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Control strategies for a population dynamics model of *Aedes aegypti* with seasonal variability and their effects on dengue incidence

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A B S T R A C T

Aedes aegypti female mosquitoes are the principal transmitters of dengue and other vector-borne infections. This species is closely associated with human habitation, due to its blood-feeding habits and the presence of breeding sites widely available around households. In this paper, we introduce a mathematical model for the life cycle of *Aedes aegypti* mosquitoes comprising two stages, aerial and aquatic, that reflects seasonal changes in the mosquito abundance. This model is further amended by three season-dependent control actions. Two coercive actions are introduced during the *hot seasons* characterized by higher abundance and enhanced growth rates of mosquitoes. They consist in the application of two chemical substances, insecticide and larvicide, acting upon the aerial and aquatic mosquito stages, respectively. During the *cool seasons*, characterized by the slower growth rates of mosquitoes and abundance of quiescent unhatched eggs, we introduce a preventive vector control measure consisting in mechanical elimination of mosquito breeding sites. Using the framework of optimal control in combination with the cost-benefit approach and epidemiological assessment, we identify the most efficient strategy capable of essentially reducing the population of adult and immature mosquitoes during both seasons and provide a sketch for its modus operandi.

1. Introduction

Aedes aegypti is the most common and abundant vector which is closely associated with human habitation [1–3] and this species is capable of transmitting different diseases such as dengue, yellow fever, chikungunya, and zika.

Among vector-borne diseases, dengue is the most rapidly spreading one in all tropical and subtropical regions of the world, and its persistence constitutes the public health emergency [1–3].

During the 1960s, there was an eradication campaign of *Aedes aegypti* in the Americas [4]. Unfortunately, some countries were unable to eradicate the vector because the control measures were not sustained for sufficiently long time. After that,

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re-infestations of *Aedes aegypti* had ubiquitously occurred and then caused numerous dengue outbreaks in Latin America. Since then it is observed that dengue is spreading with cyclical outbreaks appearing every 3–5 years [3,4]. Therefore, vector control programs are essential to mitigate the risk of dengue and other vector-borne infections [2].

There are some works claiming that endemo-epidemic patterns in dengue propagation are caused by seasonal changes in daily temperatures that usually affect the mosquito development, reproduction, and abundance. In other words, mosquitoes entomological parameters are closely related with environmental conditions that induce recurrent changes in mosquito abundance which, in their turn, positively correlate with periodic dengue outbreaks [5–9].

There is no vaccine against dengue; therefore, controlling the vector still remains the primary method for prevention of dengue and other vector-borne diseases. In particular, vector control interventions seek to reduce the population of immature and adult mosquitoes to the levels at which the transmission of dengue virus between the mosquitoes and human hosts significantly slows down [3].

There are different methods to control the mosquito population. Chemical control (use of larvicides and insecticides) decrease the sizes of aquatic and adult mosquito populations. Mechanical control consists of eliminating mosquito breeding sites around households where female mosquitoes lay their eggs. Genetic control is implemented by introducing sterile male mosquitoes into the population in order to reduce the overall offspring size. Finally, releases of *Aedes aegypti* carrying *Wolbachia* symbiont[1] and introduction of natural predators of mosquito larvae are regarded as biological control measures.

Mathematical models are useful tools for finding the best strategies in the implementation of different types of vector control interventions and for assessing their impact on the disease propagation. Some authors had studies only one type of vector control interventions, such as insecticide spraying [11–15], Sterile Insect Technique (or SIT, [16]), *Wolbachia* infestation [17–20] and introduction of natural predators of mosquito larvae [21]. Others had focused on combinations of various types of vector control, namely, the combined effects of insecticide spraying with personal protection measures [22] or educational campaigns [23,24], interventions that complement the insecticide spraying with the use of larvicides [25,26] or with genetic control of SIT type [27–30], or with both [30].

In this paper, we take into account seasonal variations in mosquito abundance and design optimal two-stage strategies for integrated vector control where chemical interventions (use of larvicides and insecticides) targeting immature and adult mosquitoes are alternated with mechanical control measures consisting in elimination of mosquito breeding sites.

It is worth noting that chemical interventions are considered *coercive* measures. Therefore, they should be implemented during the periods with more favorable conditions for mosquito development and reproduction (e.g., higher average daily temperatures), characterized by enhanced mosquito growth rates, which are strongly correlated with dengue outbreaks. In this work, such "favorable" periods are conventionally called *hot seasons*.

On the other hand, mechanical control is regarded as a *preventive* measure and its application should be carried out during the periods with less favorable conditions for mosquito development and reproduction (e.g., lower average daily temperatures), characterized by slow growth rates of mosquitoes and abundance of quiescent unhatched eggs. Such "unfavorable" periods will be further referred to as *cool seasons* by convention.

In order to model the mosquito life cycle during the hot and cool seasons, we have used two different sets of entomological parameters which bear changes with respect to fluctuations in the average daily temperatures as observed in various studies [5–9]. For each season, we have designed optimal control strategies targeting to reduce the population of immature and adult mosquitoes while minimizing the overall cost of control interventions.

It is worth pointing out that our goal was to designed the *season-dependent* strategies for control intervention. The latter marks the principal difference between our work and [31] where seasonality effects were not accounted for and all three types of control measures (larvicide, insecticide, and mechanical elimination of mosquitoes breeding sites) have been applied simultaneously.

Speaking of the effectiveness of different vector control measures, a comparative analysis of single-type control strategies performed in [32] had revealed that insecticide spraying is the most effective control measure, followed by mechanical control, while the use of larvicides constitutes the most ineffective one. In order to provide arguments in favor or opposing these outcomes, we have analyzed four single-type strategies for chemical control, two of them involving only insecticide spraying and another two based solely on the use of larvicide while employing chemical substances with high and low lethalities and underlying costs. Having access to two types of substances and trying to optimize the cost-benefit is a common situation. For example, when the agency in charge of the intervention is offered substances from two different laboratories or when existing resources are not sufficient to acquire only high-lethal insecticides.

Further, we have also assessed four mix-type strategies which are the combinations of insecticides and larvicides bearing either low or high lethality and underlying costs. While analyzing the impact of eight strategies on the reduction of immature and adult mosquito populations, we have intrinsically sought for cogent answers to the following two questions:

1. What kind of chemicals (larvicide, insecticide, or their combination) should be used for reaching better effects of vector control interventions per unit of invested costs during hot seasons?
2. Which season (hot or cool) is more appropriate for initial introduction of season-dependent control interventions?

[1] *Wolbachia* is a maternally inherited bacterial symbiont that thwart the mosquitoes ability to transmit the dengue and other vector-borne infections [10].

The answers to these questions constitute the major practical contribution of this study. They are provided in Sections 4 and 5 on the grounds of cost-benefit approach and epidemiological assessment of the impact of control strategies on the disease incidence.

The paper is organized as follows. Formulation of the mathematical model is given in Section 2. Section 3 describes the optimal control approach using three control actions that depend on the seasonality. In Section 4, we present the numerical solutions of two optimal control problems formulated in the Section 3 and perform the cost-effectiveness analysis that leads us to cogent answers for two questions stated above. In Section 5 we illustrate the impact of the most cost-effective two-stage control strategy on the dynamics of dengue transmission among human hosts. Finally, Section 6 summarizes the conclusions of our work.

2. Mathematical model of mosquito population dynamics

Let us introduce a system of nonlinear differential equations that models the life cycle of mosquitoes *Aedes aegypti*. We consider two phases of the mosquito development, the aquatic phase (comprising three immature stages: egg, larvae, and pupae) and the aerial phase of mature female insects or vectors. Furthermore, we take into account that the entomological parameters depend on the ambient temperature which may significantly affect the development of the immature stages of mosquitoes.

We denote by $m(t)$ the density of mature female mosquitoes (*imago* stage), and by $p(t)$ the density of mosquitoes in pre-adult stage (pupae). The population of adult females, $m(t)$, increases at the per-capita rate of development ω from pupae to adult stage, and declines at the natural mortality rate ϵ (cf. (1a) below).

The population of pupae, $p(t)$, declines due to natural mortality π and development into adult ω (cf. last term in (1b) below) and its per-capita growth rate is expressed by the positive term in (1b). This term includes the fraction κ of mosquitoes that become females, the fraction ζ of larvae that arrive to pupae through larvae competition, the fraction χ of egg that hatch into larvae stage and the oviposition rate $\phi\left(1-\frac{p}{C}\right)$, where ϕ stands for intrinsic oviposition rate at low densities and C denotes the carrying capacity related with available breeding sites.

Thus, the population dynamics of both stages $m(t)$ and $p(t)$ is modeled the following system of two differential equations, where we consider the entomological parameters (ω, ϵ, ζ, χ, ϕ, and π) be dependent on the ambient temperature:

$$\frac{dm(t)}{dt} = f_1(m,p) = \omega p(t) - \epsilon m(t), \tag{1a}$$

$$\frac{dp(t)}{dt} = f_2(m,p) = \kappa\zeta\chi\phi\left(1-\frac{p(t)}{C}\right)m(t) - (\pi+\omega)p(t). \tag{1b}$$

As we can see the parameter corresponding to the carrying capacity C appears in Eq. (1b) through a term that describes the logistic behaviour of the mosquito population in the aquatic state. It is easy to see that both trajectories $m(t)$, $p(t)$ of (1) engendered by nonnegative initial conditions $m(0)$, $p(0)$ are bounded for all $t \geq 0$ when the model's parameters remain constant. It was proved in [7] that the system's trajectories $m(t)$ and $p(t)$ belong to the positively invariant set

$$\Omega = \left\{ (m,p) \in \mathbb{R}^2_+ \;\middle|\; m \geq 0 \text{ and } 0 \leq p < C \right\}$$

for all $t \geq 0$ whenever $(m(0), p(0)) \in \Omega$. Keeping in mind that $0 \leq p(t) \leq C$, we have from the equation (1a) that

$$\frac{dm}{dt} + \epsilon m = \kappa\omega p \leq \kappa\omega C = C_o.$$

After multiplying both sides of the above relationship by $e^{\epsilon t}$ and integrating over $[0, t]$ we obtain

$$\frac{d}{dt}\left(m(t)e^{\epsilon t}\right) \leq C_o e^{\epsilon t} \quad \Rightarrow \quad m(t) \leq m(0) + \frac{C_o}{\epsilon}.$$

Previous study [7] has shown that stability of the dynamical system (1) depends on the threshold value

$$R_M = \frac{\kappa\omega\zeta\chi\phi}{\epsilon(\pi+\omega)} > 0 \tag{2}$$

(known as *basic offspring number*) when the entomological parameters of the model (1) remain constant and the system's trajectories $m(t)$ and $p(t)$ belong to the positively invariant set

$$\Omega = \left\{ (m,p) \in \mathbb{R}^2_+ \;\middle|\; m \geq 0 \text{ and } 0 \leq p < C \right\}$$

for all $t \geq 0$ whenever $(m(0), p(0)) \in \Omega$.

To be more specific, it was proved in [7] that:

1. If $R_M < 1$, the system (1) admits only the trivial steady-state (0,0) which is locally asymptotically stable node and implies eventual extinction of the mosquito population (however, this outcome is hardly expectable in the real-life settings).

2. If $R_M > 1$, the system (1) admits two steady-states, namely:
   - The trivial stationary solution (0,0), which is unstable and is a saddle point.
   - The non-trivial stationary solution

$$(\tilde{m}, \tilde{p}) = \left(C\frac{\omega}{\epsilon}\frac{(R_M - 1)}{R_M}, C\frac{(R_M - 1)}{R_M}\right),$$

   which is a locally asymptotically stable node.

Thus, the second condition (which is quite realistic) characterizes the persistence of mosquito population and appeals for implementation of external actions aimed at vector control.

In this work, we focus in three control actions. First, the adult mosquito population, $m(t)$, can be reduced by increasing the natural mortality of adult mosquitoes (ϵ) via insecticide spraying. Second, the proportion of larvae that become pupae (ζ) can be decreased by larvicide application and the latter should reduce the population of pre-adult mosquitoes in pupae stage, $p(t)$. Finally, mechanical elimination of mosquito breeding sites around households, induced by educational campaigns, can reduce the carrying capacity C and impair the mosquito prolification.

In the following section we introduce the mathematical models with underlying controls corresponding to three actions indicated above.

3. Model with control

In order to consider the entomological parameters of the model (1) dependable on environmental conditions (like ambient temperature) while keeping it mathematically tractable, we divide our study of the controlled system in two periods. Within each period, the entomological parameters will be kept constant, but between these periods the parameters will differ.

In the first period, $[0,\ \tilde{t}]$, we suppose that mosquitoes have rather favorable environmental conditions for development and reproduction (for example, during late spring, summer time, and early autumn). In this case, we consider the underlying set of entomological parameters denoted by $(\omega_1, \epsilon_1, \zeta_1, \chi_1, \phi_1, \pi_1, C_1)$.

In the second period, $[\tilde{t},\ T]$, we suppose that mosquito development and reproduction is impaired by environmental conditions (for example, during late autumn, winter time, and early spring). In this case, we consider another set of entomological parameters denoted by $(\omega_2, \epsilon_2, \zeta_2, \chi_2, \phi_2, \pi_2, C_2)$.

It seems reasonable to suppose that the carrying capacity within both periods remains the same, that is, $C_1 = C_2$.

In the period with favorable environmental conditions, $[0,\ \tilde{t}]$, we introduce an optimal control problem with two actions of chemical control that target to reduce the population of adult and pre-adult mosquitoes. In other words, we introduce two control variables, $u_1(t)$ and $u_2(t)$, expressing the application of insecticide and larvicide, respectively:

$$u_1(t) : [0, \tilde{t}] \mapsto [0, u_\epsilon], \quad u_2(t) : [0, \tilde{t}] \mapsto [0, u_\zeta]. \tag{3}$$

Here, $0 < u_\epsilon < 1$ and $0 < u_\zeta < 1$ stand for the maximum efficiency of insecticide and larvicide, respectively. Both variables $u_1(t)$ and $u_2(t)$ should be chosen in order to minimize the adult and pre-adult populations, as well as the cost of control effort. That is, we propose to minimize the following objective functional:

$$J_1\big(u_1,\ u_2\big) = \int_0^{\tilde{t}} \left(A_1 m(t) + A_2 p(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t)\right)dt \tag{4}$$

subject to the controlled dynamical system

$$\frac{dm(t)}{dt} = \omega_1 p(t) - \big(\epsilon_1 + u_1(t)\big)m(t), \quad m(0) = m_o \tag{5a}$$

$$\frac{dp(t)}{dt} = \kappa\big(\zeta_1 - u_2(t)\big)\chi_1\phi_1 m(t)\left(1 - \frac{p(t)}{C_1}\right) - (\omega_1 + \pi_1)p(t), \quad p(0) = p_o, \tag{5b}$$

where initial conditions $(m_o,\ p_o)$ are specified in the initial endpoint of the interval $[0,\ \tilde{t}]$, while $u_1(t)$, $u_2(t)$ are defined in (3) and belong to the following *set of admissible controls*:

$$\Gamma_1 = \left\{\big(u_1, u_2\big)\ \middle|\ u_i(\cdot) \in PC[0, \tilde{t}] \text{ and satisfy (3) for i=1,2} \right\}. \tag{6}$$

It is worth pointing out that $u_1(t)$ and $u_2(t)$ act upon the rate of adult mosquito mortality (ϵ_1, see (5a)) and the transition rate from larvae to pupae stage (ζ, see (5b)), respectively. Therefore, they target to reduce the overall density of the adult insects and pupae.

In the objective function (4), the weight coefficients $A_1 > 0$ and $A_2 > 0$ express the priorities of reducing the mosquito densities in aerial and aquatic phases, respectively, while $B_1,\ B_2 \geq 0, B_1 + B_2 > 0$ stand for underlying weight (or marginal unit costs, assumed constant) related to vector control actions $u_1(t)$ and $u_2(t)$, respectively. The magnitudes of this coefficients are thus chosen to give each term in the cost functional its relative importance.

The quadratic form the objective functional $J(u_1, u_2)$ with respect to control variables $u_1(t)$ and $u_2(t)$ clearly states that total marginal cost of the control strategy (that is, $B_1u_1(t) + B_2u_2(t)$) effectively depends on the amount of insecticide and larvicide used during the strategy implementation. As marginal cost is the change in total cost, the integral $J_1(u_1, u_2)$ is quadratic with respect to control variables. This approach is rather conventional in epidemiological modelling where optimal control methods are applied. It has been justified for optimal treatment and vaccination policies [33–37] as well as their combinations with vector control efforts [22,38–41].

Thus, our ultimate goal is to reduce the vector proliferation by minimizing the density of adult females $m(t)$ and pupae $p(t)$ during the period $[0,\ \tilde{t}]$, while trying to minimize the costs of chemical substances (insecticide and larvicide) needed for implementation of the control intervention. In mathematical terms, we look for an optimal control strategy $\left(u_1^*, u_2^*\right)$, such that

$$J_1\left(u_1^*, u_2^*\right) = \min\left\{J_1\left(u_1, u_2\right)\ \middle|\ \left(u_1, u_2\right) \in \Gamma_1\right\} \quad \text{almost for all } [0,\ \tilde{t}].$$

In the second period, $[\tilde{t},\ T]$, when mosquito development and reproduction is delayed by environmental conditions, we implement the control action targeting to eliminate the breeding sites around households, and introduce another control variable

$$u_3(t) : [\tilde{t},\ T] \mapsto [0, u_c], \quad 1 < u_c \le 3 \tag{7}$$

where u_c stands for the maximum efficiency in breeding sites elimination and can be interpreted in the following way. If $u_3(t) = 1$, there is no mechanical control meaning that the carrying capacity C_2 remains unchanged under this control action $(C_2/u_3(t) = C_2/1 = C_2)$. Alternatively, if $u_3(t) = 3$, the carrying capacity C_2 of mosquito breeding sites can be reduced to its third part by applying this control action with maximum effort (that is, $C_2/u_3(t) = C_2/3$). It is worth to mention that from field experience, it has been observed that breeding sites can be reduced to a third of their original capacity by applying mechanical control. Thus, we propose to minimize the following objective functional:

$$J_2\left(u_3\right) = \int_{\tilde{t}}^{T} \left(A_3 m(t) + A_4 p(t) + \frac{B_3}{2} u_3^2(t)\right) dt \tag{8}$$

subject to the controlled dynamical system

$$\frac{dm(t)}{dt} = \omega_2 p(t) - \epsilon_2 m(t), \quad m\left(\tilde{t}\right) = m_f \tag{9a}$$

$$\frac{dp(t)}{dt} = \kappa\zeta_2\chi_2\phi_2 m(t)\left(1 - u_3(t)\frac{p(t)}{C_2}\right) - (\pi_2 + \omega_2)p(t), \quad p\left(\tilde{t}\right) = p_f, \tag{9b}$$

where initial conditions (m_f, p_f) are specified in the initial endpoint of the interval $[\tilde{t},\ T]$, while $u_3(t)$ is defined in (7) and belongs to the following *set of admissible controls*:

$$\Gamma_2 = \left\{u_3\ \middle|\ u_3(\cdot) \in PC[\tilde{t},\ T] \text{ and satisfies (7)}\right\}. \tag{10}$$

In the objective function (8), the weight coefficients $A_3 > 0$ and $A_4 > 0$ express the priorities of reducing the mosquito densities in aerial and aquatic phases, respectively, while $B_3 > 0$ stands for underlying weight (or marginal unit cost, assumed constant) related to mechanical control actions $u_3(t)$.

Our ultimate goal here consists in minimizing the overall vector proliferation, while trying to minimize the costs of mechanical control needed for implementation of this strategy. In mathematical terms, we look for an optimal control strategy u_3^*, such that

$$J_2\left(u_3^*\right) = \min\left\{J_2\left(u_3\right)\ \middle|\ u_3 \in \Gamma_2\right\} \quad \text{almost for all } [\tilde{t},\ T].$$

Remark 1. There is a natural link between two optimal control problems (4)–(6) and (8)–(10) formulated above. Namely, optimal states $(m^*(t), p^*(t))$ of the first problem (4)–(6), evaluated at $t = \tilde{t}$, define the initial conditions (m_f, p_f) for dynamical system (9) of the second one (8)–(10). Therefore, these optimal control problems should be solved successively, rather than separately or in parallel.

It is worth noting that optimal control problems (4)–(6) and (8)–(10) make sense only if the population of mosquitoes persists; therefore, we suppose that condition (2) is fulfilled for all the parameters of the original system (1) within both periods $[0,\ \tilde{t}]$ and $[\tilde{t},\ T]$, so we have

$$R_M^{(1)} = \frac{\kappa\omega_1\zeta_1\chi_1\phi_1}{\epsilon_1(\pi_1 + \omega_1)} > 1, \quad R_M^{(2)} = \frac{\kappa\omega_2\zeta_2\chi_2\phi_2}{\epsilon_2(\pi_2 + \omega_2)} > 1. \tag{11}$$

The fundamental issue regarding both optimal control problems posed above consists in proving the existence of their optimal solutions and finding the characterizations of optimal controls. To deal with that issue, we provide the following two statements below.

Theorem 1. *Then optimal control problems (4)–(6) and (8)–(10) have non-trivial solutions* $(u_1^*, u_2^*) \in \Gamma_1$ *and* $u_3^* \in \Gamma_2$ *such that*

$$\min_{(u_1,u_2)\in\Gamma_1} J_1(u_1,u_2) = J_1(u_1^*,u_2^*) \quad \text{and} \quad \min_{u_3\in\Gamma_2} J_2(u_3) = J_2(u_3^*)$$

Existence of optimal controls can be justified by using the classical result of Filippov–Cesari existence theorem (thoroughly described in [42–44]) and the formal proof of Theorem 1 can be found in Appendix A.

Before focusing on determination of the optimal control characterizations, let us introduce the Hamiltonian functions related to the optimal control problems (4)–(6) and (8)–(10).

The Hamiltonian function $H(m, p, u_1, u_2, \lambda_1, \lambda_2) : \Omega \times \Gamma_1 \times \mathbb{R}^2 \mapsto \mathbb{R}$ associated with the optimal control problem (4)–(6) is defined as

$$\begin{aligned} H(m, p, u_1, u_2, \lambda_1, \lambda_2) &= A_1 m + A_2 p + \frac{B_1}{2}u_1^2 + \frac{B_2}{2}u_2^2 \\ &\quad + \lambda_1\left[\omega_1 p - (\epsilon_1 + u_1)m\right] \\ &\quad + \lambda_2\left[\kappa(\zeta_1 - u_2)\chi_1\phi_1 m\left(1 - \frac{p}{C_1}\right) - (\omega_1 + \pi_1)p\right] \end{aligned} \tag{12}$$

where $\boldsymbol{\lambda}(t) = (\lambda_1(t), \lambda_2(t))'$ denote the *adjoint vector-function* or *costate* that satisfies the adjoint dynamical system with corresponding transversality condition specified in the final endpoint of the interval $[0,\ \tilde{t}]$, that is,

$$\frac{d\boldsymbol{\lambda}}{dt} = \begin{pmatrix} -H_m \\ -H_p \end{pmatrix}, \qquad \boldsymbol{\lambda}(\tilde{t}) = \begin{pmatrix} 0 \\ 0 \end{pmatrix}. \tag{13}$$

In the above expression, H_m and H_p denote the partial derivatives of (12) with respect to m and p.

On the other hand, the Hamiltonian function $\mathcal{H}(m, p, u_3, \mu_1, \mu_2) : \Omega \times \Gamma_2 \times \mathbb{R}^2 \mapsto \mathbb{R}$ associated with the optimal control problem (8)–(10) is defined as

$$\begin{aligned} \mathcal{H}(m, p, u_3, \mu_1, \mu_2) &= A_3 m + A_4 p + \frac{B_3}{2}u_3^2 \\ &\quad + \mu_1\left[\omega_2 p - \epsilon_2 m\right] \\ &\quad + \mu_2\left[\kappa\zeta_2\chi_2\phi_2 m\left(1 - u_3(t)\frac{p}{C_2}\right) - (\omega_2 + \pi_2)p\right] \end{aligned} \tag{14}$$

where $\boldsymbol{\mu}(t) = (\mu_1(t), \mu_2(t))'$ denote the *adjoint vector-function* or *costate* that satisfies the adjoint dynamical system with corresponding transversality condition specified in the final endpoint of the interval $[\tilde{t},\ T]$, that is,

$$\frac{d\boldsymbol{\mu}}{dt} = \begin{pmatrix} -\mathcal{H}_m \\ -\mathcal{H}_p \end{pmatrix}, \quad \boldsymbol{\mu}(T) = \begin{pmatrix} 0 \\ 0 \end{pmatrix}. \tag{15}$$

In the above expression, $\mathcal{H}_m$ and $\mathcal{H}_p$ denote the partial derivatives of (14) with respect to m and p.

It is worth pointing out that both adjoint vector-functions $\boldsymbol{\lambda}(t)$ and $\boldsymbol{\mu}(t)$ defined by (13) and (15) can be viewed as two-dimensional time-dependent Lagrange multipliers associated with differential constraints (5) and (9), respectively. These functions express the marginal variation in the value of objective functionals $J_1(u_1, u_2)$ and $J_2(u_3)$ with respect to the state variables m and p. In other words, $\boldsymbol{\lambda}(t)$ and $\boldsymbol{\mu}(t)$ can be viewed as additional benefits or costs associated with changes in the state variable and they are necessary elements of the *Pontryagin maximum principle* [45,46].

In general terms, the Pontryagin maximum principle affirms the following. If $(u_1^*(t), u_2^*(t))$ and corresponding $(m^*(t), p^*(t))$ are optimal solutions to the problem (4)–(6), then there exists a piecewise differentiable adjoint function $\boldsymbol{\lambda}(t)$ satisfying (13) such that

$$H(m^*(t), p^*(t), u_1^*(t), u_2^*(t), \lambda_1(t), \lambda_2(t)) \le H(m^*(t), p^*(t), u_1, u_2, \lambda_1(t), \lambda_2(t))$$

for all $(u_1, u_2) \in \Gamma_1$ and almost for all $t \in [0,\ \tilde{t}]$. The above expression implies that Hamiltonian function H associated with optimal control problem (4)–(6) and defined by (12) attains its minimum in $(u_1^*(t), u_2^*(t))$ over the set of admissible controls Γ_1 (in a point-wise sense) almost for all $t \in [0,\ \tilde{t}]$ along the optimal trajectories $(m^*(t), p^*(t))$.

A similar statement is valid for the optimal control problem (8)–(10). Namely, if $u_3^*(t)$ and corresponding $(m^*(t), p^*(t))$ are optimal solutions to the problem (8)–(10), then there exists a piecewise differentiable adjoint function $\boldsymbol{\mu}(t)$ satisfying (15) such that

$$\mathcal{H}(m^*(t), p^*(t), u_3^*(t), \mu_1(t), \mu_2(t)) \le \mathcal{H}(m^*(t), p^*(t), u_3, \mu_1(t), \mu_2(t))$$

for all $u_3 \in \Gamma_2$ and almost for all $t \in [\tilde{t},\ T]$. The latter implies that Hamiltonian function $\mathcal{H}$ associated with optimal control problem (8)–(10) and defined by (14) attains its minimum in $u_3^*(t)$ over the set of admissible controls Γ_2 (in a point-wise sense) almost for all $t \in [\tilde{t},\ T]$ along the optimal trajectories $(m^*(t), p^*(t))$.

Thus, minimization of the objective functionals (4) and (8) can be viewed as "point-wise" minimization of the Hamiltonian functions H and $\mathcal{H}$ at almost all $t \in [0,\ \tilde{t}]$ and $t \in [\tilde{t},\ T]$ along the optimal state trajectories $(m^*(t),\ p^*(t))$, and the following result can be resumed.

Proposition 1. *Given the optimal controls* $\left(u_1^*, u_2^*\right)$ *and* $u_3^*(t)$, *as well as optimal states* m^* *and* p^* *defined as solutions of the corresponding dynamical systems (5) and (9), respectively, there exist two absolutely continuous adjoint vector-functions* $\boldsymbol{\lambda}(t) : [0, \tilde{t}] \mapsto \mathbb{R}^2$ *and* $\boldsymbol{\mu}(t) : [\tilde{t}, T] \mapsto \mathbb{R}^2$ *such that*

$$\frac{d\lambda_1}{dt} = -A_1 + \lambda_1\left(\epsilon_1 + u_1^*(t)\right) - \lambda_2\left(\kappa\left(\zeta_1 - u_2^*(t)\right)\chi_1\phi_1\left(1 - \frac{p^*(t)}{C_1}\right)\right) \tag{16a}$$

$$\frac{d\lambda_2}{dt} = -A_2 - \omega_1\lambda_1 + \lambda_2\left(\frac{\kappa\left(\zeta_1 - u_2^*(t)\right)\chi_1\phi_1 m^*(t)}{C_1} + \omega_1 + \pi_1\right) \tag{16b}$$

$$\lambda_1(\tilde{t}) = 0, \quad \lambda_2(\tilde{t}) = 0 \tag{16c}$$

and

$$\frac{d\mu_1}{dt} = -A_3 + \epsilon_2\mu_1(t) - \mu_2(t)\left(\kappa\zeta_2\chi_2\phi_2\left(1 - u_3^*(t)\frac{p^*(t)}{C_2}\right)\right) \tag{17a}$$

$$\frac{d\mu_2}{dt} = -A_4 - \omega_2\mu_1(t) + \mu_2(t)\left(\frac{\kappa\zeta_2\chi_2\phi_2 m^*(t)}{C_2} + \omega_2 + \pi_2\right) \tag{17b}$$

$$\mu_1(T) = 0, \quad \mu_2(T) = 0 \tag{17c}$$

Furthermore, the characterizations of optimal controls $u_1^*(t)$, $u_2^*(t)$ *and* $u_3^*(t)$ *can be written as*

$$u_1^*(t) = \min\left\{\max\left\{\frac{1}{B_1}m^*(t)\lambda_1(t), 0\right\}, u_\epsilon\right\} \tag{18a}$$

$$u_2^*(t) = \min\left\{\max\left\{\frac{1}{B_2}\kappa\chi_1\phi_1 m^*(t)\left(1 - \frac{p^*(t)}{C_1}\right)\lambda_2(t), 0\right\}, u_\zeta\right\} \tag{18b}$$

$$u_3^*(t) = \min\left\{\max\left\{\frac{1}{B_3}\kappa\zeta_2\chi_2\phi_2\frac{m^*(t)p^*(t)}{C_2}\mu_2(t), 0\right\}, u_c\right\} \tag{18c}$$

The proof of Proposition 1 is almost immediate and provides interesting insights into economic interpretation of the Pontryagin maximum principle [46].

First, we note that adjoint Eqs. (16) and (17) can be directly obtained from (13) and (15). Second, optimal controls $\left(u_1^*, u_2^*\right)$ and $u_3^*(t)$ minimize the Hamiltonian function H and $\mathcal{H}$ over $(u_1,\ u_2) \in \Gamma_1$ and $u_3 \in \Gamma_2$, respectively. Therefore, they must comply with the necessary conditions of optimality, that is,

$$H_{u_1} = 0, \qquad H_{u_2} = 0, \qquad \mathcal{H}_{u_3} = 0 \tag{19}$$

whenever $\left(u_1^*, u_2^*\right) \in \text{int}\,\Gamma_1, u_3^* \in \text{int}\,\Gamma_2$ or take values on the border of admissible control sets $\Gamma_1,\ \Gamma_2$ otherwise. Third, given that $u_i(t), i = 1, 2, 3$ are bounded functions (cf. (3), (7)), the necessary conditions of optimality can be expressed in the following compact form (see [45] for more details):

$$\begin{cases} u_1^*(t) = 0 & \text{if} \quad H_{u_1} > 0 \\ 0 \le u_1^*(t) \le u_\epsilon & \text{if} \quad H_{u_1} = 0 \\ u_1^*(t) = u_\epsilon & \text{if} \quad H_{u_1} < 0 \end{cases} \qquad \begin{cases} u_2^*(t) = 0 & \text{if} \quad H_{u_2} > 0 \\ 0 \le u_2^*(t) \le u_\zeta & \text{if} \quad H_{u_2} = 0 \\ u_2^*(t) = u_\zeta & \text{if} \quad H_{u_2} < 0 \end{cases} \tag{20}$$

$$\begin{cases} u_3^*(t) = 0 & \text{if} \quad \mathcal{H}_{u_3} > 0 \\ 1 \le u_3^*(t) \le u_c & \text{if} \quad \mathcal{H}_{u_3} = 0 \\ u_3^*(t) = u_c & \text{if} \quad \mathcal{H}_{u_3} < 0 \end{cases} \tag{21}$$

Eqs. (19), with partial derivatives given by

$$H_{u_1} = B_1 u_1 - m\lambda_1, \tag{22a}$$

$$H_{u_2} = B_2 u_2 - \kappa\chi_1\phi_1 m\left(1 - \frac{p}{C_1}\right)\lambda_2, \tag{22b}$$

$$\mathcal{H}_{u_3} = B_3 u_3 - \kappa\zeta_2\chi_2\phi_2\frac{p\,m}{C_2}m\mu_2. \tag{22c}$$

effectively state that, in the optimal controls $u_i^*(t), i = 1, 2, 3,$ the marginal cost of each control action $u_i^*(t)$ (expressed by the respective terms $B_i u_i^*(t)$ in the right-hand sides of (22)) should be equal to the marginal benefit of this strategy (expressed by last terms in the right-hand sides of (22)).

However, if the marginal cost of $u_i^*(t)$ exceeds its marginal benefit (that is, if $H_{u_i} > 0, i = 1, 2$ or $\mathcal{H}_{u_3} > 0$), then it is optimal not to apply this strategy and set $u_i^*(t) = 0$ (cf. first rows in (20) and (21)). Alternatively, if the marginal cost of $u_i^*(t)$ stays below its marginal benefit (that is, if $H_{u_i} < 0, i = 1, 2$ or $\mathcal{H}_{u_3} < 0$), then it is optimal to employ all available resources and set $u_i^*(t)$ equal to its maximum level (cf. third rows in (20) and (21)). The above argument leads us directly to the compact forms (18) of optimal control characterizations, and this concludes the proof of Proposition 1. □

Finally, the Pontryagin maximum principle helps us reduce both optimal control problems (4)–(6) and (8)–(10) to a successive solution of two boundary-value problems generally known as *optimality systems*. The first one is composed by four ordinary differential equations with four endpoint conditions, that is, two equations with initial conditions given by (5) plus two equations with transversality conditions given by (16), where the control functions $u_1(t)$ and $u_2(t)$ should be replaced by their respective characterizations (18a) and (18b). It is worth pointing out that this optimality system is defined for the period $[0, \tilde{t}]$, during which the mosquitoes have favorable environmental conditions for their development and reproduction.

The second boundary value problem is also composed four ordinary differential equations with four endpoint conditions, that is, two equations with initial conditions given by (9) plus two equations with transversality conditions given by (17), where the control function $u_3(t)$ should be replaced by its respective characterization (18c). This optimality system is defined for the period $[\tilde{t}, T]$, during which the mosquitoes development and reproduction is impaired by environmental conditions.

It should be noted that both optimality systems are linked to each other in the sense that optimal state solutions ($m^*(t)$, $p^*(t)$) of the first optimality system, evaluated at $t = \tilde{t}$, define the initial state conditions (m_f, p_f) for the second one (see Remark 1).

Furthermore, the transversality conditions (16c) and (17c) guarantee that both chemical control actions should be suspended by the end of period $[0, \tilde{t}]$, that is, $u_1^*(\tilde{t}) = 0$ and $u_2^*(\tilde{t}) = 0$, while mechanical control must be suspended by the end of period $[\tilde{t}, T]$, that is, $u_3^*(T) = 0$.

Due to non-linearity and high dimension of both optimality systems described above, they can only be solved numerically, and the forthcoming section is fully devoted to this issue.

4. Numerical results and discussion

In what follows, we should refer to successive numerical solutions of two optimal control problems (4)–(6) and (8)–(10) (as well as their possible sequential combinations), even though, in practice, we will be solving the underlying optimality systems obtained by the application of Pontryagin maximum principle.

For the study, we consider two seasons that we will call “hot” and “cool” seasons. This is to resemble the approximate yearly behavior of the climate in a broad area of Mexico. The “hot” season corresponds to the months of rain in Mexico that goes from June to September (4 months), in that period the conditions for the development of the vector are maintained. The “cool” season corresponds to the months from October to May (8 months), in this season there are temperatures which slowdown the development of the mosquito.

Among different software solvers developed for numerical solution of optimal control problems, we have chosen the *GPOPS-II package*[2] designed for MATLAB platform and thoroughly described in [47], while its concise description is also provided in Appendix B of [20]. This solver implements an adaptive combination of direct and orthogonal collocation techniques, which is also known as *Radau pseudospectral method* [48].

The primary limitation of GPOPS-II package regards to requiring continuity of the first- and second-order derivatives of the Hamiltonian function with respect to all its variables. However, all optimal control models considered in this paper meet this condition.

4.1. Description of two main scenarios and combined control strategies

In order to decide which season (hot or cool) is more appropriate for initial introduction of season-dependent control interventions, and thus to provide a cogent answer to the second question proposed in Introduction (see p. 2), we should consider and thoroughly analyze two sequential scenarios. One initiating with hot season and following with the cold season and the other initiating with the hot season following with the cold season. This two scenarios can show us in which season is best to start the intervention. In addition a third season is added to both scenarios in order to find the best strategy for a continuous intervention.

Case A: hot-cool-hot. Start in the beginning of hot season with chemical control interventions (for about 4 months), followed by mechanical control measures during cool season (approx. 8 months), and concluding with chemical control again during the next hot season (for additional 4 months).

[2] For more information regarding GPOPS-II solver please visit http://gpops2.com/.

Table 1
Schematic description of two sequential scenarios (**Case A** and **Case B**).

Cases	Sequential solution of optimal control problems		
A	Chemical control (4)–(6) $t \in [0, \tilde{t}] = [0, 120]$	Mechanical control (8)–(10) $t \in [\tilde{t}, T] = [120, 365]$	Chemical control (4)–(6) $t \in [T, T + \tilde{t}] = [365, 485]$
B	Mechanical control (8)–(10) $t \in [0, \tilde{t}] = [0, 245]$	Chemical control (4)–(6) $t \in [\tilde{t}, T] = [245, 365]$	Mechanical control (8)–(10) $t \in [T, T + \tilde{t}] = [365, 610]$

Table 2
Reference values for each set of entomological parameters borrowed from the existing literature [49–53].

Parameters	ϕ_i	ϵ_i	π_i	ω_i	χ_i	ζ_i	C_i
Hot season $(i = 1)$	10	0.07	0.05	0.07	0.5	0.8	1000
Cool season $(i = 2)$	10	0.05	0.05	0.05	0.12	0.3	1000

Case B: cool-hot-cool. Start in the beginning of cool season with mechanical control measures (for about 8 months), followed by chemical control interventions during hot season (approx. 4 months), and concluding with mechanical control measures again during the next cool season (for additional 8 months).

Table 1 summarizes both scenarios described above and indicates the underlying sequences of three optimal control problems to be solved numerically. Hot season corresponds to late spring, summertime and early autumn (about 120 days), so it is assumed shorter that cool season which corresponds to the rest of the year (from mid-autumn to mid-spring, about 245 days)[3].

It should be pointed out that during each season (hot and cool), we assume that mosquitoes possess different entomological parameters regarding their development and reproduction. Therefore, we take two sets of different entomological parameter (see Table 2), where the first set $(i = 1)$ corresponds to hot seasons (with temperatures between 24°C and 30°C which are the most favorable for mosquito development and reproduction), while the second set $(i = 2)$ corresponds to cool seasons (with temperatures between 15°C and 20°C which are less favorable for mosquito development and reproduction). For both periods, we assume the same carrying capacity of available breeding sites, that is, $C_1 = C_2$[4].

We also assumed that, before application of the control measures, the mosquito population has time to reach the equilibrium during the previous season. Therefore, initial conditions for both cases at $t = 0$ are assigned as

$$\big(m(0), p(0)\big) = (\tilde{m}, \tilde{p}) = \left(C_i \frac{\omega_i}{\epsilon_i} \frac{\big(R_M^{(i)} - 1\big)}{R_M^{(i)}}, C_i \frac{\big(R_M^{(i)} - 1\big)}{R_M^{(i)}} \right)$$

where $R_M^{(i)}, i = 1, 2$ are defined by (11). On the other hand, both scenarios consist of three stages (see Table 1), and the initial conditions for optimal control problems corresponding to the second and third stages (that is, at $t = \tilde{t}$ and $t = T$) are assumed equal to the terminal endpoints of states, $\big(m(\tilde{t}), p(\tilde{t})\big)$ and $(m(T), p(T))$, obtained in the previous stage, either the first or the second, respectively.

In order to decide what kind of chemicals (larvicide, insecticide, or their combination) should be used for reaching better effects of vector control interventions during hot seasons and thus to give a cogent answer to the first question proposed in Introduction (see p. 2), we should consider different types of insecticides and larvicides along with their possible combinations.

There are some studies showing that effectiveness of insecticides and larvicides exhibits a rather wide range of variations. According to [54], the range of vector mortality due to insecticide spraying may vary between 15% and 98%, while the vector mortality due to larvicide use is between 23% and 98%. Other scholars claim that lethality of new-generation larvicides may get as high as 50–98% [55,56] or does not exceed 60–70% [57]. Using these data as reference along with an idea borrowed from [22], we consider two types of insecticides and two types of larvicides, as well as their possible combinations. In

[3] It is plausible to point out that our subdivision of a year into one hot and one cool seasons is contingent with climatic conditions of some particular regions. In a more general sense, a year can comprise more than one hot or cool season(s). Nonetheless, the methodology employed in this study can be easily adopted to a set of multiple intercalating seasons within or beyond a year.

[4] Generally speaking, the carrying capacity which is present in various population dynamics models does not have a "physical" sense but expresses the maximal population size that the environment can sustain indefinitely, given the food, habitat, and other necessary resources. Therefore, it is conventional to normalize or round-up the value of carrying capacity.

Table 3
Detailed description of eight strategies for chemical control.

Strategies	Description	Value of u_ϵ	Weight B_1	Value of u_ζ	Weight B_2
Strategy 1	High-lethality expensive insecticide only	0.8	1000	0	0
Strategy 2	Low-lethality cheap insecticide only	0.2	250	0	0
Strategy 3	Hight-lethality expensive larvicide only	0	0	0.7	1000
Strategy 4	Low-lethality cheap larvicide only	0	0	0.2	250
Strategy 5	High-lethality expensive insecticide combined with high-lethality expensive larvicide	0.8	1000	0.7	1000
Strategy 6	High-lethality expensive insecticide combined with low-lethality cheap larvicide	0.8	1000	0.2	250
Strategy 7	Low-lethality cheap insecticide combined with high-lethality expensive larvicide	0.2	250	0.7	1000
Strategy 8	Low-lethality cheap insecticide combined with low-lethality cheap larvicide	0.2	250	0.2	250

mathematical formulation, we define the following sets of upper borders u_ϵ and u_ζ of $u_1(t)$ and $u_2(t)$, respectively:

$$u_\epsilon = \begin{cases} 20\% \text{ low-lethality cheap insecticide} \\ 80\% \text{ high-lethality expensive insecticide} \end{cases}$$

$$u_\zeta = \begin{cases} 20\% \text{ low-lethality cheap larvicide} \\ 70\% \text{ high-lethality expensive larvicide} \end{cases}$$

Possible combinations of these two types of insecticides and larvicides define eight strategies of chemical control which are presented in Table 3 along with corresponding weight coefficients B_1, B_2 expressing the underlying (unit) costs of these chemical substances. This values were chosen to reflect the cost-relation between an expensive and a cheap substance. Other weight coefficients in the objective functionals (4) and (8) are defined as follows:

$$A_1 = A_2 = 1, \qquad A_3 = 1, \quad A_4 = 50, \qquad B_3 = 3000.$$

We have chosen this weight constant values in the objective functionals to balance the vector population and control functions as their magnitudes are on a different scale. This criterion is standard in epidemiology [38,39,58].

The above values imply that, during hot seasons, elimination of both aerial and aquatic mosquito stages are equally important, while during cool seasons, elimination of immature mosquitoes is more important and has a higher (unit) cost.

4.2. Simulations for ***Case A*** (hot-cool-hot sequence)

Let us recall that **Case A** begins at $t = 0$ with a chemical control campaign that lasts for 120 days, that is, during the period $[0, \tilde{t}] = [0, 120]$. Further, mechanical elimination of mosquito breeding sites goes on for 245 consequent days (that is, for $t \in [\tilde{t}, T] = [120, 365]$), and the intervention finally ends with an application of chemical control for 120 more days, i.e., during $[T, T + \tilde{t}] = [365, 485]$ (see details in Table 1).

Further, we perform numerical simulations of eight strategies (described in Table 3) and for each strategy Table 4 provides numerical values of optimal state variables $m^*(t)$ and $p^*(t)$ at the initial and final end-points of three sub-intervals of time, which are denoted by m_o, p_o and m_f, p_f, respectively.

By revising the values of m_f in the second and fourth columns of Table 4, we observe that *Strategy 7* has the best potential to reduce the population of adult mosquitoes that are capable of transmitting dengue and other vector-borne infections. Therefore, our description presented in this section will be centered on the last two strategies from Table 3, *Strategies 7* and *8*. Other numerical results related to the implementation of *Strategies 1–6* are presented in Appendix B.

Figs. 1 and 2 display optimal trajectories $m^*(t), p^*(t)$ and optimal control functions u_i^*, $i = 1, 2, 3$ obtained under *Strategy 7* (red solid lines) and *Strategy 8* (blue dashed lines). It is worth pointing out that the impact of *Strategy 7* on the populations of adult and immature mosquitoes is very similar to that of the *Strategy 5* (cf. red solid curves in the two upper rows of Figs. B.3 and 1) during the hot seasons. In other words, a high-lethality larvicide, if combined with either high- or low-lethality insecticide, is capable of reducing drastically both mosquito populations. However, an insecticide bearing high lethality is more expensive and may do more lateral damage to non-target species (other insects, birds, plants) than a low-lethality insecticide. Therefore, it seems plausible to choose *Strategy 7* over *Strategy 5* for practical applications.

On the other hand, a low-lethality larvicide only “attenuates” the larval competition (as under *Strategy 4*, see Fig. B.2) so that $p^*(t)$ remains almost in the stationary state during the hot seasons when *Strategy 8* is performed (see blue dashed curves in columns (a) and (c) of the second row, Fig. 1). Therefore, the use of low-lethality larvicide must be complemented by spraying of an insecticide bearing high lethality (as under *Strategy 6*, see Fig. B.3) to obtain acceptable results.

Table 4
Case A: end-point conditions for state variables under *Strategies 1–8*. The initial condition is $\big(m(0), p(0)\big) = (\tilde{m}, \tilde{p}) = (664.2857, 930)$.

Strategies	Chemical control $t \in [0, \tilde{t}] = [0, 120]$	Mechanical control $t \in [\tilde{t}, T] = [120, 365]$	Chemical control $t \in [T, T + \tilde{t}] = [365, 485]$
1	$m_f = 67.1268$ $p_f = 414.7682$	$m_o = 67.1268$ $m_f = 271.3915$ $p_o = 414.7682$ $p_f = 310.8467$	$m_o = 271.3915$ $m_f = 66.6134$ $p_o = 310.8467$ $p_f = 411.7832$
2	$m_f = 135.1852$ $p_f = 730$	$m_o = 135.1852$ $m_f = 271.5675$ $p_o = 730$ $p_f = 310.9794$	$m_o = 271.5675$ $m_f = 135.1852$ $p_o = 310.9794$ $p_f = 730$
3	$m_f = 334.2064$ $p_f = 678.1741$	$m_o = 334.2064$ $m_f = 271.6921$ $p_o = 678.1741$ $p_f = 311.0734$	$m_o = 271.6921$ $m_f = 318.6222$ $p_o = 311.0734$ $p_f = 663.1593$
4	$m_f = 648.6406$ $p_f = 922.6189$	$m_o = 648.6406$ $m_f = 271.8679$ $p_o = 922.6189$ $p_f = 311.2058$	$m_o = 271.8679$ $m_f = 648.3815$ $p_o = 311.2058$ $p_f = 922.5892$
5	$m_f = 26.0072$ $p_f = 157.4305$	$m_o = 26.0072$ $m_f = 270.8145$ $p_o = 157.4305$ $p_f = 310.4109$	$m_o = 270.8145$ $m_f = 25.6200$ $p_o = 310.4109$ $p_f = 155.1013$
6	$m_f = 45.8608$ $p_f = 263.0405$	$m_o = 45.8608$ $m_f = 271.1997$ $p_o = 263.0405$ $p_f = 310.7019$	$m_o = 271.1997$ $m_f = 44.9672$ $p_o = 310.7019$ $p_f = 257.5688$
7	$m_f = 24.2745$ $p_f = 163.9678$	$m_o = 24.2745$ $m_f = 270.8245$ $p_o = 163.9678$ $p_f = 310.4185$	$m_o = 270.8245$ $m_f = 23.7747$ $p_o = 310.4185$ $p_f = 160.8855$
8	$m_f = 124.0735$ $p_f = 658.2061$	$m_o = 124.0735$ $m_f = 271.5438$ $p_o = 658.2061$ $p_f = 310.9616$	$m_o = 271.5438$ $m_f = 124.0731$ $p_o = 310.9616$ $p_f = 658.2056$

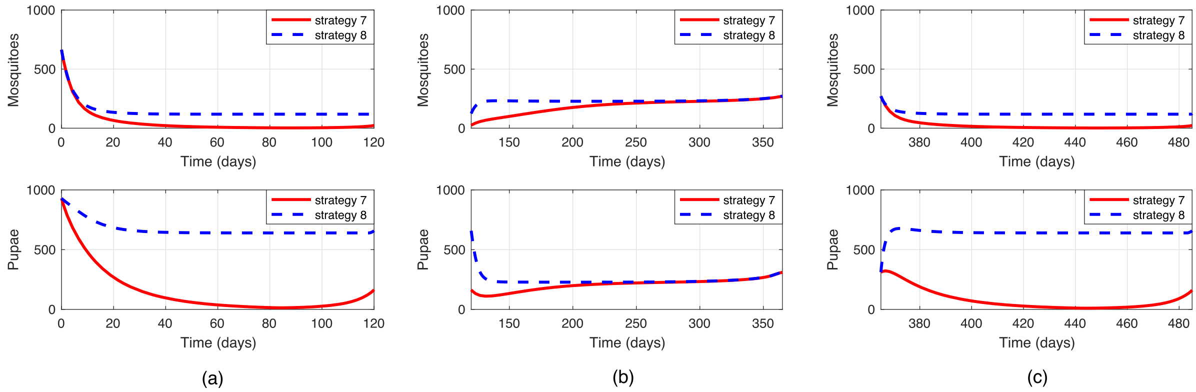

Fig. 1. Case A: optimal trajectories $m^*(t)$, $p^*(t)$ of (4), (5) over $[0, \tilde{t}] \cup [T, T + \tilde{t}]$ (columns (a) and (c)) and optimal trajectories $^*(t)$, $p^*(t)$ of (8), (9) over $[\tilde{t}, T]$ (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 8* – low-lethality cheap insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

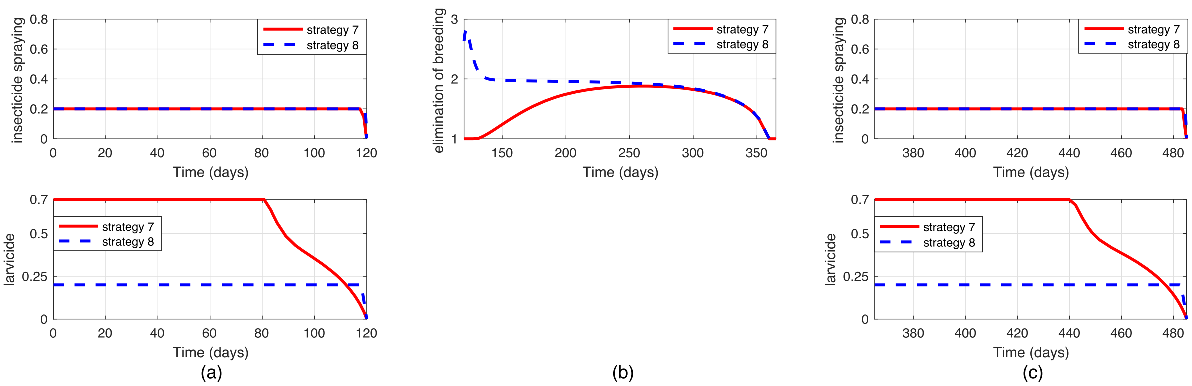

Fig. 2. Case A: optimal controls $u_1^*(t)$, $u_2^*(t)$ designed for (4), (5) over $[0, \tilde{t}] \cup [T, T + \tilde{t}]$ (columns (a) and (c)) and optimal control $u_3^*(t)$ designed for (8), (9) over $[\tilde{t}, T]$ (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 8* – low-lethality cheap insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 5
Case B: end-point conditions for state variables under *Strategies 1–8*. The initial condition is $\big(m(0), p(0)\big) = (\tilde{m}_o, \tilde{p}_o) = (444.44, 444.44)$.

Strategies	Mechanical control $t \in [0, \tilde{t}] = [0, 245]$	Chemical control $t \in [\tilde{t}, T] = [245, 365]$	Mechanical control $t \in [T, T + \tilde{t}] = [365, 610]$
1	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 66.6143$	$m_o = 66.6143$ $m_f = 271.3889$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 411.7884$	$p_o = 411.7884$ $p_f = 310.8447$
2	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 135.1852$	$m_o = 135.1852$ $m_f = 271.5675$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 730$	$p_o = 730$ $p_f = 310.9794$
3	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 318.6253$	$m_o = 318.6253$ $m_f = 271.6808$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 663.1623$	$p_o = 663.1623$ $p_f = 311.0648$
4	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 648.3818$	$m_o = 648.3818$ $m_f = 271.8678$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 922.5851$	$p_o = 922.5851$ $p_f = 311.2057$
5	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 25.6204$	$m_o = 25.6204$ $m_f = 270.7996$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 155.1039$	$p_o = 155.1039$ $p_f = 310.3997$
6	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 44.9694$	$m_o = 44.9694$ $m_f = 271.1884$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 257.5814$	$p_o = 257.5814$ $p_f = 310.6934$
7	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 23.7758$	$m_o = 23.7758$ $m_f = 270.8054$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 160.8927$	$p_o = 160.8927$ $p_f = 310.4040$
8	$m_f = 271.7361$	$m_o = 271.7361$ $m_f = 124.0731$	$m_o = 124.0731$ $m_f = 271.5440$
	$p_f = 311.1065$	$p_o = 311.1065$ $p_f = 658.2056$	$p_o = 658.2056$ $p_f = 310.9617$

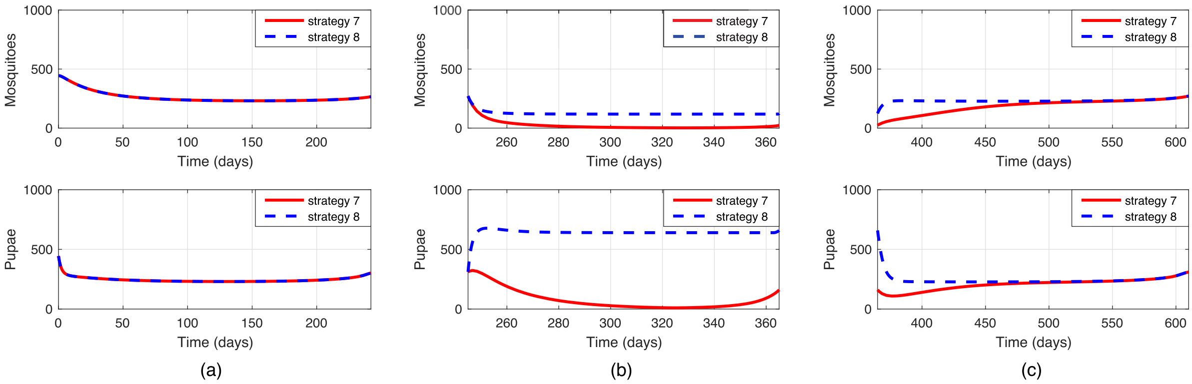

Fig. 3. Case B: optimal trajectories $m^*(t)$, $p^*(t)$ of (8), (9) over $[0, \tilde{t}] \cup [T, T + \tilde{t}]$ (columns (a) and (c)) and optimal trajectories $m^*(t)$, $p^*(t)$ of (4), (5) over $[\tilde{t}, T]$ (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 8* – low-lethality cheap insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

*4.3. Simulations for **Case B** (cool-hot-cool sequence)*

As underlined in Table 1, **Case B** begins at $t = 0$ with a mechanical elimination of mosquito breeding sites that lasts for 245 days, that is, during the period $[0, \tilde{t}] = [0, 245]$. Further, chemical control campaign goes on for 120 consequent days (that is, for $t \in [\tilde{t}, T] = [245, 365]$), and the intervention ends with mechanical elimination of mosquito breeding sites that lasts again for 245 days, i.e., during the period $[T, T + \tilde{t}] = [365, 610]$.

In this subsection, we perform numerical simulations of eight strategies (described in Table 3) and for each strategy Table 5 provides numerical values of optimal state variables $m^*(t)$ and $p^*(t)$ at the initial and final end-points of three sub-intervals of time, which are denoted by m_o, p_o and m_f, p_f, respectively.

According to the values of m_f displayed in the third column of Table 5 and similar to the sequence "hot-cool-hot" (Subsection 4.2), *Strategy 7* shows the best potential to reduce the population of adult mosquitoes. For that reason, only the outcomes of *Strategies 7* and *8* are displayed here (see Figs. 3 and 4), while other results related to *Strategies 1–6* are presented in Appendix B. It is worth pointing out that column (a) in Figs. 3, 4 and B.4, B.5 and B.6.

By comparing Figs. 3 and B.6 from Appendix B, it become clear that *Strategy 7* performs almost as good as *Strategy 5*, despite the fact that these two strategies require to employ insecticides bearing different lethalities. Fig. 3 also shows that a combination of two chemical substances with low lethalities is incapable of suppressing the population of immature mosquitoes which persists at its steady-state level during the hot season. A similar outcome has been already observed in Section 4.2 with regards to **Case A** (*Strategies 4* and *8* described in Appendix B) and the underlying explanation relates to the fact that low-lethality larvicide only attenuates the larval competition without actually affecting the population size of $p(t)$.

It is worth pointing out that the application mode of mechanical control remains almost the same for both cool seasons ($[0, \tilde{t}]$ and $[T, T + \tilde{t}]$) under *Strategies 2–4* and *8*. On the other hand, prior application of chemical control actions $u^*(t)$ and

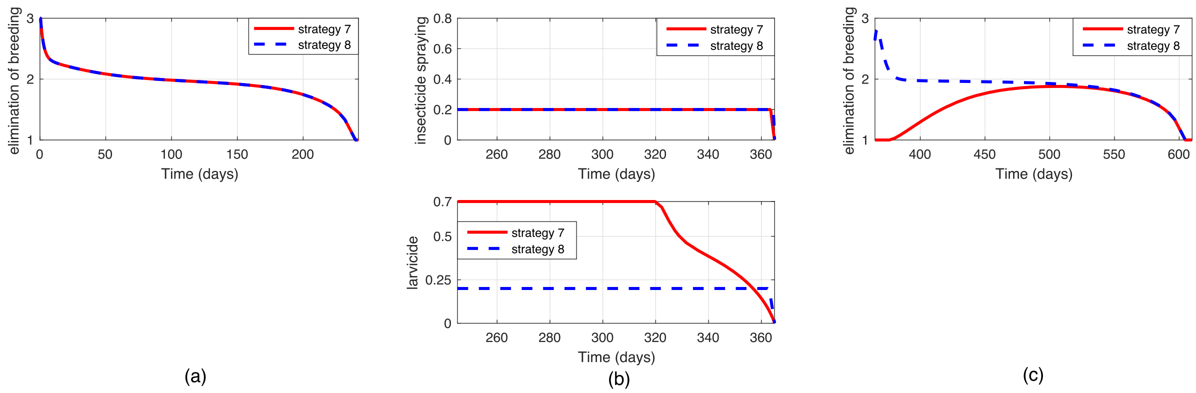

Fig. 4. Case B: optimal control $u_3^*(t)$ designed for (8), (9) over $[0,\tilde{t}]\cup[T,T+\tilde{t}]$ (columns (a) and (c)) and optimal control $u_1^*(t)$, $u_2^*(t)$ designed for (4), (5) over $[\tilde{t},T]$ (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 8* – low-lethality cheap insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

$u_2^*(t)$ under *Strategies 1* and *5–7* alters the application mode of $u_3^*(t)$, requires for less intensive mechanical control and reduces its underlying costs (cf. lower charts in columns (a) versus (c) of Figs. B.4, B.5, B.6 and 3).

As demonstrated by Figs. B.4, B.5, B.6 and 3, all considered strategies contribute, to higher or lesser extent, in suppressing the population of adult mosquitoes that transmit dengue and other vector-borne diseases. On the other hand, these strategies also require for considerable investments that guarantee their implementation, and each strategy bears associated costs. Choosing the best or most adequate strategy for vector control is a challenging task that requires to assess the benefits rendered by each strategy versus its underlying costs. In the following subsection, we employ the so-called "cost-benefit" approach to provide formal rationale and finally decide which strategy renders higher benefits per unit of invested costs.

4.4. Cost-effectiveness analysis

Sixteen optimal control strategies presented in the Sections 4.2 and 4.3 have been obtained on the basis of the maximum principle under two sequential modes. However, it is not clear which strategy would render better results if applied in practice. When dealing with external control interventions, it is recommended to use the so-called cost-effectiveness analysis that allows to assess the benefits of each control intervention and estimate its underlying costs.

The standard measure of cost-effectiveness is the indicator called *Average Cost-Effectiveness Ratio* (ACER) that evaluates each intervention strategy $\big(u_1^*(t), u_2^*(t), u^*(t)\big)$ against its baseline option (e.i., no intervention, that is, $u_1(t)=u_2(t)=0, u_3(t)=1$ for all $t\in[0,T+\tilde{t}]$). Thus, in the case of vector control interventions, the ACER indicator can be calculated as

$$\text{ACER}(\textit{Strategy } j) = \frac{\text{Cost of } \textit{Strategy } j}{\text{Benefit of } \textit{Strategy } j}, \qquad j=1,\dots,8 \tag{23}$$

for each case (**Case A** and **Case B**). To make use of the above formula, we should provide a plausible way to estimate the benefits of all strategies and their underlying costs.

The prime goal of vector control interventions consists in suppressing the sizes of aquatic and aerial mosquito populations. Therefore, the benefit of each strategy can be measured by the expected reduction of both mosquito populations with respect to their steady-state values throughout the intervention period, that is,

$$\text{Benefit} \quad m\big(u_1^*, u_2^*, u_3^*\big) = \tilde{m} - m^*(T+\tilde{t}),$$
$$\text{Benefit} \quad p\big(u_1^*, u_2^*, u_3^*\big) = \tilde{p} - p^*(T+\tilde{t}).$$

To assess the costs of control intervention strategies, we can use a linear relationship of unit cost per effort or amount spent, which is in line with marginal costs of each $u_i^*(t), i=1,2,3,$ that is,

$$\text{Cost}\big(u_1^*, u_2^*, u_3^*\big) = \text{Cost}\big(u_1^*, u_2^*\big) + \text{Cost}\big(u_3^*\big) \tag{24}$$

where

$$\begin{aligned}\text{Cost}\big(u_1^*, u_2^*, u_3^*\big)\Big|_{\textbf{Case A}} &= \int_0^{\tilde{t}} \Big[B_1u_1^*(t)+B_2u_2^*(t)\Big]dt + \int_{\tilde{t}}^{T} B_3u_3^*(t)dt \\ &\quad + \int_T^{T+\tilde{t}} \Big[B_1u_1^*(t)+B_2u_2^*(t)\Big]dt, \\ \text{Cost}\big(u_1^*, u_2^*, u_3^*\big)\Big|_{\textbf{Case B}} &= \int_0^{\tilde{t}} B_3u_3^*(t)dt + \int_{\tilde{t}}^{T} \Big[B_1u_1^*(t)+B_2u_2^*(t)\Big]dt + \int_T^{T+\tilde{t}} B_3u_3^*(t)dt.\end{aligned}$$

Table 6
Case A: Estimations of total costs, benefits, and the respective ACERs for *Strategies 1–8*.

Strategy	Cost	**Benefit** m	**ACER** m	**Benefit** p	**ACER** p
7	1368692.6	640.511	**2136.8740**	769.1145	**1779.5693**
5	1,379,282	638.6657	2159.6396	774.8987	1779.9513
6	1457903.6	619.3185	2354.0449	672.9312	2168.1082
1	1486520.6	597.6723	2487.1833	518.2168	2868.5303
8	1466823.5	540.2126	2715.2708	271.7944	5396.8128
2	1427705.7	529.1005	2698.3639	200	7138.5285
3	1568375.5	345.6637	4537.28	266.8407	5877.5722
4	1477962.9	15.9042	92929.0942	7.4108	199433.65

Table 7
Case B: Estimations of total costs, benefits, and the respective ACERs for *Strategies 1–8*.

Strategy	Cost	**Benefit** m	**ACER** m	**Benefit** p	**ACER** p
7	2675985.1	173.6346	**15411.5890**	134.036	**19964.6744**
5	2680106.37	173.6444	15434.4532	134.0443	19994.1837
6	2761631.9	173.2511	15940.0540	133.7466	20648.2403
1	2806945.9	173.0511	16220.32	133.5953	21010.8132
2	2808065.1	172.8725	16243.5615	133.4606	21040.4051
8	2823489.4	172.896	16330.5651	133.4783	21153.1687
4	2858595.4	172.5722	16564.63	133.2343	21455.4014
3	2887271.9	172.7592	16712.6954	133.3752	21647.7418

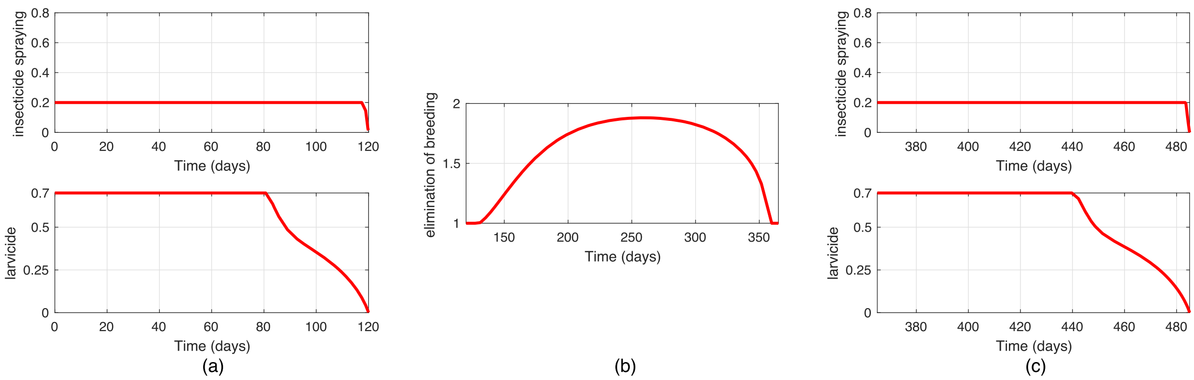

Fig. 5. Case A: optimal controls over "hot season" (columns (a) and (c)) and optimal solutions over "cool season" (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide.

In the above formulas, it is naturally understood that no mechanical control (that is, $u_3^*(t) = 1$) is carried on during the hot season(s), and no chemical control is performed during the cool season(s), so that $u_1^*(t) = u_2^*(t) = 0$.

Tables 6 and 7 provide estimations of total costs, benefits and the respective ACERs for *Strategies 1–8* designed for **Case A** and **Case B**, respectively. In both tables, all strategies are arranged in ascending order regarding their cost-effectiveness indicators (ACERs).

As shown in Tables 6 and 7, *Strategy 7* (see Fig. 5 for hot-cool-hot sequence, and Fig. 6 for cool-hot-cool sequences) renders the best cost-effectiveness result, expressed through the smallest value of ACER, for both considered sequences (**Cases A** and **B**). Therefore, it is plausible to conclude that a combination of low-lethality insecticide and high-lethality larvicide is the best measure for vector control. This gives an outright answer to the first question formulated in the Introduction (see p. 2).

On the other hand, *Strategies 3* and *4* based on the sole use of larvicides (with high or low lethality) constitute the least efficient measure of vector control (see two lower rows in Tables 6 and 7). The underlying explanation (already given in Sections 4.2 and 4.3) basically relate to the fact that an application of larvicides only "attenuates" the larval competition and about the same share of larvae are still able to survive thought the pupae stage to adulthood.

5. Control effects on the dengue incidence

In this section we introduce a epidemiological mathematical model for dengue transmission in order to assess the effect of *Strategy 7* (considered the most appropriate for vector control) on dengue incidence among human hosts. The model includes susceptible, infective, and recovered compartments of human hosts (denoted by $S(t)$, $I(t)$, and $R(t)$, respectively) as

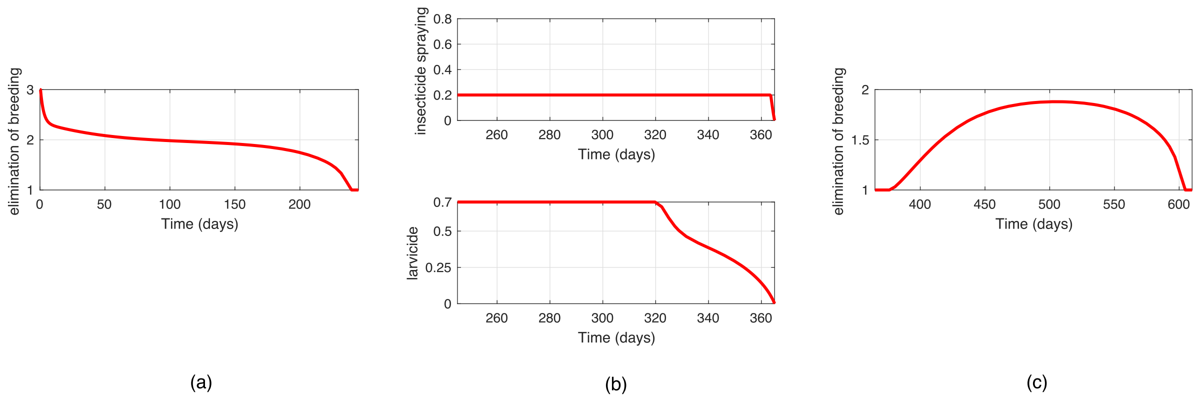

Fig. 6. Case B: optimal control over "cool season" (columns (a) and (c)) and optimal controls over "hot season" (column (b)) under *Strategy 7* – low-lethality cheap insecticide combined with high-lethality expensive larvicide.

well as susceptible/infective compartments of adult female mosquitoes and pupae (denoted by $m_S(t)$, $m_I(t)$ and $p_S(t)$, $p_I(t)$, respectively)[59]:

$$\frac{dS(t)}{dt} = \eta_i N - \alpha_i \frac{m_I(t)}{N} S(t) - \eta_i S(t) \tag{25a}$$

$$\frac{dI(t)}{dt} = \alpha_i \frac{m_I(t)}{N} S(t) - \eta_i I(t) - \gamma_i I(t) \tag{25b}$$

$$\frac{dR(t)}{dt} = \gamma_i I(t) - \eta_i R(t) \tag{25c}$$

$$\frac{dm_S(t)}{dt} = \omega_i p_S(t) - \beta_i \frac{I(t)}{N} m_S(t) - \epsilon_i m_S(t) \tag{25d}$$

$$\frac{dm_I(t)}{dt} = \omega_i p_I(t) + \beta_i \frac{I(t)}{N} m_S(t) - \epsilon_i m_I(t) \tag{25e}$$

$$\begin{aligned}\frac{dp_S(t)}{dt} &= \kappa \zeta_i \chi_i \phi_i m_S(t)\left(1 - \frac{p_S(t)+p_I(t)}{C_i}\right)\\ &\quad + (1-\nu_i)\kappa \zeta_i \chi_i \phi_i m_I(t)\left(1 - \frac{p_S(t)+p_I(t)}{C_i}\right) - (\pi_i + \omega_i) p_S(t)\end{aligned} \tag{25f}$$

$$\frac{dp_I(t)}{dt} = \nu_i \kappa \zeta_i \chi_i \phi_i m_I(t)\left(1 - \frac{p_S(t)+p_I(t)}{C_i}\right) - (\pi_i + \omega_i) p_I(t) \tag{25g}$$

In the above system, we suppose seasonal dependency of the model's parameters with $i = 1$ referring to the hot seasons and $i = 2$ corresponding to the cool seasons.

For the sake of simplicity, the total population of human hosts is assumed constant, that is, $S(t) + I(t) + R(t) = N$ for all $t \geq 0$. Eqs. (25a)–(25c) describe evolution of three human classes with $\eta_i > 0$ denoting the demographic inflow and outflow (human birth and death rates) and $\gamma_i > 0$ expressing the human recovery rate. Thus, human hosts are considered infective (i.e., capable of transmitting the virus) during $1/\gamma_i$ days, while female mosquitoes remain infective until they die.

It worth pointing out that the model (25) does not contemplate the re-infection of human hosts after their recovery while assuming an essentially invariable human population size. However, the model (25) does account for newborn human hosts and demographic changes in the human population since there are studies indicating that newborns are rather susceptible to dengue [60]. The mosquito-to-human transmission of dengue virus occurs at the effective contact rate $\alpha_i > 0$ (see Eqs. (25a) and (25b)), while the inverse human-to-mosquito transmission occurs at the effective contact rate $\beta_i > 0$ (see Eqs. (25d) and (25e)).

In accordance with existent evidence [61], we assume the presence of partial (or imperfect) vertical transmission of the dengue pathogen in mosquitoes. The latter is expressed by Eqs. (25f) and (25g) where a share $0 < \nu_i < 1$ of eggs laid by infective female mosquitoes carry the virus.

Table 8
Reference values for parameters related to the model (25) borrowed from the existing literature [22,61,62].

Parameters	η_i	α_i	γ_i	β_i	ν_i	N
Hot season $(i=1)$	$1/(75 \cdot 365)$	0.67	1/12	0.67	0.3	1000
Cool season $(i=2)$	$1/(75 \cdot 365)$	0.50	1/12	0.5	0.3	1000

In concordance with other mathematical models describing dengue transmission, we assume that the presence of dengue virus in mosquitoes does not affect their entomological parameters [5,8,15,24], and consider the same two sets of season-dependent entomological parameters as in Table 2 while the rest of parameters included in the dengue transmission model (25) have values assigned in Table 8.

To assess the effect of the *Strategy 7*, which is considered the best in terms of cost-effectiveness (see Section 4.4) and consists in combining a low-lethality insecticide with a high-lethality larvicide, we can compare the trajectories of $I(t)$ and $I^*(t), t \in [0, T+\tilde{t}]$ of the dengue transmission model (25) obtained as follows:

1. Trajectory $I(t), t \in [0, T+\tilde{t}]$ represents the solution of dengue transmission system (25) without control intervention while taking into account the seasonal changes of the model's parameters given in Tables 2 and 8.
2. Trajectory $I^*(t), t \in [0, T+\tilde{t}]$ stands for the solution of dengue transmission system (25) under *Strategy 7* represented by the control functions $\big(u_1^*(t), u_2^*(t), u_3^*(t)\big)$.

To obtain $I^*(t)$, Eqs. (25d)–(25g) in the system (25) should be replaced by their controlled versions, that is,

$$\frac{dm_S(t)}{dt} = \omega_i p_S(t) - \beta_i \frac{I(t)}{N} m_S(t) - \big(\epsilon_i + u_1^*(t)\big) m_S(t) \tag{26a}$$

$$\frac{dm_I(t)}{dt} = \omega_i p_i(t) + \beta_i \frac{I(t)}{N} m_S(t) - \big(\epsilon_i + u_1^*(t)\big) m_I(t) \tag{26b}$$

$$\begin{aligned}\frac{dp_S(t)}{dt} &= \kappa\big(\zeta_i - u_2^*(t)\big)\chi_i\phi_i m_S(t)\left(1 - u_3^*(t)\frac{p_S(t)+p_I(t)}{C_i}\right) \\ &\quad + \kappa(1-\nu_i)\big(\zeta_i - u_2^*(t)\big)\chi_i\phi_i m_I(t)\left(1 - u_3^*(t)\frac{p_S(t)+p_I(t)}{C_i}\right) - (\omega_i + \pi_i)p_S(t)\end{aligned} \tag{26c}$$

$$\frac{dp_I(t)}{dt} = \kappa\nu_i\big(\zeta_i - u_2^*(t)\big)\chi_i\phi_i m_I(t)\left(1 - u_3^*(t)\frac{p_S(t)+p_I(t)}{C_i}\right) - (\omega_i + \pi_i)p_I(t) \tag{26d}$$

with $i=1$ and $i=2$ referring to the set of parameters for the hot and cool seasons as given in Tables 2 and 8. It is also understood that the parameter values are switched from $i=1$ to $i=2$ or vice versa exactly at $t=\tilde{t}$ and $t=T$ in accordance with a sequential scenario (**Case A** or **Case B**, see Table 1). Therefore, prior to simulation of two sequential scenarios, we designate that:

- for $i=1$ (hot seasons), optimal controls $u_1^*(t)$ and $u_2^*(t)$ are numerical functions plotted by red-colored solid curves in two lower rows of Figs. 2(a), (c) and 4(b), while $u_3^*(t)=1$;
- for $i=2$ (cool seasons), optimal controls $u_3^*(t)$ are numerical functions plotted by red-colored solid curves in the lower rows of Figs. 2(b) and 4(a) and (c), while $u_1^*(t)=u_2^*(t)=0$.

The results of numerical simulations of the system composed by (25a)–(25c), (26) are presented in Fig. 7 for **Case A** (upper chart) and **Case B** (lower chart).

Fig. 7 helps us to answer the second question posed in the Introduction (see p. 2). Let us compare the impact of optimal controls $u_i^*(t), i=1,2,3$ on the reduction of human infections by contrasting $I(t)$ versus $I^*(t)$ in both charts. When control intervention starts in the beginning of hot season (**Case A**, upper chart in Fig. 7), one expects a lesser number of human infections during the following year $[0, T]=[0, 365]$ than in **Case B** (vector control commencement in the cool season). Moreover, if the control intervention is extended to the second year (that is, for $t \in [T, T+\tilde{t}]$) the impact of $\big(u_1^*(t), u_2^*(t)\big)$ on $I^*(t)$ becomes even more noticeable during the second hot season (**Case A**).

Therefore, the hot season is more appropriate for initial introduction of season-dependent measures for vector control, and the latter cogently responds to the second question posed in the Introduction (see p. 2).

6. Conclusions

In this paper, we have introduced a stylized model for the life cycle of *Aedes aegypti* mosquitoes that accounts for seasonal variation in the mosquito abundance. The latter is a typical feature for many (sub)tropical areas in Mexico and other

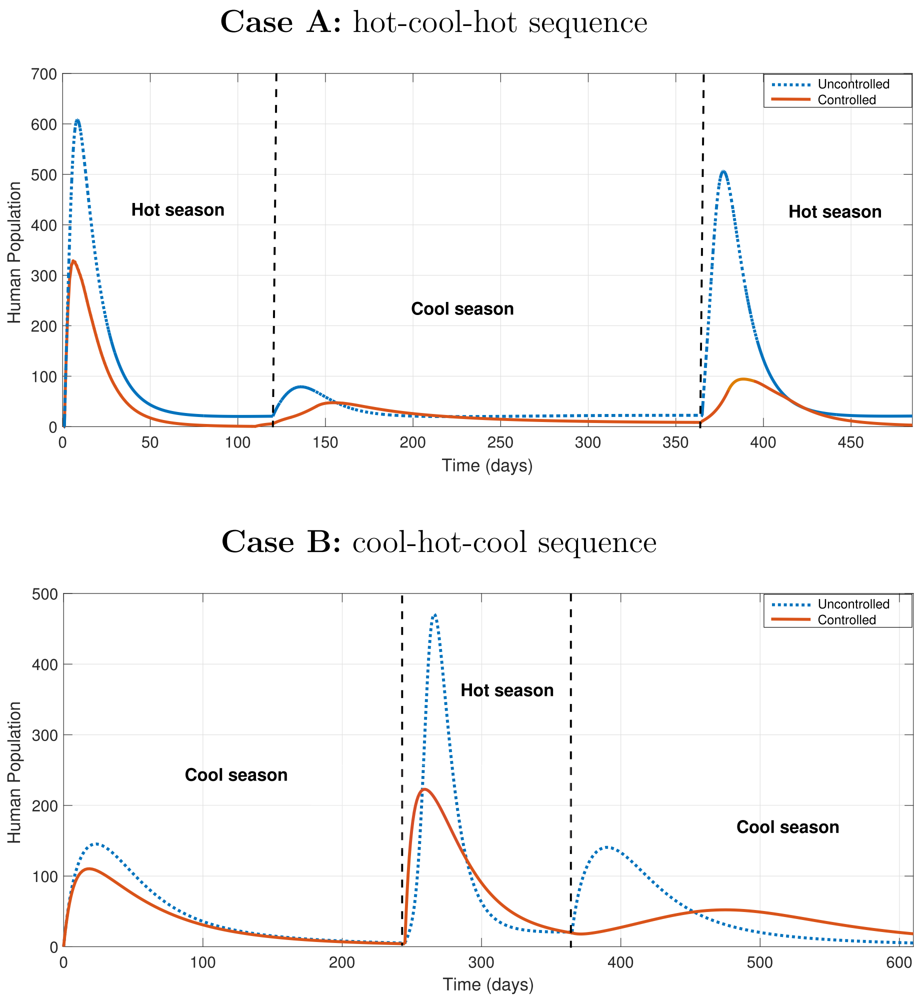

Fig. 7. Population of human hosts infected with dengue for **Case A** (upper chart) and **Case B** (lower chart); trajectories $I(t)$ are plotted by blue dotted lines, and trajectories $I^*(t)$ are sketched by red solid lines. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

countries exhibiting endemo-epidemic patterns of dengue infections among human residents. Highest peaks of dengue epidemics usually occur during the summertime (or hot seasons) when the disease transmitters (*Aedes aegypti* mosquitoes) have favorable climatic conditions for their fast development and reproduction, while outside this period (that is, during cool seasons) dengue infections persist at a relatively low level.

By considering two underlying sets of entomological parameters related to the mosquito life cycle during each season and using the optimal control framework at sequential solution mode, we have designed a series of season-dependent vector control strategies projected for the whole year and aimed at suppressing the overall mosquito population (aerial and aquatic stages).

Our principal goal was to identify the most appropriate type of chemicals (that is, larvicides or/and insecticides bearing different lethalities and underlying costs) rendering the best effects on reduction of vector population during the hot season. According to the analysis performed in Section 4 the most efficient chemical control action should be the combination of a cheap low-lethality insecticide with an expensive high-lethality larvicide. It is worth pointing out that the above mentioned chemical control action showed the best results under two setting: before and after mechanical elimination of mosquito breeding sites during the preceding or subsequent cool season.

Furthermore, in Section 5 this particular chemical control action was tested on the epidemiological model describing dengue transmission between mosquitoes and human hosts. The underlying results of epidemiological assessment gave us sufficient ground to conclude that season-dependent control interventions should be launched in the commencement of hot season in order to prevent more human infection during the following year.

Thus, our findings send a clear message to the healthcare authorities responsible for integrated programs of vector control and plainly indicate the modus operandi of season-dependent control intervention targeting to suppress the overall population of *Aedes aegypti* mosquitoes in dengue-affected areas.

Acknowledgments

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Appendix A. Proof of the Theorem 1

To proof this theorem, we employ the classical approach based on the Filippov-Cesari theorem [42–44] while taking into account the specific characteristics of the optimal control problems (4)–(6) and (8)–(10). Roughly speaking, we have to show that both optimal control problems (4)–(6) and (8)–(10) fulfil the following sufficient conditions for existence of optimal solutions:

(i) Solutions of the dynamical systems (5) and (9) are well-defined and unique for each admissible $(u_1, u_2) \in \Gamma_1$ and $u_3 \in \Gamma_2$, respectively.
(ii) The sets of solutions to the systems (5) and (9) are non-empty and bounded for all admissible control functions $(u_1, u_2) \in \Gamma_1$ and $u_3 \in \Gamma_2$, respectively.
(iii) The sets of all initial and terminal states $(m(0), p(0))$, $\big(m(\tilde{t}), p(\tilde{t})\big)$, $(m(T), p(T))$ are closed and bounded in $\mathbb{R}^2$.
(iv) The control sets Γ_1 and Γ_2 are closed, bounded and convex in $\mathbb{R}^2$ and $\mathbb{R}$, respectively.
(v) The right-hand sides of the dynamical systems (5) and (9) are linear in controls (u_1, u_2) and u_3, respectively.
(vi) The integrands of (4) and (8) are convex in (u_1, u_2) and u_3, respectively, and satisfy

$$A_1 m(t) + A_2 p(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) \geq \mathcal{C}_1 \left\| \big(u_1, u_2\big) \right\|^{\beta} - \mathcal{C}_2 \tag{A-1a}$$

$$A_1 m(t) + A_2 p(t) + \frac{B_3}{2} u_3^2(t) \geq \mathcal{K}_1 \left\| u_3 \right\|^{\theta} - \mathcal{K}_2 \tag{A-1b}$$

with some constants $\mathcal{C}_1, \mathcal{K}_1 > 0,\ \beta, \theta > 1,$ and $\mathcal{C}_2, \mathcal{K}_2$.

Item (i) holds since the admissible control sets Γ_1, Γ_2 contain piecewise continuous bounded function and the right-hand sides of (5) and (9) are Lipschitz continuous with respect to both state variables *m, p* for each admissible $(u_1(t), u_2(t)) \in \Gamma_1$ and $u_3(t) \in \Gamma_2$. Using the *Picard-Lindelöf theorem* (see, e.g., [63]), there exists a unique solution $(m(t), p(t)) \in \Omega$ corresponding to each admissible control $\big(u_1(t), u_2(t)\big) :\ \mathbb{R}_+ \mapsto [0, u_\epsilon] \times [0, u_\zeta]$ and $u_3(t) :\ \mathbb{R}^+ \mapsto [1, u_c]$.

When control variables are in their lower bounds, that is $u_1(t) = u_2(t) = 0$ and $u_3(t) = 1$ in (5) and (9), we arrive to the initial model without control (1) whose trajectories $m(t)$, $p(t)$ engendered by $(m(0), p(0)) \in \Omega$ are bounded for all $t \geq 0$.

It is worthwhile to note that system (1) is *quasimonotone increasing* or *cooperative* in the sense that

$$\frac{\partial f_1(m,p)}{\partial p} \geq 0, \quad \frac{\partial f_2(m,p)}{\partial m} \geq 0 \tag{A-2}$$

for all $(m, p) \in \Omega$. On the other hand, the controlled systems (5) and (9) are also cooperative in the sense of relationships (A-2), and their right-hand sides are decreasing with respect to the control variables $u_i, i = 1, 2, 3$. Therefore, solutions of the systems (5) and (9) with $u_1(t) = u_2(t) = 0$ and $u_3(t) = 1$ can be regarded as their *super-solutions*.

Alternatively, when control variables are at their upper bounds, that is $u_1(t) = u_\epsilon, u_2(t) = u_\zeta$ and $u_3(t) = u_c$, the underlying solutions of the systems (5) and (9) can be regarded as their *sub-solutions*. The monotonicity properties (A-2) give grounds for application of the *comparison theorem* (see, e.g., [64, p.112]) that guarantees that both trajectories $m(t)$ and $p(t)$ will remain between their super-solutions and sub-solutions for all admissible controls $(u_1, u_2) \in \Gamma_1$, $u_3 \in \Gamma_2$ and for all $t \geq 0$. The latter implies that item (ii) holds. Additionally, item (iii) is also true due to the boundedness of both trajectories $m(t)$ and $p(t)$ for all $t \geq 0$.

The forms of admissible control sets Γ_1 and Γ_2 defined by (6) and (10) plainly indicate that these sets are closed, bounded, and convex in $\mathbb{R}^2$ and $\mathbb{R}$, respectively. Thus, item (iv) holds.

A mere glance at the right-hand sides of the dynamical systems (5) and (9) reveals that they are linear in the control variables (u_1, u_2) and u_3. Therefore, item (v) is also fulfilled.

Finally, the integrands of (4) and (8) are quadratic in (u_1, u_2) and u_3, respectively, and therefore convex. Conditions (A-1) are fulfilled with $\mathcal{C}_2 = \mathcal{K}_2 = 0, \beta = \theta = 2 > 1, \mathcal{K}_1 = \frac{B_3}{2} > 0$ and $\mathcal{C}_1 = \frac{\hat{B}}{2} > 0$ where

$$\hat{B} = \begin{cases} B_1 & \text{if} \quad B_2 = 0 \\ B_2 & \text{if} \quad B_1 = 0 \\ \min\{B_1, B_2\} & \text{otherwise} \end{cases}$$

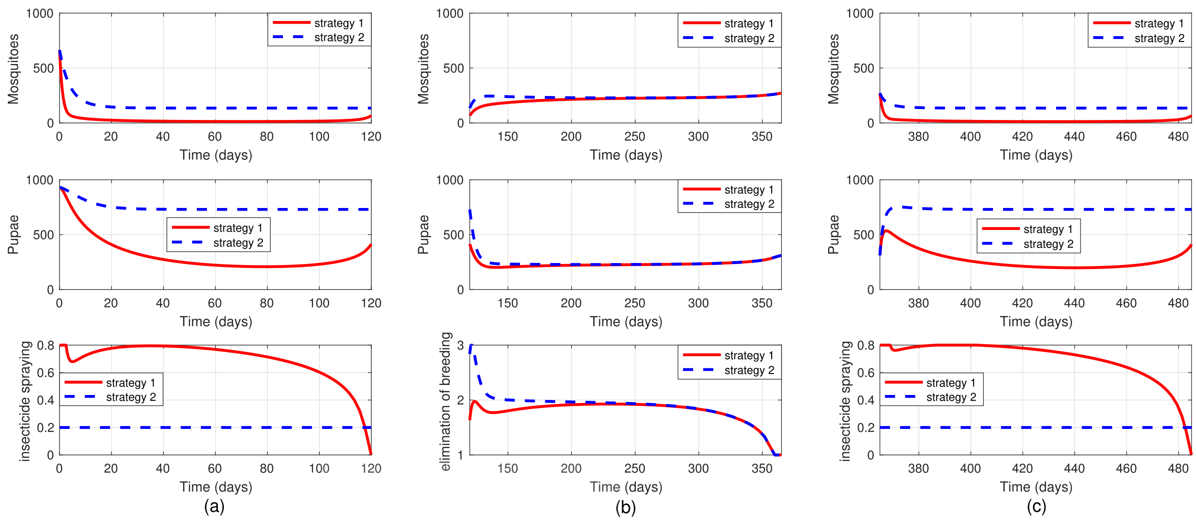

Fig. B1. Case A: optimal solutions of (4), (5) over $[0,\tilde{t}]\cup[T,T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (8), (9) over $[\tilde{t},T]$ (column (b)) under *Strategy 1* – high-lethality expensive insecticide only (red solid lines) and *Strategy 2* – low-lethality cheap insecticide only (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Thus, it holds that

$$A_1 m(t) + A_2 p(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t) \geq \frac{\hat{B}}{2}\left\|\left(u_1(t), u_2(t)\right)\right\|^2,$$
$$A_1 m(t) + A_2 p(t) + \frac{B_3}{2}u_3^2(t) \geq \frac{B_3}{2}\left\|u_3(t)\right\|^2.$$

This concludes the proof of Theorem 1 and justifies the existence of optimal controls for problems (4)–(6) and (8)–(10). □

Appendix B. Numerical outcomes of *Strategies 1–6* under Cases A and B

Simulations for Case A (hot-cool-hot sequence)

Fig. B.1 displays the optimal solutions obtained for **Case A** under *Strategy 1* (red solid lines) and *Strategy 2* (blue dashed lines).

First we note that for both strategies the functional forms of $u_1^*(t)$ are very similar within the initial $[0,\tilde{t}]$ and closing $[T,T+\tilde{t}]$ sub-periods (cf. left and right charts in the last row of Fig. B.1). However, the operational mode of *Strategies 1* is time-dependent while that of the *Strategy 2* is constant ($u_1^*(t)=u_\epsilon, t\in[0,\tilde{t}]\cup[T,T+\tilde{t}]$). Indeed, the low cost of insecticide employed under *Strategy 2* guarantees that the marginal benefit of this control action exceeds its marginal cost[5]; therefore, it is optimal to use all available resources during the whole course of this control action.

During hot seasons, the density of adult mosquitoes $m^*(t)$ exhibits greater reduction under *Strategy 1* than under *Strategy 2* (cf. red solid curves versus blue dashed curves in columns (a) and (c) of the first row in Fig. B.1). This outcome is quite expectable due to the higher lethality of insecticide employed for *Strategy 1* than for *Strategy 2*. Moreover, the application of high-lethality insecticide notably reduces the density of immature stages $p^*(t)$ too (cf. left and right charts in the second row of Fig. B.1) while the effect of low-lethality insecticide has almost no reflection upon the density of $p^*(t)$. This is exactly the reason why the mechanical control $u_3^*(t)$ requires more effort for *Strategy 2* (plotted by the blue dashed curve in last row of Fig. B.1(b)) at the beginning of cool season. The latter counterpoises the effect of $u_3^*(t)$ upon $m^*(t)$ and $p^*(t)$ during the cool season ($t\in[\tilde{t},T]$), and both state trajectories $m^*(t)$ and $p^*(t)$ become almost identical under *Strategies 1* and *2* after the day $t=180$ (see two upper charts in Fig. B.1(b)).

Fig. B.2 displays the optimal solutions obtained for **Case A** under *Strategy 3* (red solid lines) and *Strategy 4* (blue dashed lines). First we observe that during the hot seasons, even a full-force application of the low-lethality larvicide (*Strategy 4* with $u_2^*(t)=u_\zeta=0.2$) has no effect on the mosquito population since both $m^*(t)$ and $p^*(t)$ remain basically in the steady state $(\tilde{m},\tilde{p})$. In effect, a low-lethality larvicide eliminates, in average, about 20% of larvae and "attenuates" the larval competition thus ensuring that the densities of both pupae and adult insects remain close to their steady-state values. On the other hand, a full-force application of high-lethality larvicide (*Strategy 3* with $u_2^*(t)=u_\zeta=0.7$) renders about 50% reduction of mosquito population in aquatic and aerial stages (see red solid curve in the columns (a) and (c) of Fig. B.2). In the course

[5] This implies that $H_{u_1}<0$ for all $t\in[0,\tilde{t}]\cup[T,T+\tilde{t}]$ in accordance with the left-hand relationship in (20).

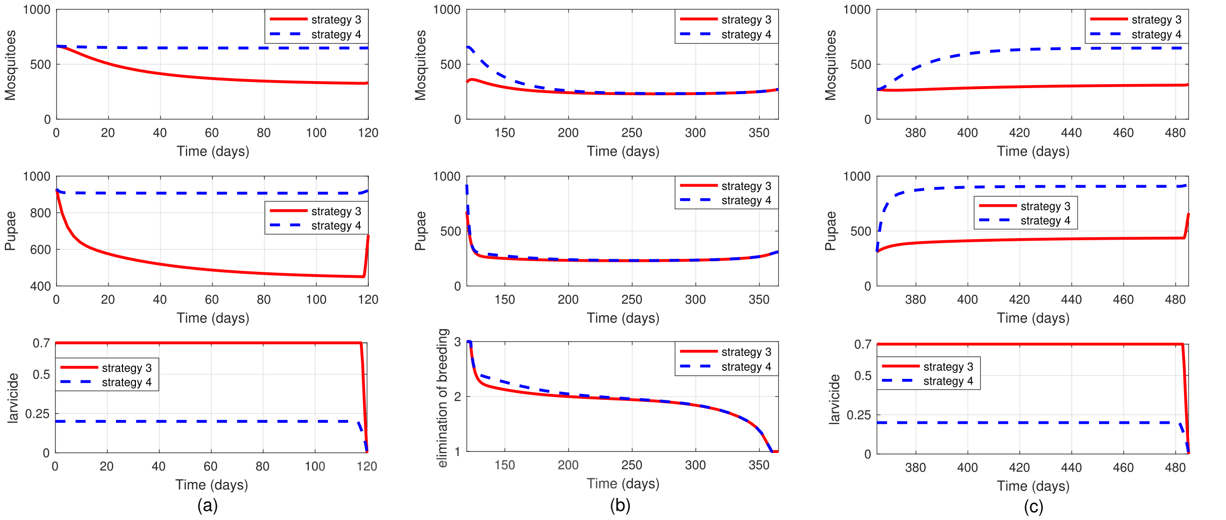

Fig. B2. Case A: optimal solutions of (4), (5) over $[0, \tilde{t}] \cup [T, T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (8), (9) over $[\tilde{t}, T]$ (column (b)) under *Strategy 3* – high-lethality expensive larvicide only (red solid lines) and *Strategy 4* – low-lethality cheap larvicide only (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

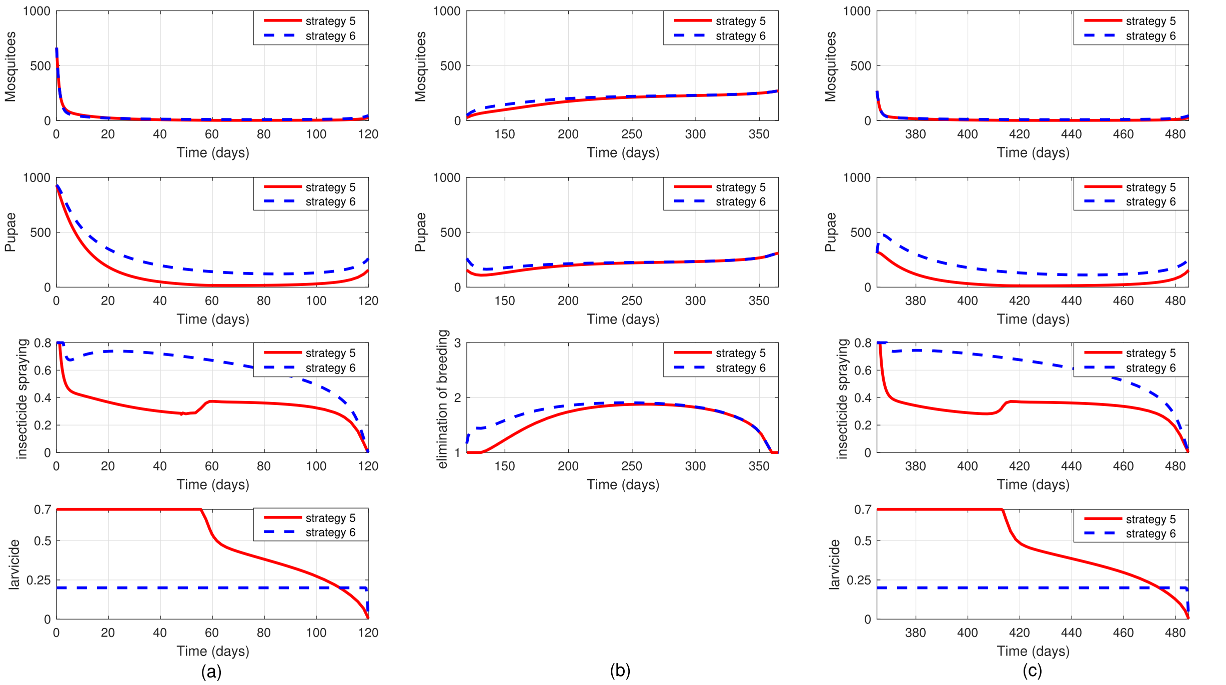

Fig. B3. Case A: optimal solutions of (4), (5) over $[0, \tilde{t}] \cup [T, T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (8), (9) over $[\tilde{t}, T]$ (column (b)) under *Strategy 5* – high-lethality expensive insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 6* – high-lethality expensive insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of cool season, the optimal trajectory corresponding to mechanical control, $u_3^*(t)$, behaves similarly for *Strategies 3* and *4* and has the same effect on mosquito populations $m^*(t)$ and $p^*(t)$ (see Fig. B.2(b)).

Fig. B.3 displays the optimal solutions obtained for **Case A** under *Strategy 5* (red solid lines) and *Strategy 6* (blue dashed lines). Both strategies have very remarkable effect on the densities of adult mosquitoes (which become almost extinct during the hot seasons). Aquatic stages also exhibit rather low densities when high-lethality larvicide is applied (*Strategy 5*) what naturally lead to fewer larvae that reach the adult state and lesser quantity of high-lethality insecticide needed for mosquito control under this strategy in comparison with *Strategy 6* (cf. red solid curves versus blue dashed curves in the columns (a) and (c) of the third row of Fig. B.3).

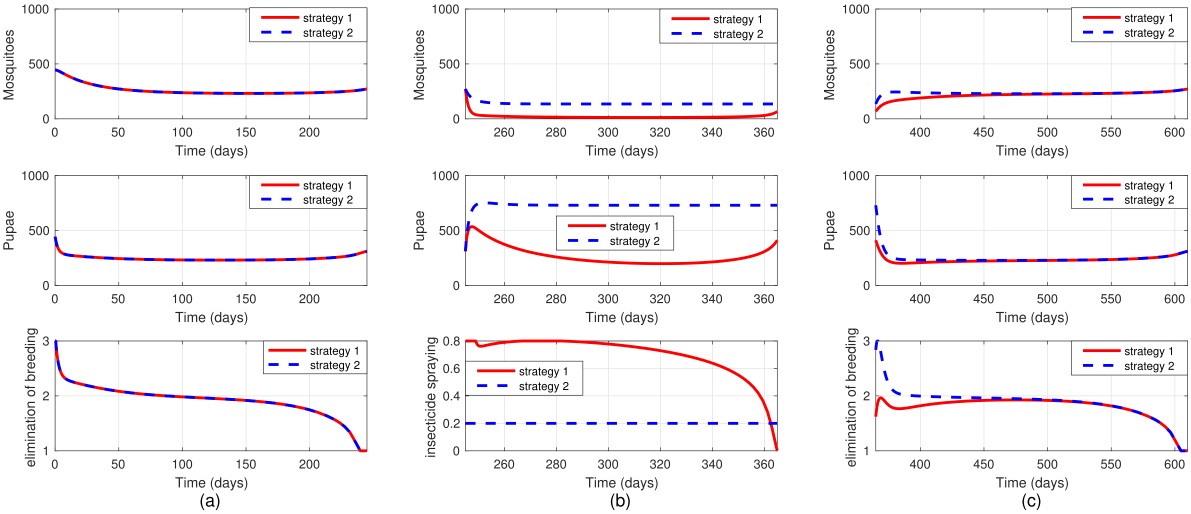

Fig. B4. Case B: optimal solutions of (8), (9) over $[0, \tilde{t}] \cup [T, T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (4), (5) over $[\tilde{t}, T]$ (column (b)) under *Strategy 1* – high-lethality expensive insecticide only (red solid lines) and *Strategy 2* – low-lethality cheap insecticide only (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

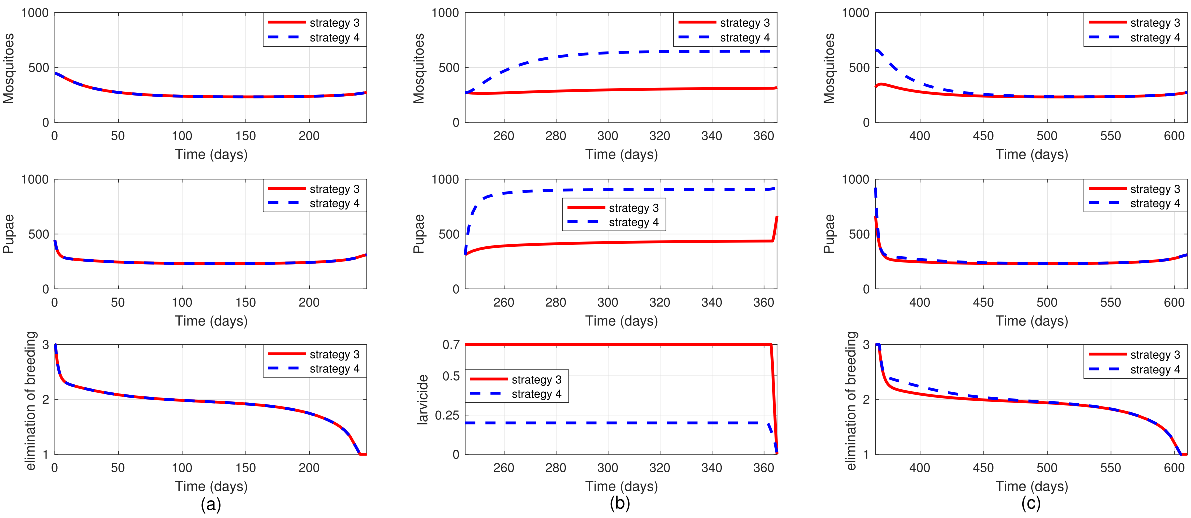

Fig. B5. Case B: optimal solutions of (8), (9) over $[0, \tilde{t}] \cup [T, T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (4), (5) over $[\tilde{t}, T]$ (column (b)) under *Strategy 3* – high-lethality expensive larvicide only (red solid lines) and *Strategy 4* – low-lethality cheap larvicide only (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

In the commencement of the cool season, more intensive mechanical control $u_3^*(t)$ is required for implementation of the *Strategy 6* since this strategy (based on low-lethality larvicide) leaves behind higher density of immature mosquitoes by the end of the hot season than *Strategy 5* does. In regards to *Strategy 5*, it is interesting to observe that the pre-adult population $p^*(t)$ becomes almost extinct around the mid-point $t \approx 0.5\tilde{t}$ of the initial hot season. Therefore, the use of larvicide is reduced just before this mid-point. At the same time, the use of insecticide is slightly enhanced in order to eliminate the greater number of remaining adults and to prevent their oviposition. This explains a “peculiar change of directions” in the middle of the chart located in the third row of columns (a) and (c) in Fig. B.3.

Simulations for Case B (cool-hot-cool sequence)

Fig. B.4 (b) shows that immature mosquitoes quickly reach their steady state at the commencement of the hot season since the sole application of low-lethality insecticide (*Strategy 2*) even at maximum force and during the whole hot season cannot reduce sufficiently the population of adults (see blue dashed curve on two upper charts in Fig. B.4(b)). However, *Strategy 1* which is based on the sole application high-lethality insecticide is capable of reducing the size of immature

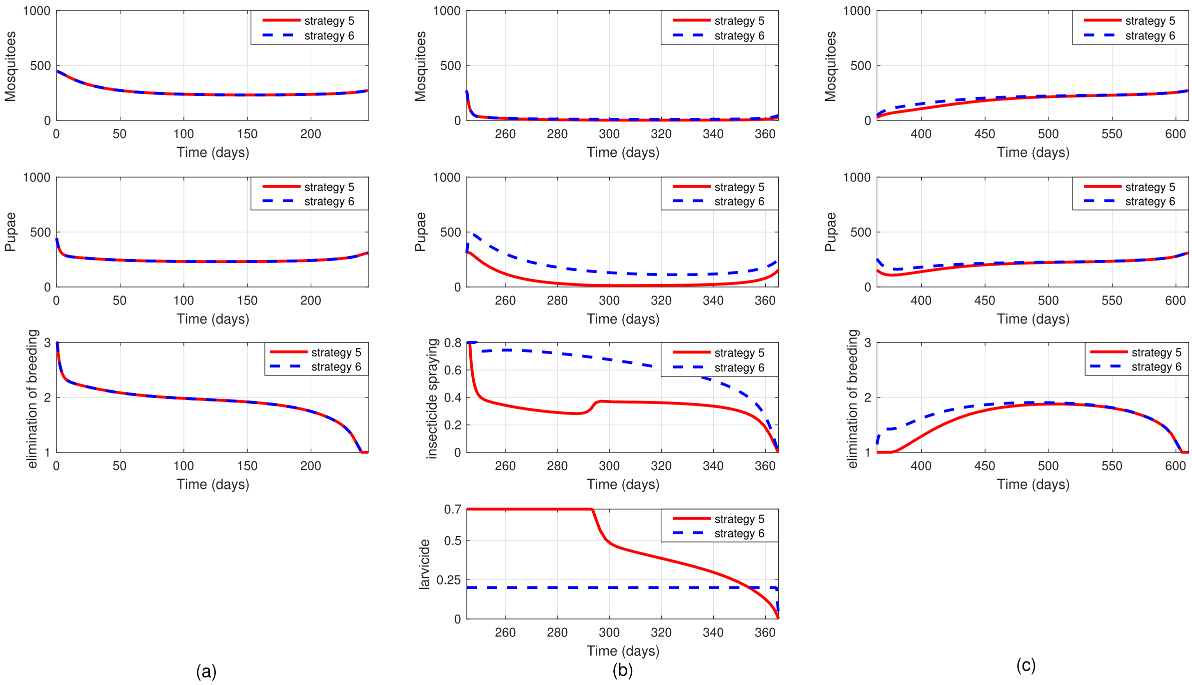

Fig. B6. Case B: optimal solutions of (8), (9) over $[0, \tilde{t}] \cup [T, T+\tilde{t}]$ (columns (a) and (c)) and optimal solutions of (4), (5) over $[\tilde{t}, T]$ (column (b)) under *Strategy 5* – high-lethality expensive insecticide combined with high-lethality expensive larvicide (red solid lines) and *Strategy 6* – high-lethality expensive insecticide combined with low-lethality cheap larvicide (blue dashed lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

population during the hot season, and the latter is counterpoised by a less intensive mechanical control at the beginning of subsequent cool season (see the chart in the lower row of Fig. B.4(c)).

Strategy 3 is capable of reducing the densities of $m(t)$ and $p(t)$ by about 50% with regards to their steady-state values but requires for full-force spraying of a high-lethality larvicide during the entire hot season (see red solid curves in Fig. B.5(b)). On the other hand, an application of a low-lethality larvicide (*Strategy 4*) seems completely useless, since both populations $m(t)$ and $p(t)$ quickly reach their steady-state values in the beginning of hot season (see blue dashed curve in Fig. B.5(b)).

According to Fig. B.6(b), *Strategy 5* has excellent performance and also allows to postpone for a couple of week the mechanical elimination of mosquito breeding sites, while *Strategy 6* also performs relatively well but requires immediate mechanical control action at the commencement of the second cool season (see the lower chart of Fig. B.6(c)).

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