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OPTIMAL CONTROL OF CHIKUNGUNYA DISEASE: LARVAE REDUCTION, TREATMENT AND PREVENTION

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Abstract. Since the 1980s, there has been a worldwide re-emergence of vector-borne diseases including Malaria, Dengue, Yellow fever or, more recently, chikungunya. These viruses are arthropod-borne viruses (arboviruses) transmitted by arthropods like mosquitoes of *Aedes* genus. The nature of these arboviruses is complex since it conjugates human, environmental, biological and geographical factors. Recent researchs have suggested, in particular during the Réunion Island epidemic in 2006, that the transmission by *Aedes albopictus* (an *Aedes* genus specie) has been facilitated by genetic mutations of the virus and the vector capacity to adapt to non tropical regions. In this paper we formulate an optimal control problem, based on biological observations. Three main efforts are considered in order to limit the virus transmission. Indeed, there is no vaccine nor specific treatment against chikungunya, that is why the main measures to limit the impact of such epidemic have to be considered. Therefore, we look at time dependent breeding sites destruction, prevention and treatment efforts, for which optimal control theory is applied. Using analytical and numerical techniques, it is shown that there exist cost effective control efforts.

1. **Introduction.**

The chikungunya virus, is an arthropod-borne virus (arbovirus) transmitted by mosquitoes of *Aedes* genus. The chikungunya term, used for both the virus and the disease comes from the Makonde Plateau language in Tanzania, where the virus was first identified in 1953 [31, 39]. It means "that which bends up" in reference to symptoms observed on affected people, like cardiovascular manifestation and fever [37]. The mosquito responsible of this first epidemic is the *Aedes aegypti* [40]. This mosquito is most known for being the main vector of the dengue

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fever [25], the most rapidly spreading mosquito-borne viral disease in the world. Indeed, in the last 50 years, the incidence of this virus has increased with increasing geographic expansion to new countries, and in the last decades, from urban to rural settings. Moreover, approximately one billion people live in dengue endemic countries and annually, an estimated 50 million dengue infections occur [47]. Like dengue epidemic, which is a major public health problem in several countries, chikungunya appears also to be one of the most important vector-borne disease.

Many factors have influenced the resurgence of such vector-borne diseases like the increase of travel and exchanges [9] or the development of insecticide and drug resistance [4]. Studies have suggested that human activities help carrying eggs on eventually long distances whereas once hatched a mosquito may not have a perimeter wider that 200 meters. This means that people, rather than mosquitoes, rapidly help the spread of the virus within and between communities. Nevertheless, each of these species has a particular ecological behaviour and geographical distribution.

In the fifties, various outbreaks of chikungunya have been observed like in Thaïland (1960s and 1995) [29], or in Senegal (1972 to 1986)[15]. After a break of twenty years, severals epidemics have been reported in India [44, 41], in Europe, or in the Indian Ocean Islands like in Mayotte, Comoros archipelago [42], or in the Réunion Island [43]. In the last one, one third of the total population has been infected by this virus in 2006.
Usually transmitted by *Aedes aegypti*, it has been observed during recent epidemics that the virus is additionally transmitted by *Aedes albopictus* [26], also called Asian tiger mosquito and native from Southeast Asia [27]. Indeed, the *Aedes aegypti* mosquito is a tropical and a subtropical specie widely distributed around the world, while the *Aedes albopictus* has developed capabilities to adapt to non tropical regions. The chikungunya used to be localized in tropical regions but, nowadays, because of climate changes that create suitable conditions for outbreaks of diseases, they slowly start to spread all over the world, Europe included where the *Aedes albopictus* mosquito is also present since a long time. For instance, an outbreak of chikungunya occurred in the Emilia Romagna region, in Italy [14, 38, 46], in 2007, with 254 cases of infection. It was the first case of chikungunya transmission within Europe.
Moreover, recent research [21] suggested that in the case of the Réunion Island epidemic, the transmission by *Aedes albopictus* has been facilitated by genetic mutations of the virus. Indeed, during the recent outbreaks reported in the Indian ocean island, the identified chikungunya virus was characterized by a genetic mutation in the E1 glycoprotein gene (E1-226V). This mutation allowed the virus to be present in the mosquito saliva only two days after the infection, instead of approximately seven days [18]. This greatly helped the transmission by *Aedes albopictus*. Moreover this mosquito is present in several parts of the world, like in Albania [3], Spain [10], USA and Australia [7].

Unfortunately, this disease has no specific treatment nor vaccine, that is why preventing or reducing chikungunya virus transmission depends mainly on control of the mosquito vectors or interruption of human-vector contact. Actions focus on individual protection against mosquito bites, symptomatic treatment of patients and mosquito proliferation control. For instance, the number of breeding sites are reduced by eliminating container habitats that are favorable oviposition sites and that permit the development of aquatic stages. Indeed, the *Aedes albopictus* female lays its eggs in wet places adjacent to the surface of water in all sorts of receptacles: vases, rainwater barrels, used tyres, *etc.* Moreover, as winter approaches, eggs may enter a diapause, that is to say the progression from egg to adult is interrupted by a period of dormancy [24]. In this stage, eggs are resistant to cold climates and droughts, and can wait until next spring to hatch. This diapause may explain the adaptation of the mosquito to temperate climate [34, 32].

Recently, a number of studies have been conducted to explore optimal control theory in some mathematical models for infectious diseases including HIV diseases [2, 1], tuberculosis [28] and vector-borne diseases [8]. Authors in [8] derive the optimal control efforts for treatment and prevention in order to prevent the spread of a vector-borne disease using a system of ordinary differential equations (ODEs) for the host and vector populations. In our effort, we investigate such optimal strategies for prevention, treatment and vector control using two systems of ODEs which consist of a stage structure model for the vector and a SI/SIR type model for the vector/host population.

In this paper, using models described in [33] for the mosquito population dynamics and the transmission virus, we formulate the associated control model in order to derive optimal prevention and treatment strategies with minimal implementation cost. Controls used here are based on three main actions applied in the recent epidemics.

The paper is organized as follows. In section 2, we present the compartmental model used in [33] to describe the *Aedes albopictus* population dynamics and the chikungunya virus transmission to the human population.

In section 3, we formulate an optimal control problem; first, we investigate the existence of an optimal control, then we derive the optimality system which characterizes the optimal control using Pontryagin's Maximum Principle [36]. In section 4 numerical results illustrate our theoretical results.

2. **The basic model.**

We have proposed two models [33] to describe the population dynamics of the *Aedes albopictus* mosquito population and the transmission of the virus to human population. For the reader convenience, we briefly recall here main results which are developed in this work.

i. The vector population is described by a stage-structured model based on the biological life cycle. It consists in four main stages described by the following compartment: egg (E), larvae and pupae (L) which are biologically very closed stages, and the adult stage (A) which contains only females because they are responsible for the transmission. The density variation of each stage is easily done by making the input-output balance in each evolution stage. The *per capita* mortality rate of eggs, larvae and adults are denoted by d, d_L and d_m respectively. The net oviposition rate per female insect is proportional to their density, but it is also regulated by a carrying capacity effect depending on the occupation of the available breeder sites. Moreover, it has been observed that females are able to detect the best breeding sites for the egg development, that is to say breeding sites where eggs and then larvae will be able to develop easily. Thus, in this model, we assume that the *per capita* oviposition rate is also proportional to the number of females and given by $bA(t)(1 - E(t)/K_E)$, where K_E is the carrying capacity related to the amount of available nutrients and space, and b is the intrinsic oviposition rate. The egg population becomes larvae at a *per capita* transfer rate s and the larvae population becomes mosquito female at a *per capita* rate s_L. In addition to the transfer rate

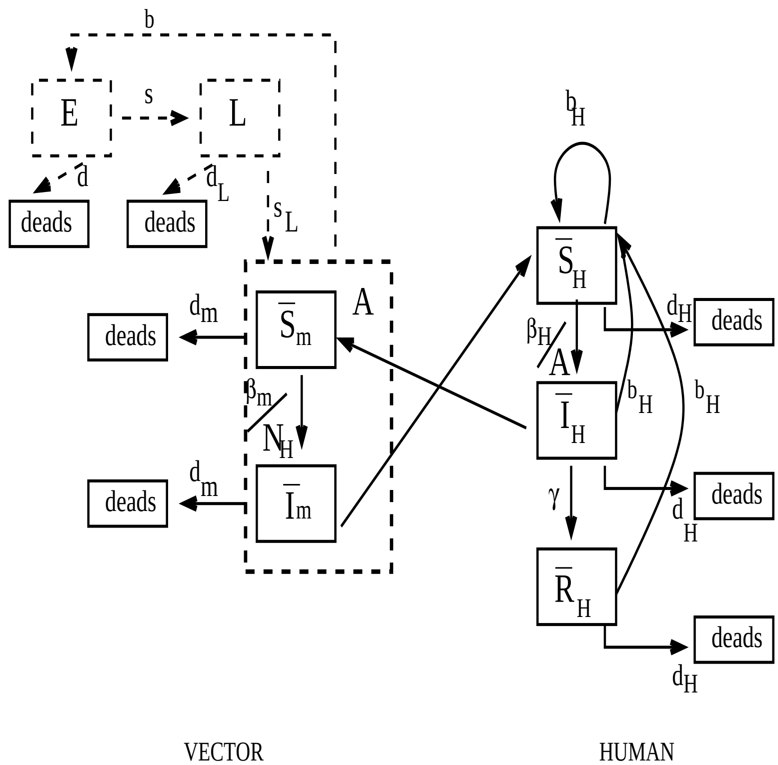

FIGURE 1. Transmission diagram. Coupling of a stage structured model for *Aedes albopictus* population dynamics (dashed line) and a compartmental model describing the transmission of the virus between adult mosquito and human population.

s, the flows from eggs to larvae is regulated by a carrying capacity K_L due to the intra-specific competition with young larvae. Thus the number of new larvae is given by $sE(t)(1 - L(t)/K_L)$. All this hypothesis may be summarize in figure (1) (dashed line) which describes the input-output of each mosquito stages. Therefore, the mosquito population dynamics is described by:

$$\begin{cases} \dfrac{dE}{dt}(t) = bA(t)\left(1 - \dfrac{E(t)}{K_E}\right) - (s+d)E(t) \\ \dfrac{dL}{dt}(t) = sE(t)\left(1 - \dfrac{L(t)}{K_L}\right) - (s_L + d_L)L(t) \\ \dfrac{dA}{dt}(t) = s_L L(t) - d_m A(t) \end{cases} \tag{1}$$

This system is defined on the bounded subset of $\mathbb{R}^3$,

$$\Delta = \left\{ (E, L, A) \ \middle|\ \begin{array}{l} 0 \le E \le K_E \\ 0 \le L \le K_L \\ 0 \le A \le \dfrac{s_L}{d_m} K_L \end{array} \right\} \tag{2}$$

Let us introduce the following threshold parameter:

$$r = \frac{b}{s+d}\frac{s}{s_L + d_L}\frac{s_L}{d_m}$$

which, as we will see, governs the asymptotic behavior of the mosquito population.

Theorem 2.1.

- *System (1) always has the mosquito free equilibrium* $X_0^* = (0,0,0)$ *which is globally asymptotically stable iff* $r \leq 1$.
- *If* $r > 1$, *there is a unique non-trivial equilibrium, which is globally asymptotically stable and given by*

$$X^* = \left(1 - \frac{1}{r}\right)\left(\frac{K_E}{\gamma_E}; \frac{K_L}{\gamma_L}; \frac{s_L}{d_m}\frac{K_L}{\gamma_L}\right)^T = (E^*; L^*; A^*),$$

where

$$\gamma_E = 1 + \frac{(s+d)d_m K_E}{b s_L K_L} \qquad \text{and} \qquad \gamma_L = 1 + \frac{(s_L + d_L)K_L}{s K_E}.$$

Proof. The global stability of both equilibrium points is given using Lyapunov function theory. This function is obtained by the construction of a symmetric matrix. The detailed proof is given in [33]. □

Then, by the previous theorem, we observe that the mosquito population may have two different behaviors. All populations may die out if the threshold parameter r is less than one or tends to an endemic equilibrium which corresponds to the coexistence of species.

ii. The second model uses SI and SIR schemes, which are ordinary differential equations describing the numbers of susceptible, infective and recovered individuals during an epidemic. Indeed, the adult mosquito population (A) is described thanks to a SI model, because an infected vector remains infective until its death, whereas human population is described by an SIR model.

With respect to the circulation of chikungunya virus among adults mosquitoes, they are sub-divided into susceptible ($\bar{S}_m$) and infectious ($\bar{I}_m$). The total size of the population is $A = \bar{S}_m + \bar{I}_m$, where A is given previously in system (1). The chikungunya infection occurs when susceptible mosquitoes ($\bar{S}_m$) are infected during the blood meal from infectious humans ($\bar{I}_H$). The *per capita* incidence rate among mosquitoes $\beta_m \dfrac{\bar{I}_h}{N_H}$ depends on the fraction of infectious humans $\dfrac{\bar{I}_H}{N_H}$, where N_H is the total human population size. This rate takes into account the encounters between susceptible mosquitoes and infectious humans, given by the contact rate β_m, which is related to the frequency of bites. We assume that the mortality rates related to susceptible and infectious mosquitoes are equals and given by d_m. Biological observations allow us to assume that there is no vertical transmission, *i.e.* all new births are susceptible and after recovering, humans become immune.

The chikungunya infection among humans occurs when susceptible individuals $\bar{S}_H$ are bitten by infectious mosquitoes $\bar{I}_m$ during the blood meal. The *per capita* incidence rate among susceptible humans depends on the fraction of infectious mosquitoes $\dfrac{\bar{I}_m}{A}$ and takes into account the encounters between susceptible humans and infectious mosquitoes, designed by β_H. These infected individuals enter in the recovered class ($\bar{R}_H$) at a constant rate γ_H. Moreover we assume that N_H is constant, *i.e.* $b_H = d_H$. Then the hypothesis leads to the following virus transmission model:

$$\begin{cases} \dfrac{d\bar{S}_H}{dt}(t) = b_H N_H - \beta_H \dfrac{\bar{I}_m(t)}{A(t)} \bar{S}_H(t) - d_H \bar{S}_H(t) \\ \dfrac{d\bar{I}_H}{dt}(t) = \beta_H \dfrac{\bar{I}_m(t)}{A(t)} \bar{S}_H(t) - \gamma \bar{I}_H(t) - d_H \bar{I}_H(t) \\ \dfrac{d\bar{R}_H}{dt}(t) = \gamma \bar{I}_H(t) - d_H \bar{R}_H(t) \\ \dfrac{d\bar{S}_m}{dt}(t) = s_L L(t) - d_m \bar{S}_m(t) - \beta_m \dfrac{\bar{I}_H(t)}{N_H} \bar{S}_m(t) \\ \dfrac{d\bar{I}_m}{dt}(t) = \beta_m \dfrac{\bar{I}_H(t)}{N_H} \bar{S}_m(t) - d_m \bar{I}_m(t). \end{cases} \tag{3}$$

System (3) is defined on the bounded subset of $\mathbb{R}^5$,

$$\left\{ (\bar{S}_H, \bar{I}_H, \bar{R}_H, \bar{S}_m, \bar{I}_m) \;\middle|\; \begin{array}{l} \bar{S}_H + \bar{I}_H + \bar{R}_H = N_H, \\ \bar{S}_m + \bar{I}_m = A \end{array} \right\},$$

where A corresponds to the female adult mosquito stage of system (1) and is bounded by $\dfrac{s_L}{d_m} K_L$.

Introducing proportions $S_H = \bar{S}_H/N_H$, $I_H = \bar{I}_H/N_H$, $R_H = \bar{R}_H/N_H$, $S_m = \bar{S}_m/A$, $I_m = \bar{I}_m/A$ in system (3) by using relations $\bar{S}_H + \bar{I}_H + \bar{R}_H = N_H$ and $\bar{S}_m + \bar{I}_m = A$ and the derivative $dS_H/dt = (d\bar{S}_H/dt)(1/N_H)$, $dI_H/dt = (d\bar{I}_H/dt)(1/N_H)$ and $dI_m/dt = (1/A^2)((d\bar{I}_m/dt)A - \bar{I}_m(dA/dt))$, we obtain the following system,

$$\begin{cases} \dfrac{dS_H}{dt}(t) = -\left(b_H + \beta_H I_m(t)\right) S_H(t) + b_H \\ \dfrac{dI_H}{dt}(t) = \beta_H I_m(t) S_H(t) - (\gamma + b_H) I_H(t) \\ \dfrac{dI_m}{dt}(t) = -\left(s_L \dfrac{L(t)}{A(t)} + \beta_m I_H(t) \right) I_m(t) + \beta_m I_H(t). \end{cases} \tag{4}$$

Remark 1. Due to this classical variable changes, mathematical study of system (3) may reduce to the study of (4).

Our transmission virus model including mosquito population dynamic is then given by:

$$\left\{\begin{array}{ll}\left\{\begin{array}{l}\dfrac{dE}{dt}(t) = bA(t)\left(1-\dfrac{E(t)}{K_E}\right) - (s+d)E(t)\\ \dfrac{dL}{dt}(t) = sE(t)\left(1-\dfrac{L(t)}{K_L}\right) - (s_L+d_L)L(t)\\ \dfrac{dA}{dt}(t) = s_L L(t) - d_m A(t)\end{array}\right. & (a)\\ \left\{\begin{array}{l}\dfrac{dS_H}{dt}(t) = -\left(b_H + \beta_H I_m(t)\right) S_H(t) + b_H\\ \dfrac{dI_H}{dt}(t) = \beta_H I_m(t) S_H(t) - (\gamma + b_H) I_H(t)\\ \dfrac{dI_m}{dt}(t) = -\left(s_L \dfrac{L(t)}{A(t)} + \beta_m I_H(t)\right) I_m(t) + \beta_m I_H(t).\end{array}\right. & (b)\end{array}\right. \tag{5}$$

defined on $\Delta \times \Omega$, where Δ is given by (2) and

$$\Omega = \left\{ (S_H, I_H, I_m) \in \mathbb{R}^3_+ \;\middle|\; \begin{array}{l} 0 \le S_H + I_H \le 1 \\ 0 \le I_m \le 1 \end{array} \right\}. \tag{6}$$

Remark 2. Note that this system has two different time scales, since the subsystem (5a) describes the dynamics of our different mosquito stages, while the subsystem (5b) describes the dynamics of the proportion of susceptible and infected populations. In this paper we consider proportions rather than quantities in the proposed model. We believe it is more convenient for the reader since it refers more easily to the study proposed in [33]. A switch back to a system without densities is straightforward, thanks to the variable change proposed earlier. Besides, considering proportions allows us to use mathematical results on competitive theory for 3-dimensional systems and second compound matrix to study the global stability of the endemic equilibrium of subsystem (5b).

Let us introduce the following reproduction number [16, 17], which is defined as the average number of secondary infections produced by an infected individual in a completely susceptible population

$$R_0 = \frac{\beta_m \beta_H}{d_m(\gamma + b_H)}. \tag{7}$$

Theorem 2.2. *Assume that $r > 1$.*

- *System (4) always has the disease free equilibrium $N_0^* = (1, 0, 0)$ which is globally asymptotically stable iff $R_0 \le 1$.*
- *If $R_0 > 1$, there is a unique globally asymptotically stable endemic equilibrium given by*

$$N^* = \begin{pmatrix} \dfrac{b_H}{\beta_H + b_H} + \dfrac{\beta_H}{(\beta_H + b_H)R_0} \\ \dfrac{d_m b_H}{\beta_m(\beta_H + b_H)}(R_0 - 1) \\ \dfrac{b_H}{\beta_H + b_H R_0}(R_0 - 1) \end{pmatrix} = \begin{pmatrix} S_H^* \\ I_H^* \\ I_m^* \end{pmatrix}.$$

Proof. We use Lyapunov function and competitive system theory. The detailed proof is given in [33]. □

Remark 3. Note that in this model we have considered a non classical incidence rate among humans depending on the total vector population (as in [22, 48]). A simple variable change allows us to consider a classical incidence rate substituing β_H by $\beta_H \dfrac{A(t)}{N_H}$ in system (3). The second reproduction number is then given by:

$$\begin{aligned} R_0 &= \frac{\beta_m \beta_H}{d_m(\gamma + b_H)} \frac{A^*}{N_H} \\ &= \frac{\beta_m \beta_H}{d_m(\gamma + b_H)} \frac{1}{N_h} \left(1 - \frac{1}{r}\right) \frac{s K_E s_L K_L}{d_m\big(s K_E + (s_L + d_L) K_L\big)}. \end{aligned}$$

Biological and modeling details of the previous model and a study of the asymptotic dynamics are given in [33].

3. **A model for optimal control.** There are several possible interventions in order to reduce or limit the proliferation of mosquitoes and the explosion of the number of infected people.

Using previous models (1) and (4), we formulate the associated control model in order to derive optimal prevention and treatment strategies with minimal implementation cost. Controls used here are based on effective actions applied in the recent epidemics.

- The first control u_1 represents efforts made for prevention on a time interval $[0, T]$. It mainly consists in reducing the number of vector-host contacts due to the use of repulsive against adult mosquitoes and protection with mosquito nets or wearing appropriate clothing. Indeed *Aedes albopictus* has a peak of activity during fresh temperatures, early in the morning and late in the afternoon.
- The second control u_2 represents efforts made for treatment on a time interval $[0, T]$. It mainly consists in isolating infected patients in hospitals, installing an anti-mosquito electric diffuser in the hospital room, or symptomatic treatments. Because, there are no vaccine nor completely satisfying drug to treat all symptoms [11], which can persist several months after the infection [35], the vector control remains a major tool to prevent and control the illness.

  More precisely, only symptomatic treatments are used in order to alleviate the symptoms. Their efficacy varies from one person to another, using for instance corticosteroids, paracetamol and non-steroidal anti-inflammatory drugs.
- Finally the third control u_3 represents the effect of interventions used for the vector control. It mainly consists in the reduction of breeding sites with chemical application methods, for instance using larvicides like BTI (Bacillus Thuringensis Israelensis) which is a biological larvicide, or by introducing larvivore fish. This control focuses on the reduction of the number of larvae, and thus eggs, of any natural or artificial water-filled container. Moreover, in France, one other type of intervention is the use of traps. This consists in using simple black buckets (black colour is recognized as being attractive), with a capacity of one liter of water, three-quarters full with tannic water (water macerated for 3 days with dead branches and leaves). This traps contain laying sites (little plates of square extruded polystyrene placed on the surface of the water [5]. Finally tablets of bio-insecticide (Dimilin) are introduced in the traps in order to neutralise the potential development of larvae.

We will not consider the use of Deltamethrin, a chemical adulticide, because it has a negative effect on the environment. Moreover the sensitiveness to this adulticide depends on the area, for instance in Martinique Island, a French department, 60% of *Aedes* population have rapidly developed a resistance to Deltamethrin. Let us remark that we have not converted this control by a reduction of eggs and larvae carrying capacity. Indeed, while it is possible to reduce the number of artificial breeding sites, the only possibility to reduce natural ones is to dry them rather than to destroy them. This solution is of course not realistic. Moreover, even if artificial breeding sites are man-made, it is impossible to inventory them all because they are often temporary or random.

Another approach using a biological control consists in the introduction of sterile insects [45]. This method allows to reduce the number of mosquitoes thanks to a decrease of the oviposition rate.

Therefore, our transmission and optimal control model of chikungunya disease reads as

$$\begin{cases} \dfrac{dE}{dt}(t) = bA(t)\left(1-\dfrac{E(t)}{K_E}\right) - (s+d+\varepsilon u_3(t))E(t) \\ \dfrac{dL}{dt}(t) = sE(t)\left(1-\dfrac{L(t)}{K_L}\right) - (s_L+d_L)L(t) - d_c u_3(t)L(t) \\ \dfrac{dA}{dt}(t) = s_L L(t) - d_m A(t) \\ \dfrac{dS_H}{dt}(t) = -\left(b_H + \beta_H(1-u_1(t))I_m(t)\right)S_H(t) + b_H \\ \dfrac{dI_H}{dt}(t) = \beta_H(1-u_1(t))I_m(t)S_H(t) - (\gamma+\gamma_0 u_2(t)+b_H)I_H(t) \\ \dfrac{dI_m}{dt}(t) = -s_L\dfrac{L(t)}{A(t)}I_m(t) + \beta_m(1-u_1(t))I_H(t)(1-I_m(t)). \end{cases} \tag{8}$$

where $u_1 \in [0,1]$ corresponds to prevention effort, thus if $u_1 = 1$ there is no contact between humans and mosquitoes and if $u_1 = 0$ the infection rate is maximal and equal to β_H or β_m; $u_2 \in [0,1]$ corresponds to the treatment effort and γ_0 is the proportion of effective treatment (thus $\gamma_0 u_2(t)$ is the *per capita* recovery rate induced by treatment); $u_3 \in [0,1]$ corresponds to the reduction of the mosquito proliferation effort, and ε and d_c are eggs and larvae mortality rates induced by chemical intervention respectively.

Theorem 3.1. *$\Delta \times \Omega$ is positively invariant under system (8).*

Proof. On the one hand, one can easily see that it is possible to get,

$$\begin{cases} \frac{dE}{dt} \geq -(\frac{b}{K_E} + s + d + \varepsilon)E \\ \frac{dL}{dt} \geq -(\frac{s}{K_L} + s_L + d_L + d_c)L \\ \frac{dA}{dt} \geq -d_m A \\ \frac{dS_H}{dt} \geq -(b_H + \beta_H)S_H \\ \frac{dI_H}{dt} \geq -(\gamma + \gamma_0 + b_H)I_H \\ \frac{dI_m}{dt} \geq -(s_L + \beta_m)I_m, \end{cases} \tag{9}$$

for $E_i(0), L_i(0), A_i(0), S_H(0), I_H(0), I_m(0) \geq (0)$. Thus, solutions with initial value in $\Delta \times \Omega$ remain nonnegative for all $t \geq 0$. On the other hand, we have

$$\begin{cases} \frac{dE}{dt} \leq bA\left(1 - \frac{E}{K_E}\right) - (s + d)E \\ \frac{dL}{dt} \leq sE\left(1 - \frac{L}{K_L}\right) - (s_L + d_L)L \\ \frac{dA}{dt} \leq s_L L - d_m A \\ \frac{dS_H}{dt} \leq (b_H + \beta_H I_m)\, S_H + b_H \\ \frac{dI_H}{dt} \leq \beta_H I_m S_H - (\gamma + b_H)I_H \\ \frac{dI_m}{dt} \leq \left(s_L \frac{L}{A} + \beta_m I_H\right) I_m + \beta_m I_H. \end{cases} \tag{10}$$

The right hand side of the inequality corresponds to the transmission model without control (1) and (3) for which we have shown in [33] that solutions remain in $\Delta \times \Omega$. Then using Gronwall's inequality as before, we deduce that solutions of (8) are bounded. □

Using system (8), we consider an optimal control problem with the objective (cost) functional given by

$$J(u_1, u_2, u_3) = \int_0^T \left(A_1 I_H(t) + A_2 I_m(t) + A_3 L(t) + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2\right) dt. \tag{11}$$

The first three terms represent benefit of I_H, I_m and L populations. Positive constants B_1, B_2 and B_3 are weight for prevention, treatment and vector control effort respectively, which regularize the optimal control. These costs are given in quadratic form as usually done in the literature. Our goal is to limit the number of I_H and I_m populations and control the proliferation of the vector population by minimizing the number of larvae and pupae L. We look for an optimal control

(u_1^*, u_2^*, u_3^*) such that

$$J(u_1^*, u_2^*, u_3^*) = min\left\{J(u_1,u_2,u_3)|(u_1,u_2,u_3) \in \Gamma\right\}, \tag{12}$$

where

$$\begin{aligned}\Gamma \quad = \quad & \{(u_1,u_2,u_3)|u_i(t) \text{ is piecewise continuous function on} \\ & [0,T] \text{ such that } a_i \leq u_i(t) \leq b_i, i = 1,2,3\}\end{aligned}$$

is the control set and a_i, b_i are constants in $[0,1]$, $i = 1,2,3$. The basic framework of this problem is to prove the following:

- the existence of the optimal control;
- the characterization of the optimal control.

3.1. **Existence and characterization of an optimal control.** The existence of an optimal control can be obtained by using a result of Fleming and Rishel [23].

Theorem 3.2. *Consider the control problem with system* (8). *There exists* $(u_1^*, u_2^*, u_3^*) \in \Gamma$ *such that*

$$\min_{(u_1,u_2,u_3)\in\Gamma} J(u_1,u_2,u_3) = J(u_1^*, u_2^*, u_3^*).$$

Proof. To use an existence result, theorem III.4.1 from [23], we must check if the following properties are satisfied:

1. the set of controls and corresponding state variables is non empty;
2. the control set Γ is convex and closed;
3. the right hand side of the state system is bounded by a linear function in the state and control;
4. the integrand of the objective functional is convex;
5. there exist constants $c_1, c_2, c_3 > 0$, and $\beta > 0$ such that the integrand of the objective functional is bounded below by $c_1(|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\beta}{2}} - c_2$.

In order to verify these properties, we use a result from Lukes [30] to give the existence of solutions for the state system (8) with bounded coefficients, which gives condition 1. The control set Γ is bounded by definition, then, condition 2 is satisfied. The right hand side of the state system (8) satisfies condition 3 since the state solutions are bounded. The integrand of our objective functional is clearly convex on Γ, which gives condition 4. Finally, there are $c_1, c_2 > 0$ and $\beta > 1$ satisfying $A_1 I_H(t) + A_2 I_m(t) + A_3 L(t) + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2 \geq c_1(|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\beta}{2}} - c_2$, because the states variables are bounded.

We conclude that there exists an optimal control (u_1^*, u_2^*, u_3^*) that minimizes the objective functional $J(u_1,u_2,u_3)$. □

Now, that we have established, the existence of an optimal control, we focus on the determination of an optimal control.
Let $Z = (E, L, A, S_H, I_H, I_m) \in \Delta \times \Omega$, $U = (u_1,u_2,u_3) \in \Gamma$ and the adjoint variables $\Pi = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6)$.

Let us define the Lagrangian of our problems as follows:

$$
\begin{aligned}
&\mathcal{L}(Z,U,\Pi) = A_1 I_H(t) + A_2 I_m(t) + A_3 L(t)\\
&+B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2\\
&+\lambda_1 \left(bA(t)\left(1 - \frac{E(t)}{K_E}\right) - (s + d + \varepsilon u_3(t))E(t) \right)\\
&+\lambda_2 \left(sE(t)\left(1 - \frac{L(t)}{K_L}\right) - (s_L + d_L + d_c u_3(t))L(t) \right)\\
&+\lambda_3 \left(s_L L(t) - d_m A(t) \right)\\
&+\lambda_4 \left(-\left(b_H + \beta_H(1-u_1(t))I_m(t)\right) S_H(t) + b_H \right)\\
&+\lambda_5 \left(\beta_H (1-u_1(t)) I_m(t) S_H(t) - (\gamma + \gamma_0 u_2(t) + b_H) I_H(t) \right)\\
&+\lambda_6 \left(-s_L \frac{L(t)}{A(t)} I_m(t) + \beta_m I_H(t)(1-u_1(t))(1-I_m(t)) \right)\\
&-w_{11}(u_1 - a_1) - w_{12}(b_1 - u_1) - w_{21}(u_2 - a_2)\\
&-w_{22}(b_2 - u_2) - w_{31}(u_3 - a_3) - w_{32}(b_3 - u_3),
\end{aligned}
\tag{13}
$$

where $w_{ij}(t) \geq 0$ are the penalty multipliers satisfying

$$w_{11}(t)(u_1(t) - a_1) = w_{12}(t)(b_1 - u_1(t)) = 0 \text{ at optimal control } u_1^*,$$

$$w_{21}(t)(u_2(t) - a_2) = w_{22}(t)(b_2 - u_2(t)) = 0 \text{ at optimal control } u_2^*$$

and

$$w_{31}(t)(u_3(t) - a_3) = w_{32}(t)(b_3 - u_3(t)) = 0 \text{ at optimal control } u_3^*.$$

Theorem 3.3. *Given an optimal control (u_1^*, u_2^*, u_3^*) and solutions E, L, A, S_H, I_H, and I_m of the corresponding state system (8), there exist adjoint variables $\Pi = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6)$ satisfying,*

$$
\begin{aligned}
\dot{\lambda_1} &= -\left(\lambda_1[-b\frac{A}{K_E} - (s + d + \varepsilon u_3)] + \lambda_2 s(1 - \frac{L}{K_L}) \right)\\
\dot{\lambda_2} &= -\left(A_3 + \lambda_2[-s\frac{E}{K_L} - (s_L + d_L + d_c u_3)] + \lambda_3 s_L - \lambda_6 s_L \frac{I_m}{A} \right)\\
\dot{\lambda_3} &= -\left(\lambda_1 b(1 - \frac{E}{K_E}) - \lambda_3 d_m + \lambda_6 s_L \frac{L}{A^2} I_m \right)\\
\dot{\lambda_4} &= -\left(-\lambda_4[(b_H + \beta_H(1-u_1)I_m)] + \lambda_5 \beta_H (1-u_1) I_m \right)\\
\dot{\lambda_5} &= -\left(A_1 - \lambda_5(\gamma + \gamma_0 u_2 + b_H) + \lambda_6 \beta_m (1-u_1)(1-I_m) \right)\\
\dot{\lambda_6} &= -\Big(A_2 - \lambda_4 \beta_H (1-u_1) S_H + \lambda_5 \beta_H (1-u_1) S_H\\
&-\lambda_6 \Big[s_L \frac{L}{A} + \beta_m I_H (1-u_1) \Big] \Big),
\end{aligned}
\tag{14}
$$

with the terminal condition

$$\lambda_i(T) = 0 \qquad \textit{for} \qquad i = 1, ..., 6. \tag{15}$$

Furthermore, u_1^*, u_2^* *and* u_3^* *are represented by*

$$\begin{aligned}
&u_1^* = \\
&max\left\{a_1, min\left\{b_1, \frac{1}{2B_1}[(\lambda_5-\lambda_4)\beta_H I_m S_H + \lambda_6\beta_m I_H(1-I_m)]\right\}\right\} \\
&u_2^* = max\left\{a_2, min\left\{b_2, \frac{1}{2B_2}(\lambda_5\gamma_0 I_H)\right\}\right\} \\
&u_3^* = max\left\{a_3, min\left\{b_3, \frac{1}{2B_3}(\lambda_1\varepsilon E + \lambda_2 d_c L)\right\}\right\}.
\end{aligned} \tag{16}$$

Proof. The form of the adjoint equations and terminal conditions are standard results from Pontryagin's Maximum Principle [36]. We differentiate the Lagrangian (which is the Hamiltonian augmented with penalty terms for the control constraints) with respect to states and then the adjoint system can be written as

$$\dot{\lambda_1} = -\frac{\partial\mathcal{L}}{\partial E}, \qquad \dot{\lambda_2} = -\frac{\partial\mathcal{L}}{\partial L}, \qquad \dot{\lambda_3} = -\frac{\partial\mathcal{L}}{\partial A},$$
$$\dot{\lambda_4} = -\frac{\partial\mathcal{L}}{\partial S_H}, \qquad \dot{\lambda_5} = -\frac{\partial\mathcal{L}}{\partial I_H}, \qquad \dot{\lambda_6} = -\frac{\partial\mathcal{L}}{\partial I_m}.$$

To obtain the optimal control given by (16), we also differentiate the Lagrangian $\mathcal{L}$, with respect to $U = (u_1, u_2, u_3)$ and set it equal to zero.

$$\begin{aligned}
\frac{\partial\mathcal{L}}{\partial u_1} &= 2B_1u_1 + \lambda_4\beta_H I_m S_H - \lambda_5\beta_H I_m S_H \\
&\quad -\lambda_6\beta_m I_H(1-I_m) - w_{11} + w_{12} = 0, \\
\frac{\partial\mathcal{L}}{\partial u_2} &= 2B_2u_2 - \lambda_5\gamma_0 I_H - w_{21} + w_{22} = 0, \\
\frac{\partial\mathcal{L}}{\partial u_3} &= 2B_3u_3 - \lambda_1\varepsilon E - \lambda_2 d_c L - w_{31} + w_{32} = 0.
\end{aligned}$$

Solving for the optimal control, we obtain

$$u_1^* = \frac{1}{2B_1}[(\lambda_5-\lambda_4)\beta_H I_m S_H + \lambda_6\beta_m I_H(1-I_m) + w_{11} - w_{12}],$$
$$u_2^* = \frac{1}{2B_2}[\lambda_5\gamma_0 I_H + w_{21} - w_{22}],$$
$$u_3^* = \frac{1}{2B_3}[(\lambda_2 d_c L) + w_{31} - w_{32}].$$

To determine an explicit expression for the optimal control without w_{11}, w_{12}, w_{21}, w_{22}, w_{31} and w_{32}, we use a standard optimality technique involving the bounds of control. We consider the three following cases.

- On the set $\{t \mid a_1 < u_1^* < b_1\}$, we have
$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \Rightarrow w_{11} = w_{12} = 0.$$
Hence the optimal control is
$$u_1^* = \frac{1}{2B_1}[(\lambda_5-\lambda_4)\beta_H I_m S_H + \lambda_6\beta_m I_H(1-I_m)].$$
- On the set $\{t \mid u_1^* = b_1\}$, we have
$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \Rightarrow w_{11} = 0.$$

Hence,

$$b_1 = u_1^* = \frac{1}{2B_1}[(\lambda_5 - \lambda_4)\beta_H I_m S_H + \lambda_6 \beta_m I_H (1 - I_m) - w_{12}],$$

and then,

$$\frac{1}{2B_1}[(\lambda_5 - \lambda_4)\beta_H I_m S_H + \lambda_6 \beta_m I_H (1 - I_m) \geq b_1 \text{ since } w_{12}(t) > 0.$$

- On the set $\{t \mid u_1^* = a_1\}$, we have

$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \Rightarrow w_{12} = 0.$$

Hence,

$$a_1 = u_1^* = \frac{1}{2B_1}[(\lambda_5 - \lambda_4)\beta_H I_m S_H + \lambda_6 \beta_m I_H (1 - I_m) - w_{11}],$$

and then,

$$\frac{1}{2B_1}[(\lambda_5 - \lambda_4)\beta_H I_m S_H + \lambda_6 \beta_m I_H (1 - I_m)] \leq a_1 \text{ since } w_{11}(t) > 0,$$

which, in compact notation, reads as

$$u_1^* = max\left\{a_1, min\left\{b_1, \frac{1}{2B_1}[(\lambda_5 - \lambda_4)\beta_H I_m S_H + \lambda_6 \beta_m I_H (1 - I_m)]\right\}\right\}.$$

- On the set $\{t \mid a_2 < u_2^* < b_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \Rightarrow w_{21} = w_{22} = 0.$$

Hence the optimal control is

$$u_2^* = \frac{1}{2B_2}[\lambda_5 \gamma_0 I_H].$$

- On the set $\{t \mid u_2^* = b_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \Rightarrow w_{21} = 0.$$

Hence,

$$b_2 = u_2^* = \frac{1}{2B_2}[\lambda_5 \gamma_0 I_H + w_{22}],$$

and then,

$$\frac{1}{2B_2}[\lambda_5 \gamma_0 I_H] \geq b_2 \text{ since } w_{22}(t) \geq 0.$$

- On the set $\{t \mid u_2^* = a_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \Rightarrow w_{22} = 0.$$

Hence,

$$a_2 = u_2^* = \frac{1}{2B_2}[\lambda_5 \gamma_0 I_H - w_{21}],$$

and then,

$$\frac{1}{2B_2}[\lambda_5 \gamma_0 I_H] \leq a_2 \text{ since } w_{12}(t) \geq 0,$$

which, in compact notation, reads as

$$u_2^* = max\left\{a_2, min\left\{b_2, \frac{1}{2B_2}(\lambda_5 \gamma_0 I_H)\right\}\right\}.$$

- On the set $\{t \mid a_3 < u_3^* < b_3\}$, we have
$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \Rightarrow w_{31} = w_{32} = 0.$$
Hence the optimal control is
$$u_3^* = \frac{1}{2B_3}(\lambda_1 \varepsilon E + \lambda_2 d_c L).$$
- On the set $\{t \mid u_3^* = b_3\}$, we have
$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \Rightarrow w_{31} = 0.$$
Hence
$$b_3 = u_3^* = \frac{1}{2B_3}[\lambda_1 \varepsilon E + \lambda_2 d_c L + w_{32}],$$
and then,
$$\frac{1}{2B_3}(\lambda_2 d_c L) \geq b_3 \text{ since } w_{32}(t) \geq 0.$$
- On the set $\{t \mid u_3^* = a_3\}$, we have
$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \Rightarrow w_{32} = 0.$$
Hence,
$$a_3 = u_3^* = \frac{1}{2B_3}[\lambda_1 \varepsilon E + \lambda_2 d_c L - w_{31}],$$
and then,
$$\frac{1}{2B_3}(\lambda_1 \varepsilon E + \lambda_2 d_c L) \leq a_3 \text{ since } w_{13}(t) \geq 0,$$

which, in compact notation, reads as
$$u_3^* = max\left\{a_3, min\left\{b_3, \frac{1}{2B_3}(\lambda_1 \varepsilon E + \lambda_2 d_c L)\right\}\right\}.$$

□

The optimality system contains the state system (8) with initial condition $Z(0)$, the adjoint system (14) with terminal condition (15), and the optimality condition (16).

4. **Numerical results.** First of all, note that the optimality system is a two-point boundary problem. Indeed the state (8) is solved forward in time with initial conditions $Z(0) = (100, 40, 10, 0.9, 0.1, 0.2)$ while the adjoint (or costate) system (14) is solved backward in time with terminal conditions $\Pi(T) = (0, 0, 0, 0, 0, 0)$, where $T = 100$ days. We implemented a gradient method, using standard Matlab routines, to solve numerically the optimality system . First of all, we solve the state system and the costate system with an initial guess control $(u_1(t), u_2(t), u_3(t)) = (0, 0, 0)$. The state system is solved forward in time while the costate system is solved backward in time. Then, we update control functions using the optimality condition given by (16) in each iteration. Iterations continue until convergence is achieved.

In the objective functional (11) weight constant values are chosen as follows:
$$A1 = A2 = 10000,\ A_3 = 1,\ B_1 = B_2 = B_3 = 10,$$
since the mosquito population dynamic and the virus transmission dynamics and control functions are on different scales. The other parameters are given in table 1.

Parameter	Description	Value
b	*per capita* oviposition rate	1 or 6
K_E	carrying capacity for eggs	1000
ε	chemical eggs mortality rate	0.001
K_L	carrying capacity for larvae	500
s	transfer rate from eggs to larvae	0.7
s_L	transfer rate from larvae to mosquitoes	0.5
d	eggs death rate	0.2 or 0.4
d_L	larvae natural mortality rate	0.2 or 0.4
d_c	chemical larvae mortality rate	0.3
d_m	adult mosquitoes mortality rate	0.25 or 0.5
b_H	human birth rate	0.0000457
β_H	effective contact rate human $\to$ vector	0.2 or 0.75
β_m	effective contact rate vector $\to$human	0.1 or 0.5
γ_H	natural recovery rate	0.1428
γ_0	recovery rate induced by treatment	0.3

Table 1. Values of parameters in the chikungunya model. Most of the values were obtained from entomologists and given for instance in [6, 13, 20, 12, 19].

At first, we look for three optimal control functions u_1, u_2 and u_3 for prevention, treatment and proliferation mosquito control respectively. Numerical results are obtained for different values of b (oviposition rate), d_E, d_L, d_m (mortality rates), β_H and β_m (effective contact rates), while keeping the remaining parameters unchanged in each simulation.

By performing numerical simulations with different parameter sets, we investigate effects of the threshold parameter, r, and the basic reproduction, R_0, governing the dynamics of the mosquito stage population and the proportion of individuals in each class, respectively.

$$\begin{aligned}
\text{Data 1}: \quad & b = 1,\ d = 0.4,\ d_L = 0.4,\ d_m = 0.5,\ \beta_H = 0.2, \\
& \beta_m = 0.1.\ \text{In this case } r = 0.7071,\ R_0 = 0.2800. \\
\text{Data 2}: \quad & b = 1,\ d = 0.4,\ d_L = 0.4,\ d_m = 0.5,\ \beta_H = 0.75, \\
& \beta_m = 0.5.\ \text{In this case } r = 0.7071,\ R_0 = 5.2504 \\
\text{Data 3}: \quad & b = 6,\ d = 0.2,\ d_L = 0.2,\ d_m = 0.25,\ \beta_H = 0.2, \\
& \beta_m = 0.1.\ \text{In this case } r = 13.3333,\ R_0 = 0.5600. \\
\text{Data 4}: \quad & b = 6,\ d = 0.2,\ d_L = 0.2,\ d_m = 0.25,\ \beta_H = 0.75, \\
& \beta_m = 0.5.\ \text{In this case } r = 13.3333,\ R_0 = 10.5008.
\end{aligned}$$

Optimal strategies, optimal solutions, the threshold parameter, r and the basic reproduction, R_0 suggested by Data 1, Data 2, Data 3 and Data 4, are illustrated in Figs. 2-Fig. 5, respectively. These optimal solutions (solid line), together with non-optimal solutions (dashed line) corresponding to no control functions (that is, $u_1 = u_2 = u_3 = 0$) are presented in (b) and (c) for comparison. In Data 1 and 2, all stages of the vector population without any control become extinct. By contrast, in Data 3 and 4, a certain level of all stages of the vector population is maintained, as we expect in Theorem 2.1 (see (c) in all figures). From (a) in all figures, we observe that, in the case of Data 1 and Data 2, that is for $r < 1$, almost no efforts on the vector control u_3 are recommended, while the full efforts on the vector control are needed in the case of Data 3 and Data 4, that is for $r > 1$. Notable features include that the shapes of optimal solutions (solid line) are much better than those of solutions (dashed line) of the system without control (see (b) and (c) in all figures). For example, the number of susceptible human with optimal control keeps staying on high level, and the number of infected human with optimal control keeps staying on low level.

Indeed, in Fig.2 and Fig.3, the adapted threshold parameter including control function, given by $r(t) = \dfrac{b}{(s + d + \varepsilon u_3(t))} \dfrac{s}{(s_L + d_L + d_c u_3(t))} \dfrac{s_L}{d_m}$ remains less than one in both cases, hence, the mosquito population density is described by a rapidly decreasing function on the time interval $[0, T]$.

In the cases of Fig. 4 and Fig. 5, the reduction of the density of all infected populations is due to a reduction of the second reproduction number given by $R_0(t) = \dfrac{\beta_m \beta_H (1 - u_1(t))^2}{d_m(s_L + d_L + d_c u_2(t))}$ (see Fig. 5(e)) when applying control functions while the threshold parameter $r(t)$ remains larger than 1. In Fig. 4, optimal control allows to reduce the function $R_0(t)$ less than 1 in the interval of high epidemic level, Fig. 4(e). In this case, there is only one trivial equilibrium point which is stable and then all trajectories tend to (1,0,0), Fig. 4(b). Moreover in Fig. 5, at the beginning of the epidemic, we have to apply full efforts for all controls.

Then, effort on prevention u_1 have to be more important than effort for treatment, since the epidemics tends to extinction. Thus, efforts have to focus on the prevention that will stabilize populations in order to prevent the appearance of another epidemic peak. Of course, at the end of control measures time T, $R_0(t)$ returns to its initial value. As said before, in the case of $R_0(t) < 1$, full effort has to be applied at the beginning of the epidemic, until the peak is reached, then unlike the previous case, more effort focus on the treatment of patients, since the epidemic tends to the trivial equilibrium. Thus, numerical results suggest that the optimal strategies should be changed depending on the dynamics of the vector population and the transmission of the virus to human population.

5. **Conclusion.** In this paper, an optimal control model to assess the effectiveness of three measures to reduce the number of chikungunya infected humans is done. Several governmental plans, like in France, focus in the use of insecticides to eradicate in the areas where the *Aedes albopictus* mosquito is newly established. Moreover, even if in several regions, infection has not been yet observed, recommendations and information to limit the mosquito proliferation to population are done. Of course, all interventions or strategies may not be efficient without human mobilization. For instance, after each rainfall, it is advisable to check around the houses regularly and systematically empty or clean all the water receptacles where mosquitoes could lay eggs.

The first action, consists in the reduction of the number of host-vector contact rate due to human prevention. Time dependent intervention strategies have been implemented, in the present work, to limit the bad effects of vector-borne disease on a finite time interval. This model allows to determine activities to be intensified in appropriate time intervals $[0, T]$ relevant to disease outbreak. Of course, such strategies allow to control the epidemic on a short time interval and not to predict the long term of the disease dynamics. In this paper we analyzed the optimal control using the functional J in terms of quadratic forms. Minimizing the cost, we obtained the optimal controls u_1,u_2 and u_3, where I_H, I_m and L are minimized. The main conclusion based on results furnished by all these strategies, when the mosquito is established, is that high application of larvicide or measures to control the proliferation of mosquitoes is needed during all the interval $[0, T]$ even if the peak of epidemic is passed. Then, we observe various scenarios depending on the mosquito population and virus transmission dynamics. Specific strategies may be considered in case of an ongoing epidemic. Moreover strategies depend on the expected objectives (prevention of an epidemic, focus on patients treatment, etc.). If we are only interested in weakening the vector independently of the virus, then our attention will focus on the model describing the vector dynamics. Therefore, we only have to consider the first three equations of system (8). The optimal control consists, in this case, in the control u_3.

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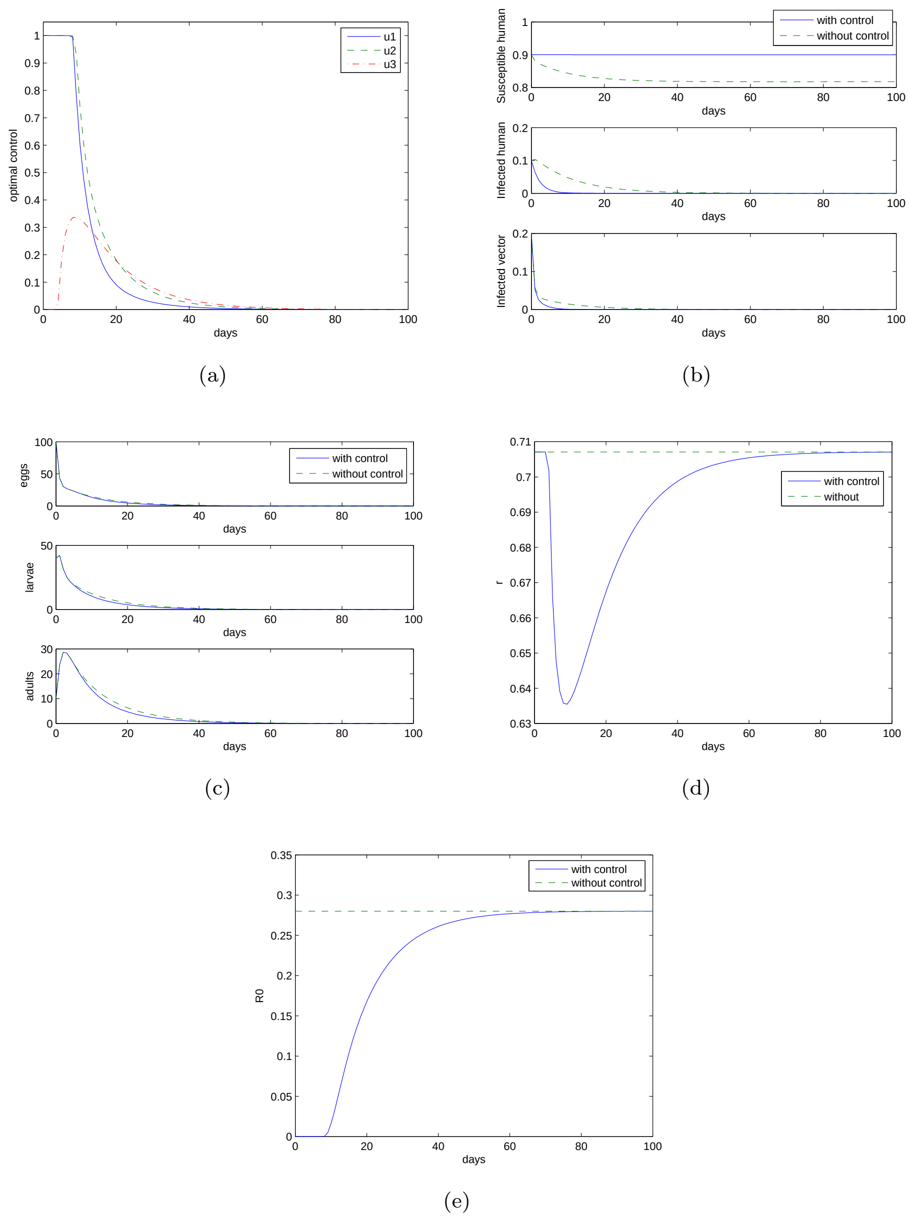


FIGURE 2. Numerical simulations with $b = 1$, $d = 0.4$, $d_L = 0.4$, $d_m = 0.5$, $\beta_H = 0.2$ and $\beta_m = 0.1$. On this case $r = 0.7071 < 1$ and $R_0 = 0.2800 < 1$. (a) Optimal control functions: prevention (–), treatment (– –), vector control (–·); (b) Solutions for susceptible and infected human and infected vector: optimal solutions (–), solutions without controls (– –); (c) Solutions for eggs, larvae and adults of vector: optimal solutions (–), solutions without controls (– –); (d) Threshold parameter with the optimal control functions (–) and without the control functions (– –); (e) Second reproductive number with the optimal control functions (–) and without the control functions (– –).

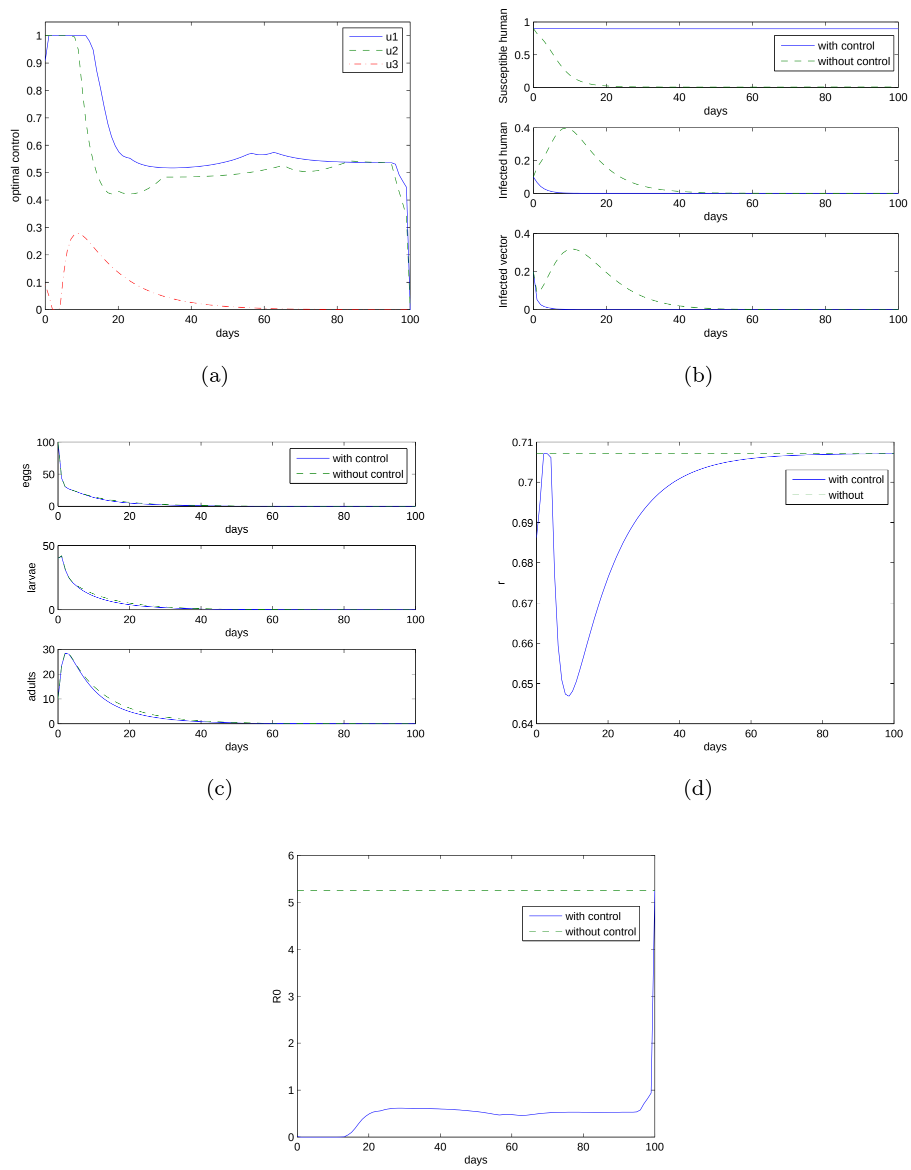


FIGURE 3. Numerical simulations with $b = 1$, $d = 0.4$, $d_L = 0.4$, $d_m = 0.5$, $\beta_H = 0.75$, and $\beta_m = 0.5$. On this case $r = 0.7071 < 1$ and $R_0 = 5.2504 > 1$. (a) Optimal control functions: prevention (–), treatment (– –), vector control (–·); (b) Solutions for susceptible and infected human and infected vector: optimal solutions (–), solutions without controls (– –); (c) Solutions for eggs, larvae and adults of vector: optimal solutions (–), solutions without controls (– –); (d) Threshold parameter with the optimal control functions (–) and without the control functions (– –); (e) Second reproductive number with the optimal control functions (–) and without the control functions (– –).

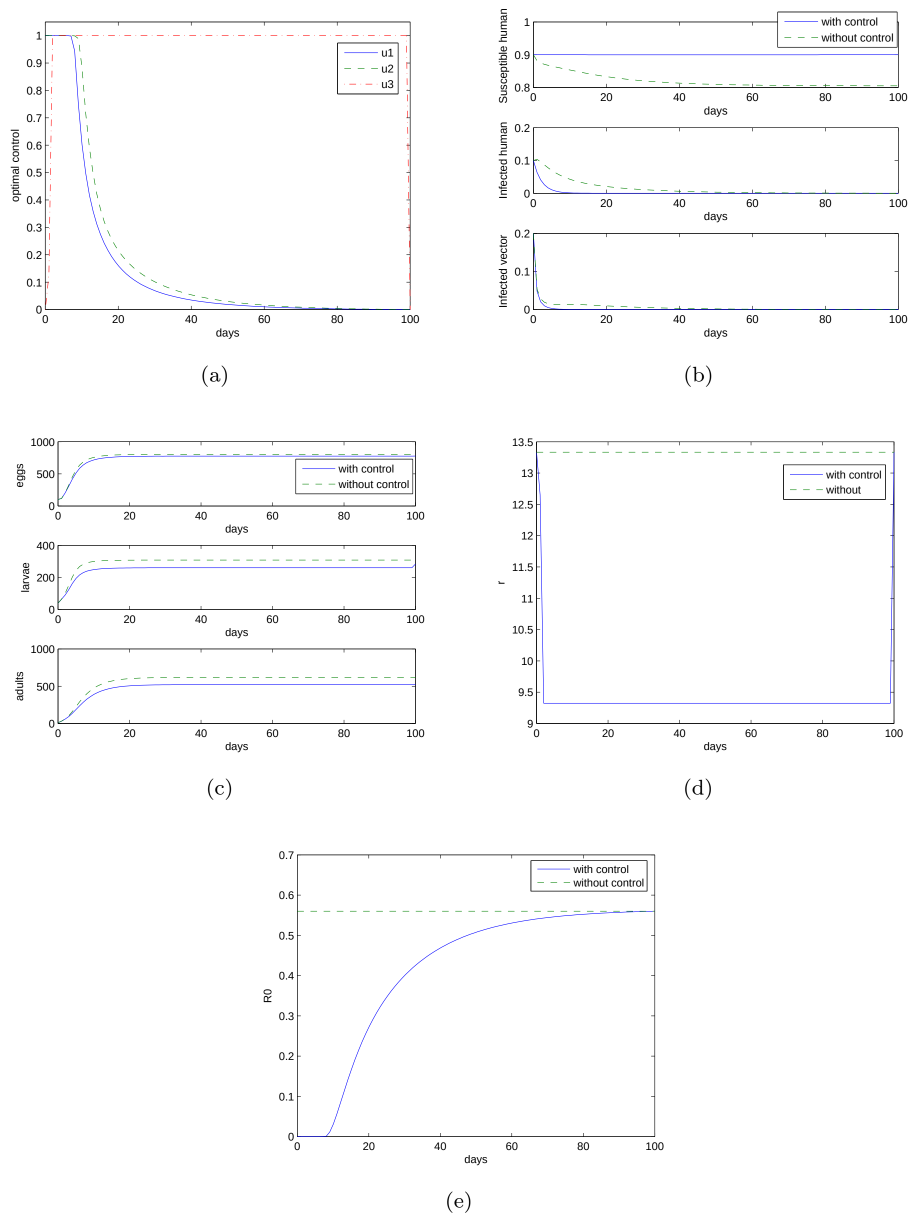
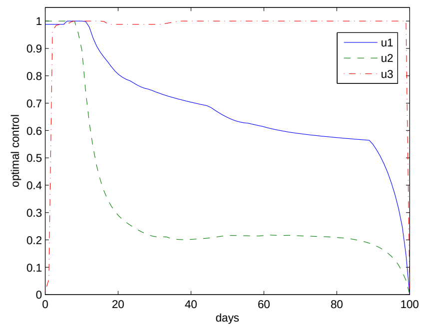


FIGURE 4. Numerical simulations with $b = 6$, $d = 0.2$, $d_L = 0.2$, $d_m = 0.25$, $\beta_H = 0.2$, and $\beta_m = 0.1$. On this case $r = 13.3333 > 1$ and $R_0 = 0.5600 < 1$. (a) Optimal control functions: prevention (–), treatment (– –), vector control (–·); (b) Solutions for susceptible and infected human and infected vector: optimal solutions (–), solutions without controls (– –); (c) Solutions for eggs, larvae and adults of vector: optimal solutions (–), solutions without controls (– –); (d) Threshold parameter with the optimal control functions (–) and without the control functions (– –); (e) Second reproductive number with the optimal control functions (–) and without the control functions (– –).



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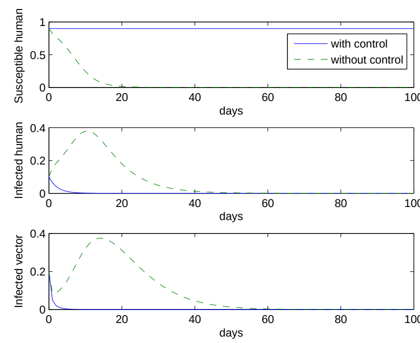

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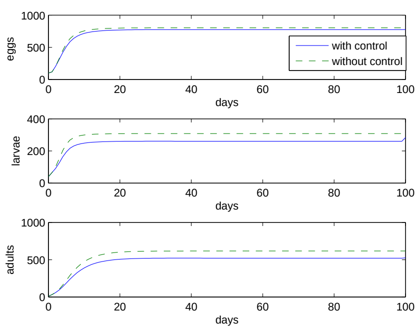

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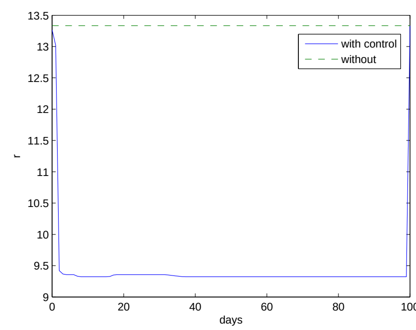

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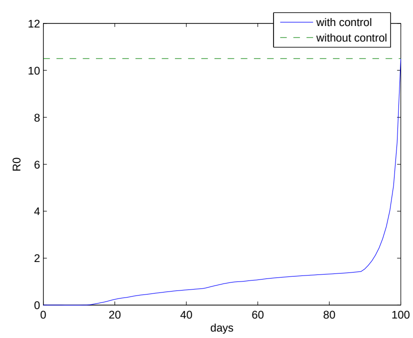

(e)

FIGURE 5. Numerical simulations with $b = 6$, $d = 0.2$, $d_L = 0.2$, $d_m = 0.25$, $\beta_H = 0.75$, and $\beta_m = 0.5$. On this case $r = 13.3333 > 1$ and $R_0 = 10.5008 > 1$. (a) Optimal control functions: prevention (–), treatment (– –), vector control (–·); (b) Solutions for susceptible and infected human and infected vector: optimal solutions (–), solutions without controls (– –); (c) Solutions for eggs, larvae and adults of vector: optimal solutions (–), solutions without controls (– –); (d) Threshold parameter with the optimal control functions (–) and without the control functions (– –); (e) Second reproductive number with the optimal control functions (–) and without the control functions (– –).