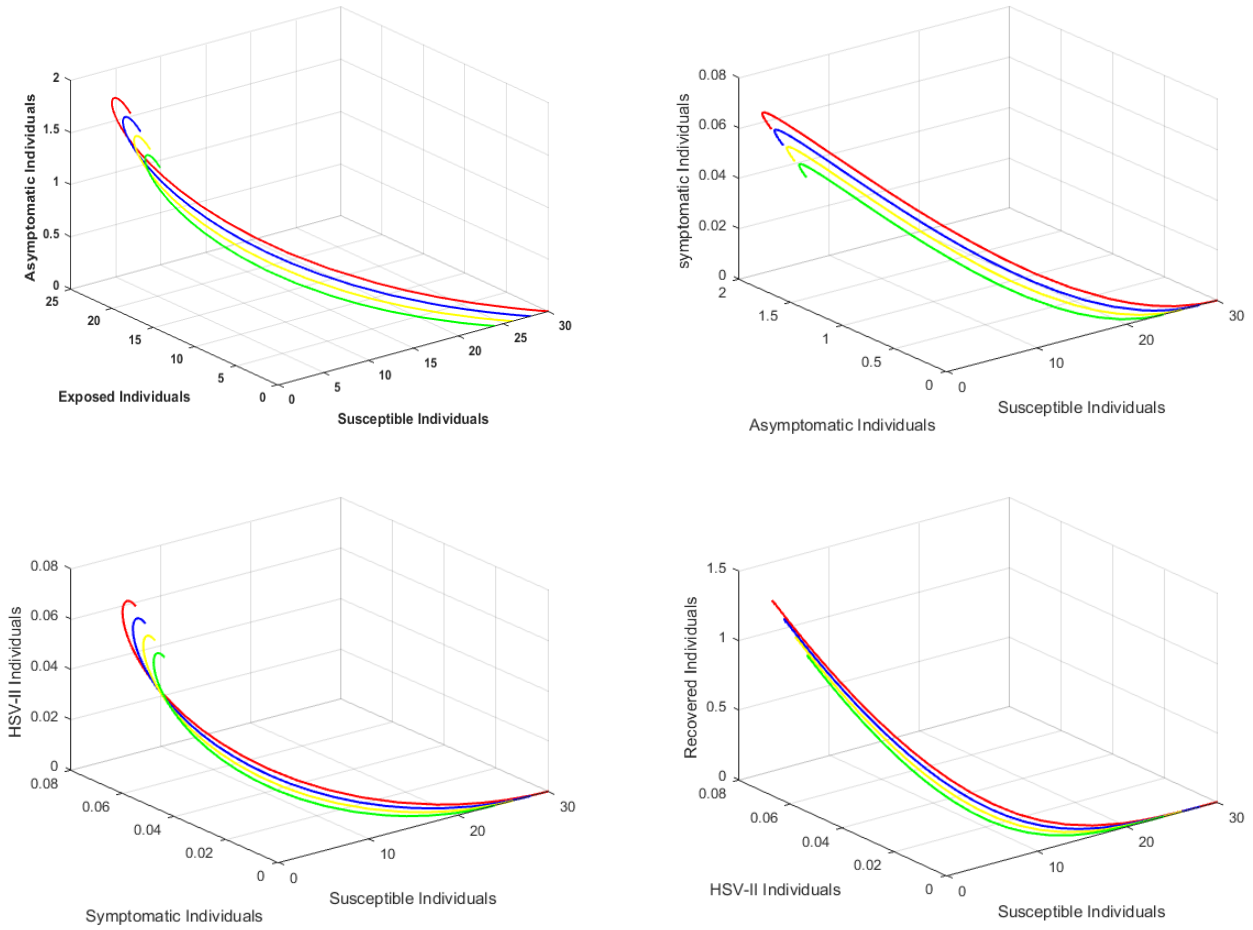
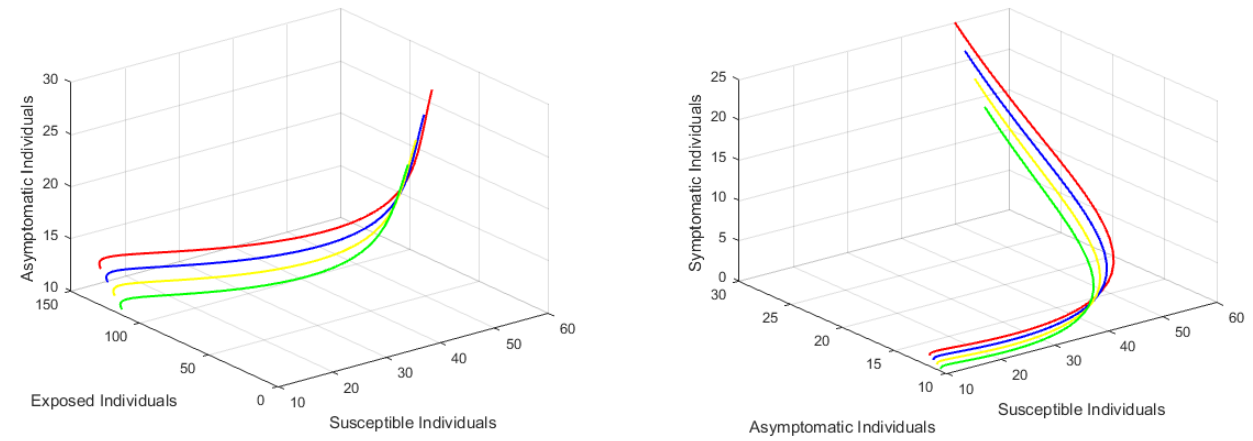


Figure 1. Disease free solution trajectories



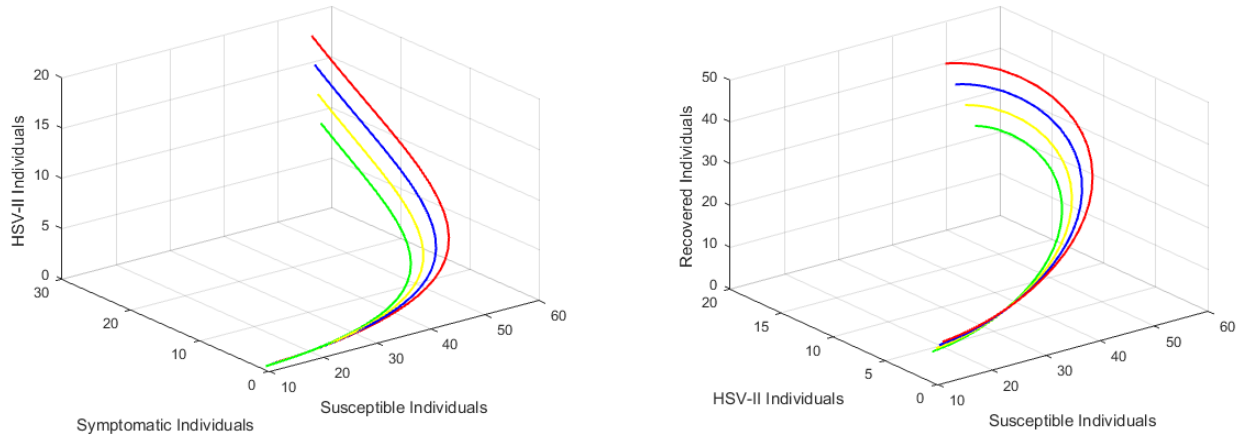


Figure 2. Endemic solution trajectories

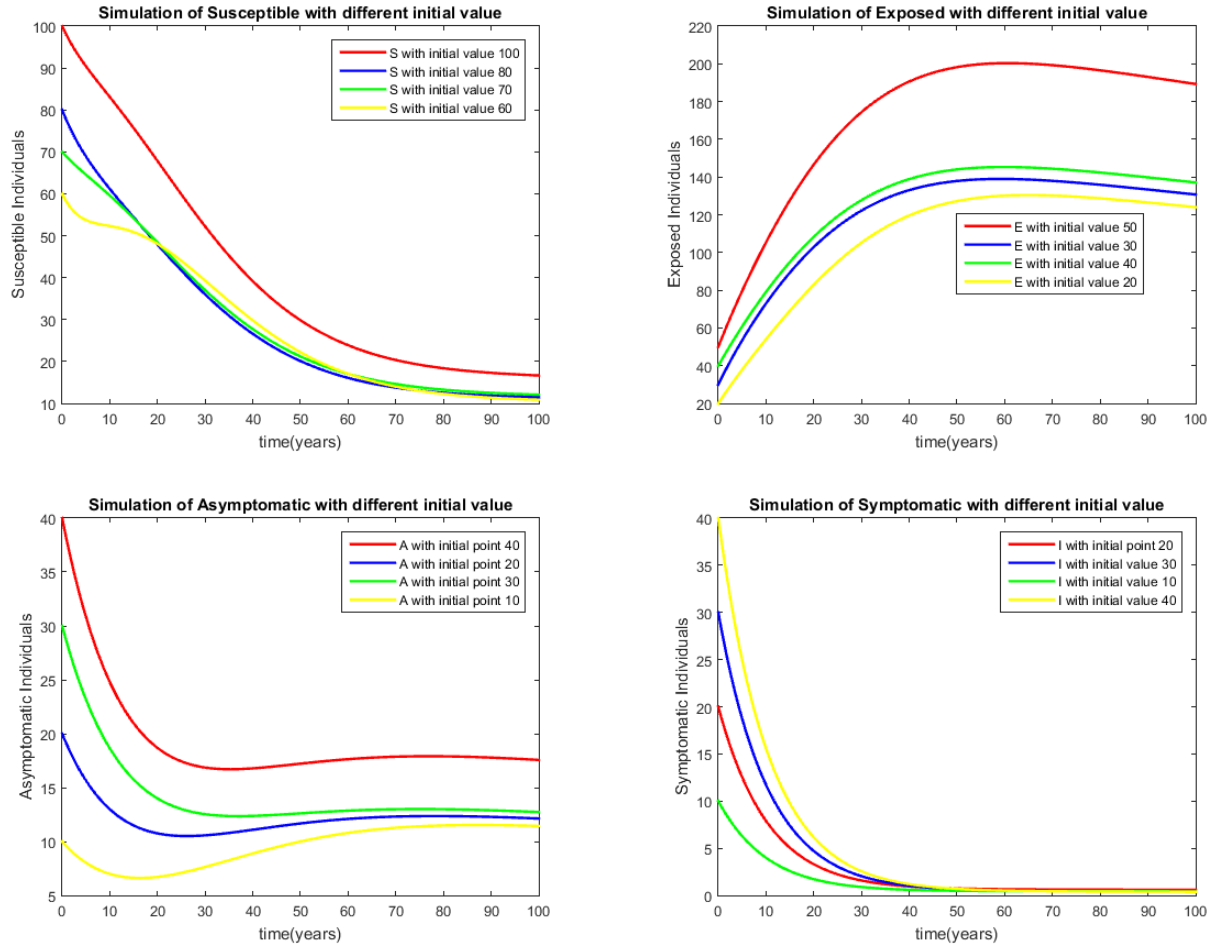


Figure 3. Time series of the trajectories of susceptible, exposed, asymptomatic and symptomatic individuals with different initial point

6.2. Simulation of the Optimal Control Problem

In this subsection we discuss numerical results of Equation (2) to show the effect of various control strategies on the spread of HSV-II.

Strategy 1: Implementing Prevention and Treatment

In this strategy, we applied prevention and treatment as intervention to control HSV-II. Figures 5 and 6 shows that all individuals have gone to zero over the period of implementation of this intervention strategy. Therefore, control with prevention and treatment reduces the burden to some extent but it is not eliminate HSV-II totally from the community.

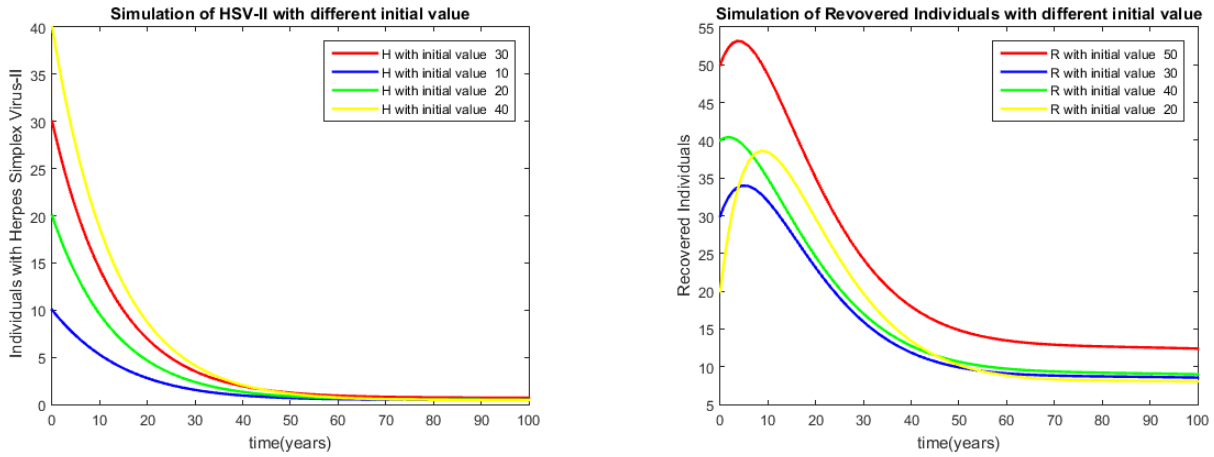


Figure 4. Time series of the trajectories of HSV-II and recovered individuals with different initial point.

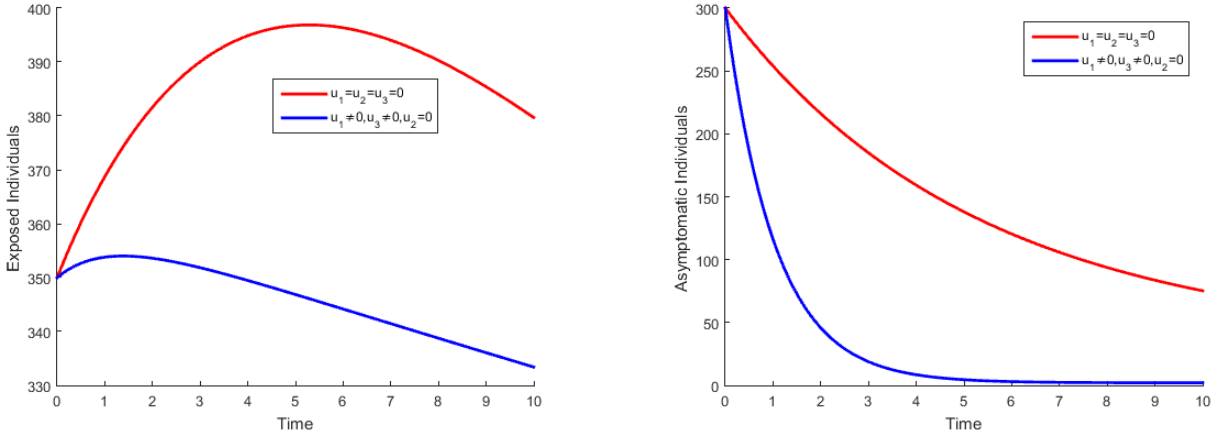


Figure 5. Exposed and Asymptomatic individuals with prevention and treatment

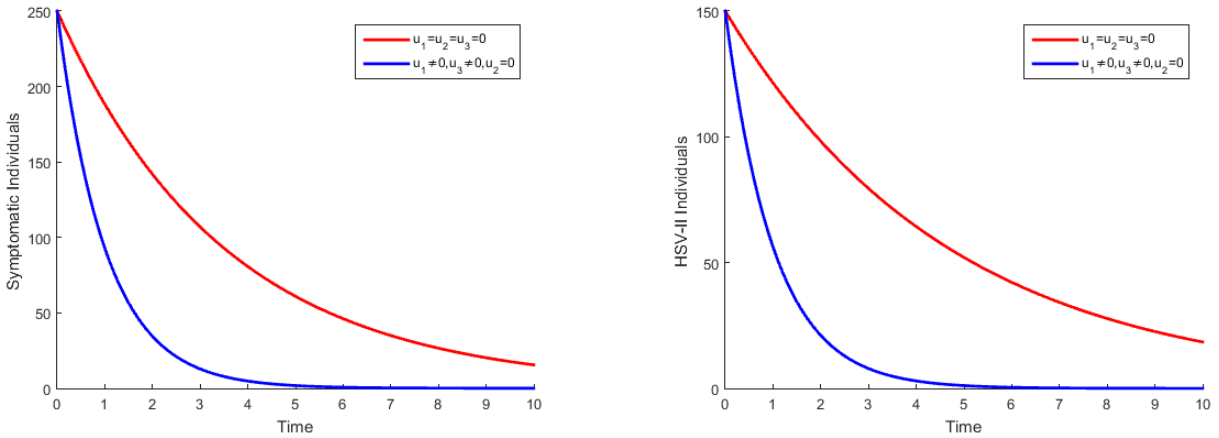


Figure 6. Symptomatic and HSV-II individuals with prevention and treatment

Strategy 2: Implementing screening and treatment

We simulate the optimality system using a combination of screening and treatment as intervention strategy for control of HSV-II in the community. Figures 7 and 8 clearly show that infectious individuals have gone to zero at the end of the implementation period.

Strategy 3: Implementing prevention, screening and treatment

In this strategy, we implemented all the three controls (prevention, screening and treatment) as intervention to eradicate HSV-II from the community. Figures 9 and 10 shows that an infectious individual goes to zero at the end of the implementation period. Therefore, applying this strategy is effective in eradicating HSV-II from the community in a specified period of time.

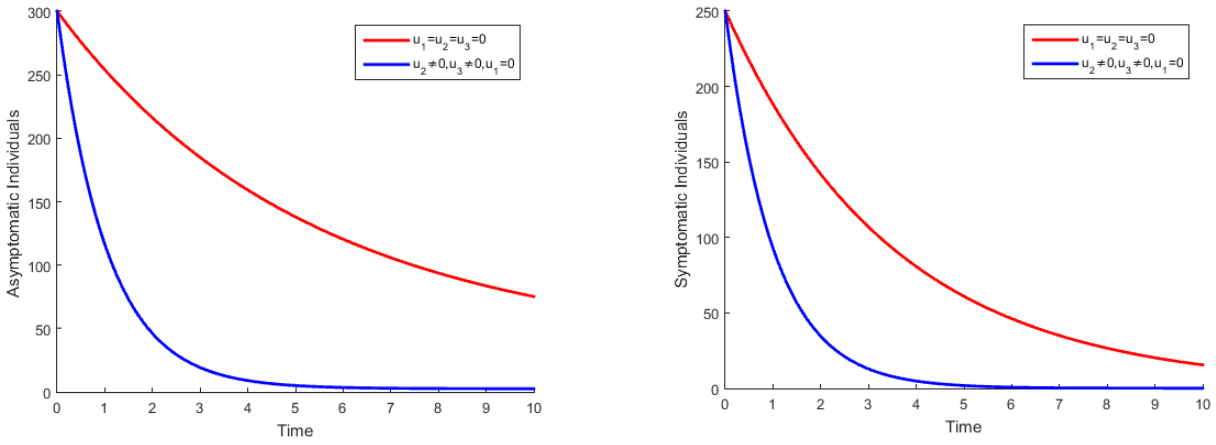


Figure 7. Asymptomatic and symptomatic individuals with screening and treatment

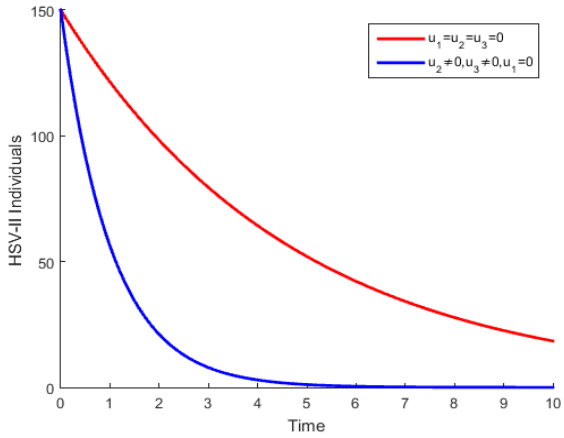


Figure 8. HSV-II individuals with screening and treatment

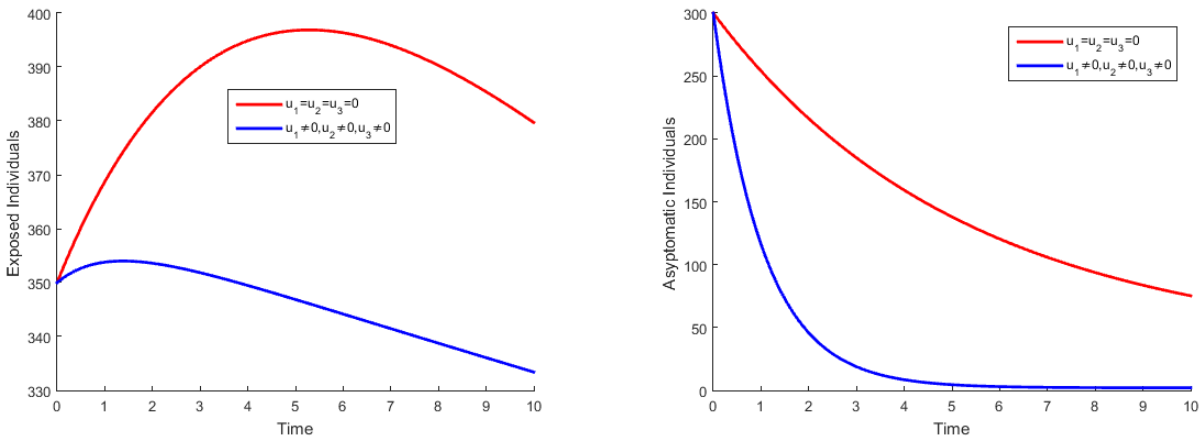


Figure 9. Exposed and asymptomatic individuals with prevention, screening and treatment

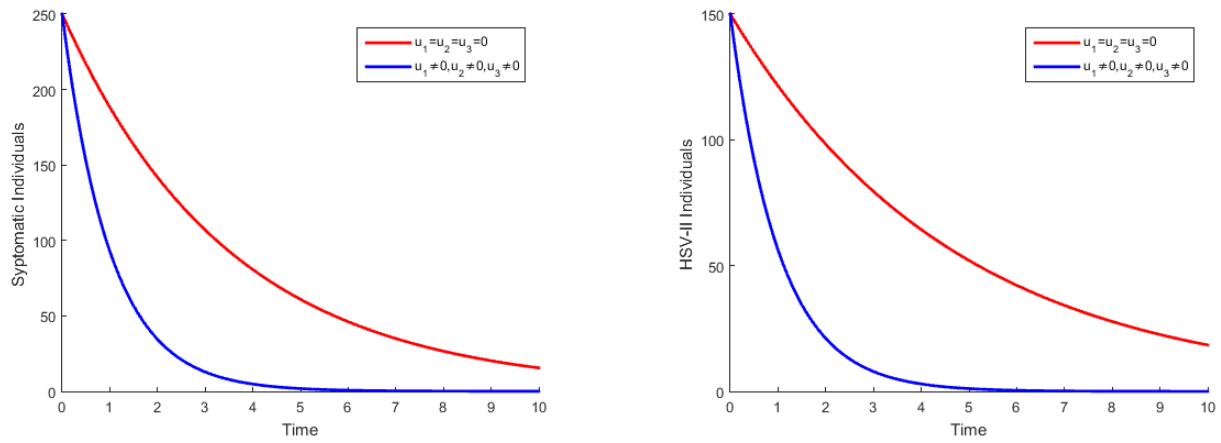


Figure 10. Symptomatic and HSV-II individuals with prevention,screening and treatment

7. CONCLUSION

In this paper, an optimal control problem was formulated and analysed to study the effects of implementing continuous controls on HSV-II model [11]. In this process, we have designed an optimal control problem that minimizes the cost for implementation of the controls while also minimizing the total infectious individuals over the intervention interval.The existence of optimal controls and characterization was established using Pontryagin's Maximum Principle. The findings from the optimal control problem revealed that a combination of prevention, screening and treatment are the most effective strategy to eradicate the disease from the community. HSV-II infection remain a challenge especially in developing countries, but from results of this study we recommend that, the government should introduce education programmers on the importance of voluntary and routinely screening on HSV-II infection. For the future work, we plan to extend the study by incorporating protected and treatment class to HSV-II transmission dynamics.

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