

# Assessing the effects of vector control on dengue transmission <sup>☆</sup>

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## Abstract

The dengue virus is an arbovirus transmitted to humans through mosquito *Aedes aegypti*. To describe the dynamics of dengue disease within these two populations we develop a compartment model taking into account chemical controls and mechanical control applied on the mosquitoes, which are the currently available controlling mechanisms to prevent dengue disease. To mimic seasonal variations, some parameters of the model are allowed to depend on time in order to divide a calendar year in favorable and unfavorable periods regarded to the development of vector population.

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## 1. Introduction

The dengue virus, a *flavivirus* transmitted by arthropod of the genus *Aedes*, is prevalent in different parts of the world, presents only one epidemiological cycle (urban) which comprises the human (host) and the mosquito *Aedes aegypti* (vector). As a result of being pathogenic for humans and capable of transmission in heavily populated areas, dengue virus (arbovirus) can cause widespread and serious epidemics, which constitute major public health problems in many tropical and subtropical regions of the world where *A. aegypti* and other appropriate mosquito vectors are present [1].

There are four different serotypes of dengue virus presenting low cross immunity among them, which can result in secondary infections after an infection with one serotype had been occurred. It is known that an individual infected with one serotype can be infected with other serotype six months later the first exposure, but there is not evidence of reinfection with the same serotype. Dengue viruses of all four serotypes cause three distinct syndromes: classic dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Although caused by the same viruses, dengue and dengue hemorrhagic fever are pathogenically, clinically

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and epidemiologically distinct. Dengue virus appear to replicate in macrophages at the site of the mosquito bite, in regional lymph nodes, and then throughout the reticuloendothelial system.

The epidemiological cycle occurs as follows. Female mosquitoes are infected during the blood meal from infectious individuals (in the viremic period). After a period of time (the extrinsic incubation period, the time elapsed since the ingestion of the blood infected with virus dengue to the achievement of the infective stage) the mosquito transmits the infection. The range of the extrinsic incubation period situates between 7 and 10 days. It is accepted that the infection in the mosquitoes does not induce immunity and they transmit the virus probably throughout the life-span. An infectious mosquito can transmit the virus to a susceptible host during the bite and feeding. When an infectious mosquito injects the dengue virus in a susceptible host during the blood meal, after a period of time, called the incubation period, which varies in average from 4 to 6 days (minimum of 3 and maximum of 10 days), the dengue disease can evolve from asymptomatic or classical dengue fever to the hemorrhagic dengue, which can lead to the death of the host. The manifestation of the symptoms vary between 3 and 7 days, which corresponds roughly to the infectious period. Thereafter, the individual develops the life long specific immunity against the disease [2].

The prevention against the dengue disease is restricted to the controlling mechanisms applied on the vector, because immunization by vaccine is not available yet. In order to assess different vector controlling mechanisms available to control the dengue disease, a mathematical model taking into account the three aquatic forms and the adult mosquito is considered. The model regarded to the vector population is coupled to the human population to describe the overall dengue transmission dynamics [3]. In this dengue transmission dynamics the per-capita incidence rate (or force of infection) is assumed to be proportional to the fraction of infectious individuals [4,5].

The paper is organized as follows: in Section 2 we develop a mathematical model to describe the dynamics of the dengue transmission taking into account the controlling mechanisms applied on the mosquito population; this model is treated analytically and numerically in Section 3; in Section 4 we present the conclusion.

## 2. Dynamics of dengue transmission

The dengue virus infection among female (omitted hereafter) mosquitoes neither diminishes the longevity nor induces immunity. However, this infection among humans induces a life long immunity and in the case of prime infection we have the dengue fever, which does not lead to death.

With respect to the circulation of dengue virus among mosquitoes, they are sub-divided into susceptible ( $W_1$ ), exposed (infected but not infectious,  $W_2$ ) and infectious ( $W_3$ ). The total size of the mosquito population is  $W = W_1 + W_2 + W_3$ . The dengue infection occurs when susceptible mosquitoes ( $W_1$ ) are infected during the blood meal from infectious individuals ( $I$ ). The per-capita incidence rate among mosquitoes (or the force of infection  $\eta_w(I) = \beta_w \frac{I}{N}$ ) depends on the fraction of infectious individuals  $I/N$ , where  $N$  is the human population size, and takes into account the encounter between susceptible mosquitoes and infectious individuals, designed by  $\beta_w$  (the contact rate or transmission coefficient), which is related to the frequency of bites. The exposed mosquitoes are removed from this stage at a constant rate  $\gamma_w$ , where  $\gamma_w^{-1}$  is the extrinsic period of dengue virus (in mosquitoes), and enter to the infective stage. We assume that mortality rates related to susceptible, exposed and infectious mosquitoes are given by  $\mu_w$ .

The dengue infection among humans (we are dealing with the transmission of a unique serotype of dengue) occurs when susceptible individuals ( $S$ ) are bitten by infectious mosquitoes ( $W_3$ ) during blood meal. The per-capita incidence rate among humans (or the force of infection  $\eta_h(W_3) = \beta_h \frac{W_3}{W}$ ) depends on the fraction of infectious mosquitoes  $W_3/W$ , and takes into account the encounter between susceptible individuals and infectious mosquitoes, designed by  $\beta_h$  (the contact rate or transmission coefficient), which is related to the frequency of bites. These infected individuals enter to the exposed class ( $\bar{E}$ ) and are removed from this class to infectious stage ( $I$ ) at a constant rate  $\gamma_h$ , where  $\gamma_h^{-1}$  is the (intrinsic) incubation period of virus (in humans). Finally, these individuals are removed from this class to recovered (or immune) stage ( $\bar{R}$ ) at a constant rate  $\sigma_h$ , where  $\sigma_h^{-1}$  is the infectious (or recovery) period. The total human population is considered constant (natality replacing mortality, that is,  $\Phi N = \mu_h N$ , where  $\Phi$  and  $\mu_h$  are, respectively, the per-capita natality and mortality rates),  $N = S + \bar{E} + I + \bar{R}$ , and we are not considering neither the loss of immunity nor the maternally derived antibodies.

The aquatic phases of the mosquito’s life cycle and controlling mechanisms are described briefly. The egg, larva and pupa compartments are represented by  $E$ ,  $L$  and  $P$ , respectively. The total capacity of the recipients is  $C = \sum_{i=1}^k C_i$ , which is comprised by  $k$  different kinds (form, size, etc.) of recipients  $C_i$ , where  $i = 1, 2, \dots, k$ . The parameters  $\phi$ ,  $\sigma_e$ ,  $\sigma_l$  and  $\sigma_p$  are rates of, respectively, oviposition, transformation (from egg to larva), changing (from larva to pupa) and emerging (from pupa to mosquito). The parameters  $\mu_e$ ,  $\mu_l$  and  $\mu_p$  are the mortality rates of, respectively, eggs, larvae and pupae. With respect to the controlling mechanisms, the mechanical control removes a fraction  $f_i$ ,  $i = 1, 2, \dots, k$ , of each kind of recipients, so the remaining carrying capacity is  $C' = \sum_{i=1}^k (1 - f_i)C_i$ . The larvicide, of long duration (three months, due to the residual action), is assessed by the additional mortality rates  $\mu'_l$  and  $\mu'_p$ . Finally, the insecticide to eliminate the adult mosquitoes, which is applied inside and surrounding houses (in severe epidemic situations heavy duty application of insecticide can be used), is assessed by the additional mortality rate  $\mu'_w$ . Differently of larvicide, insecticide application does not present long residual action.

The dynamics of dengue infection among mosquitoes is described by

$$\begin{cases} \frac{d}{dt}E(t) = \phi \left[1 - \frac{E(t)}{C'}\right] W(t) - (\sigma_e + \mu_e)E(t), \\ \frac{d}{dt}L(t) = \sigma_e E(t) - (\sigma_l + \mu_l + \mu'_l)L(t), \\ \frac{d}{dt}P(t) = \sigma_l L(t) - (\sigma_p + \mu_p + \mu'_p)P(t), \\ \frac{d}{dt}W_1(t) = \sigma_p P(t) - \left[\beta_w \frac{I(t)}{N} + \mu_w + \mu'_w\right] W_1(t), \\ \frac{d}{dt}W_2(t) = \beta_w \frac{I(t)}{N} W_1(t) - (\gamma_w + \mu_w + \mu'_w)W_2(t), \\ \frac{d}{dt}W_3(t) = \gamma_w W_2(t) - (\mu_w + \mu'_w)W_3(t) \end{cases} \tag{1}$$

and the dynamics of dengue transmission in human population is described by

$$\begin{cases} \frac{d}{dt}s(t) = \mu_h - \left[\beta_h \frac{W_3(t)}{W(t)} + \mu_h\right]s(t), \\ \frac{d}{dt}e(t) = \beta_h \frac{W_3(t)}{W(t)} s(t) - (\gamma_h + \mu_h)e(t), \\ \frac{d}{dt}i(t) = \gamma_h e(t) - (\sigma_h + \mu_h)i(t), \\ \frac{d}{dt}r(t) = \sigma_h i(t) - \mu_h r(t), \end{cases} \tag{2}$$

where the fractions of susceptible ( $s$ ), exposed ( $e$ ), infectious ( $i$ ) and recovered ( $r$ ) individuals are obtained dividing, respectively,  $S$ ,  $\bar{E}$ ,  $I$  and  $\bar{R}$  by the population size  $N$ . The effective dengue infection occurs when a mosquito bites an infectious individual (ingesting the virus), survives the extrinsic incubation period  $\gamma_w^{-1}$ , and bites a susceptible individual (inoculating the virus). This system of equations is valid for  $W > 0$ , because we have  $N > 0$  due to  $\mu_h > 0$ .

The model is analyzed in two cases. First, all the parameters do not depend on time, in which case we present brief steady state analysis. Afterwards we allow some parameters to depend on time, in which case we treat the dynamical system numerically.

### 3. Analysis of the model

Briefly we present some analytical results of the model given by the system of equations (1) and (2), which are followed by numerical simulations [6].

#### 3.1. Steady state analysis

The steady state of the dengue transmission among humans is analyzed assuming that all parameters of the model do not depend on time [7]. The steady state is designed by the same dynamical variables withdrawing the time  $t$ . The corresponding autonomous modelling has three equilibrium points [8,9] described below.

3.1.1. Human population free of mosquitoes

The null (with respect to mosquito) equilibrium point is given by

$$\begin{cases} E = L = P = W_1 = W_2 = W_3 = 0, \\ s = 1, \\ e = i = r = 0. \end{cases} \tag{3}$$

The stability of this point is given by the system of equations regarded to mosquito population (1).

The analysis of the local stability is done based on the characteristic equation:

$$A(\lambda) = \det(J^* - \lambda \bar{I}) = 0,$$

where  $J^*$  is the Jacobian matrix (linearization of the dynamics system) evaluated at the equilibrium point and  $\bar{I}$  is the identity matrix. The corresponding characteristic equation is

$$A(\lambda) = (\rho_e + \lambda)(\rho_l + \lambda)(\rho_p + \lambda)(\rho_w + \lambda) - \sigma_e \sigma_l \sigma_p \phi = 0,$$

where the global outcomes from egg, larva, pupa and (susceptible) mosquito compartments are, respectively,  $\rho_e = \sigma_e + \mu_e$ ,  $\rho_l = \sigma_l + \mu_l + \mu'_l$ ,  $\rho_p = \sigma_p + \mu_p + \mu'_p$  and  $\rho_w = \mu_w + \mu'_w$ . All the coefficients of  $A(\lambda)$  are positive, except the independent term of  $\lambda$  given by

$$a^0 = \rho_e \rho_l \rho_p \rho_w - \sigma_e \sigma_l \sigma_p \phi = \sigma_e \sigma_l \sigma_p \phi \left( \frac{1}{Q} - 1 \right),$$

where the number of offsprings is defined by  $Q = \phi / \phi_{th}$ , which is the average number of viable mosquitoes produced by one mosquito during survival period, with the threshold oviposition rate  $\phi_{th}$  being given by

$$\phi_{th}^{-1} = \frac{\sigma_e \sigma_l \sigma_p}{\rho_e \rho_l \rho_p \rho_w}. \tag{4}$$

Parameter  $a^0$  is positive for  $Q < 1$  (or  $\phi < \phi_{th}$ ), so the null equilibrium point is locally asymptotically stable for  $\phi < \phi_{th}$  [10], in which case the mosquito population cannot be established in a community, eradicating also the dengue disease.

3.1.2. Human population infested with mosquito but free of dengue

The trivial (with respect to the disease) equilibrium point is given by

$$\begin{cases} E = C' \left( 1 - \frac{1}{Q} \right), \\ L = \frac{\sigma_e}{\rho_l} E, \\ P = \frac{\sigma_e \sigma_l}{\rho_l \rho_p} E, \\ W_1 = W = \frac{\sigma_e \sigma_l \sigma_p}{\rho_l \rho_p \rho_w} E, \\ W_2 = W_3 = 0, \\ s = 1, \\ e = i = r = 0, \end{cases} \tag{5}$$

which is biologically acceptable when  $Q > 1$  (or  $\phi > \phi_{th}$ ) and  $R_c < 1$ , with the reproduction ratio (of dengue)  $R_c$  being given by

$$R_c = \frac{\gamma_w \gamma_h \varepsilon^2 \beta_w \beta_h}{\rho_2 \rho_3 \rho_h \rho_i} = \frac{\varepsilon \beta_h}{\rho_3} \times \frac{\gamma_h}{\rho_h} \times \frac{\varepsilon \beta_w}{\rho_i} \times \frac{\gamma_w}{\rho_2}, \tag{6}$$

where the overall outcome rates from the compartments of exposed and infectious mosquitoes and humans are, respectively,  $\rho_2 = \gamma_w + \mu_w + \mu'_w$ ,  $\rho_3 = \mu_w + \mu'_w$ ,  $\rho_h = \gamma_h + \mu_h$  and  $\rho_i = \sigma_h + \mu_h$ .

With respect to the stability, the characteristic equation related to the equilibrium point given by Eq. (5) has two eigen-values given by  $\lambda_1 = \lambda_2 = -\mu_h$  plus the roots of the following characteristic equation:

$$A(\lambda) = P_1(\lambda)P_2(\lambda) = 0, \tag{7}$$

where the fourth-order polynomials  $P_1(\lambda)$  and  $P_2(\lambda)$  are

$$\begin{cases} P_1(\lambda) = (\rho_c R_c + \lambda)(\rho_1 + \lambda)(\rho_p + \lambda)(\rho_w + \lambda) - \phi_{th} \sigma_c \sigma_1 \sigma_p, \\ P_2(\lambda) = (\rho_2 + \lambda)(\rho_3 + \lambda)(\rho_h + \lambda)(\rho_i + \lambda) - \gamma_w \gamma_h \beta_w \beta_h. \end{cases}$$

All the coefficients of both polynomials are positive, except the independent terms of  $\lambda$  given, respectively, by

$$\begin{cases} a_1^0 = \rho_c \rho_1 \rho_p \rho_w (Q - 1), \\ a_2^0 = \rho_2 \rho_3 \rho_h \rho_i (1 - R_c). \end{cases}$$

The independent terms are positive when  $Q > 1$  (or  $\phi > \phi_{th}$ ) and  $R_c < 1$ , so the trivial equilibrium point is locally asymptotically stable for  $\phi > \phi_{th}$  and  $R_c < 1$  [10], in which case the mosquito population can be established in a community but the dengue disease fades out.

If there are not any kind of control mechanisms being applied, we have the basic reproduction ratio  $R_0$  given by

$$R_0 = \frac{\gamma_w \gamma_h \beta_w \beta_h}{(\gamma_w + \mu_w) \mu_w (\gamma_h + \mu_h) (\sigma_h + \mu_h)}. \tag{8}$$

Thus  $R_0$ , the number of secondary cases of dengue infection produced by one primary case during infectious period, depends on the product of transmission coefficients  $\beta_w \beta_h$ , that is, a new case occurs only after double bites from same mosquito.

### 3.1.3. Dengue prevalent in human population

This non-trivial equilibrium point is given by

$$\begin{cases} L = \frac{\sigma_c}{\rho_1} C' \left(1 - \frac{\phi_{th}}{\phi}\right), \\ P = \frac{\sigma_1}{\rho_p} \frac{\sigma_c}{\rho_1} C' \left(1 - \frac{\phi_{th}}{\phi}\right), \\ W_1 = \frac{\sigma_p}{\rho_w} \frac{\sigma_1}{\rho_p} \frac{\sigma_c}{\rho_1} C' \left(1 - \frac{\phi_{th}}{\phi}\right) \frac{1}{1 + \frac{\gamma_h \beta_w}{\rho_w \rho_i} e}, \\ W_2 = \frac{\sigma_p}{\rho_w} \frac{\sigma_1}{\rho_p} \frac{\sigma_c}{\rho_1} C' \left(1 - \frac{\phi_{th}}{\phi}\right) \frac{\gamma_h \beta_w}{\rho_2 \rho_i \left(1 + \frac{\gamma_h \beta_w}{\rho_w \rho_i} e\right)} e, \\ W_3 = \frac{\sigma_p}{\rho_w} \frac{\sigma_1}{\rho_p} \frac{\sigma_c}{\rho_1} C' \left(1 - \frac{\phi_{th}}{\phi}\right) \frac{\gamma_w}{\rho_3} \frac{\gamma_h \beta_w}{\rho_2 \rho_i \left(1 + \frac{\gamma_h \beta_w}{\rho_w \rho_i} e\right)} e, \\ s = \frac{1}{R_c} \left[1 + \frac{\gamma_h \beta_w (\gamma_w + \rho_3)}{\rho_2 \rho_3 \rho_i} e\right], \\ i = \frac{\gamma_h}{\rho_i} e, \\ r = \frac{\sigma_h}{\mu_h} \frac{\gamma_h}{\rho_i} e, \end{cases} \tag{9}$$

where the fraction of exposed individuals  $e$ , given by

$$e = \frac{\gamma_w \mu_h \beta_h}{\rho_h [\mu_h (\gamma_w + \rho_3) + \gamma_w \beta_h]} \left(1 - \frac{1}{R_c}\right) \tag{10}$$

is biologically viable when  $\phi > \phi_{th}$  and  $R_c > 1$ . The stability analysis is done numerically.

### 3.2. Numerical results

Dengue disease depends strongly on the amount of mosquito population, which size fluctuates with abiotic variations. We take into account the seasonal variations in a very simple way, dividing the calendar year only in two periods: unfavorable and favorable seasons regarded to the development of mosquito population. Temperature and humidity are high in favorable periods, while they are low in unfavorable periods. The difference between these periods are the values assigned to the development rates of the aquatic phases and the mortality rate of the adult mosquito. All other values of the parameters could vary, but we are assuming that they are the same in both periods.

Therefore, the following model’s parameters are assumed to be fixed in both favorable and unfavorable seasons:  $\mu_h^{-1} = 24,000$ ,  $\gamma_w^{-1} = 8$ ,  $\sigma_h^{-1} = 7$ ,  $\gamma_h^{-1} = 10$ ,  $\mu_e^{-1} = 100$ ,  $\mu_l^{-1} = 2$  and  $\mu_p^{-1} = 60$  (all in days),  $\phi = 1 \text{ days}^{-1}$  and  $C = 100$ . During the unfavorable seasons the following values are fixed:  $\sigma_e^{-1} = 5$ ,  $\sigma_1^{-1} = 15$ ,  $\sigma_p^{-1} = 11$  and  $\mu_w^{-1} = 17$  (all in days). This set of values yielded  $\phi_{th} = 0.620 \text{ days}^{-1}$ , the threshold per capita oviposition rate calculated by Eq. (4).

We consider that the unfavorable period occurs during the most part of the year, and only 75 days in a year comprise the favorable season with abundant rains and high temperature. Instead fixing a unique set of values during this favorable period, we allow two set of values (all in days) for the development rates of the aquatic phases and the mortality rate of the adult mosquito:  $\sigma_e^{-1} = 3.3$ ,  $\sigma_1^{-1} = 8$ ,  $\sigma_p^{-1} = 3.1$  and  $\mu_w^{-1} = 25$  (less favorable, for instance, corresponding to mean season temperature of 25 °C) and  $\sigma_e^{-1} = 2$ ,  $\sigma_1^{-1} = 4.4$ ,  $\sigma_p^{-1} = 1.6$  and  $\mu_w^{-1} = 35$  (more favorable, for instance, 27 °C). For instance, the mortality rate  $\mu_w$  assumes the values

$$\mu_w^{-1} \text{ (days)} = \begin{cases} 17; & 0 \leq t \leq 100, \\ 25 \text{ (or } 35); & 100 < t < 175, \\ 17; & 175 \leq t \leq 360, \end{cases}$$

during one calendar year (360 days).

In simulations, we perform the numerical analysis of the system of equations (1) and (2) allowing four parameters ( $\sigma_e$ ,  $\sigma_1$ ,  $\sigma_p$  and  $\mu_w$ ) to vary according to favorable and unfavorable periods. Additionally, during the favorable periods we choose one of the two sets of parameters according to the probabilities  $P$  and  $1 - P$  assigned to, respectively, more favorable and less favorable periods, as follows. A random number  $z_n \in [0, 1]$  is chosen in the beginning of the  $n$ th year of simulation and compared with  $P$ . If  $z_n \leq P$  we choose the set of parameters corresponding to more favorable in the  $n$ th year, otherwise, that related to less favorable period. All the simulations presented below were performed considering  $P = 0.75$ , that is, the more favorable periods occur in average with high probability (75% of cases) in a long run.

We measure the reduction in the mosquito population and in the number of infectious individuals when a unique controlling mechanism is introduced in a region. The specified controlling mechanism introduced to control mosquito population is taken into account in the dynamics system by appropriate parameters. The effect of insecticide acting alone on the mosquito population can be measured by the parameter  $\mu'_w$ , letting  $f = \mu'_l = \mu'_p = 0$  in the system of equations (1). The effect of larvicide is measured by  $\mu'_l$  and  $\mu'_p$ , letting  $f = \mu'_w = 0$ . Finally, the effects of mechanical control is assessed by  $f$ , letting  $\mu'_w = \mu'_l = \mu'_p = 0$ .

To compare the effects of different controlling mechanisms applied on the *Aedes aegypti*, we introduce the efficiency index, designed as  $J$ . Before, let us define the variable  $A$ , the area comprised between the curve of the mosquito population size, for instance, and the time axis during the period of time from 0 to  $T$ , as

$$A = \int_0^T W(t)dt.$$

This measures the cumulated number of adult mosquitoes during the time interval  $[0, T]$ . Hence we can define the efficiency index  $J$  as

$$J = \left(1 - \frac{A_c}{A_0}\right) \times 100, \tag{11}$$

where  $A_c$  and  $A_0$  are the cumulated number of adult mosquitoes, respectively, with and without the controlling mechanisms applied on the mosquito population. Observe that  $A_0 - A_c$  measures the cumulated (on the range from 0 to  $T$ ) reduction in the number of mosquitoes by the controlling mechanism, therefore,  $J$  is the reduction in percentage of the adult mosquitoes over the time interval  $[0, T]$ .

In the simulations, the favorable period is embedded into unfavorable period, beginning at 100th day and finishing at day 175. With respect to controlling mechanisms, we consider that insecticides are applied various times to kill mosquitoes during 10 days. Larvicide is applied only one time, but due to residual action, larvae and pupae die during 50 days. Finally, removing of breeding sites (mechanical control) occurs also only one time, but the effects is forever due to the reduction in the carrying capacity. Only during the period of time of action of chemical controls, the additional mortalities are different from zero. The efficacy of vector control is

studied considering mosquito population free of disease and the observation time restricted in one year. Then, we assess the efficacy of vector control in the dengue transmission when controlling efforts are applied during several years.

3.2.1. Vector control

We deal with the system of equations (1), because all currently available controlling mechanisms against dengue virus transmission are based on actions to reduce vector population. Parameters regarded to development rates of the aquatic phases and the mortality rate of the adult mosquito are allowed to vary to mimic the dependency of mosquito population with abiotic conditions.

First we show the dynamical system simulated in a period of one year. In Fig. 1, one of the controlling mechanisms is introduced at the 130th day, 30 days after the beginning of favorable period (this period of time is marked in figure by  $\tau$ ). The periods of time that controlling mechanisms are acting is marked in figure by  $\lambda$ : 10 (A), 50 (B) and 230 (C) days for, respectively, insecticide (multiple applications), larvicide (unique application) and mechanical control (unique removing of recipients).

Fig. 1 shows the variation in the mosquito population size due to the abiotic changes. Dashed curves are number of mosquitoes varying during one year without any controlling mechanisms. When the favorable period (in this case corresponds to less one) begins the number of mosquitoes increases and at the end, the number decreases up to the equilibrium value corresponding to unfavorable period, which is neared after 120 days. This nearing to the equilibrium point is observed when chemical controls are applied; however, the removing without replenishment of breeding sites settles the new equilibrium to low value (continuous curves). Area between dashed and continuous curves gives the total number of mosquitoes eliminated from 130th day until day 360.

Let us now assess the effects of vector control applied during one year taking into account unfavorable period and less favorable period. In order to measure the amount of mosquitoes eliminated by a specified controlling mechanism, we use the efficiency index given by Eq. (11). This index measures the elimination of mosquitoes from the varying time at which control is introduced until day 360. The index is also calculated for different control efforts.

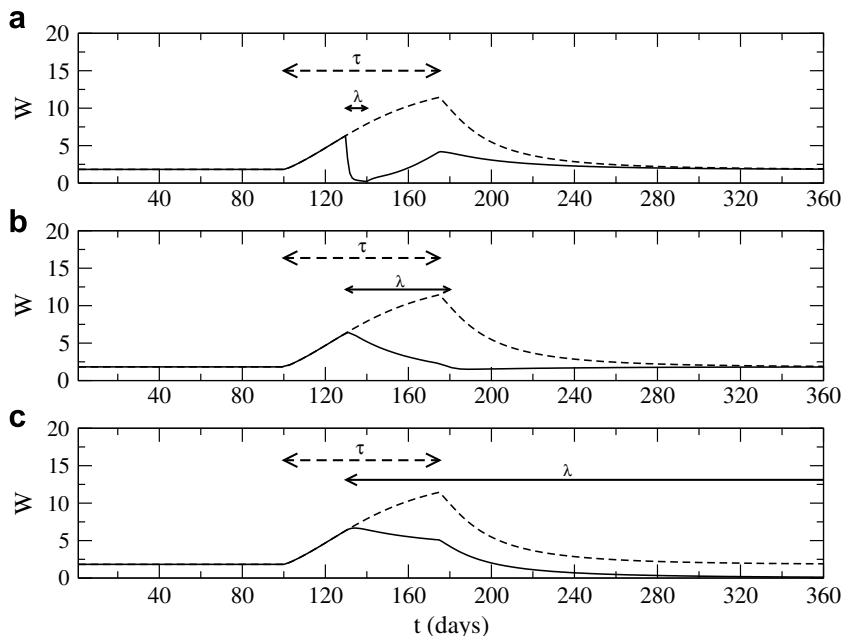


Fig. 1. Dynamics of the mosquito population. Dashed curves are dynamical system without control, and continuous curves are isolated controlling mechanism applied to population mosquito: insecticide (a), larvicide (b) and mechanic control (c). The lines labelled with  $\tau$  and  $\lambda$  are, respectively, favorable period and period of time the control is acting. The initial conditions supplied to dynamical system corresponds to the steady state given by Eq. (5).

Fig. 2 shows the efficiency index related to the application of the insecticide. The period of the action of insecticide is fixed in 10 days and we take into account  $\mu'_w$  in the dynamical system. The efficiency index is calculated considering two situations: varying the beginning of the application  $t_i$  (a) and varying the additional mortality rate induced by the insecticide, which reflects the controlling effort (b). In (a) the efficiency index is shown for  $\mu'_w = 0.5$  and  $\mu'_w = 1.0$  (days<sup>-1</sup>), and the most of the beginning times of insecticide application lay in favorable period except first and last three times. We observe an optimal value for the beginning of the insecticide application, which occurs at around  $t_i = 140$  days, which corresponds to the middle of the increasing phase of mosquito population (see Fig. 1), that is, quite in the middle of favorable period. In (b) the efficiency index is shown for  $t_i = 140$  and  $t_i = 170$  (days), which corresponds to, respectively, optimal application and quite the end of favorable period. We observe that the efficiency index increases monotonically with  $\mu'_w$ , reaching an asymptote. The efficiency index is sensitive when  $\mu'_w \leq 1$  days<sup>-1</sup> for  $t_i = 170$  days, and  $\mu'_w \leq 3$  days<sup>-1</sup> for

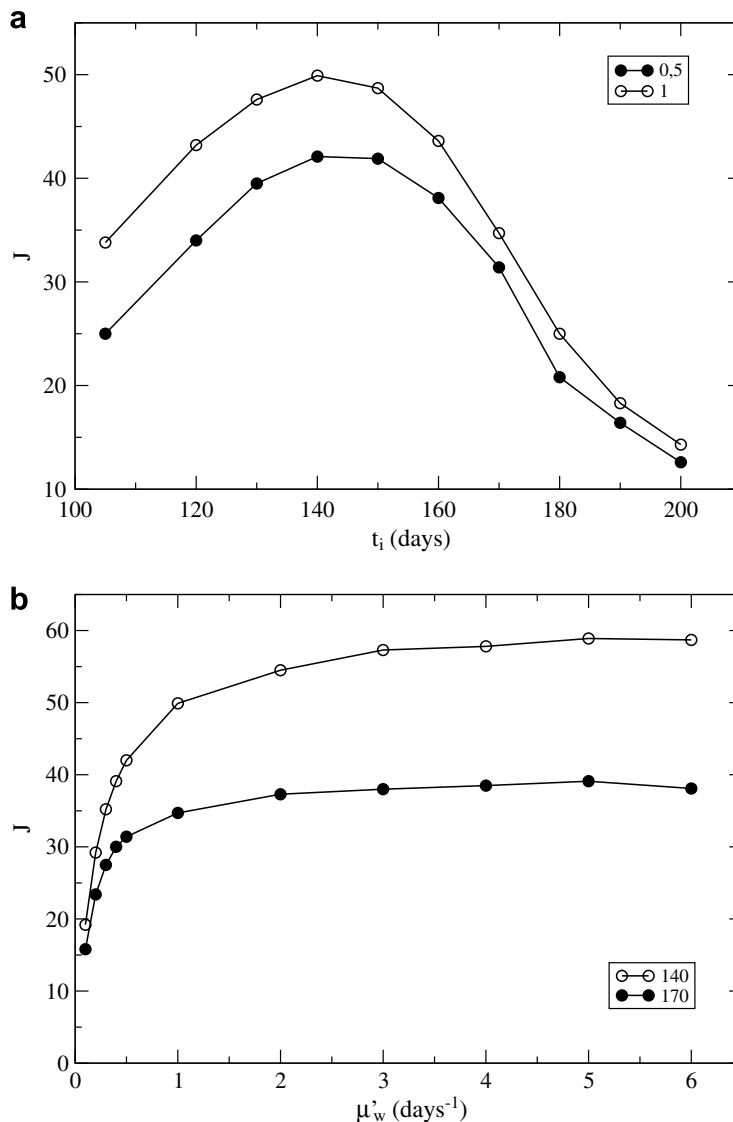


Fig. 2. The efficiency index  $J$  regarded to control of mosquitoes by insecticide. In (a)  $J$  is a function of  $t_i$ , the time at which control is introduced considering two efforts (days<sup>-1</sup>)  $\mu'_w = 0.5$  (●) and  $1.0$  (○), and in (b), a function of  $\mu'_w$ , the controlling effort considering two introduction times (days)  $t_i = 140$  (●) and  $170$  (○).



$t_i = 140$  days; thereafter, the gain in the efficiency is very small even so a great amount of insecticide could be applied.

Fig. 3 shows the efficiency index related to the application of the larvicide. The period of the action of larvicide is fixed in 50 days and we take into account  $\mu'_i$  in the dynamical system. The efficiency index is calculated considering two situations: varying the beginning of the application  $t_i$  (a) and varying the additional mortality rate induced by the larvicide, which reflects the controlling effort (b). In (a) the efficiency index is shown for  $\mu'_i = 1.0$  and  $\mu'_i = 2.0$  (days<sup>-1</sup>), and the beginning times of insecticide application lay in favorable period and the preceding unfavorable period. We observe an optimal value for the beginning of the larvicide application, which occurs at around  $t_i = 110$  days, which corresponds to the beginning of the increasing phase of mosquito population (see Fig. 1), that is, 10 days after the beginning of favorable period. In (b) the efficiency index is shown for  $t_i = 110$  and  $t_i = 140$  (days), which corresponds to, respectively, optimal application and quite

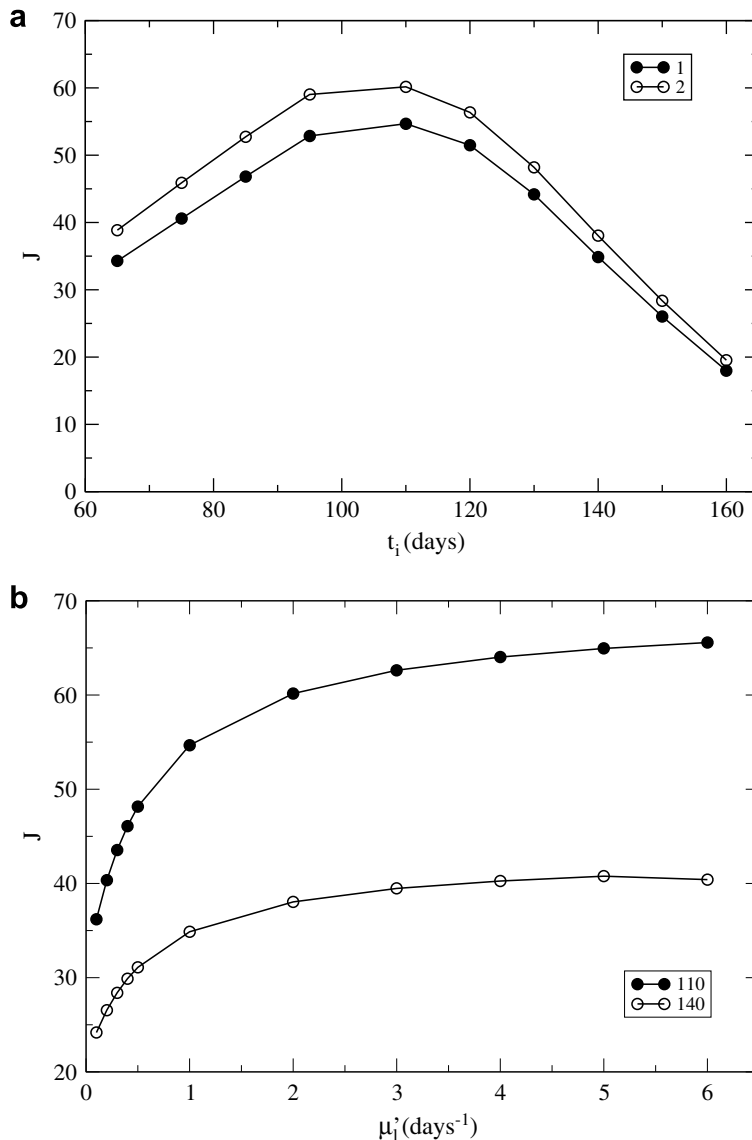


Fig. 3. The efficiency index  $J$  regarded to control of mosquitoes by larvicide. In (a)  $J$  is a function of  $t_i$ , the time at which control is introduced considering two efforts (days<sup>-1</sup>)  $\mu'_w = 1.0$  (●) and  $2.0$  (○), and in (b), a function of  $\mu'_i$ , the controlling effort considering two introduction times (days)  $t_i = 110$  (●) and  $140$  (○).

middle of favorable period. We observe that the efficiency index increases monotonically with  $\mu'_1$ , reaching an asymptote. The efficiency index is sensitive when  $\mu'_1 \leq 2 \text{ days}^{-1}$  for  $t_i = 140$  days, and  $\mu'_1 \leq 5 \text{ days}^{-1}$  for  $t_i = 110$  days; thereafter, the gain in the efficiency is very small even so a great amount of larvicide could be applied.

Fig. 4 shows the efficiency index related to the mechanical control that removes the breeding sites in the community. This removing occurs at time  $t_i$  and we take into account the fraction of removed recipients  $f$  in the dynamical system. The efficiency index is calculated considering two situations: varying the beginning of the application  $t_i$  (a) and varying the fraction of recipients removed, which reflects the controlling effort (b). In (a) the efficiency index is shown for  $f = 0.2$  and  $f = 0.4$ , and in (b) the efficiency index is shown for  $t_i = 100$  and  $t_i = 170$  (days). The efficiency index decreases monotonically with the delay in the remotion of recipients (a), and the efficiency index increases with the fraction of removed recipients without an asymptote (b). For instance, from (b), for  $f = 0.8$ , the efficiency indexes are 37% and 86%, for the remotion of breeding sites

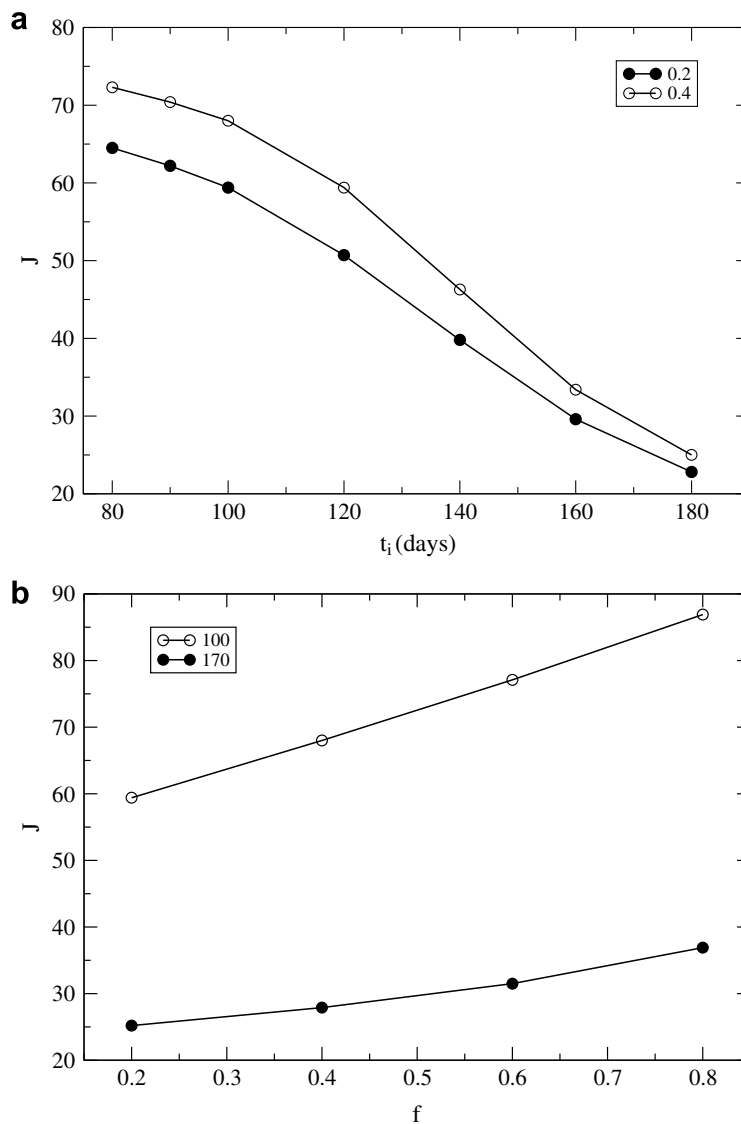


Fig. 4. The efficiency index  $J$  regarded to control of mosquitoes by mechanical control. In (a)  $J$  is a function of  $t_i$ , the time at which control is introduced considering two efforts  $f = 0.2$  (●) and  $0.4$  (○), and in (b), a function of  $f$ , the controlling effort considering two introduction times (days)  $t_i = 100$  (●) and  $170$  (○).

occurring, respectively, in the beginning and at the end of favorable period. When the breeding sites are removed after the favorable period, the number of mosquitoes during favorable period was not reduced, and probably dengue transmission could be occurred at high level.

One of the major role in the efficiency of controlling mechanisms is played by the periods of time at which they act on the mosquito population. With respect to chemical controls, we note that the elimination of the larvae is more efficient when the larvicide is applied at the beginning of the favorable period (around  $t_i = 110$  days). The insecticide must be applied at middle of favorable period (around  $t_i = 140$  days) to obtain better efficiency. If we take into account the period of time that vector control acts, the deviation from the optimal time to initiate the chemical control does not catch the time when the mosquito population can grow abundantly. Conversely, the efficiency of mechanical control does not depend on the seasons, and it must be applied as soon as possible.

The efficiency index  $J$  provides us an important tool to design the control strategy. Taking into account Figs. 2–4, controlling mechanisms can be combined and applied on the community to yield better efficiency according to the initiation time of application and available budget.

### 3.2.2. Vector control and dengue transmission

To measure the effects of controlling mechanisms applied on the vector population in the overall transmission of dengue virus, we deal with the system of equations (1) and (2) in a long run.

First, we present simulation of dynamical system without controlling efforts, but seasonal variation is taken into account: unfavorable period and two favorable periods. The values of parameters are those given above, and the value of the transmission coefficients  $\beta_w$  and  $\beta_h$  are, respectively, 0.013 and 0.01 ( $\text{days}^{-1}$ ). Fig. 5 shows the dynamical trajectories of the susceptible mosquitoes,  $W_1(t)$ , and the fraction of infectious humans,  $i(t)$ . In this simulation two less favorable periods were chosen after four more favorable periods. The first inter-epidemic period is 3 years, and very low epidemics is observed at 4.5 years. Between two major epidemic outbreaks we observe a time gap of 5 years. In both favorable and unfavorable periods, the corresponding basic reproduction ratio are above unity. However, if we simulate letting the basic reproduction ratios to

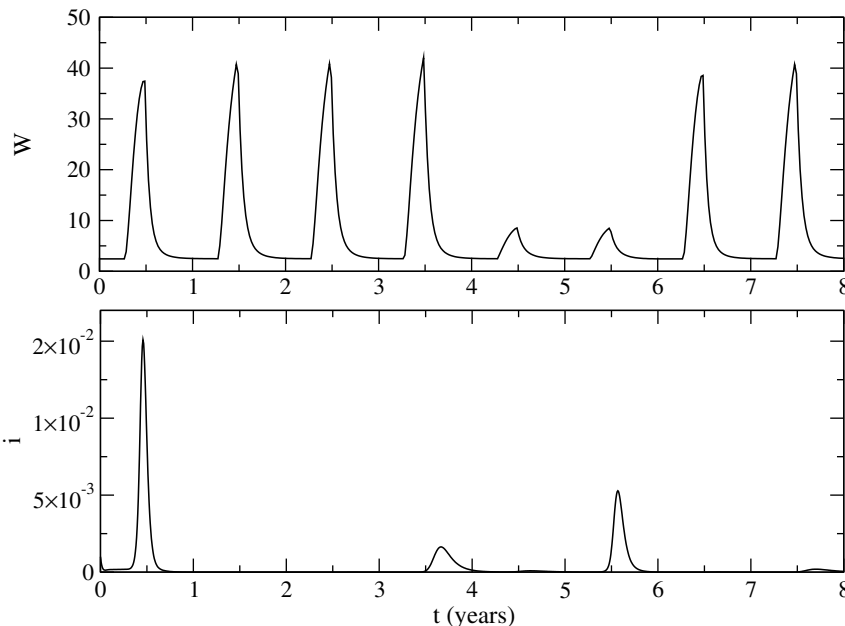


Fig. 5. Dynamics of dengue transmission, for transmission coefficients  $\beta_w$  and  $\beta_h$  assuming, respectively, 0.013 and 0.01 ( $\text{days}^{-1}$ ). The initial conditions supplied to dynamical system corresponds to the steady state given by Eq. (9) for mosquito population and  $s(0) = 0.999$ ,  $e(0) = 0.0$ ,  $i(0) = 0.001$  and  $r(0) = 0.0$  for humans. The simulation shows the number of susceptible mosquitoes (top) and the fraction of infectious individuals (bottom).

assume very lower than unity and just above unity, respectively, to the unfavorable and favorable periods, the disease can be maintained in the community, even so the average basic reproduction ratio situates lower than unity over a year.

The epidemic outbreaks are characterized by both epidemic levels and inter-epidemic periods, but both features can be estimated with some accuracy [11]. In general a very intense epidemic is followed by mild outbreak after a very long time lag. However, epidemic outbreaks become unpredictable (both epidemic level and inter-epidemic period) if stochasticity is introduced in the dynamical system. Fig. 5 is a deterministic modelling where ‘the tossing of coin’ chooses values of the parameters in favorable periods. Bearing in mind this aspect of epidemic outbreaks, we measure the effects of vector control in dengue transmission.

The controls of mosquitoes are repeatedly introduced at day 110 in each year, with the periods of time they are acting on vector population are those given in Fig. 1. At  $t = 0$ , which coincides with the beginning of the calendar year, we start the simulation with initial conditions being equal to those values used in previous simulations. With respect to the efficiency index, we calculate  $J$  on the range  $[t_i, \Delta t]$ , where  $t_i$  is the time at which controlling mechanism is introduced at first time, and  $\Delta t = t - t_i$ , where  $\Delta t$  is the time elapsed since the introduction of vector control. The efficiency index  $J$  is calculated to mosquito and human populations:  $J_{W_j} = (1 - A_c^{W_j}/A_0^{W_j}) \times 100$ , with  $j = 1, 2$  and  $3$ , measures the percentage of the susceptible, latent and infectious mosquitoes eliminated by the control mechanisms, and  $J_H = (1 - A_c^H/A_0^H) \times 100$  measures the percentage of human population protected by the control mechanisms. Note that  $J_H$  is regarded to the infectious individuals  $i$ , therefore this index provides the percentage of humans that avoided the disease due to the control applied on the vector.

Fig. 6 shows the efficiency index as function of the time elapsed  $\Delta t$  after the introduction of the insecticide (acting during 10 days) and larvicide (acting during 50 days) applied annually, and one unique application of mechanical control. The transmission coefficients are  $\beta_w = 0.013$  and  $\beta_h = 0.005$  (days<sup>-1</sup>). With respect to the susceptible mosquitoes  $W_1$ , after initial perturbation the asymptotic value is reached. However, the latent  $W_2$  and infectious  $W_3$  mosquitoes and also infectious individuals  $i$  show similar behavior, but do not follow regular pattern. These behaviors can be explained due to the fact that the susceptible mosquitoes are in high number and the epidemic outbreaks are ‘unpredictable’ (not completely), and also due to the controlling mechanisms being applied regularly, disregarding the occurrence or not of epidemic at each year.

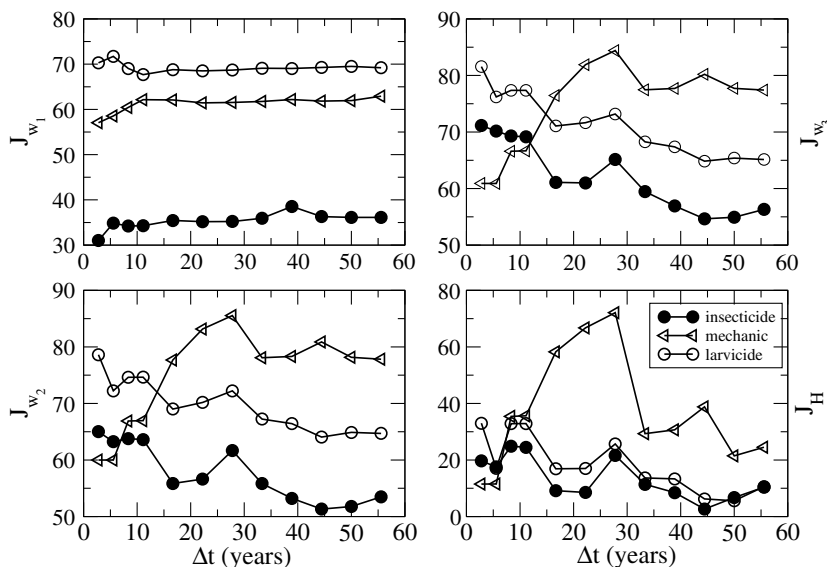


Fig. 6. The efficiency index  $J$  considering dengue transmission with  $\beta_w = 0.013$  and  $\beta_h = 0.005$  (days<sup>-1</sup>). Chemical controls are introduced at day  $t_i = 110$  of each year, and a fraction  $f = 0.4$  of breeding sites are removed only one time at  $t_i = 110$  of first year. During the periods of time that controls are acting, we have  $\mu'_w = 1.0$  days<sup>-1</sup> for insecticide (●),  $\mu'_i = 5.0$  and  $\mu'_p = 2.0$  (days<sup>-1</sup>) for larvicide (○) and mechanical control acts only one time in the beginning (<).

Fig. 6 shows that insecticide and mechanical control diminished the number of latent and infectious mosquitoes more than the susceptible mosquitoes, except larvicide, which eliminated more susceptible mosquitoes. The high proportion of mosquitoes being eliminated does not reproduce with respect to humans: the human protection did not surpass 40%, if we disregard the three most efficient mechanical control.

#### 4. Conclusion

The dengue vector mosquitoes *A. aegypti* were coupled to the human population in order to analyze the overall dengue transmission. First, we analyzed the autonomous modelling. The eradication can be achieved when the reproduction ratio  $R_c$  is diminished below unity. Therefore, the eradication of the disease is attained acting only on the parameters directly involved in the generation of new cases of infection, whatever be the oviposition rate value  $\phi$ . Or, the disease can be eradicated if we eliminate the mosquito population when the condition  $Q < 1$  is reached by controlling mechanisms applied on the mosquito population.

The autonomous model furnishes the eradication of the disease when the basic reproduction ratio is decreased below unity. However, the non-autonomous model shows that the transmission can be maintained even when we have the one year average transmission rates resulting in  $R_c < 1$ . In this situation the disease is maintained due to high transmission in the favorable period, as a result of abiotic variations. Besides this seasonal variations that maintain the dengue disease, we have the gap of several years in the successive outbreaks of severe dengue epidemics, which is strongly dependent on the threshold number of susceptible individuals. For instance, let us suppose that due to the unfavorable dry seasons an endemic region experimented low incidence rates during some years. Then, when favorable wet season is predicted, then if public health authorities are not aware of, we can expect very intense incidence rate due to the accumulation of susceptible individuals.

Finally, the simulations showed ‘unpredictable’ epidemic outbreaks when abiotic variations are taken into account. Due to this characteristic, if controlling mechanisms are introduced regularly (with respect to time of introduction and effort) every year, we observe the decline of the efficiency index with the elapsed time. This kind of inefficient control can be improved by indexing the effort and introduction time of controlling mechanisms with ‘the memory’ regarded to past epidemics. For instance, after mild epidemic outbreaks, and if the time elapsed after a peak of epidemic outbreak did not reached 5 years (Fig. 5), very intense control of mosquitoes must be applied in order to avoid another peak of epidemics.

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