OPTIMAL CONTROL AND COST-EFFECTIVENESS ANALYSIS
OF A THREE AGE-STRUCTURED TRANSMISSION DYNAMICS
OF CHIKUNGUNYA VIRUS

FOLASHADE B. AGUSTO

Department of Ecology and Evolutionary Biology
University of Kansas
Lawrence KS 66045, USA

ABSTRACT. Chikungunya is an RNA viral disease, transmitted to humans by infected Aedes aegypti or Aedes albopictus mosquitoes. In this paper, an age-structured deterministic model for the transmission dynamics of Chikungunya virus is presented. The model is locally and globally asymptotically stable when the reproduction number is less than unity. A global sensitivity analysis using the reproduction number indicates that the mosquito biting rate, the transmission probability per contact of mosquitoes and of humans, mosquito recruitment rate and the death rate of the mosquitoes are the parameters with the most influence on Chikungunya transmission dynamics. Optimal control theory was then applied, using the results from the sensitivity analysis, to minimize the number infected humans, with time dependent control variables (impacting mosquito biting rate, transmission probability, death rate and recovery rates in humans).

The numerical simulations indicate that Chikungunya can be reduced by the application of these controls. The benefits associated with these health interventions are evaluated using cost-effectiveness analysis and these shows that using mono-control strategy involving treatment of infected individuals is the most cost-effective strategy of this category. With pairs of control, the pairs involving treatment of infected individuals and mosquitoes adulticiding, is the most cost-effective strategy of this category and is more cost-effective than using the triple control strategy involving personal protection, treatment of infected humans and mosquitoes adulticiding.

1. Introduction. Chikungunya is a viral disease transmitted to humans from an infected mosquito of the Aedes genus (particularly the Aedes aegypti and Aedes albopictus mosquitoes [8, 53]). It is an RNA virus that belongs to alphavirus genus of the family togaviridae [54]. It was first described about 1952 during an outbreak in southern Tanzania [54]. Chikungunya in the Kimakonde language (the language from where the name was derived) means to become contorted or “bend over” [54]. The incubation period is usually between 3-7 days following an effect bite from an infected mosquitoes [8, 53], the symptoms include fever, headache, nausea, fatigue, rash and severe joint-pain (including lower back, ankle, knees, wrists or phalanges) [8, 53]. There are no antiviral medicines to treat the disease [8, 53]; all the treatment are directed at relieving the disease symptoms [54]. There are no preventative
vaccines for Chikungunya [54]; however, there is a promising experimental vaccine in an early-stage clinical trial which prompts an immune response in all 25 trial volunteers [9]. Chikungunya rarely causes death, and infected individuals are expected to make full recovery with life-long immunity [53]. However, there are some cases where individuals experience joint pains for several months or years after the initial infection [54]. There have also been reports of eye, neurological, heart complications and gastrointestinal complaints [54]. Generally, the disease symptoms are mild and the infection may go unrecognized. However, newborns infected about the time of birth, older adults (≥ 65 years), and people with medical conditions (such as high blood pressure, diabetes, or heart disease) are at risk for more severe disease [8].

There have been numerous cases of Chikungunya re-emergence in Africa, Asia, Europe, and more recently the Caribbean [14]. The virus was isolated in the 1960s in Bangkok, then in 1964, the virus surfaced again in parts of India cities such as Vellore, Calcutta, and Maharastha [38]. Other outbreaks include Sri Lanka in 1969; Vietnam in 1975; Myanmar in 1975; and Indonesia in 1982 [38]. From 1999-2000, a large Chikungunya outbreak occurred in the Democratic Republic of the Congo [54]. From 2005-2007, islands of the Indian Ocean saw occurrences of Chikungunya outbreaks. Gabon experienced an outbreak in 2007 [54]. Since 2005 over 1.9 million cases have been encountered in India, Indonesia, Thailand, Maldives, and Myanmar [54]. By 2007, the disease had spread to Europe with 197 recorded cases [54].

In December 2013, two laboratory-confirmed autochthonous (native) cases were reported in the French part of the Caribbean island of St. Martin [14] [54]. Since then, local transmission has been confirmed in the Dutch part of Saint Martin (St Maarten), Anguilla, British Virgin Islands, Dominica, French Guiana, Guadeloupe, Martinique and St Barthelemy [54]. As of October 2014, over 776,000 suspected cases of Chikungunya have been recorded in the Caribbean islands, Latin American countries and some South American countries [54]. 152 deaths have also been attributed to this disease during the same period. Mexico and the USA have also recorded imported cases. On 21 October 2014, France confirmed four cases of Chikungunya locally-acquired infection in Montpellier, France [54].

From 2005-2006 major Chikungunya outbreaks occurred on numerous islands in the Indian Ocean, most notably was the outbreak on La Reunion Island where one-third of the population was infected [15]. According to Schuffenecker et al. [44] and Vazeille et al. [52], in two parallel studies, the Chikungunya virus strains in the Reunion Island outbreak mutated to facilitate the disease transmission by Aedes albopictus (Tiger mosquito) [15] [18]. The mutation was a point mutation in one of the viral envelope genes (E1 glycoprotein gene (E1-226V)) [47] [49]. Dubrulle et al. [15] found that this mutation allowed the virus to be present in the mosquito saliva only two days after the infection, instead of approximately seven days and that Aedes albopictus is slightly more efficient host than Aedes aegypti in transmitting the variant E1-226V of Chikungunya virus. Hence, this result indicates that other areas where the tiger mosquitoes are present could be at greater risk of an outbreak with an enhanced transmission of Chikungunya virus by Aedes albopictus.

Some studies have been carried out to study the Chikungunya virus, considering different factors that affect the outbreak of the disease (see [16] [30] [33] [54] [40] [41] [43] [57]). Diego Ruiz-Moreno et al. [43] analyzed the potential risk of Chikungunya introduction into the US, their study combines a climate-based mosquito population dynamics stochastic model with an epidemiological model to identify temporal windows that have an epidemic risk. Dumont et al. [16] propose a model, including
human and mosquito compartments, which is associated with the time course of the first epidemic of Chikungunya in Reunion Island. Using entomological results, they investigated the links between the 2005 episodes and the 2006 outbreak. Manore et al. [30] investigated via an adapted mathematical model the differences in transient and endemic behavior of Chikungunya and dengue; the risk of emergence for different virus-vector assemblages; and the role that virus evolution plays in disease dynamics and risk. Poletti et al. [40] developed a Chikungunya transmission model for the spread of the epidemic in both humans and mosquitoes; the model involves a temporal dynamics of the vector (Aedes albopictus) depending on climatic factors. In the study, they provided estimates of the transmission potential of the virus and assessed the efficacy of the measures undertaken by public health authorities to control the epidemic spread in Italy. Yakob et al. [57] developed a simple, deterministic mathematical model for the transmission of the virus between humans and mosquitoes. They fitted the model to the large Reunion epidemic data and estimated the type-reproduction number for Chikungunya; their model provided a close approximation of both the peak incidence of the outbreak and the final epidemic size. Pongsumpun and Sangsawang [41] developed and studied theoretically an age-structured model for Chikungunya involving juvenile and adult human populations, giving conditions for the disease free and endemic states respectively. They also suggested an alternative way of controlling the disease.

The aim of this study is to develop a new deterministic transmission model to gain qualitative insight into the transmission dynamics of Chikungunya virus and to apply optimal control to curtail the spread of the virus in the community. A notable feature of the model is the incorporation of three different human age classes involving juvenile, adult and senior human populations; the model also involves two infectious human classes, notably the asymptomatic and symptomatic classes. The paper is organized as follows: the model is formulated in Section 2, while in Section 3 the analysis of the mathematical properties of the model is carried out. The sensitivity analysis of the model is investigated in Section 3.3. Following the results obtained from the sensitivity analysis, optimal control theory is applied in Section 4. Numerical simulations involving the application of optimal control to curtail disease spread is implemented in Section 5. Cost-effectiveness analysis is investigated in Section 6. The key theoretical and epidemiological results from this study are summarized in Section 7.

2. Model formulation. This paper considers the Chikungunya model formulated and developed in [1]. The model divides the total human population into juvenile, adult and senior sub-populations. The sub-population is further divided into susceptible (S_i), exposed (E_i), symptomatic (I_{Si}), asymptomatic (I_{Ai}) and recovered (R_i), where i = J, A, S for the juvenile, adult and senior sub-populations. Thus, the total human population is \( N_H(t) = S_J(t) + E_J(t) + I_{AJ}(t) + I_{SJ}(t) + R_J(t) + S_A(t) + E_A(t) + I_{AA}(t) + I_{SA}(t) + R_A(t) + S_S(t) + E_S(t) + I_{AS}(t) + I_{SS}(t) + R_S(t) \). The mosquito population is divided into three classes consisting of susceptible mosquitoes (S_M), exposed mosquitoes (E_M) and infected mosquitoes (I_M). Hence, the total mosquito population is \( N_M(t) = S_M(t) + E_M(t) + R_M(t) \).

The model for the transmission dynamics of Chikungunya virus in a population is given by the following deterministic system of non-linear differential equations:
\[
\begin{align*}
\frac{dS_J}{dt} &= \pi_J - \frac{\beta_j b_M S_J I_M}{N_H} - \alpha S_J - \mu J S_J \\
\frac{dE_J}{dt} &= \frac{\beta_j b_M S_J I_M}{N_H} - \alpha E_J - (\sigma_j + \mu J) E_J \\
\frac{dI_{AJ}}{dt} &= \varepsilon J \sigma J E_J - \alpha I_J - (\gamma_{AJ} + \mu J) I_J \\
\frac{dI_{SJ}}{dt} &= (1 - \varepsilon_j) \sigma J E_J - \alpha I_{SJ} - (\gamma_{SJ} + \mu J) I_{SJ} \\
\frac{dR_J}{dt} &= \gamma_{AJ} I_{AJ} + \gamma_{SJ} I_{SJ} - \alpha R_J - \mu J R_J \\
\frac{dS_A}{dt} &= \alpha S_J - \frac{\beta_a b_M S_A I_M}{N_H} - \xi S_A - \mu A S_A \\
\frac{dE_A}{dt} &= \alpha E_J + \frac{\beta_a b_M S_A I_M}{N_H} - \xi E_A - (\sigma_A + \mu_A) E_A \\
\frac{dI_{AA}}{dt} &= \alpha I_{AJ} + \varepsilon_A \sigma_A E_A - \xi I_{AA} - (\gamma_{AA} + \mu_A) I_{AA} \\
\frac{dI_{SA}}{dt} &= \alpha I_{SJ} + (1 - \varepsilon_A) \sigma_A E_A - \xi I_{SA} - (\gamma_{SA} + \mu_A) I_{SA} \\
\frac{dR_A}{dt} &= \alpha R_J + \gamma_{AA} I_{AA} + \gamma_{SA} I_{SA} - \xi R_A - \mu_A R_A \\
\frac{dS_S}{dt} &= \xi S_A - \frac{\beta_s b_M S_S I_M}{N_H} - \mu S S \\
\frac{dE_S}{dt} &= \xi E_A + \frac{\beta_s b_M S_S I_M}{N_H} - (\sigma_S + \mu_S) E_S \\
\frac{dI_{AS}}{dt} &= \xi I_{AA} + \varepsilon_S \sigma_S E_S - (\gamma_{AS} + \mu_S) I_{AS} \\
\frac{dI_{SS}}{dt} &= \xi I_{SA} + (1 - \varepsilon_S) \sigma_S E_S - (\gamma_{SS} + \mu_S) I_{SS} \\
\frac{dR_S}{dt} &= \xi R_A + \gamma_{AS} I_{AS} + \gamma_{SS} I_{SS} - \mu_S R_S
\end{align*}
\]
\[
\frac{dS_M}{dt} = \pi_M - \beta_M b_M \left[ \frac{I_{AJ} + I_{SJ} + I_{AA} + I_{SA} + I_{AS} + I_{SS}}{N_H} \right] S_M
\]

(2)

\[
\frac{dE_M}{dt} = \beta_M b_M \left[ \frac{I_{AJ} + I_{SJ} + I_{AA} + I_{SA} + I_{AS} + I_{SS}}{N_H} \right] S_M
- (\mu_M + \sigma_M) E_M
\]

\[
\frac{dI_M}{dt} = \sigma_M E_M - \mu_M I_M.
\]

The parameter \( \pi_J \) is the recruitment rate, and \( \mu_J \) is the natural death rate of juveniles. The juvenile maturation rate is given by \( \alpha \). The parameter \( b_M \) denotes the average number of mosquito bites received by humans. The parameter \( \beta_J \) is the probability that a bite from an infectious mosquito leads to infection of the susceptible juvenile; while \( \beta_M \) is the transmission probability per contact from an infectious juvenile to a susceptible mosquito. The parameters \( (1 - \varepsilon_J) \sigma_J \) is the rate at which \( (1 - \varepsilon_J) \) fraction of exposed juveniles enters the asymptomatic class and \( \varepsilon_J \sigma_J \) is the remaining fraction \( \varepsilon_J \) that goes into the symptomatic class. The asymptomatic juvenile population recovery rate (either naturally or via the use of treatment) is given by \( \gamma_{AJ} \); while the juvenile symptomatic population recovery rate is \( \gamma_{SJ} \). The parameters for the adult and senior populations are similarly defined (with the subscript \( J \) replaced by \( A \) and \( S \) respectively). Additionally, the parameter \( \xi \) presents the maturation rate from the adult population into the senior class. The parameter \( \pi_M \) represent mosquito recruitment rate while \( \mu_M \) is the natural death rate in mosquitoes. The parameter \( \sigma_M \) is the mosquito progression rate from the exposed class to the infected class.

The flow diagram of the age-structured Chikungunya model (1)-(2) is depicted in Figure 1 and the associated variables and parameters are described in Table 1.

3. Analysis of the model.

3.1. Basic qualitative properties.

3.1.1. Positivity and boundedness of solutions. For the age-structured Chikungunya transmission model (1)-(2) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time. In other words, solutions of the model system (1)-(2) with non-negative initial data will remain non-negative for all time \( t > 0 \).

Lemma 3.1. Let the initial data \( F(0) \geq 0 \), where \( F(t) = (S_J, E_J, I_{AJ}, I_{SJ}, R_J, S_A, E_A, I_{AA}, I_{SA}, R_A, S_S, E_S, I_{AS}, I_{SS}, R_A, S_M, E_M, I_M) \). Then the solutions \( F(t) \) of the age-structured Chikungunya model (1)-(2) are non-negative for all \( t > 0 \). Furthermore

\[
\limsup_{t \to \infty} N_H(t) = \frac{\pi_J}{\mu_H}, \quad \text{and} \quad \limsup_{t \to \infty} N_M(t) = \frac{\pi_M}{\mu_M}
\]

where \( \mu_H = \max\{\mu_J, \mu_A, \mu_S\} \) and
Figure 1. Systematic flow diagram of age-structured Chikungunya Model (1)-(2)

\[ N_H(t) = S_J(t) + E_J(t) + I_{AJ}(t) + I_{SJ}(t) + R_J(t) + S_A(t) + E_A(t) + I_{AA}(t) + I_{SA}(t) + R_A(t) + S_S(t) + E_S(t) + I_{AS}(t) + I_{SS}(t) + R_S(t), \]

\[ N_M(t) = S_M(t) + E_M(t) + R_M(t). \]

The proof of Lemma 3.1 is given in [1].

3.1.2. Invariant regions. The age-structured Chikungunya model (1)-(2) will be analyzed in a biologically-feasible region as follows. Consider the feasible region

\[ \Omega = \Omega_H \times \Omega_M \subset \mathbb{R}_+^{15} \times \mathbb{R}_+^3, \]

with,
Table 1. Description of the variables and parameters of the age-structured Chikungunya model (1)-(2)

$$\Omega_H = \left\{ S_J, E_J, I_{S_J}, I_{A_J}, R_J, S_A, I_{S_A}, I_{A_A}, R_A, S_S, I_{S_S}, I_{A_S}, R_S : N_H(t) \leq \frac{\pi_J}{\mu_H} \right\},$$

and

$$\Omega_M = \left\{ S_M, E_M, R_M : N_M(t) \leq \frac{\pi_M}{\mu_M} \right\}.$$

Lemma 3.2. The region $\Omega \subset \mathbb{R}^{18}_+$ is positively-invariant for the age-structured Chikungunya model (1)-(2) with non-negative initial conditions in $\mathbb{R}^{18}_+$.

In the next section, the conditions for the existence and stability of the equilibria of the model (1)-(2) are stated.

3.2. Stability of disease-free equilibrium (DFE). The age-structured Chikungunya model (1)-(2) has a disease-free equilibrium (DFE), obtained by setting the right-hand sides of the equations in the model to zero, given by
The linear stability of $\mathcal{E}_0$ can be established using the next generation operator method on the system (1)-(2). Taking $E_J, I_{SA}, I_{AJ}, E_A, I_{SA}, I_{AA}, E_S, I_{SS}, I_{AS}, E_M, I_M$, as the infected compartments, then using the notation in [51], the Jacobian matrices $F$ and $V$ for the new infection terms and the remaining transfer terms are respectively given by,

$$F = \begin{pmatrix}
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\end{pmatrix},$$

where $\Phi_J = \frac{\beta J b M M \mu H}{k_1}$, $\Phi_A = \frac{\beta A b M \alpha}{k_1}$, $\Phi_S = \frac{\beta S b M \xi \alpha}{\mu H k_1}$, $\Phi_M = \frac{\tau M \beta M b M \mu H}{\mu M \mu J}$, and

$$V = \begin{pmatrix}
k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
-\xi J \sigma J & k_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
-\Psi J & 0 & k_4 & 0 & 0 & 0 & 0 & 0 & 0 \\
-\alpha & 0 & 0 & k_7 & 0 & 0 & 0 & 0 & 0 \\
0 & -\alpha & 0 & -\xi A \sigma A & k_8 & 0 & 0 & 0 & 0 \\
0 & 0 & -\alpha & -\Psi A & 0 & k_9 & 0 & 0 & 0 \\
0 & 0 & 0 & -\xi & 0 & 0 & k_11 & 0 & 0 \\
0 & 0 & 0 & 0 & -\xi & 0 & -\xi S \sigma S & k_{12} & 0 \\
0 & 0 & 0 & 0 & 0 & -\Psi S & 0 & k_{13} & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & k_{14} & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\sigma M & \mu M \\
\end{pmatrix},$$

where: $\Psi_J = (1 - \varepsilon J) \sigma J$, $\Psi_A = (1 - \varepsilon A) \sigma A$, $\Psi_S = (1 - \varepsilon S) \sigma S$, $k_2 = \alpha + \sigma J + \mu J$, $k_3 = \alpha + \gamma A J + \mu J$, $k_4 = \alpha + \gamma S J + \mu J$, $k_7 = \xi + \sigma A + \mu A$, $k_8 = \xi + \gamma A A + \mu A$, $k_9 = \xi + \gamma S A + \mu A$, $k_{11} = \sigma S + \mu S$, $k_{12} = \gamma A S + \mu S$, $k_{13} = \gamma S S + \mu S$, $k_{14} = \sigma M + \mu M$.

It follows that the basic reproduction number of the age-structured Chikungunya model (1)-(2), is given by:

$$R_0 = \rho(FV^{-1}) = \sqrt{(R_J + R_A + R_S)R_M},$$

where $\rho$ is the spectral radius and
\[ \mathcal{R}_J = \beta J b_M S J^* \left[ k_{11} k_{12} k_{13} \sigma J k_{7} k_{8} k_{9} \left( (1 - \varepsilon_J) k_3 + \varepsilon_J k_4 \right) + \alpha k_{11} k_{12} k_{13} (1 - \varepsilon_J) k_{3} k_{8} + \varepsilon_J k_{9} k_{4} \right] + \sigma A k_{4} k_{3} \left( (1 - \varepsilon_A) k_{8} + \varepsilon_A k_{9} \right) + \xi \alpha \left( (1 - \varepsilon_J) k_{3} k_{8} k_{12} + \varepsilon_J k_{4} k_{9} k_{13} \right) + \sigma_A k_{3} k_{4} k_{11} \left( (1 - \varepsilon_A) k_{8} k_{12} + \varepsilon_A k_{9} k_{13} \right) + \varepsilon_A k_{9} k_{13} + \sigma_S k_{3} k_{4} k_{8} k_{9} \left( (1 - \varepsilon_S) k_{12} + \varepsilon_S k_{13} \right) \right], \\
\mathcal{R}_A = \beta A b_M S A^* k_{2} k_{3} k_{4} \left[ \sigma A k_{12} k_{11} k_{13} \left( (1 - \varepsilon_A) k_{8} + \varepsilon_A k_{9} \right) + \xi \left( (1 - \varepsilon_A) k_{3} k_{8} k_{12} + \varepsilon_A k_{9} k_{13} \right) + \sigma_S k_{8} k_{9} \left( (1 - \varepsilon_S) k_{12} + \varepsilon_S k_{13} \right) \right], \\
\mathcal{R}_S = \beta S b_M S _{S}^* k_{2} k_{3} k_{4} k_{7} k_{9} \left( (1 - \varepsilon_S) k_{12} + k_{13} \varepsilon_S \right), \\
\mathcal{R}_M = \sigma M b_S S _{S}^* \mu_H b_M / \left( k_{3} k_{4} k_{8} k_{7} k_{9} k_{11} k_{12} k_{13} k_{14} \mu_M \pi^2 \right). \\
\]

**Figure 2.** Simulation of the age-structured Chikungunya model \(^1-^2\) as a function of time when \( \mathcal{R}_0 < 1 \). (a) Total number of infectious (asymptomatic and symptomatic) juveniles (b) Total number of infectious (asymptomatic and symptomatic) adults (c) Total number of infectious (asymptomatic and symptomatic) seniors (d) Total number of infectious mosquitoes. Parameter values used are as given in Table 2.

Furthermore, the expression \( \mathcal{R}_J \) is the number of secondary infections among the juveniles by one infectious mosquito, \( \mathcal{R}_A \) is the number of secondary infections in the adults population by the introduction of one infectious mosquito, \( \mathcal{R}_S \) is the number of secondary infections among the seniors as a result of one infectious mosquito, and lastly \( \mathcal{R}_M \) is the number of secondary infections in the mosquitoes population.
resulting from a newly introduced infectious juvenile, adult and senior respectively. Hence, using Theorem 2 in [51], the following result is established.

**Lemma 3.3.** The disease-free equilibrium ($E_0$) of the age-structured Chikungunya model (1)-(2) is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

The basic reproductive number $R_0$ is defined as the average number of new infections that result from one infectious individual in a population that is fully susceptible [5, 13, 22, 51]. The epidemiological significance of Lemma 3.3 is that, Chikungunya will be eliminated from the community if the reproduction number ($R_0$) can be brought to (and maintained at) a value less than unity. Figures 2 shows convergence of the solutions of the model (1)-(2) to the DFE ($E_0$) for the case when $R_0 < 1$ (in accordance with Lemma 3.3).

**Theorem 3.4.** The disease-free equilibrium ($E_0$), of the age-structured Chikungunya model (1)-(2), is globally asymptotically stable (GAS) whenever $R_0 \leq 1$.

The proof of Theorem 3.4 is given in [1].

Let $E_1 = (S^*_J, E^*_J, I^*_J, S^*_A, I^*_A, S^*_M, E^*_M, I^*_M)$ be an arbitrary endemic equilibrium of model (1)-(2).

**Lemma 3.5.** The age-structured Chikungunya model (1)-(2) has a unique positive endemic equilibrium whenever $R_0 > 1$.

The proof of Lemma 3.5 is given in [1]. Numerical simulations of the age-structured Chikungunya model (1)-(2), depicted in Figure 3, show convergence to an endemic equilibrium when $R_0 > 1$ (suggesting that the unique EEP of the model (1)-(2) is asymptotically stable when it exists).

### 3.3. Sensitivity analysis

Sensitivity analysis [6, 29, 32] is carried out, on the parameters of the model (1)-(2), to determine which of the parameters have the most significant impact on the outcome of the numerical simulations of the model. Figure 4(a) depicts the partial rank correlation coefficient (PRCC) values for each parameter of the models, using the ranges and baseline values tabulated in Table 2 (with the basic reproduction numbers, $R_0$, as the response function), from which it follows that the parameters that have the most influence on Chikungunya transmission dynamics are the mosquito biting rate ($b_M$), the transmission probability per contact in mosquitoes ($\beta_M$) and in humans ($\beta_S$), mosquito recruitment rate ($\pi_M$) and the death rate of the mosquitoes ($\mu_M$). It is interesting to note from Figure 4(a) that the transmission probability per contact in juvenile and adult ($\beta_J$ and $\beta_A$) is not as significant as that of the seniors.

Thus, this study identifies the most important parameters that drive the transmission mechanism of the disease. The identification of these key parameters is vital to the formulation of effective control strategies for combating the spread of the disease. In other words, the results of this sensitivity analysis suggest that a strategy that reduces the mosquito biting rate (reduce $b_M$), the mosquito recruitment rate (reduce $\pi_M$), the transmission probability per contact in mosquitoes (reduce $\beta_M$) and in humans (reduce $\beta_S$) and increases the death rate of the mosquito (increase $\mu_M$) will effectively curtail the spread of Chikungunya virus in the community.
In summary, the sensitivity analysis of the age-structured Chikungunya model shows that the dominant parameters are the mosquito biting rate ($b_M$), the transmission probability per contact in mosquitoes ($\beta_M$) and in humans ($\beta_S$), mosquito recruitment rate ($\pi_M$) and the natural death rate ($\mu_M$).

4. The optimal control problems. Introducing controls impacting the mosquito biting rate, the transmission probability, mosquito recruitment and death rates, and human recovery rate, the age-structured Chikungunya transmission model (1)-(2) becomes:

\[
\frac{dS_J}{dt} = \pi_J - \frac{(1-u_P)\beta_J b_M S_J I_M}{N_H} - \alpha S_J - \mu_J S_J \\
\frac{dE_J}{dt} = \frac{(1-u_P)\beta_J b_M S_J I_M}{N_H} - \alpha E_J - (\sigma_J + \mu_J) E_J \\
\frac{dI_{AJ}}{dt} = \varepsilon_J \sigma_J E_J - \alpha I_{AJ} - (u_J \gamma_{AJ} + \mu_J) I_{AJ}
\]
Figure 4. PRCC values for the age-structured Chikungunya model (1)-(2), using the basic reproduction number ($R_0$) as the response function. Parameter values (baseline) and ranges used are as given in Table 2.

\[
\begin{align*}
\frac{dI_{SJ}}{dt} &= (1 - \varepsilon_J)\sigma_J E_J - \alpha I_{SJ} - (u_J\gamma_{SJ} + \mu_J)I_{SJ} \\
\frac{dR_J}{dt} &= u_J\gamma_{AJ} I_{AJ} + u_J\gamma_{SJ} I_{SJ} - \alpha R_J - \mu_J R_J \\
\frac{dS_A}{dt} &= \alpha S_J - \frac{(1 - u_P)\beta_A b_M S_A I_M}{N_H} - \xi S_A - \mu_A S_A \\
\frac{dE_A}{dt} &= \alpha E_J + \frac{(1 - u_P)\beta_A b_M S_A I_M}{N_H} - \xi E_A - (\sigma_A + \mu_A)E_A \\
\frac{dI_{AA}}{dt} &= \alpha I_{AJ} + \varepsilon_A \sigma_A E_A - \xi I_{AA} - (u_A\gamma_{AA} + \mu_A)I_{AA} \\
\frac{dI_{SA}}{dt} &= \alpha I_{SJ} + (1 - \varepsilon_A)\sigma_A E_A - \xi I_{SA} - (u_A\gamma_{SA} + \mu_A)I_{SA} \\
\frac{dR_A}{dt} &= \alpha R_J + u_A\gamma_{AA} I_{AA} + u_A\gamma_{SA} I_{SA} - \xi R_A - \mu_A R_A
\end{align*}
\]
\[
\begin{align*}
\frac{dS}{dt} &= \xi S_A - \frac{(1-u_P)\beta b m S_I M}{N_H} - \mu S S \\
\frac{dE}{dt} &= \xi E_A + \frac{(1-u_P)\beta b m S_I M}{N_H} - (\sigma S + \mu S)E_S \\
\frac{dI_A}{dt} &= \xi I_A + \varepsilon S \sigma S E_S - (u_S \gamma_{AS} + \mu_S)I_A S \\
\frac{dI_S}{dt} &= \xi I_S + (1-\varepsilon S)\sigma S E_S - (u_S \gamma_{SS} + \mu_S)I_S S \\
\frac{dR}{dt} &= \xi R_A + u_S \gamma_{AS} I_A S + u_S \gamma_{SS} I_S S - \mu S R_S \\
\frac{dS_M}{dt} &= \pi_M - (1-u_P)\beta b M \left[ \frac{I_A J + I_S J + I_A A + I_S A + I_A S + I_S S}{N_H} \right] S_M \\
&\quad - \mu M S_M - u M S_M \\
\frac{dE_M}{dt} &= (1-u_P)\beta b M \left[ \frac{I_A J + I_S J + I_A A + I_S A + I_A S + I_S S}{N_H} \right] S_M \\
&\quad - (\sigma M + \mu M)E_M - u M R_M \\
\frac{dI_M}{dt} &= \sigma M E_M - \mu M I_M - u M I_M.
\end{align*}
\]

Table 2. Parameters values of the age-structured Chikungunya model (1)-(2)
The problem here is to minimize the cost function defined as

\[
J(u_*, u_+; u_0) = \int_0^{t_f} \left\{ A_1(I_{AJ} + I_{SJ} + I_{AA} + I_{SA} + I_{AS} + I_{SS} + I_M) + A_2[u_J I_{AJ} + u_J I_{SJ} + u_A I_{AA} + u_A I_{SA} + u_S I_{SS} + u_S I_{SB}] + u_S I_{SS} + u_M(S_M + E_M + I_M) + C_1 u_P^2 + C_2 u_A^2 + C_3 u_A^2 + C_4 u_S^2 + C_5 u_M^2 \right\} dt
\]

subject to the differential equations (3)-(4), where \( t_f \) is the final time. This performance specification involves the numbers of infected humans and mosquitoes, along with the cost of applying the controls \( (u_P(t), u_J(t), u_A(t), u_S(t) \) and \( u_M(t)) \). In this paper, a quadratic objective functional is implemented for measuring the control cost, such a cost has been frequently used \[23, 24, 25, 26, 28, 55\]. The quintuple \((u_P(t), u_J(t), u_A(t), u_S(t) \) and \( u_M(t)) \) are bounded, Lebesgue integrable functions \[24, 56\]. And we seek to find optimal controls \( u_+^*, u_+^*, u_A^*, u_S^* \) and \( u_M^* \), such that

\[
J(u_+^*, u_+^*, u_A^*, u_S^*, u_M^*) = \min_{u} \{ J(u_P, u_J, u_A, u_S, u_M) \}
\]

where the control set,

\[
U = \{(u_P(t), u_J(t), u_A(t), u_S(t), u_M(t)), u_i: [0, t_f] \rightarrow [a_i, b_i], i = 1, \cdots, 5, \text{ is Lebesgue measurable}\}, \quad 0 \leq a_i < b_i.
\]

**Characterization of optimal controls.** The necessary conditions that an optimal control quintuple must satisfy come from the Pontryagin’s Maximum Principle \[42\]. This principle converts (3)-(4) and (5) into a problem of minimizing pointwise a Hamiltonian \( H \), with respect to the controls \((u_P, u_J, u_A, u_S, u_M) \). First we formulate the Hamiltonian from the cost functional (5) and the governing dynamics (3)-(4) to obtain the optimality conditions.

\[
H = A_1(I_{AJ} + I_{SJ} + I_{AA} + I_{SA} + I_{AS} + I_{SS} + I_M) + A_2[u_J I_{AJ} + u_J I_{SJ} + u_A I_{AA} + u_A I_{SA} + u_S I_{SS} + u_S I_{SB}] + u_S I_{SS} + u_M(S_M + E_M + I_M) + C_1 u_P^2 + C_2 u_A^2 + C_3 u_A^2 + C_4 u_S^2 + C_5 u_M^2 + \lambda_{S_J}(\tau - \lambda_J S_J - k_i S_J) + \lambda_{E_J}(\lambda_J S_J - k_2 E_J) + \lambda_{I_{AJ}}(\varepsilon_1 \sigma_J E_J - k_3 I_{AJ} - u_J I_{AJ}) + \lambda_{I_{SJ}}[(1 - \varepsilon_1) \sigma_J E_J - k_4 I_{SJ} - u_J I_{SJ}] + \lambda_{R_J}(u_J I_{AJ} + u_J I_{SJ} - k_5 R_J) + \lambda_{S_A}(\alpha S_J - \lambda_A S_A - k_6 S_A) + \lambda_{E_A}(\alpha E_J + \lambda_A S_A - k_7 E_A) + \lambda_{I_{AA}}(\alpha I_{AJ} + \varepsilon_2 \sigma_A E_A - k_8 I_{AA} - u_A I_{AA}) + \lambda_{I_{SA}}(\alpha I_{AJ} + (1 - \varepsilon_2) \sigma_A E_A - k_9 I_{SA} - u_A I_{SA}) + \lambda_{R_A}(\alpha R_J + u_A I_{AA} + u_A I_{SA} - k_10 R_A) + \lambda_{S_S}(S_A - \lambda_S S_S - \mu_M S_S) + \lambda_{E_S}(E_A + \lambda_S S_S - k_{11} E_S) + \lambda_{I_{AS}}(\xi I_{AA} + \varepsilon_3 \sigma_A E_S - k_{12} I_{AS} - u_S I_{AS}) + \lambda_{I_{SS}}(\xi I_{AA} + (1 - \varepsilon_3) \sigma_S E_S - k_{13} I_{SS} - u_S I_{SS}) + \lambda_{R_S}(\xi R_A + u_S I_{AS} + u_S I_{SS} - \mu_R R_S) + \lambda_{S_M}(\pi_M - \lambda_M S_M - \mu_M S_M - u_M S_M) + \lambda_{E_M}(\lambda_M E_M - k_{14} E_M - u_M E_M) + \lambda_{I_{M}}(\sigma_M E_M - \mu_M I_M - u_M I_M)
\]
where $\lambda_{S_J}, \lambda_{I_{AJ}}, \lambda_{I_{SJ}}, \lambda_{R_J}, \lambda_{S_A}, \lambda_{I_{AA}}, \lambda_{I_{SA}}, \lambda_{R_A}, \lambda_{S_S}, \lambda_{S_M}, \lambda_{I_M}$ are the associated adjoints for the states $S_J, E_J, I_{AJ}, I_{SJ}, R_J, S_A, E_A, I_{AA}, I_{SA}, R_A, S_S, E_S, I_{AS}, I_{SS}, R_S, S_M, E_M, I_M$. The system of adjoint equations is found by taking the appropriate partial derivatives of the Hamiltonian (7) with respect to the associated state and control variables.

**Theorem 4.1.** Given an optimal control quintuple $(u^*_p, u^*_j, u^*_A, u^*_S, u^*_M)$ and solutions $S_J^*, E_J^*, I_{AJ}^*, I_{SJ}^*, R_J^*, S_A^*, E_A^*, I_{AA}^*, I_{SA}^*, R_A^*, S_S^*, E_S^*, I_{AS}^*, I_{SS}^*, R_S^*, S_M^*, E_M^*, I_M^*$ of the corresponding state system (3)-(4) that minimizes $J(u^*_p, u^*_j, u^*_A, u^*_S, u^*_M)$ over $\mathcal{U}$. Then there exists adjoint variables $\lambda_{S_J}, \lambda_{I_{AJ}}, \lambda_{I_{SJ}}, \lambda_{R_J}, \lambda_{S_A}, \lambda_{I_{AA}}, \lambda_{I_{SA}}, \lambda_{R_A}, \lambda_{S_S}, \lambda_{I_{AS}}, \lambda_{I_{SS}}, \lambda_{R_S}, \lambda_{S_M}, \lambda_{I_M}$ satisfying

$$-\frac{d\lambda_i}{dt} = \frac{\partial H}{\partial i}$$

and with transversality conditions

$$\lambda_i(t_f) = 0, \text{ where } i = S_J, E_J, I_{AJ}, I_{SJ}, R_J, S_A, E_A, I_{AA}, I_{SA}, R_A, S_S, E_S, I_{AS}, I_{SS}, R_S, S_M, E_M, I_M.$$  

Furthermore, the control quintuple $(u^*_p, u^*_j, u^*_A, u^*_S, u^*_M)$ are given as

$$u^*_p = \min \left\{ b_1, \max \left[ a_1, b_H((\lambda_{E_J} - \lambda_{S_J})\beta_J I_MS_J + (\lambda_{E_A} - \lambda_{S_A})\beta_A I_MS_A + (\lambda_{E_S} - \lambda_{S_S})\beta_S I_MS_S + \beta_M S_M(\lambda_{E_M} - \lambda_{S_M})(I_{AJ} + I_{SJ} + I_{AA} + I_{SA} + I_{AS} + I_{SS})/(2C_1 N_H) \right] \right\},$$

$$u^*_j = \min \left\{ b_2, \max \left[ a_2, -[A_2(I_{AJ} + I_{SJ}) - \lambda_{I_{AJ}} I_{AJ} - \lambda_{I_{SJ}} I_{SJ} + \lambda_{R_J} I_{AJ} + \lambda_{R_J} I_{SJ}]/(2C_2) \right] \right\},$$

$$u^*_A = \min \left\{ b_3, \max \left[ a_3, -[A_2(I_{AA} + I_{SA}) - \lambda_{I_{AA}} I_{AA} - \lambda_{I_{SA}} I_{SA} + \lambda_{R_A} I_{AA} + \lambda_{R_A} I_{SA}]/(2C_3) \right] \right\},$$

$$u^*_S = \min \left\{ b_4, \max \left[ a_4, -[A_2(I_{AS} + I_{SS}) - \lambda_{I_{AS}} I_{AS} - \lambda_{I_{SS}} I_{SS} + \lambda_{R_S} I_{AS} + \lambda_{R_S} I_{SS}]/(2C_4) \right] \right\},$$

$$u^*_M = \min \left\{ b_5, \max \left[ a_5, -[A_2(S_M + E_M + I_M) - \lambda_{E_M} E_M - \lambda_{S_M} S_M - \lambda_{I_M} I_M]/(2C_5) \right] \right\}.$$
obtained by the differentiation of the Hamiltonian function, evaluated at the optimal controls. Thus, the adjoint system can be written as,

\[
\begin{align*}
-\frac{d\lambda_{S_j}}{dt} &= \frac{\partial H}{\partial S_j}, \quad \lambda_{S_j}(t_f) = 0, \\
\ldots \\
-\frac{d\lambda_{S_A}}{dt} &= \frac{\partial H}{\partial S_A}, \quad \lambda_{S_A}(t_f) = 0, \\
\ldots \\
-\frac{d\lambda_{S_S}}{dt} &= \frac{\partial H}{\partial S_S}, \quad \lambda_{S_S}(t_f) = 0, \\
\ldots \\
-\frac{d\lambda_{S_M}}{dt} &= \frac{\partial H}{\partial S_M}, \quad \lambda_{S_M}(t_f) = 0, \\
\ldots \\
-\frac{d\lambda_{I_M}}{dt} &= \frac{\partial H}{\partial I_M}, \quad \lambda_{I_M}(t_f) = 0,
\end{align*}
\]

evaluated at the optimal controls and corresponding state variables, results in the stated adjoint system (8) and (9). Furthermore, differentiating the Hamiltonian function with respect to the control variables in the interior of the control set and then solving for controls \((u^*_P, u^*_J, u^*_A, u^*_S, u^*_M)\) result in the optimality conditions given as

\[
\begin{align*}
u^*_P &= b_P[\beta_J I_M S_J (\lambda_{E_J} - \lambda_{S_J}) + \beta_A I_M S_A (\lambda_{E_A} - \lambda_{S_A}) + \beta_S I_M S_S (\lambda_{E_S} - \lambda_{S_S}) \\
&\quad + \beta_M S_M (\lambda_{E_M} - \lambda_{S_M}) (I_{A_J} + I_{S_J} + I_{S_A} + I_{AS} + I_{SS} + I_{AA})]/(2N_H C_1), \\
u^*_J &= -[A_2 (I_{A_J} + I_{S_J}) - \lambda_{I_{A_J}} I_{A_J} - \lambda_{I_{S_J}} I_{S_J} + \lambda_{R_{A_J}} I_{A_J} + \lambda_{R_{S_J}} I_{S_J}]/2C_2, \\
u^*_A &= -[A_2 (I_{A_A} + I_{S_A}) - \lambda_{I_{S_A}} I_{S_A} - \lambda_{R_{A_A}} I_{A_A} + \lambda_{R_{S_A}} I_{S_A}]/2C_3, \\
u^*_S &= -[A_2 (I_{A_S} + I_{S_S}) - \lambda_{I_{A_S}} I_{A_S} - \lambda_{I_{S_S}} I_{S_S} + \lambda_{R_{A_S}} I_{A_S} + \lambda_{R_{S_S}} I_{S_S}]/2C_4, \\
u^*_M &= -[A_2 (S_M + E_M + I_M) - \lambda_{E_M} E_M - \lambda_{S_M} S_M - \lambda_{I_M} I_M]/2C_5.
\end{align*}
\]

Using the bounds on the controls, the characterization (10) can be derived. \(\square\)

**Remark 1.** Due to the a priori boundedness of the state and adjoint functions and the resulting Lipschitz structure of the ODE’s, the uniqueness of the optimal control for small time \((t_f)\) was obtained. The uniqueness of the optimal control quintuple follows from the uniqueness of the optimality system, which consists of (3)-(4) and (8), (9) with characterization (10). The restriction on the length of the time interval is to guarantee the uniqueness of the optimality system, the smallness in the length of time is due to the opposite time orientations of (3)-(4), (8), and (9); the state problem has initial values, and the adjoint problem has final values. This restriction is very common in control problems (see \([2, 3, 4, 23, 24, 25, 26]\)).

Next, we discuss the numerical solutions of the optimality system, the corresponding optimal control and the interpretations from various cases.
5. **Numerical results.** The following algorithm was used to compute the optimal controls and state values using a Runge-Kutta method of the fourth order. First, an initial estimate for the control quintuple is made. Then the state variables are solved forward in time using the dynamics (3)-(4). The results obtained for the state variables are plugged into the adjoint equations (8). These adjoint equations with given final conditions (10) are then solved backward in time, employing the backward fourth order Runge-Kutta method. Both the state and adjoint values are then used to update the control quintuple, and the process is repeated until the current state, adjoint, and controls values converge sufficiently [28].

To illustrate the optimal control strategies, the following values were taken for the initial conditions:

- \( S_J(0) = 929 \)
- \( E_J(0) = 24 \)
- \( I_{AJ}(0) = 25 \)
- \( I_{SJ}(0) = 14 \)
- \( R_J(0) = 9 \)
- \( S_A(0) = 1529 \)
- \( E_A(0) = 224 \)
- \( I_{AA}(0) = 125 \)
- \( I_{SA}(0) = 114 \)
- \( R_A(0) = 29 \)
- \( S_S(0) = 529 \)
- \( E_S(0) = 24 \)
- \( I_{AS}(0) = 35 \)
- \( I_{SS}(0) = 24 \)
- \( R_S(0) = 19 \)
- \( S_M(0) = 1000 \)
- \( E_M(0) = 150 \)
- \( I_M(0) = 125 \)

For the weight factors we choose \( A_1 = 100 \), \( A_2 = 100 \), \( C_1 = C_2 = C_3 = C_4 = C_5 = 1 \). It should be pointed out that the weights in the simulations here are only of theoretical sense to illustrate the control strategies proposed in this paper. Using parameter values in Table 2, the reproduction numbers is given as \( R_0 = 3.58 \), thus indicating that the disease is endemic in the population.

**Figure 5.** Simulation of the age-structured Chikungunya model (3)-(4) as a function of time without control and with optimal control for:

- (a). Total number of infected juvenile;
- (b). Total number of infected adult;
- (c). Total number of infected seniors;
- (d). Total number of infected mosquitoes.
The results of the optimal control simulations of the age-structured Chikungunya model (3)-(4) are depicted in Figures 5(a) - 5(d). From Figure 5(a) it is observed that the total number of infected juveniles is reduced considerably with the applications of the optimal controls compared to the total number of infected in the absence of controls. The total number of infected adults and seniors are shown in Figures 5(b) and 5(c) and the total number of infected mosquitoes are depicted in Figure 5(d). There are more infected in the absence of controls compared to the total number of infected with the applications of the optimal controls. The corresponding time-dependent control quintuple \((u_J(t), u_A(t), u_S(t), u_P(t) \text{ and } u_M(t))\) are depicted in Figures 6(a)-6(e). The juveniles and seniors time-dependent controls \(u_J(t)\) and \(u_S(t)\) are observed to be at the upper bound set at unity for about 20 days and then gradually reduced till the end of the simulation period. The adult time-dependent control \(u_A(t)\) is at the upper bound for about 25 days, while the time-dependent control \(u_P(t)\) on personal protection is at the upper bound for about 18 days and the mosquito adulticiding time-dependent control \(u_M(t)\) is at the upper bound for about 10 days. These results suggest that during an outbreak, its optimal to treat the adult for a longer period than the juveniles and seniors. The results also suggest that mosquito adulticiding and use of personal-protection should be carried out only for a short period of time and then turned off.

In summary, numerical simulations of the age-structured Chikungunya control model (3)-(4) show that Chikungunya can be reduced in the community by the application of time dependent control quintuple \((u_J(t), u_A(t), u_S(t), u_P(t) \text{ and } u_M(t))\).

6. **Cost-effectiveness analysis.** The benefits associated with health intervention(s) or strategy (strategies) such as treatment, screening, vaccination or educational intervention are evaluated using cost-effectiveness analysis, so as to justify the costs associated with the strategy (strategies) [2, 7, 19, 21, 36, 39].

**Incremental cost-effectiveness ratio.** The most cost effective strategy to use in the control of Chikungunya in the population is determine using cost-effectiveness analysis (using as control interventions personal protection only, treatment of infected individuals only, adulticiding only and the combination of personal protection, treatment of infected humans and adulticiding). This is obtained by calculating the incremental cost-effectiveness ratio (ICER) which is described as the additional cost per additional health outcome; this is achieved by comparing the differences between the costs and health outcomes of these interventions. When comparing two or more competing intervention strategies incrementally, one intervention is compared with the next-less-effective alternative. The ICER numerator includes the differences in intervention costs, averted disease costs, costs of prevented cases and averted productivity losses if applicable. The ICER denominator is the differences in health outcomes (e.g. number of susceptibility cases prevented, the total number of infections averted; the number of infection averted is the difference between the total infectious individuals in the absence of control and the total infectious individuals in the presence of control). The costs of the controls are assumed to be directly proportional to the number of controls deployed.

To access the most cost-effective strategy to use in the control of Chikungunya in the population, mono-control strategies are first used in the model simulation, and the results are arranged in increasing order of effectiveness in averting infection, the control strategies are then ranked. The control considered are interventions involving personal protection only (Strategy A), treatment of infected individuals
Figure 6. The optimal controls of the age-structured Chikungunya model (3)-(4) for: (a). Juvenile treatment; (b). Adult treatment; (c). Seniors treatment; (d). Personal protection control; (e). Mosquitoes adulticiding control.

only (Strategy B) and adulticiding only (Strategy C). Figures 7(a) - 7(d) depict the result of the simulation of the age-structured Chikungunya model (3)-(4) as a function of time using strategies A, B and C for a total number of infected juvenile, the total number of infected adult, the total number of infected seniors and the total number of infected mosquitoes. The results of the corresponding optimal controls are depicted in Figures 8(a) - 8(e) for juvenile treatment, adult treatment, seniors treatment, personal protection control and mosquitoes adulticiding controls. The results from these simulations are arranged in increasing order of effectiveness in
averting infection, and the ranking of the control strategies based on the ICER is given in Table 3.

![Graphs showing infection dynamics](image)

**Figure 7.** Simulation of the age-structured Chikungunya model (3)-(4) as a function of time using strategies A, B and C for: (a). Total number of infected juvenile; (b). Total number of infected adult; (c). Total number of infected seniors; (d). Total number of infected mosquitoes.

| Strategies | Total infection averted | Total Cost | ICER    |
|------------|------------------------|------------|---------|
| Strategy C | $2.4390 \times 10^6$   | $9.5014 \times 10^7$ | 38.1361 |
| Strategy A | $2.7536 \times 10^6$   | $6.5306 \times 10^7$ | −88.0737 |
| Strategy B | $3.3176 \times 10^6$   | $2.2384 \times 10^7$ | −76.1028 |

**Table 3.** Incremental cost-effectiveness ratio in increasing order of total infection averted.

The ICER is obtained by the following computation:
Figure 8. The optimal controls of the age-structured Chikungunya model (3)-(4) using strategies A, B and C for: (a) Juvenile treatment; (b) Adult treatment; (c) Seniors treatment; (d) Personal protection control; (e) Mosquitoes adulticiding control.

\[
\text{ICER(C)} = \frac{9.3014 \times 10^7}{2.4390 \times 10^6} = 38.1361
\]
\[
\text{ICER(A)} = \frac{6.5306 \times 10^7 - 9.3014 \times 10^7}{2.7536 \times 10^6 - 2.4390 \times 10^6} = -88.0737
\]
\[
\text{ICER(B)} = \frac{2.2384 \times 10^7 - 6.5306 \times 10^7}{3.3176 \times 10^6 - 2.7536 \times 10^6} = -76.1028
\]
Now, comparing ICER (C) and ICER (A) from Table 3, a cost saving of 0.0737 is observed for Strategy A over Strategy C. The lower ICER for Strategy A indicates that Strategy A is less dominated over C which is strongly dominated. That is, Strategy A is less costly and more effective than Strategy C which is more costly and less effective than Strategy A. Therefore, Strategy C is left out from the set of alternative control strategies, so it does not consume limited resources.

| Strategies | Total infection averted | Total Cost | ICER |
|------------|-------------------------|------------|------|
| Strategy A | $2.7536 \times 10^6$   | $6.5306 \times 10^7$ | 23.7166 |
| Strategy B | $3.3176 \times 10^6$   | $2.2384 \times 10^7$  | $-76.1028$ |

Table 4. Incremental cost-effectiveness ratio in increasing order of total infection averted.

The ICER in Table 4 is obtained as follows:

\[
\text{ICER(A)} = \frac{6.5306 \times 10^7}{2.7536 \times 10^6} = 23.7166
\]

\[
\text{ICER(B)} = \frac{2.2384 \times 10^7 - 6.5306 \times 10^7}{3.3176 \times 10^6 - 2.7536 \times 10^6} = -76.1028
\]

Comparing strategies A and B, a cost saving of 76.1028 for Strategy B over Strategy A is observed. The high ICER for Strategy A indicates that Strategy A is strongly dominated over Strategy B. That is, Strategy A is more costly and less effective than Strategy B. Hence, it can be concluded that Strategy B has the least ICER and therefore is more cost-effective than Strategy A.

Next, pairs of controls from a combination of two strategies are implemented at the same time in the model simulation in order to access the most cost-effective strategy to use in the control of Chikungunya in the population. These combinations of control strategies include interventions involving treatment of infected individuals and personal protection (Strategy D), treatment of infected individuals and adulticiding (Strategy E) and the combination of personal protection and adulticiding (Strategy F). Figures 9(a) - 9(d) depict the result of the simulation of the age-structured Chikungunya model (3)-(4) as a function of time using strategies D, E and F for the total number of infected juvenile, the total number of infected adult, the total number of infected seniors and the total number of infected mosquitoes. The results of the corresponding optimal controls are depicted in Figures 10(a) - 10(e) for juvenile treatment, adult treatment, seniors treatment, personal protection control and mosquitoes adulticiding controls.

Table 5 shows the arrangement of the simulation results in increasing order of effectiveness in averting infection and the ICER ranking of the control strategies. Following the ranking approach for the mono-control strategies, it follows that Strategy E with the least ICER value is the most cost effective strategy.

Next, we compare the most cost effective strategy obtained from the mono-control strategy (B), the paired control strategy (E) and the combination of the triple
strategy involving personal protection, treatment of infected humans and adulticiding (Strategy G). Figures 12(a) - 12(c) depict the results of the simulations of the age-structured Chikungunya model (3)-(4) as a function of time using strategies B, E and G for optimal controls for juvenile treatment, adult treatment, and seniors treatment. Figures 12(a) - 12(c) shows that in order for Strategy B (involving mono-control) to avert as much infection as we observed in Table 6, the controls need to be set at the upper bound of one for a much longer time compare to controls for Strategies E and G.

Observe in Table 6 that Strategy E has the least ICER value and is, therefore, the most cost effective strategy. And this is followed by Strategy G, then Strategy B. In other words, the paired-control strategy is more cost effect that the tripled-control strategy.

| Strategies | Total infection averted | Total Cost | ICER  |
|------------|------------------------|------------|-------|
| Strategy F | $2.7536 \times 10^6$   | $6.1476 \times 10^6$ | 22.32536 |
| Strategy E | $3.3444 \times 10^6$   | $3.3421 \times 10^6$ | $-98.30986$ |
| Strategy D | $3.3475 \times 10^6$   | $6.5525 \times 10^6$ | 1035.6129 |

Table 5. Incremental cost-effectiveness ratio in increasing order of total infection averted.
Figure 10. The optimal controls of the age-structured Chikungunya model (3)-(4) using strategies D, E and F for: (a). Juvenile treatment; (b). Adult treatment; (c). Seniors treatment; (d). Personal protection control; (e). Mosquitoes adulticiding control.

In summary, the mono-control strategy (Strategy B) has the least ICER and therefore is most cost-effective of all the mono-strategies. With paired-control strategies, the strategy involving treatment of infected individuals and mosquitoes adulticiding (Strategy E) is the most cost effective strategy of all the paired-control strategies with the least ICER value. However, comparison of these strategies (mono-and paired-control) with the tripled-control interventions involving all control strategies (personal protection, treatment of infected humans and mosquitoes adulticiding, i.e., Strategy G) indicate that Strategy E is the most cost effective
Table 6. Incremental cost-effectiveness ratio in increasing order of total infection averted.

| Strategies   | Total infection averted | Total Cost | ICER       |
|--------------|-------------------------|------------|------------|
| Strategy B   | $3.3176 \times 10^6$   | $2.2384 \times 10^6$ | 6.7470     |
| Strategy E   | $3.3444 \times 10^6$   | $3.3421 \times 10^6$ | $-710.5187$ |
| Strategy G   | $3.3475 \times 10^6$   | $2.7131 \times 10^6$ | $-202.9032$ |

Furthermore, this results (in terms of cost effectiveness) suggest that the paired-control strategy is cheaper to implement than the mono- and tripled-control strategies. Further, the result suggests that the paired-control strategy is just as good as the tripled-control strategy in terms of the infection averted. These control strategies emphasize the importance of treating the infected humans and coupling this with mosquito adulticiding.

Figure 11. Simulation of the age-structured Chikungunya model (3)-(4) as a function of time using strategies B, E and G for: (a). Total number of infected juvenile; (b). Total number of infected adult; (c). Total number of infected seniors; (d). Total number of infected mosquitoes.

7. Conclusion. In this paper, a system of ordinary differential equations for an age structure transmission dynamics of Chikungunya virus is formulated and analyzed.
Some of the theoretical and epidemiological findings of this study are summarized below:

(i). The model (1) is locally and globally asymptotically stable (LAS) when $R_0 < 1$ and unstable when $R_0 > 1$;

(ii). The sensitivity analysis of the model shows that the dominant parameters are the mosquito biting rate ($b_M$), the transmission probability per contact in mosquitoes ($\beta_M$) and in humans ($\beta_S$), mosquito recruitment rate ($\pi_M$) and the natural death rate of the mosquitoes ($\mu_M$);
Numerical simulations of the age-structured Chikungunya control model \([3]-[4]\) show that Chikungunya can be reduced in the community by the application of time-dependent controls.

Using mono-control strategy, involving treatment of infected individuals (Strategy B) is the most cost-effective of this category; with pairs of control strategies, the control pairs involving treatment of infected individuals and mosquitoes adulticiding (Strategy E) is the most cost effective strategy of its category and incidentally, is more cost effective than using the triple control strategy which includes personal protection, treatment of infected humans and mosquitoes adulticiding (Strategy G).

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E-mail address: fbagusto@gmail.com