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Optimal control in a model for Zika transmission with stratification by sex

Control óptimo en un modelo para la transmisión del Zika con estratificación por sexo

Erick Manuel Delgado Moya and Aymée Marrero Severo

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Abstract

This paper presents an optimal control strategy for the Zika virus disease with sexual transmission. A mathematical model for the transmission of the Zika virus is considered with three preventive measures as control, namely: the prevention of the sexual contagion with the use of condoms and the orientation in the transmission of Zika in the homosexual and heterosexual relations, the campaigns against vectors and the protection of the society regarding the contagion by mosquito bites. We examine the implementation of various combinations of the control strategies in order to determine the most cost-effective one. The necessary conditions for the optimal controls are determined using Pontryaguin's maximum principle and the optimality problem is solved using Runge-Kutta fourth order scheme. Based on the computational results, we conclude that the most efficient control strategy is when it is applied on the infections in homosexual relationships combined with the control in the transmission by vectors.

Keywords . Model, sexual transmission, strategy, optimal control, Zika.

Resumen

Este trabajo presenta una estrategia óptima de control para la enfermedad del virus Zika con transmisión sexual. Se considera un modelo matemático para la transmisión del virus Zika con tres medidas preventivas como control: la prevención del contagio sexual con el uso de preservativos y la orientación en la transmisión del Zika en las relaciones homosexuales y heterosexuales, las campañas contra los vectores y la protección de la sociedad respecto al contagio por picaduras de mosquitos. Examinamos la aplicación de diversas combinaciones de las estrategias de control para determinar la más eficaz en función de los costos. Las condiciones necesarias para los controles óptimos se determinan utilizando el principio del máximo de Pontryaguin y el problema de la optimización se resuelve utilizando el esquema de cuarto orden de Runge-Kutta. Basándonos en los resultados computacionales, concluimos que la estrategia de control más eficiente es cuando se combina la estrategia de prevención en las relaciones homosexuales con el control en la transmisión por vectores.

Palabras clave. Control óptimo, estrategia, modelo, transmisión sexual, Zika.

1. Introduction. Zika fever (also known as Zika virus disease) is an illness caused by the Zika virus. The disease is spread through the bite of daytime-active Aedes mosquitoes such as the A. aegypti and A. albopictus (these are the same mosquitoes that spread dengue and chikungunya viruses). Its name comes from Zika forest in Uganda, where the virus was first isolated from a rhesus monkey in 1947. The first

*IME- University of São Paulo, Rua do Matão, 1010, SP-Brazil (erickmath@ime.usp.br).
†MATCOM- University of Havana, Edificio Felipe Poey. San Lázaro y L. Colina Universitaria, Havana-Cuba (aymee@matcom.uh.cu).

human cases were reported in Nigeria in 1954. The first documented outbreak among people occurred in 2007, in the Federated State of Micronesia [2].

The disease of Zika virus is transmitted from infected Aedes mosquitoes to humans through mosquito bites [1]. It can also be transmitted from human to human through the blood and semen of an infected human, and through an infected pregnant woman to the fetus. Zika is a cause of microcephaly and other severe brain defects [5].

There is no specific treatment or vaccine currently available for Zika virus disease. Prevention and control relies on reducing mosquitoes through source reduction (removal and modification of breeding sites), and reducing contacts between mosquitoes and people.

Education about the Zika virus mode of transmission and ways of preventing transmission are essential in order to halt mosquito growth and thus Zika spread among a community or population, at regional, national, and global levels. Control measures available are limited and include the use of insect repellents to protect humans against mosquito bites and sex protection while engage in sexual activities. The Zika virus can also be transmitted through sexual intercourse and has been detected in semen, blood, urine, amniotic fluid and saliva, as well as in body fluids found in the brain and spinal cord [5, 6].

Optimal control is also an important mathematical method deciding a strategy regarding epidemic control with provided scenarios [11, 12]. There are some studies of the optimal control of several diseases such as dengue [13], chikungunya [14], and HIV [15]. The results show that optimal control helps in reducing the number of infected individuals and the spread of the virus. The objective of this work is to present a model for the transmission of Zika with the presence of sexual contagion and stratified by sex. In the model, there are controls referring to the control over the contagion by mosquito bites and the sexual contagion by homosexual and heterosexual relationships. Study the optimal control problem and carry out computer simulations. The paper is organized as follows. Section 2 is devoted to a Zika model. Section 3 presents the Optimal control problem. Section 4 is devoted to computer simulations. Section 5 are the conclusions of paper.

2. Formulation of Mathematical Model. The model variables are susceptible men H_s, susceptible women M_s, exposed men H_E, exposed women M_E, infected men H_I, infected women M_I, recovered men H_R, recovered women M_R, susceptible mosquitoes V_s, exposed mosquitoes V_E and infected mosquitoes V_I. The model is SEIR type (susceptible-exposed-infected-recovered) for humans and SEI (susceptible-exposed-infected) for mosquitoes, because mosquitoes do not recover. The model is compartmentalized by sex because we take into account sexual contagion in the dynamics of Zika transmission. The description of the parameters of model (2.1) are in Table (2.1).

Assumptions for the construction of model:

- we assumed immunity in the recovered state.
- The death by natural causes is equal in any state, the death of mosquitoes will be due to environmental factors because no control strategy is applied.
- The $H_s, M_s, H_E, M_E, H_I, M_I, H_R, M_R, V_s, V_E$ and V_I are continuous functions and positive or null (because we work with human and mosquitoes populations).
- The model is defined in an interval $[0, t_f]$, where t_f is finite.

Let:

β_{y_1} : (number of times a single mosquito bites a human per unit time $\times$ probability of pathogen transmission from an infectious mosquito to a susceptible human given that a contact between the two occurs)/the total population of human within the model).

To define β_{y_2}, β_{y_5}, β_{y_4} and β_{y_3} we did an analogous study but taking into account the sexual contacts (homosexual and heterosexual respectively) and the probability of infecting these contacts, the force of infection from infected man to susceptible man by sexual contact β_{y_2}, the force of infection from infected woman to susceptible woman by sexual contact β_{y_5}, the force of infection from infected man to susceptible woman by sexual contact β_{y_3} and the force of infection from infected woman to susceptible man by sexual contact β_{y_3}.

The β_x : (number of times a single mosquito bites a human per unit time $\times$ probability of pathogen transmission from an infectious human to a susceptible mosquito given that a contact between the two occurs)/the total population of vectors within the model.

Let l_1, l_2, l_3 the life expectancy of men, women and mosquitoes. We define $\mu_1 = \dfrac{1}{l_1}$, $\mu_2 = \dfrac{1}{l_2}$ and $\eta = \dfrac{1}{l_3}$ such as death rates for men, women and mosquitoes respectively.

The control strategy for the outbreak is proposed considering campaigns and suggestions from WHO and health organizations regarding Zika virus infection. Considering the vector transmission and sexual transmission, three control parameters are introduced for constructing the control model. The control variable $u_1(t)$ is the use of preventive measures such as insect repellent or mosquito net to reduce the contacts between human and mosquito. The control variable $u_2(t)$ is the control over homosexual contacts (use of condoms and information campaigns). The control variable $u_3(t)$ is the is the control over heterosexual sexual contacts. Consequently, from control strategy, the forces of infection in the human population are reduced by the factors of $(1 - u_1(t))$, $(1 - u_2(t))$ and $(1 - u_3(t))$.

Parameters	Description	Value
β_{y_1}	The force of infection from infected mosquito to susceptible human	0.7
β_{y_2}	The force of infection from infected man to susceptible man	0.34
β_{y_5}	The force of infection from infected woman to susceptible woman	0.1
β_{y_3}	The force of infection from infected man to susceptible woman	0.3
β_{y_4}	The force of infection from infected woman to susceptible man	0.2
β_x	The force of infection from infected human to susceptible mosquito	0.5
μ_1, μ_2, η	Man, woman and mosquito mortality rate	0.45, 0.3, 0.95
$\omega_1, \omega_2, \omega_3$	The rate of progression of men, women and mosquitoes from the exposed state to the infectious state	0.25, 0.25, 0.35
ϵ_1, ϵ_2	Disease-induced death rate for humans (men and women respectively)	0.15, 0.15
r_1, r_2	Per capital recovery rate for humans from the infectious (men and women respectively)	0.90, 0.94
N_1, N_2, N_3	Recruitment rate of men, women and mosquitoes	0.5, 0.55, 0.75

Table 2.1: Description of parameters used in the model (2.1).

The transmission of the Zika is modeled by the system (2.1).

$$
\begin{aligned}
\frac{dH_s}{dt} &= N_1 - (1-u_1)\beta_{y_1} V_I H_s - (1-u_2)\beta_{y_2} H_I H_s - (1-u_3)\beta_{y_4} M_I H_s - \mu_1 H_s,\\
\frac{dM_s}{dt} &= N_2 - (1-u_1)\beta_{y_1} V_I M_s - (1-u_2)\beta_{y_5} M_I M_s - (1-u_3)\beta_{y_3} H_I M_s - \mu_2 M_s,\\
\frac{dH_E}{dt} &= (1-u_1)\beta_{y_1} V_I H_s + (1-u_2)\beta_{y_2} H_I H_s + (1-u_3)\beta_{y_4} M_I H_s - (\omega_1 + \mu_1) H_E,\\
\frac{dM_E}{dt} &= (1-u_1)\beta_{y_1} V_I M_s + (1-u_2)\beta_{y_5} M_I M_s + (1-u_3)\beta_{y_3} H_I M_s - (\omega_2 + \mu_2) M_E,\\
\frac{dH_I}{dt} &= \omega_1 H_E - (\epsilon_1 + \mu_1 + r_1) H_I,\\
\frac{dM_I}{dt} &= \omega_2 M_E - (\epsilon_2 + \mu_2 + r_2) M_I,\\
\frac{dH_R}{dt} &= r_1 H_I - \mu_1 H_R,\\
\frac{dM_R}{dt} &= r_2 M_I - \mu_2 M_R,\\
\frac{dV_s}{dt} &= N_3 - \beta_x (H_I + M_I) V_s - \eta V_s,\\
\frac{dV_E}{dt} &= \beta_x (H_I + M_I) V_s - (\omega_3 + \eta) V_E,\\
\frac{dV_I}{dt} &= \omega_3 V_E - \eta V_I. \qquad (2.1)
\end{aligned}
$$

Initial conditions:

$$
\begin{aligned}
&H_s(0) = h_s > 0, && M_s(0) = m_s \geq 0, && H_I(0) = h_i > 0,\\
&M_I(0) = m_i > 0, && H_R(0) = h_r \geq 0, && M_R(0) = m_r \geq 0,\\
&H_E(0) = h_e \geq 0, && M_E(0) = m_e \geq 0, && V_s(0) = v_s > 0,\\
&V_I(0) = v_i > 0, && V_E(0) = v_e \geq 0.
\end{aligned}
$$

Analysis of Model. In this section, we will prove that the solutions of system (2.1) with positive initial conditions remain positive for all time $t \geq 0$. We have the following result:

Theorem 2.1. *Let the initial data for the model (2.1) be* $H_s(0) \geq 0, M_s(0) \geq 0, H_E(0) \geq 0, M_E(0) \geq 0, H_I(0) \geq 0, M_I(0) \geq 0, H_R(0) \geq 0, M_R(0) \geq 0, V_s(0) \geq 0, V_E(0) \geq 0, V_I(0) \geq 0$. *Then the solutions*

$(H_s(t), M_s(t), H_E(t), M_E(t), H_I(t), M_I(t), H_R(t), M_R(t), V_s(t), V_E(t), V_I(t))$, *of the model (2.1), with positive initial data, will remain positive for all time* $t \geq 0$.

Proof: Under the given initial conditions, it is easy to prove that the components of solutions of the model system (2.1) are positive; if not we assume a contradiction: that the exists a first time

$t_1 : H_s(t_1) = 0, \dfrac{dH_s}{dt}(t_1) < 0, M_s(t_1) > 0, H_E(t_1) > 0, M_E(t_1) > 0, H_I(t_1) > 0, M_I(t_1) > 0, H_R(t_1) > 0,$

$M_R(t_1) > 0, V_s(t_1) > 0, V_E(t_1) > 0, V_I(t_1) > 0$, for $0 < t < t_1$, or there exist a

$t_2 : M_s(t_2) = 0, \dfrac{dM_s}{dt}(t_2) < 0, H_s(t_2) > 0, H_E(t_2) > 0, M_E(t_2) > 0, H_I(t_2) > 0, M_I(t_2) > 0, H_R(t_2) > 0,$

$M_R(t_2) > 0, V_s(t_2) > 0, V_E(t_2) > 0, V_I(t_2) > 0$, for $0 < t < t_2$, or there exist a

$t_3 : H_E(t_3) = 0, \dfrac{dH_E}{dt}(t_3) < 0, H_s(t_3) > 0, M_s(t_3) > 0, M_E(t_3) > 0, H_I(t_3) > 0, M_I(t_3) > 0, H_R(t_3) > 0,$

$M_R(t_3) > 0, V_s(t_3) > 0, V_E(t_3) > 0, V_I(t_3) > 0$, for $0 < t < t_3$, or there exist a

$t_4 : M_E(t_4) = 0, \dfrac{dM_E}{dt}(t_4) < 0, H_s(t_4) > 0, M_s(t_4) > 0, H_E(t_4) > 0, H_I(t_4) > 0, M_I(t_4) > 0, H_R(t_4) > 0,$

$M_R(t_4) > 0, V_s(t_4) > 0, V_E(t_4) > 0, V_I(t_4) > 0$, for $0 < t < t_4$, or there exist a

$t_5 : H_I(t_5) = 0, \dfrac{dH_I}{dt}(t_5) < 0, H_s(t_5) > 0, M_s(t_5) > 0, H_E(t_5) > 0, M_E(t_5) > 0, M_I(t_5) > 0, H_R(t_5) > 0,$

$M_R(t_5) > 0, V_s(t_5) > 0, V_E(t_5) > 0, V_I(t_5) > 0$, for $0 < t < t_5$, or there exist a

$t_6 : M_I(t_6) = 0, \dfrac{dM_I}{dt}(t_6) < 0, H_s(t_6) > 0, M_s(t_6) > 0, H_E(t_6) > 0, M_E(t_6) > 0, H_I(t_6) > 0, H_R(t_6) > 0,$

$M_R(t_6) > 0, V_s(t_6) > 0, V_E(t_6) > 0, V_I(t_6) > 0$, for $0 < t < t_6$, or there exist a

$t_7 : H_R(t_7) = 0, \dfrac{dH_R}{dt}(t_7) < 0, H_s(t_7) > 0, M_s(t_7) > 0, H_E(t_7) > 0, M_E(t_7) > 0, H_I(t_7) > 0, M_I(t_7) > 0,$

$M_R(t_7) > 0, V_s(t_7) > 0, V_E(t_7) > 0, V_I(t_7) > 0$, for $0 < t < t_7$, or there exist a

$t_8 : M_R(t_8) = 0, \dfrac{dM_R}{dt}(t_8) < 0, H_s(t_8) > 0, M_s(t_8) > 0, H_E(t_8) > 0, M_E(t_8) > 0, H_I(t_8) > 0, M_I(t_8) > 0,$

$H_R(t_8) > 0, V_s(t_8) > 0, V_E(t_8) > 0, V_I(t_8) > 0$, for $0 < t < t_8$, or there exist a

$t_9 : V_s(t_9) = 0, \dfrac{dV_s}{dt}(t_9) < 0, H_s(t_9) > 0, M_s(t_9) > 0, H_E(t_9) > 0, M_E(t_9) > 0, H_I(t_9) > 0, M_I(t_9) > 0,$

$H_R(t_9) > 0, M_R(t_9) > 0, V_E(t_9) > 0, V_I(t_9) > 0$, for $0 < t < t_9$, or there exist a

$t_{10} : V_E(t_{10}) = 0, \dfrac{dV_E}{dt}(t_{10}) < 0, H_s(t_{10}) > 0, M_s(t_{10}) > 0, H_E(t_{10}) > 0, M_E(t_{10}) > 0, H_I(t_{10}) > 0,$

$M_I(t_{10}) > 0, H_R(t_{10}) > 0, M_R(t_{10}) > 0, V_s(t_{10}) > 0, V_I(t_{10}) > 0$, for $0 < t < t_{10}$, or there exist a

$t_{11} : V_I(t_{10}) = 0, \dfrac{dV_I}{dt}(t_{11}) < 0, H_s(t_{11}) > 0, M_s(t_{11}) > 0, H_E(t_{11}) > 0, M_E(t_{11}) > 0, H_I(t_{11}) > 0,$

$M_I(t_{11}) > 0, H_R(t_{11}) > 0, M_R(t_{11}) > 0, V_s(t_{11}) > 0, V_E(t_{11}) > 0$, for $0 < t < t_{11}$.
In the first case we have

$$\frac{dH_s}{dt}(t_1) = N_1 > 0$$

which is a contradiction meaning that H_s remains. In the second case we have

$$\frac{dM_s}{dt}(t_2) = N_2 > 0$$

which is a contradiction meaning that M_s remains. In the third case we have

$$\frac{dH_E}{dt}(t_3) = (1-u_1)\beta_{y_1}V_IH_s + (1-u_2)\beta_{y_2}H_IH_s + (1-u_3)\beta_{y_4}M_IH_s \geq 0$$

which is a contradiction meaning that H_E remains. In the fourth case we have

$$\frac{dM_E}{dt}(t_4) = (1-u_1)\beta_{y_1}V_IM_s + (1-u_2)\beta_{y_3}H_IM_s + (1-u_3)\beta_{y_5}M_IM_s \geq 0$$

which is a contradiction meaning that M_E remains. In the fifth case we have

$$\frac{dH_I}{dt}(t_5) = \omega_1 H_E \geq 0$$

which is a contradiction meaning that H_I remains. In the sixth case we have

$$\frac{dM_I}{dt}(t_6) = \omega_2 M_E \geq 0$$

which is a contradiction meaning that M_I remains. In the seventh case we have

$$\frac{dH_R}{dt}(t_7) = r_1 H_I \geq 0$$

which is a contradiction meaning that H_R remains. In the eighth case we have

$$\frac{dM_R}{dt}(t_8) = r_2 M_I \geq 0$$

which is a contradiction meaning that M_R remains. In the ninth case we have

$$\frac{dV_s}{dt}(t_9) = N_3 > 0$$

which is a contradiction meaning that V_s remains. In the tenth case we have

$$\frac{dV_E}{dt}(t_{10}) = \beta_x(H_I + M_I)V_s \geq 0$$

which is a contradiction meaning that V_E remains. In the eleventh case we have

$$\frac{dV_I}{dt}(t_{11}) = \omega_3 V_E \geq 0$$

which is a contradiction meaning that V_I remains. Thus in all cases $(H_s(t), M_s(t), H_E(t), M_E(t), H_I(t), M_I(t), H_R(t), M_R(t), V_s(t), V_E(t), V_I(t))$ remain positive.

We show that model (2.1) is dissipative. In other words, all solution are uniformly bounded and proper subset $D \subset \mathbb{R}^{18}_{+}$. Model system (2.1) has a varying population size ($N \neq 0$). Let:

$$H_s + H_E + H_I + H_R = N, \tag{2.2}$$
$$M_s + M_E + M_I + M_R = M, \tag{2.3}$$
$$V_s + V_E + V_I = V. \tag{2.4}$$

Lemma 2.1. *The closed set*

$$D = \left\{(H_s, H_E, H_I, H_R, M_s, M_E, M_I, M_R, V_s, V_I, V_R) \in \Re^{11}_{+} : N \leq \frac{N_1}{\mu_1}, M \leq \frac{N_2}{\mu_2}, V \leq \frac{N_3}{\eta}\right\},$$

is positively-invariant and attracts all positive solutions of the model (2.1).

Proof: Differentiating both sides of (2.2), (2.3) and (2.4) with appropriate substitutions, we obtained the following differential equations:

$$N^{'} = N_1 - \mu_1 N - \epsilon_1 H_I \leq N_1 - \mu_1 N, \tag{2.5}$$
$$M^{'} = N_2 - \mu_2 M - \epsilon_2 M_I \leq N_2 - \mu_2 M, \tag{2.6}$$
$$V^{'} = N_3 - \eta V. \tag{2.7}$$

Applying Grönwall Inequality in (2.5), (2.6) and (2.7), we obtained:

$$N(t) \leq N(0)\exp(-\mu_1 t) + \frac{N_1}{\mu_1}(1 - \exp(-\mu_1 t)),$$
$$M(t) \leq M(0)\exp(-\mu_2 t) + \frac{N_2}{\mu_2}(1 - \exp(-\mu_2 t)),$$
$$V(t) \leq V(0)\exp(-\eta t) + \frac{N_3}{\eta}(1 - \exp(-\eta t)),$$

where $N(0)$, $M(0)$ and $V(0)$ represents the initial humans and mosquitoes population total.
Therefore, $0 \leq N \leq \frac{N_1}{\mu_1}$, $0 \leq M \leq \frac{N_2}{\mu_2}$ and $0 \leq V \leq \frac{N_3}{\eta}$ as $t \to \infty$. This implies, $\frac{N_1}{\mu_1}$ is an upper bound for $N(t)$, $\frac{N_2}{\mu_2}$ is an upper bound for , $M(t)$ and $\frac{N_3}{\eta}$ is an upper bound for $V(t)$ provided $N(0) \leq \frac{N_1}{\mu_1}$, $M(0) \leq \frac{N_2}{\mu_2}$ and $V(0) \leq \frac{N_3}{\eta}$.

Hence, all feasible solutions of model (2.1) enter the region Ω which is a positively invariant set. Thus, the system is biologically meaningful and mathematically well-posed in the domain of Ω. In this domain, it is sufficient to consider the dynamics of the flow generated by the model system described by (2.1).

2.1. Optimal control Problem. We define our objective function:

$$J(u_1, u_2, u_3) = \int_0^{t_f} \Big(A_1 H_E + A_2 M_E + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)\Big)dt, \tag{2.8}$$

subject to the state system of (2.1).
Next, we will find the optimal controls, namely the controls that optimize our objective function. Regarding this work, we will find a set of controls that minimizes the number of exposed human. The constants A_1 and A_2, are the weighted constants associated with exposed human. The constants B_1, B_2, and B_3 are the weighted constants of the control variables u_1, u_2 and u_3, respectively. The terms $\frac{B_1 u_1^2}{2}$, $\frac{B_2 u_2^2}{2}$ and $\frac{B_3 u_3^2}{2}$ are the costs associated with implementing each of the three controls. Let u_1^*, u_2^* and u_3^* be the optimal controls, we will find a set of control functions such that

$$J(u_1^*, u_2^*, u_3^*) = \min J(u_1, u_2, u_3), \quad (u_1, u_2, u_3) \in U_{ad}, \tag{2.9}$$

subject to the system (2.1), where the control set U_{ad} is

$$U_{ad} = \{(u_1, u_2, u_3)|u_i(t) \quad \textit{is Lebesgue measurable on} \quad [0,1], 0 \leq u_i(t) \leq 1, i = 1,2,3\}.$$

2.2. Characterization of the control problem. **Theorem 2.2.** *There exists an optimal control* (u_1^*, u_2^*, u_3^*) *to problem*

$$\min J(u_1, u_2, u_3),$$

subject to (2.1),

where
$U_{ad} = \{(u_1, u_2, u_3)|u_i(t) \quad \textit{is Lebesgue measurable on} \quad [0,1], 0 \leq u_i(t) \leq 1, i = 1,2,3\}$

Proof: We follow the requirement from theorem presents in [10] and verify non trivial requirements. Let $r(t, \vec{v}, \vec{u})$ be the right-hand of (2.1). We need to show the following conditions are satisfied:

1. r is of class C^1 and there exists a constant C such that
   $|r(t,0,0)| \leq C, \quad |r_x(t,\vec{x},\vec{u})| \leq C(1+|\vec{u}|), \quad |r_u(t,\vec{x},\vec{u})| \leq C.$
2. The admissible set $\mathbb{F}$ of all solution to system (2.1) with corresponding control in U_{ad} is non empty;
3. $r(t,\vec{x},\vec{u}) = a(t,\vec{x}) + b(t,\vec{x})\vec{u}$;
4. The control set $U = [0,1] \times [0,1] \times [0,1]$ is closed, convex and compact;
5. The integrand of the objective functional is convex in U.

We write

$$r(t,\vec{x},\vec{u}) = \begin{pmatrix} N_1 - (1-u_1)\beta_{y_1} V_I H_s - (1-u_2)\beta_{y_2} H_I H_s - (1-u_3)\beta_{y_4} M_I H_s - \mu_1 H_s \\ N_2 - (1-u_1)\beta_{y_1} V_I M_s - (1-u_2)\beta_{y_5} M_I M_s - (1-u_3)\beta_{y_3} H_I M_s - \mu_2 M_s \\ (1-u_1)\beta_{y_1} V_I H_s + (1-u_2)\beta_{y_2} H_I H_s + (1-u_3)\beta_{y_4} M_I H_s - (\omega_1+\mu_1) H_E \\ (1-u_1)\beta_{y_1} V_I M_s + (1-u_2)\beta_{y_5} M_I M_s + (1-u_3)\beta_{y_3} H_I M_s - (\omega_2+\mu_2) M_E \\ \omega_1 H_E - (\epsilon_1 + \mu_1 + r_1) H_I \\ \omega_2 M_E - (\epsilon_2 + \mu_2 + r_2) M_I \\ r_1 H_I - \mu_1 H_R \\ r_2 M_I - \mu_2 M_R \\ N_3 - \beta_x (H_I + M_I) V_s - \eta V_s \\ \beta_x (H_I + M_I) V_s - (\omega_3 + \eta) V_E \\ \omega_3 V_E - \eta V_I \end{pmatrix}.$$

Then it is easy to see that $r(t,\vec{x},\vec{u})$ is of class C^1 and

$$|r_u(t,\vec{x},\vec{u})| = \begin{vmatrix} \beta_{y_1} V_I H_s & \beta_{y_2} H_I H_s & \beta_{y_4} M_I H_s \\ \beta_{y_1} V_I M_s & \beta_{y_5} M_I M_s & \beta_{y_3} H_I M_s \\ -\beta_{y_1} V_I H_s & -\beta_{y_2} H_I H_s & -\beta_{y_4} M_I H_s \\ -\beta_{y_1} V_I M_s & -\beta_{y_5} M_I M_s & -\beta_{y_3} H_I M_s \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{vmatrix}$$

,

$$A = \begin{pmatrix} -(1-u_1)\beta_{y_1} V_s - (1-u_2)\beta_{y_2} H_I - (1-u_3)\beta_{y_4} M_I - \mu_1 & 0 & 0 \\ 0 & -(1-u_1)\beta_{y_1} V_s - (1-u_2)\beta_{y_5} M_I - (1-u_3)\beta_{y_3} H_I - \mu_2 & 0 \\ (1-u_1)\beta_{y_1} V_s + (1-u_2)\beta_{y_2} H_I + (1-u_3)\beta_{y_4} M_I & 0 & -(\omega_1+\mu_1) \\ 0 & (1-u_1)\beta_{y_1} V_s + (1-u_2)\beta_{y_5} M_I + (1-u_3)\beta_{y_3} H_I & 0 \\ 0 & 0 & \omega_1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$B = \begin{pmatrix} 0 & -(1-u_2)\beta_{y_2} H_s & -(1-u_3)\beta_{y_4} H_s & 0 & 0 & 0 & -(1-u_1)\beta_{y_1} H_s & 0 \\ 0 & -(1-u_3)\beta_{y_3} & -(1-u_2)\beta_{y_5} M_s & 0 & 0 & 0 & -(1-u_1)\beta_{y_1} M_s & 0 \\ 0 & (1-u_2)\beta_{y_2} H_s & (1-u_3)\beta_{y_4} H_s & 0 & 0 & 0 & (1-u_1)\beta_{y_1} H_s & 0 \\ -(\omega_2+\mu_2) & -(1-u_3)\beta_{y_3} & -(1-u_2)\beta_{y_5} M_s & 0 & 0 & 0 & (1-u_1)\beta_{y_1} M_s & 0 \\ 0 & -(\epsilon_1+\mu_1+r_1) & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega_2 & 0 & -(\epsilon_2+\mu_2+r_2) & 0 & 0 & 0 & 0 & 0 \\ 0 & r_1 & 0 & -\mu_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & r_2 & 0 & -\mu_2 & 0 & 0 & 0 \\ 0 & -\beta_x V_s & -\beta_x V_s & 0 & 0 & -\eta & 0 & 0 \\ 0 & \beta_x V_s & \beta_x V_s & 0 & 0 & 0 & -(\omega_3+\eta) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \omega_3 & -\eta \end{pmatrix}.$$

$$r_x(t,\vec{x},\vec{u}) = [AB],$$

and

$$|r(t,0,0)| = |\left(N_1, N_2, 0, \cdots, N_3, 0, 0\right)^T|.$$

Since all the variables are bounded, there exists a constant C such that

$$|r(t,0,0)| \leq C, \quad |r_x(t,\vec{x},\vec{u})| \leq C(1+|\vec{u}|), \quad |r_u(t,\vec{x},\vec{u})| \leq C.$$

This means that condition [1] holds.
Thanks to condition [1], there exists a unique solution to system (2.1) for a constant control, which further implies that condition [2] holds.
In addition

$$r(t,\vec{x},\vec{u}) = \begin{pmatrix} N_1 - \beta_{y_1} V_I H_s - \beta_{y_2} H_I H_s - \beta_{y_4} M_I H_s - \mu_1 H_s \\ N_2 - \beta_{y_1} V_I M_s - \beta_{y_5} M_I M_s - \beta_{y_3} H_I M_s - \mu_2 M_s \\ \beta_{y_1} V_I H_s + \beta_{y_2} H_I H_s + \beta_{y_4} M_I H_s - (\omega_1 + \mu_1) H_E \\ \beta_{y_1} V_I M_s + \beta_{y_5} M_I M_s + \beta_{y_3} H_I M_s - (\omega_2 + \mu_2) M_E \\ \omega_1 H_E - (\epsilon_1 + \mu_1 + r_1) H_I \\ \omega_2 M_E - (\epsilon_2 + \mu_2 + r_2) M_I \\ r_1 H_I - \mu_1 H_R, \\ r_2 M_I - \mu_2 M_R \\ N_3 - \beta_x (H_I + M_I) V_s - \eta V_s \\ \beta_x (H_I + M_I) V_s - (\omega_3 + \eta) V_E \\ \omega_3 V_E - \eta V_I \end{pmatrix} + r_u(t,\vec{x},\vec{u}) \times \begin{pmatrix} u_1 \\ u_2 \\ u_3 \end{pmatrix}.$$

Thus condition [3] is satisfied.
Condition [4] is obvious from the definition.
In order to show the convexity of the integrand in the objective functional $f(t,\vec{x},\vec{u})$, we have to prove had

$$(1-q)f(t,\vec{x},\vec{u}) + qf(t,\vec{x},\vec{v}) \geq f(t,\vec{x},(1-q)\vec{u} + q\vec{v}),$$

where $f(t,\vec{x},\vec{u}) = A_1 H_E + A_2 M_E + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)$ and $\vec{u}$, $\vec{v}$ are two control vectors with $q \in [0,1]$.
It follows that:

$$(1-q)f(t,\vec{x},\vec{u}) + qf(t,\vec{x},\vec{v}) =$$

$$(1-q)(A_1 H_E + A_2 M_E + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)) + q(A_1 H_E + A_2 M_E + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)) =$$

$$(1-q)(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2) + q(B_1 v_1^2 + B_2 v_2^2 + B_3 v_3^2)$$

and

$$f(t,\vec{x},(1-q)\vec{u} + q\vec{v}) = \frac{1}{2}B_1[(1-q)u_1 + qv_1]^2 + \frac{1}{2}B_2[(1-q)u_2 + qv_2]^2 + \frac{1}{2}B_3[(1-q)u_3 + qv_3]^2.$$

Furthermore, we have

$$(1-q)f(t,\vec{x},\vec{u}) + qf(t,\vec{x},\vec{v}) - f(t,\vec{x},(1-q)\vec{u} + q\vec{v}) =$$

$$\frac{1}{2}B_1[(1-q)u_1^2 + qv_1^2] + \frac{1}{2}B_2[(1-q)u_2^2 + qv_2^2] + \frac{1}{2}B_3[(1-q)u_3^2 + qv_2^3] - B_1[(1-q)u_1 + qv_1]^2 - B_2[(1-q)u_2 + qv_1]^2 -$$

$-B_3[(1-q)u_3+qv_3]^2=$

$\frac{1}{2}B_1[\sqrt{q(1-q)}u_1\sqrt{q(1-q)v_1}]^2+\frac{1}{2}B_2[\sqrt{q(1-q)}u_2\sqrt{q(1-q)v_2}]^2+\frac{1}{2}B_3[\sqrt{q(1-q)}u_3\sqrt{q(1-q)v_3}]^2=$

$$\frac{1}{2}B_1q(1-q)(u_1-v_1)^2+\frac{1}{2}B_2q(1-q)(u_2-v_2)^2+\frac{1}{2}B_3q(1-q)(u_3-v_3)^2\geq 0.$$

And so the proof is complete.

The Pontryaguin's Maximum Principle provides the necessary conditions of optimality for the problem of optimal control , but considering the characteristics of our objective functional, we use the variant of minimum of this Principle. Firstly, the Lagrangian for the optimal control problem is defined by

$$L=A_1H_E+A_2M_E+\frac{1}{2}(B_1u_1^2B_2u_2^2B_3u_3^2) \tag{2.10}$$

and the Hamiltonian

$\mathbb{H}=A_1H_E+A_2M_E+\frac{1}{2}B_1u_1^2+\frac{1}{2}B_2u_2^2+\frac{1}{2}B_3u_3^2+\lambda_1(N_1-(1-u_1)\beta_{y_1}V_IH_s-(1-u_2)\beta_{y_2}H_IH_s-(1-u_3)\beta_{y_4}M_IH_s-\mu_1H_s)+\lambda_2(N_2-(1-u_1)\beta_{y_1}V_IM_s-(1-u_2)\beta_{y_5}M_IM_s-(1-u_3)\beta_{y_3}H_IM_s-\mu_2M_s)+\lambda_3((1-u_1)\beta_{y_1}V_IH_s+(1-u_2)\beta_{y_2}H_IH_s+(1-u_3)\beta_{y_4}M_IH_s-(\omega_1+\mu_1)H_E)+\lambda_4((1-u_1)\beta_{y_1}V_IM_s+(1-u_2)\beta_{y_5}M_IM_s+(1-u_3)\beta_{y_3}H_IM_s-(\omega_2+\mu_2)M_E)+\lambda_5(\omega_1H_E-(\epsilon_1+\mu_1+r_1)H_I)+\lambda_6(\omega_2M_E-(\epsilon_2+\mu_2+r_2)M_I)+\lambda_7(r_1H_I-\mu_1H_R)+\lambda_8(r_2M_I-\mu_2M_R)+\lambda_9(N_3-\beta_x(H_I+M_I)V_s-\eta V_s)+\lambda_{10}(\beta_x(H_I+M_I)V_s-(\omega_3+\eta)V_E)+\lambda_{11}(\omega_3V_E-\eta V_I).$

where $\lambda_1,\lambda_2,\cdots,\lambda_{11}$ are the adjoint variables satisfying the following adjoint system:

$$\begin{aligned}
\lambda_1^{'}&=-\frac{d\mathbb{H}}{dH_s}=(\lambda_1-\lambda_3)((1-u_1)\beta_{y_1}V_I+(1-u_2)\beta_{y_2}H_I+(1-u_3)\beta_{y_4}M_I)+\mu_1\lambda_1,\\
\lambda_2^{'}&=-\frac{d\mathbb{H}}{dM_s}=(\lambda_2-\lambda_4)((1-u_1)\beta_{y_1}V_I+(1-u_2)\beta_{y_5}M_I+(1-u_3)\beta_{y_3}M_I)+\mu_2\lambda_2,\\
\lambda_3^{'}&=-\frac{d\mathbb{H}}{dH_E}=\omega_1(\lambda_3-\lambda_5)+\mu_1\lambda_3-A_1,\\
\lambda_4^{'}&=-\frac{d\mathbb{H}}{dM_E}=\omega_2(\lambda_4-\lambda_6)+\mu_2\lambda_4-A_2,\\
\lambda_5^{'}&=-\frac{d\mathbb{H}}{dH_I}=(\epsilon_1+\mu_1)\lambda_5+r_1(\lambda_5-\lambda_7),\\
\lambda_6^{'}&=-\frac{d\mathbb{H}}{dM_I}=(\epsilon_2+\mu_2)\lambda_6+r_2(\lambda_6-\lambda_8),\\
\lambda_7^{'}&=-\frac{d\mathbb{H}}{dH_R}=\mu_1\lambda_7,\\
\lambda_8^{'}&=-\frac{d\mathbb{H}}{dM_R}=\mu_1\lambda_8,\\
\lambda_9^{'}&=-\frac{d\mathbb{H}}{dV_s}=\beta_x(H_I+M_I)(\lambda_9-\lambda_{10})+\eta\lambda_9,\\
\lambda_{10}^{'}&=-\frac{d\mathbb{H}}{dV_E}=\omega_3(\lambda_{10}-\lambda_{11})+\eta\lambda_{10},\\
\lambda_{11}^{'}&=-\frac{d\mathbb{H}}{dV_I}=(1-u_1)\beta_{y_1}[H_s(\lambda_1-\lambda_3)+M_s(\lambda_2-\lambda_4)]+\eta\lambda_{11}.
\end{aligned} \tag{2.11}$$

The transversality conditions (or boundary conditions) are

$$\lambda_i(t_f)=0,\quad i=1,...,11, \tag{2.12}$$

where t_f is the end of the time period. By the optimality condition, we have

$$\frac{\partial\mathbb{H}}{\partial u_i}=0,i=1,2,3\rightarrow u_i^*.$$

Thus,

$$\frac{\partial\mathbb{H}}{\partial u_1}=B_1u_1+[(\lambda_1-\lambda_3)H_s+(\lambda_2-\lambda_4)M_s]\beta_{y_1}V_I=0, \tag{2.13}$$

$$\frac{\partial \mathbb{H}}{\partial u_2} = B_2 u_2 + (\lambda_1 - \lambda_3)\beta_{y_2} H_I M_s + (\lambda_2 - \lambda_4) M_s M_I \beta_{y_5} = 0, \tag{2.14}$$

$$\frac{\partial \mathbb{H}}{\partial u_3} = B_3 u_3 + (\lambda_1 - \lambda_3)\beta_{y_4} M_I H_s + (\lambda_2 - \lambda_3) M_s H_I \beta_{y_3} = 0. \tag{2.15}$$

We obtain

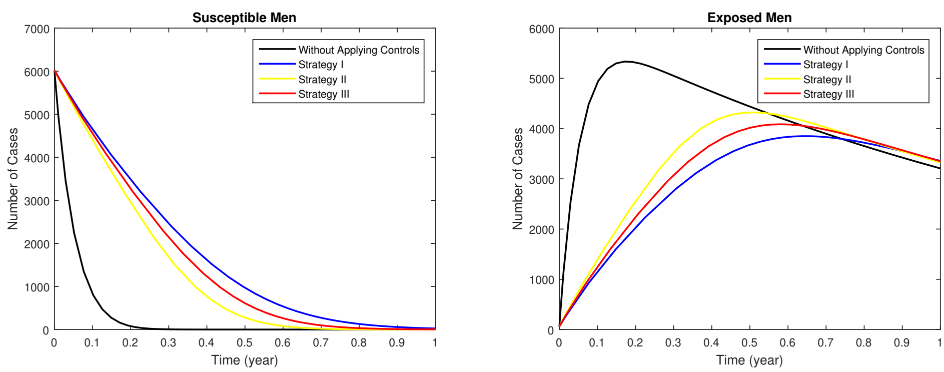
$$u_1^* = \max\left\{ \min\left\{ \frac{[(\lambda_3 - \lambda_1)H_s + (\lambda_4 - \lambda_2)M_s]\beta_{y_1} V_I}{B_1}, 1 \right\}, 0 \right\}, \tag{2.16}$$

$$u_2^* = \max\left\{ \min\left\{ \frac{[(\lambda_3 - \lambda_1)\beta_{y_2} H_I M_s + (\lambda_4 - \lambda_2) M_s M_I \beta_{y_5}}{B_2}, 1 \right\}, 0 \right\}, \tag{2.17}$$

$$u_2^* = \max\left\{ \min\left\{ \frac{[(\lambda_3 - \lambda_1)\beta_{y_4} M_I H_s + (\lambda_4 - \lambda_2) M_s H_I \beta_{y_3}}{B_3}, 1 \right\}, 0 \right\}. \tag{2.18}$$

Therefore, we obtain the optimality system which helps describe the behavior of the system with the optimal controls. The optimality system consists of the state system (2.1), initial conditions of the state variables, the adjoint system (2.11), the transversality conditions (2.12), and the characterization of the optimal control.

3. Numerical results and discussion. The goal of this section is to simulate the application of the controls in the population. First, the optimality system is numerically solved using the iterative method with the Runge-Kutta fourth order scheme. The state system (2.1) is solved by the forward Runge-Kutta method with an initial conditions, and the adjoint system (2.11) is solved by the backward Runge-Kutta method with the transversality condition [7].
For the human group, the initial number of susceptible, exposed, infected and recovered for men and women $(H_s, M_s, H_E, M_E, H_I, M_I, H_R, M_R)$ is set by $(6020, 3100, 60, 38, 20, 15, 200, 210)$. For the mosquito group, the initial number of susceptible, exposed, and infected mosquitoes (V_s, V_E, V_I) is set by $(1000, 500, 250)$. The weight constants are given as $A_1 = 0.07, A_2 = 0.06, B_1 = 30, B_2 = 10$, and $B_3 = 10$. The t_f is one year, that is, the study period is one year and the values of the parameters are extracted from [14, 13, 12, 6, 5, 4, 3, 2], see Table (2.1). We present three control strategies:
Strategy I: $u_1 = 0$, $u_2 \neq 0$ and $u_3 \neq 0$.
Strategy II: $u_1 \neq 0$, $u_2 = 0$ and $u_3 \neq 0$.
Strategy III: $u_1 \neq 0$, $u_2 \neq 0$ and $u_3 = 0$.
Because the main form of contagion is the mosquito bite and we decided in our different strategies to keep in mind the control related to mosquitoes. In practice, our strategy cannot be completely implemented, so the maximum value of each control is set to be 0.95 instead of 1.



(a) Susceptible Men (b) Exposed Men

Figure 3.1: Behavior of susceptible and exposed men, comparison of different control strategies and without the application of control.

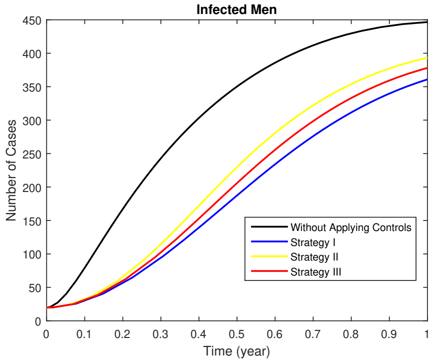
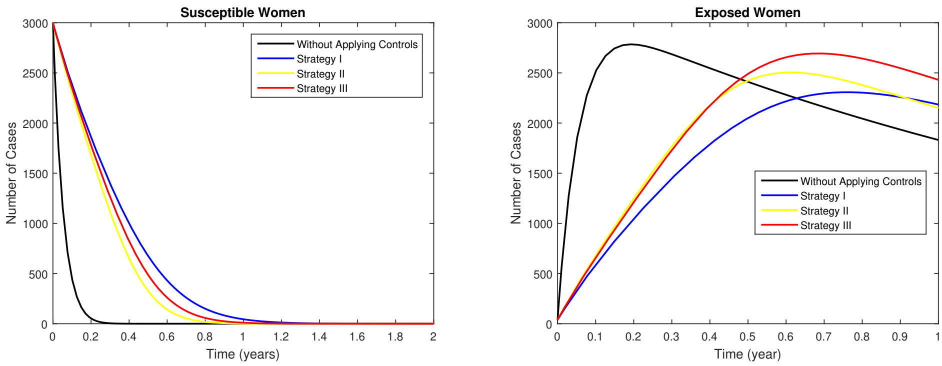


Figure 3.2: Behavior of infected men, comparison of different control strategies and without the application of control.

Figure (3.1) shows the number of susceptible and exposed men from the optimality system without control and the optimality system with controls. The figures (3.1a) show that the strategy from which all the controls will be maintained will keep the largest number of susceptible. Figure (3.1b) shows that the best control is obtained with strategy I, because the number of exposed is reduced and the process occurs with less speed, but at the end of the study period the difference between the controls is smaller and the smaller number is reported by the model without controls. This shows that at the end of the study period the efficiency of the controls should be increased. Figure (3.2) shows the number of infected men from the optimality system without control and the optimality system with controls. In the case of infected men, the least number of cases reported is by strategy I, see Figure (3.2). It is reported a lower number of exposed with the strategy I besides that with the application of control strategies the growth is lower and it takes more time to reach the peak, but at the end of the study period the differences of the controls are not significant and it is reported a lower number in the case without controls. With this results, we show that it is necessary to increase the effectiveness of controls over time. In the case of infected men, the most effective strategy in the dynamics is the activation of all controls, but the second effective option is strategy III, which demonstrates the influence that contagion through homosexual relations has on the dynamics of Zika transmission.



(a) Susceptible Women (b) Exposed Women

Figure 3.3: Behavior of susceptible and exposed women, comparison of different control strategies and without the application of control.

In the case of women, it happens analogously to the case of men but in a lesser number of cases, see Figures (3.3) and (3.4). The most effective strategy is with the activation of all controls, but the application of strategies II and III their difference is not significant as in men, in particular for those exposed and infected, see Figures (3.1b), (3.1), (3.3b) and (3.4) until the end of the study period (one year). This shows that in men in particular, infection through homosexual contact has a greater influence than in women.

The most effective strategy in the case of mosquitoes is strategy I, because it manages to maintain the highest number of susceptible and reduce the number of exposed and infected, the second most effective is strategy III, see Figures (3.5) and (3.6). Particularly for those exposed during the course of the study, the dif-

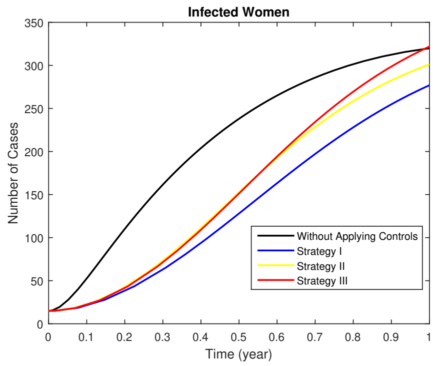
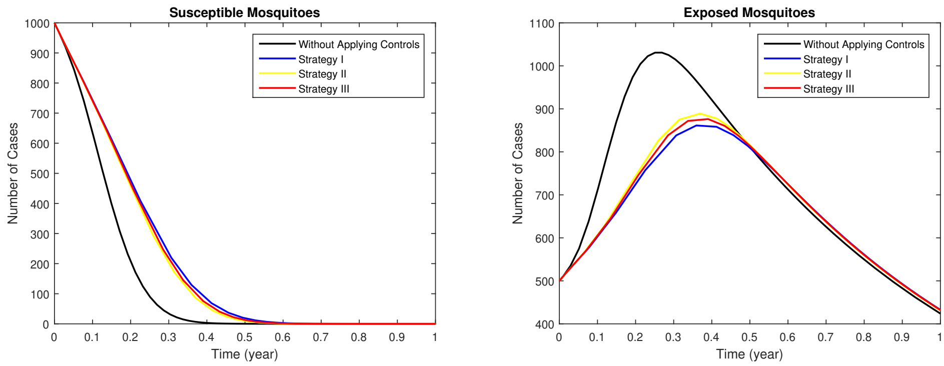


Figure 3.4: Behavior of infected women, comparison of different control strategies and without the application of control.



(a) Susceptibles Mosquitoes (b) Exposed Mosquitoes

Figure 3.5: Behavior of susceptible and exposed mosquitoes, comparison of different control strategies and without the application of control.

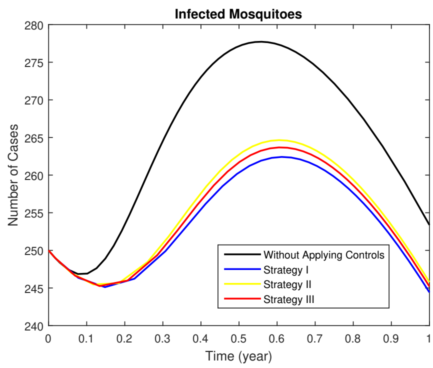


Figure 3.6: Behavior of infected mosquitoes, comparison of different control strategies and without the application of control.

ference in behavior of the strategies is not significant and even better results are achieved without applying controls, since in the dynamics we have factors such as the life cycle of the mosquito and environmental factors that are related to this behavior, see Figure (3.5b). Strategy I reports the least number of infected mosquitoes and was more efficient (in this compartment) than the other strategies and the uncontrolled model, see figure (3.6).

4. Conclusions. In this paper, we presented a control model from the deterministic model of the Zika virus infection with the presence of sexual transmission and sex stratification. The optimal control problem is proposed with three selected controls; vector-to-human contact reduction, homosexual contact control, heterosexual contact control. The optimal control problem is developed to minimize the number of exposed humans as well as the costs associated with implementing the controls. We use Pontryaguin's maximum principle to determine the necessary conditions, find the optimality system of the model and hence find the solution to the optimal control problem. Numerical simulations comparing the systems without control and the system with controls are presented. It is shown that an optimal control strategy is more effective in reducing the infected humans and vectors than without control strategy. From the numerical results, it is shown that the best strategy is to activate all the proposed controls. transmission through homosexual sexual relations in the transmission of men where the second best strategy is based on this control along with that applied to mosquitoes. This work contributes with a proposal of control policy with the objective of eradicating Zika in the community.

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Erick Manuel Delgado Moya http://orcid.org/0000-0001-5937-5374
Aymée Marrero Severo http://orcid.org/0000-0003-4823-0078

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