Rwanda Journal of Engineering, Science, Technology and Environment, Volume 4, Issue 1, June 2021
eISSN: 2617-233X | print ISSN: 2617-2321

Control measures of malaria transmission in Rwanda based on SEIR-SEI mathematical model

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DOI: 10.4314/rjeste.v4i1.9
https://dx.doi.org/10.4314/rjeste.v4i1.9

Abstract

This research paper investigated the dynamics of malaria transmission in Rwanda using the nonlinear forces of infections which are included in SEIR-SEI mathematical model for human and mosquito populations. The mathematical modeling of malaria studies the interaction among the human and mosquito populations in controlling malaria transmission and eventually eliminating malaria infection. This work investigates the optimal control strategies for minimizing the rate of malaria transmission by applying three control variables through Caputo fractional derivative. The optimal control problems for malaria model found the control parameters which minimize infection. The numerical simulation showed that the number of exposed and infected people and mosquito population are decreased due to the control strategies. Finally, this work found out that the transmission of malaria in Rwanda can be minimized by using the combination of controls like Insecticide Treated bed Nets (ITNs), Indoor Residual Spray (IRS) and Artemisinin based Combination Therapies (ACTs).

Keywords: Mathematical model, malaria, force of infection, reproduction number, Caputo fractional derivative, optimal control and numerical simulation.

1. Introduction

Malaria is a contagious disease caused by Plasmodium. The dynamics of malaria disease can be started from humans or mosquitoes. In the world, the disease is widespread in the most region such as Sub-Saharan Africa, Latin America and Asia [8]. In 2015, the World Health

Organization (WHO) reported 214 million cases of malaria and about 438 thousands resulted into deaths [14]. In fact, the disease treatment cost is heavy to poor countries. Even if malaria has been investigated for many years, it is still one of the major public health problem in the most countries where in widespread regions, pregnant women and children under five years old have a big number of malaria death [5].

In Rwanda, malaria is considered as a seasonal disease and environment related, where the Eastern region is more epidemic prone than other provinces. Malaria is one of the biggest health problem to be studied by both researchers and which the Government in Rwanda should mind [2]. In fact, the rate of malaria transmission increases during rainy seasons. Between 2012 to 2016, malaria incidence increased every year in Rwanda from 4.8% in 2012 to 40.3% in 2016 [14]. Malaria is still one of the biggest health issues in the society today, thus the epidemiologists and others are still using more effort in understanding and controlling the dynamics of malaria [5].

In 2017, the Eastern and Southern Provinces of Rwanda, were considered as the regions where malaria was most predominant. In these provinces, there are five districts, namely Bugesera, Gisagara, Gatsibo, Kirehe and Nyagatare, where malaria infection risk is highest [14].

The mathematical model is very important tool to find more information on transmission and control of infection disease [10]. In 1911, the study of malaria using mathematical model was started by Ronald Ross [9]. In 1957, Macdonald updated Ross's concept saying that, to minimize the number of mosquitoes was not enough in endemic region [3]. In 2019, Mojeeb AL et al. updated their SEIR-SEI model done in 2018 and they found that the use of the insecticide spray on the breeds grounds, treated infected individual and ITNs are the best combination in the reduction of mosquitoes [4].

In 2016, Okello Gabriel [7] found that IRS use and effort treatment are the best in endemic areas [7]. In 2007, C.E.G. Smith et al. defined a basic reproduction number as the number of secondary infections obtained from one primary infection into another susceptible. Population. The disease will continue in a population when $R_0 > 1$ otherwise it will disappear [12].

The Government of Rwanda got, in 2005, a donation from the US-Presidential Malaria Initiative (PMI) to minimize malaria deaths by using ITNs, prompt use of Artemisinin based Combination

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Therapies (ACTs) and IRS with insecticides. These involvements played a role in the reduction of malaria transmission [1].

The current aim of Rwanda National Malaria control strategic plan is to improve the healthiness of Rwandans by trying to eliminate malaria. Rwanda had adopted a strategy to realize malaria pre-eradication phase in 2017, with an ambitious target of reaching near zero deaths due to malaria [11]. In 2019, the goal of Rwanda Government was then to work with PMI which helped countries to further reduce the number of deaths and illness due to malaria, towards the goal of elimination in extended period [14].

Some researchers have been worked on the mathematical model about the control malaria transmission using SEIR-SEI model [4]. In [4], they applied the optimal control to SEIR-SEI model, then they found that malaria can be minimized in coming years. In Rwanda, the mathematical models of malaria dynamics are not frequently used, thus some people are still at risk of malaria even if there are many measures that have been taken to control it, due to the reliable information through mathematical models which are insufficient to bring malaria infection at the nearest of zero case.

This paper aims at analysis the role of controls measures of malaria transmission in Rwanda based on SEIR-SEI mathematical model and advice the policy makers to set a program that will reduce the infected individual and control disease from the country. It focuses on the study of the modified SEIR-SEI mathematical model that was done in [4] by introducing nonlinear saturating feature that inhibits the force of infection and determination of optimal controls measures through Caputo fractional derivative.

The next sections of this paper are arranged as follows: the section 2 presents the methods and material. Section 3 deals with qualitative study of mathematical model. The solution of optimal control is described in section 4. The section 5 covers the estimation of parameters. The section 6 presents the numerical test, while conclusion of the paper is finally drawn in section 7.

https://dx.doi.org/10.4314/rjeste.v4i1.9

2. Methods and material

2.1. Data set

The data help to estimate the parameters of the malaria model. Secondary data from malaria report for Rwanda were used [15]. In the US-PMI [13], the hot region of Rwanda where the mosquitoes are predominant were considered. Additionally, the data about Anopheles mosquitoes were collected in some sectors of Nyagatare, Bugesera, Kirehe and Ngoma districts in 2016, 2017 and 2018 by using human landing catch and pyrethrum spray catch. Referring to collected mosquitoes from these sectors, Enzyme-Linked Immunosorbent Assay (ELISA) test used in idendification of susceptible, exposed and infected mosquitoes, then their numbers was estimated per district.

2.2. Mathematical model formulation

Let us consider Susceptible humans (S_h), Exposed humans (E_h), Infected humans (I_h), and Recovered humans (R_h), Susceptible mosquitoes (S_m), Exposed mosquitoes (E_m), and Infected mosquitoes (I_m). The logistic function is used to model the variation of the nonlinear force of infection of malaria in human individual as

$$f_h(t) = \frac{N_h S_h(0)}{S_h(0) + (N_h - S_h(0))e^{-\alpha t}},$$

where N_h is a total human population and $S_h(0)$ is susceptible humans at initial time and α is positive number. $S_{N_h} = \frac{1}{f_h(t)}$ is a nonlinear saturating feature that inhibits the force of infection coming from infected mosquitoes to susceptible human. Similarly, the logistic function for mosquitoes is given by

$$f_m(t) = \frac{N_m S_m(0)}{S_m(0) + (N_m - S_m(0))e^{-\upsilon t}},$$

where N_m is a total mosquito population, $S_m(0)$ is susceptible mosquitoes and υ is positive coefficient. $S_{N_m} = \dfrac{1}{f_m(t)}$ is nonlinear saturating feature where the antibodies generate the antigens contacted from infected human at the rate. In line with this, a saturated force of infection from

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mosquito to the human of the form $b\beta_h S_h S_{N_h} I_m(t)$ was used, with b is the mosquito biting rate and β_h refers to the probability of biting by an infected mosquito. Considering a saturated force of infection from human to mosquito of the form $b\beta_m S_m S_{N_m} I_h(t)$, the parasite is transmitted to a susceptible mosquito at probability of biting β_m then, $\gamma_{k\tau} = \frac{ke^{-k\tau}}{1-e^{-k\tau}}$ is the rate of losing immunity with k is the rate of mean constant and partial immunity appears at an interval of τ units of time. λ_h and λ_m are recruitment rate for human and mosquito respectively. ρ_h is the rate of being recovered and δ_h is human death rate due to malaria infection. Humans and mosquitoes can be died at the natural death rates μ_h and μ_m respectively. η_h and η_m are the progression rates from E_h to I_h compartment and E_m to I_m compartment, respectively. The Figure 1 shows the schematic diagram of interaction between the seven compartments.

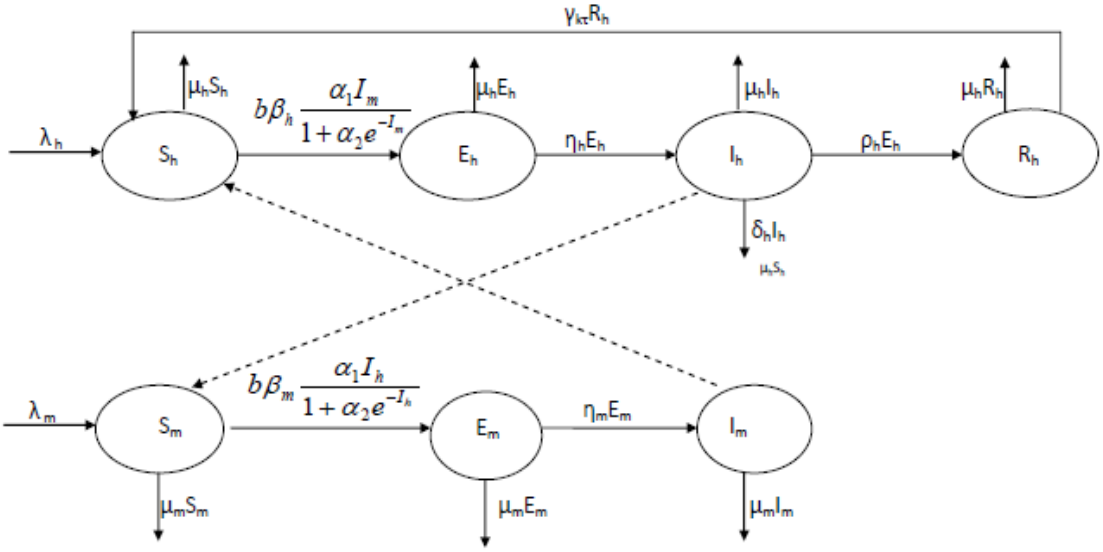

Fig. 1: Schematic diagram of malaria transmission

The following system of differential equations is obtained by applying all above assumptions.

https://dx.doi.org/10.4314/rjeste.v4i1.9

eISSN: 2617-233X | print ISSN: 2617-2321

$$\begin{cases} \frac{dS_h}{dt} = \lambda_h - b\beta_h S_h S_{N_h} I_m(t) - \mu_h S_h + \gamma_{k\tau} R_h, \\ \frac{dE_h}{dt} = b\beta_h S_h S_{N_h} I_m(t) - \left(\mu_h + \eta_h\right) E_h, \\ \frac{dI_h}{dt} = \eta_h E_h - \left(\mu_h + \delta_h + \rho_h\right) I_h, \\ \frac{dR_h}{dt} = \rho_h I_h - \left(\mu_h + \gamma_{k\tau}\right) R_h, \\ \frac{dS_m}{dt} = \lambda_m - b\beta_m S_m S_{N_m} I_h(t) - \mu_m S_m, \\ \frac{dE_m}{dt} = b\beta_m S_m S_{N_m} I_h(t) - \left(\mu_m + \eta_m\right) E_m, \\ \frac{dI_m}{dt} = \eta_m E_m - \mu_m I_m, \end{cases} \quad (1)$$

With $S_h(0) > 0\ E_h(0) \geq 0\ I_h(0) \geq 0\ R_h(0) \geq 0\ S_m(0) > 0\ E_m(0) \geq 0\ I_m(0) \geq 0$ are the initial conditions.

3. Qualitative study of mathematical model

We first focus on the positivity of solution of (1). Let us set

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t) \text{ and } N_m(t) = S_m(t) + E_m(t) + I_m(t),$$

be the total human and mosquito population size at time t respectively. We have

$$\frac{dN_h}{dt} = \frac{d}{dt}\left(S_h(t) + E_h(t) + I_h(t) + R_h(t)\right),$$

which can be written

$$\frac{dN_h}{dt} = \lambda_h - \mu_h S_h - \mu_h E_h - \mu_h I_h - \mu_h R_h - \delta_h I_h.$$

Then,

$$\frac{dN_h}{dt} = \lambda_h - \mu_h(S_h + E_h + I_h + R_h) - \delta_h I_h,$$

that is

$$\frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \delta_h I_h.$$

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Since N_h is constant, we get $\frac{dN_h}{dt} = 0$, and $\lambda_h - \mu_h N_h - \delta_h I_h = 0.$

The term $\delta_h I_h > 0$, we find that $\lambda_h - \mu_h N_h > 0$ which indicates that $N_h < \frac{\lambda_h}{\mu_h}$. Thus,

$$\lim_{t\to\infty} Sup(S_h + E_h + I_h + R_h) \le \frac{\lambda_h}{\mu_h}.$$

Taking the set for the individual population given by

$$\perp_h = \left\{(S_h,\ E_h,\ I_h,\ R_h):\ S_h + E_h + I_h + R_h \le \frac{\lambda_h}{\mu_h},\ S_h > 0,\ E_h \ge 0,\ I_h \ge 0,\ R_h \ge 0\right\}.$$

the state variables at any time are positive. Similarly, taking

$$\lim_{t\to\infty} Sup(S_m + E_m + I_m) \le \frac{\lambda_m}{\mu_m}.$$

the state variables are positive in

$$\perp_m = \left\{(S_m, E_m, I_m):\ S_m + E_m + I_m \le \frac{\lambda_m}{\mu_m}, S_m > 0, E_m \ge 0, I_m \ge 0\right\}.$$

Finally, we generalize the domain of positivity of the system (1) as follows

$$\perp = \left\{(S_h, E_h, I_h, R_h, S_m, E_m, I_m) \in \mathsf{R}_+^7\ :\ 0 \le N_h \le \frac{\lambda_h}{\mu_h}, 0 \le N_m \le \frac{\lambda_m}{\mu_m}\right\}.$$

3.1. Stability of disease free equilibrium

In this study, a disease free equilibrium (DFE) is defined as a steady state solution where the malaria infections do not exist in the population. In absence of the disease, the DFE

X_0 for SEIR-SEI model (1) is

$$X_0 = \left(S_h^0, E_h^0, I_h^0, R_h^0, S_m^0, E_m^0, I_m^0\right) = \left(\frac{\lambda_h}{\mu_h} 0,0,0, \frac{\lambda_m}{\mu_m}, 0,0\right).$$

The method of next generation matrix is used in computation of the basic reproductive number R_0 . Let

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$$\mathcal{F} = \begin{bmatrix} b\beta_h S_h S_{N_h} I_m \\ 0 \\ b\beta_m S_m S_{N_m} I_h \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad and \quad \mathcal{V} = \begin{bmatrix} (\mu_h + \eta_h) E_h \\ -\eta_h E_h + (\mu_h + \sigma_h + \rho_h) I_h \\ (\mu_m + \eta_m) E_m \\ -\eta_m E_m + \mu_m I_m \\ -\lambda_h + \mu_h S_h - \gamma_{k\tau} R_h \\ -\rho_h I_h + (\mu_h + \gamma_{k\tau}) R_h \\ -\lambda_m + \mu_m S_m \end{bmatrix}.$$

We define $F = \dfrac{\partial \mathcal{F}(X_0)}{\partial x_j}$ and $V = \dfrac{\partial \mathcal{V}(X_0)}{\partial x_j}$ where x_j is the infected variables; E_h, I_h, E_m and I_m. After calculation we get the Jacobian matrices F and V as follow

$$F = \begin{bmatrix} 0 & 0 & 0 & \frac{b\beta_h S_{N_h} \lambda_h}{\mu_h} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{b\beta_m S_{N_m} \lambda_m}{\mu_m} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \; V = \begin{bmatrix} \mu_h + \eta_h & 0 & 0 & 0 \\ -\eta_h & \mu_h + \sigma_h + \rho_h & 0 & 0 \\ 0 & 0 & \mu_m + \eta_m & 0 \\ 0 & 0 & -\eta_m & \mu_m \end{bmatrix}.$$

The basic reproduction number R_0 is defined as spectral radius $\rho\left(FV^{-1}\right)$. After calculation we get $R_0 = \rho\left(FV^{-1}\right) = \sqrt{\dfrac{b^2 \beta_h \lambda_h S_{N_h} \eta_h \beta_m \lambda_m S_{N_m} \eta_m}{\mu_h (\mu_h + \eta_h)(\mu_h + \delta_h + \rho_h) \mu_m^2 (\mu_m + \eta_m)}}$.

We have the following result which the proof focuses on the similar way used in [8]

Proposition 3.1. When $R_0 < 1$ then; DFE X_0 of system is locally asymptotically stable and it is unstable if $R_0 > 1$.

3.2. Stability of endemic equilibrium (EE) point

EE point $X^* = (S_h^*, E_h^*, I_h^*, R_h^*, S_m^*, E_m^*, I_m^*)$ is a positive steady state solution where the disease persists in the population [8].

Proposition 3.2. *The EE point of the model (1) exists when* $R_0 > 1$ *and it doesn't exist when* $R_0 < 1$.

Proof: We set the system of differential equations (1) to zero as follow

https://dx.doi.org/10.4314/rjeste.v4i1.9

eISSN: 2617-233X | print ISSN: 2617-2321

$$\begin{cases} \lambda_h - b\beta_h S_h^* S_{N_h} I_m^* - \mu_h S_h^* + \gamma_{k\tau} R_h^* = 0, \\ b\beta_h S_h^* S_{N_h} I_m^* - (\mu_h + \eta_h) E_h^* = 0, \\ \eta_h E_h^* - (\mu_h + \delta_h + \rho_h) I_h^* = 0, \\ \rho_h I_h^* - (\mu_h + \gamma_{k\tau}) R_h^* = 0, \\ \lambda_m - b\beta_m S_m^* S_{N_m} I_h^* - \mu_m S_m^* = 0, \\ b\beta_m S_m^* S_{N_m} I_h^* - (\mu_m + \eta_m) E_m^* = 0, \\ \eta_m E_m^* - \mu_m I_m^* = 0. \end{cases} \quad (3)$$

By solving this system of equations (3), we get all state variables as follow

$$\begin{cases} S_h^* = \lambda_h \frac{b\beta_m S_{N_m} I_h^* + \mu_m}{\mu_h \mu_m R_{0h} R_{0m}}, E_h^* = \frac{\mu_h + \delta_h + \rho_h}{\eta_h} I_h^*, R_h^* = \frac{\rho_h}{\mu_h + \gamma_{k\tau} I_h^*}, \\ S_m^* = \frac{\lambda_m}{b\beta_m S_{N_m} I_h^* + \mu_m}, E_m^* = \frac{\mu_m^2 R_{0m} I_h^*}{\eta_m (b\beta_m S_{N_m} I_h^* + \mu_m)}, I_m^* = \frac{\mu_m R_{0m} I_h^*}{b\beta_m S_{N_m} I_h^* + \mu_m}. \end{cases} \quad (4)$$

We transform the first equation of the system (3) using the first equation in the system (4) to get

$$w_1 (I_h^*)^2 + w_2 I_h^* + w_3 = 0,$$

where $w_1 = \mu_h b\beta_m S_{N_m} [\lambda_h b\beta_h S_{N_h} \mu_h (\mu_h + \gamma_{k\tau})(R_{0m} + 1) - R_0^2 \mu_m \gamma_{k\tau} \rho_h]$,

$$w_2 = \mu_h \mu_m [\lambda_h b(\mu_h + \gamma_{k\tau})(\beta_h S_{N_h} (R_{0m} + 1) + \beta_m S_{N_m}) - R_0^2 (\lambda_h b\beta_m S_{N_m} + \mu_h \gamma_{k\tau} \rho_h)],$$

$$w_1 = \lambda_h \mu_h^2 \mu_m (1 - R_0^2).$$

The EE point of system (1) exists when $w_3 < 0$ which gives that $R_0 > 1$ and the system (1) has no positive solution for $w_1 > 0, w_2 > 0$ and $w_3 > 0$ when $R_0 < 1$.

Proposition 3.3. *The EE point X^* of the system of equations (1) is globally asymptotically stable in the domain $\perp$ if $R_0 > 1$.*

Proof: The global stability of the EE point of the model is found by using Lyapunov function [6]. Therefore, we set nonlinear Lyapunov function $Z(S_h, E_h, I_h, R_h, S_m, E_m, I_m)$ which is positive in domain $\perp$ from the system (1) as follows

$$Z = (S_h - S_h^* \ln S_h) + (E_h - E_h^* \ln E_h) + (I_h - I_h^* \ln I_h) + (R_h - R_h^* \ln R_h) + (S_m - S_m^* \ln S_m) + (E_m - E_m^* \ln E_m) + (I_m - I_m^* \ln I_m)$$

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$$\left.\frac{dZ}{dt}\right|_{X^*} = \left(1-\frac{S_h^*}{S_h}\right)\frac{dS_h}{dt} + \left(1-\frac{E_h^*}{E_h}\right)\frac{dE_h}{dt} + \left(1-\frac{I_h^*}{I_h}\right)\frac{dI_h}{dt} + \left(1-\frac{R_h^*}{R_h}\right)\frac{dR_h}{dt} \left(1-\frac{S_m^*}{S_m}\right)\frac{dS_m}{dt} + \left(1-\frac{E_m^*}{E_m}\right)\frac{dE_m}{dt} + \left(1-\frac{I_m^*}{I_m}\right)\frac{dI_m}{dt}.$$

Finally, we get

$$\left.\frac{dZ}{dt}\right|_{X^*} = -(1-\tfrac{S_h^*}{S_h})^2\mu_h S_h - (1-\tfrac{S_m^*}{S_m})^2\mu_m S_m + H(S_h,E_h,I_h,R_h,S_m,E_m,I_m)\ ,$$

where we have set

$$H\left(S_h,E_h,I_h,R_h,S_m,E_m,I_m\right) = \left(1-\frac{S_h^*}{S_h}\right)\left(1-\frac{S_h}{S_h^*}\frac{I_m}{I_m^*}\right)b\beta_h S_{N_h} S_h^* I_m^* + \left(1-\frac{S_h^*}{S_h}\right)\left(1-\frac{R_h}{R_h^*}\right)$$
$$+\left(1-\frac{E_h^*}{E_h}\right)\left(\frac{S_h}{S_h^*}\frac{I_m}{I_m^*}-\frac{E_h}{E_h^*}\right)b\beta_h S_{N_h} S_h^* I_m^* + \left(1-\frac{I_h^*}{I_h}\right)\left(\frac{E_h}{E_h^*}-\frac{I_h}{I_h^*}\right)\eta_h E_h^* + \left(1-\frac{R_h^*}{R_h}\right)\left(\frac{I_h}{I_h^*}-\frac{R_h}{R_h^*}\right)\rho_h I_h^*$$
$$+\left(1-\frac{S_m^*}{S_m}\right)\left(1-\frac{S_m}{S_m^*}\frac{I_h}{I_h^*}\right)b\beta_m S_{N_m} S_m^* I_h^* + \left(1-\frac{E_m^*}{E_m}\right)\left(\frac{S_m}{S_m^*}\frac{I_h}{I_h^*}-\frac{E_m}{E_m^*}\right)b\beta_m S_m^* S_{N_m} I_h^* + \left(1-\frac{I_m^*}{I_m}\right)\left(\frac{E_m}{E_m^*}-\frac{I_m}{I_m^*}\right)\eta_m E_m^*$$

In Mpeshe et al. [6], $H\left(S_h,E_h,I_h,R_h,S_m,E_m,I_m\right)\le 0$ and consequently $\frac{dZ}{dt}\le 0$ if

$$\begin{aligned}&\frac{S_h}{S_h^*}\frac{I_m}{I_m^*}\ge 1, R_h^*\le R_h, \frac{E_h}{E_h^*}\le\frac{I_m}{I_m^*}\frac{S_h}{S_h^*}, E_h\le E_h^*, \frac{E_h}{E_h^*}\le\frac{I_h}{I_h^*}, I_h^*\le I_h, \frac{I_h}{I_h^*}\le\frac{R_h}{R_h^*},\\ &\frac{S_m}{S_m^*}\frac{I_h}{I_h^*}\ge 1, S_m^*\le S_m, \frac{E_m}{E_m^*}\le\frac{I_h}{I_h^*}\frac{S_m}{S_m^*}, E_m\le E_m^*, \frac{E_m}{E_m^*}\le\frac{I_m}{I_m^*}, I_m^*\le I_m, S_h^*\le S_h\end{aligned} \qquad (6)$$

By considering the calculation done in (6), it is implied that $\frac{dZ}{dt}\le 0$, thus the point X^* is globally asymptotically stable.

4. Solution of optimal control

Let us first define the notion of Caputo derivative. Consider that f is a function which defined from $[a,b]$ to $\mathbb{R}$, and let $q>0$ be a real number representing the order of Caputo derivative of f, $n-1<q<n$ if $q\notin\mathbb{N}$ and $n=q$ if $q\in\mathbb{N}$ where $n\in\mathbb{N}$. The Left Caputo Fraction Derivative

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(LCFD) is defined as

$$ {}_{a}^{c}D_{t}^{q} f(t) = {}_{a}I_{t}^{n-q} \frac{d^n}{dt^n} f(t) = \frac{1}{\Gamma(n-q)} \int_{a}^{t} (t-s)^{n-q-1} f^{(n)}(s) ds. $$

When $q = n$, we obtain that

$$ {}_{a}^{c}D_{t}^{q} f(t) = {}_{a}I_{t}^{0} \frac{d^n}{dt^n} f(t) = \frac{d^n}{dt^n} f(t). \qquad (7) $$

Then

$$ {}_{t}^{c}D_{b}^{q} f(t) = (-1)^n \, {}_{t}I_{b}^{n-q} \frac{d^n}{dt^n} f(t) = \frac{(-1)^n}{\Gamma(n-q)} \int_{t}^{b} (s-t)^{n-q-1} f^{(n)}(s) ds $$

is the Right Caputo Fraction Derivative (RCFD). When $q = n$, we find that

$$ {}_{t}^{c}D_{b}^{q} f(t) = (-1)^n \, {}_{t}I_{b}^{0} \frac{d^n}{dt^n} f(t) = (-1)^n \frac{d^n}{dt^n} f(t). \qquad (8) $$

The optimal control problem is formulated using the method of Caputo fractional derivatives. We define the set of controls as $v = (v_1, v_2, v_3)^T$, given that v_i is measurable set with $0 \le v_i(t) \le 1$, when $v_i = 1$, the proportion of control usage is maximum, $\forall t \in [0, T]$, where $i = 1, 2, 3$ and $v_1(t)$ is the use of IRS, it kills the mosquitoes in the house, $v_3(t)$ is the use of ACTs, it increases the number of recover human population, ϕ_1 is a constant rate due to the use of ITNs, ϕ_2 is constant rate due to the use of IRS and ϕ_3 is a constant rate due to the use of ACTs. The following is the inclusion of control parameters in the system (1).

https://dx.doi.org/10.4314/rjeste.v4i1.9

eISSN: 2617-233X | print ISSN: 2617-2321

$$\begin{cases} \frac{dS_h}{dt} = \lambda_h - (1-v_1)b\beta_h S_h S_{N_h} I_m - \mu_h S_h + \gamma_{k\tau} R_h, \\ \frac{dE_h}{dt} = (1-v_1)b\beta_h S_h S_{N_h} I_m - (\mu_h + \eta_h) E_h, \\ \frac{dI_h}{dt} = \eta_h E_h - (\mu_h + \delta_h + \rho_h + \phi_3 v_3) I_h, \\ \frac{dR_h}{dt} = (\rho_h + \phi_3 v_3) I_h - (\mu_h + \gamma_{k\tau}) R_h, \\ \frac{dS_m}{dt} = \lambda_m - (1-v_1)b\beta_m S_m S_{N_m} I_h - (\mu_m + \phi_1 v_1 + \phi_2 v_2) S_m, \\ \frac{dE_m}{dt} = (1-v_1)b\beta_m S_m S_{N_m} I_h - (\mu_m + \eta_m + \phi_1 v_1 + \phi_2 v_2) E_m \\ \frac{dI_m}{dt} = \eta_m E_m - (\mu_m + \phi_1 v_1 + \phi_2 v_2) I_m. \end{cases} \quad (9)$$

Definition 4.1:

We set L in the following form

$$L(x,v,t) = AE_h + BI_h + CI_m + Dv_1^2 + Ev_2^2 + Fv_3^2, \quad (10)$$

where the constants A, B and C are weight of the exposed individual population, infected individual population and mosquito population, respectively; D, E and F are weighting constants in the prevention strategies; Dv_1^2 is the cost of protection with ITNs; Ev_2^2 is the cost prevention with IRS; Fv_3^2 is the cost of treatment of infected individual population. Define the objective function as follows,

$$J(v_i) = \int_0^T L(x,v,t)dt, \quad (11)$$

subject to

$${}_0^c D_t^q x(t) = G(x,v,t),$$

where $x(t) = (S_h, E_h, I_h, R_h, S_m, E_m, I_m)^T$ vector state, $\forall t \in [0,T]$, L is Lagrangian and G is a system (9). Using the optimal control strategies $v_i(t)$, the number of exposed and infected human and mosquito population are minimized, while minimizing the cost of controls [10]. Taking (10) in (11), we find the optimal control v_i^* the solution of

$$J(v_i^*) = \min_{v_i \in V} J(v_i) \quad (12)$$

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subject to the system (9). To seek the optimal control, we first find a modified objective function

$$\bar{J}(v) = \int_0^T \left[L(x,v,t) + k\left(G(x,v,t) - {}_0^c D_t^q x(t)\right)\right] dt, \qquad (13)$$

where $k = (k_1, k_2, k_3, k_4, k_5, k_6, k_7)^T$ is the Lagrange multiplier which is called again an adjoint variable. By considering the variation of equation (13) with respect to the variables x, v and k, we obtain

$$\delta\bar{J}(v) = \int_0^T \left[\frac{\partial L}{\partial x}\delta x + \frac{\partial L}{\partial v}\delta v + \delta k\left(G - {}_0^c D_t^q x\right) + k\left(\frac{\partial G}{\partial x}\delta x + \frac{\partial G}{\partial v}\delta v - \delta\left({}_0^c D_t^q x\right)\right)\right] dt. \qquad (14)$$

Using permutation of the variation order and the fractional derivative, (14) becomes

$$\delta\bar{J}(v) = \int_0^T \left[\delta k\left(G - {}_0^c D_t^q x\right) + \delta x\left(\frac{\partial L}{\partial x} + k\frac{\partial G}{\partial x} - {}_t^c D_T^q k\right) + \delta v\left(\frac{\partial L}{\partial v} + k\frac{\partial G}{\partial v}\right)\right] dt. \qquad (15)$$

Minimization of $\bar{J}(v)$ exists when the coefficients of $\delta x, \delta u$ and δk in (15) are zero. It means that

$$\begin{cases} G - {}_0^c D_t^q x = 0 \\ \frac{\partial L}{\partial x} + k^T \frac{\partial G}{\partial x} - {}_t^c D_T^q k = 0 \\ \frac{\partial L}{\partial v} + k^T \frac{\partial G}{\partial v} = 0 \end{cases} \quad which \;\; gives \quad \begin{cases} {}_0^c D_t^q x = G(x,v,t) \\ {}_t^c D_T^q k = \frac{\partial L}{\partial x} + k^T \frac{\partial G}{\partial x} \\ \frac{\partial L}{\partial v} + k^T \frac{\partial G}{\partial v} = 0 \end{cases} \qquad (16)$$

Finding solution of controlled malaria model with fractional derivatives, the first relation of the system (16) contains LCFD which is

$${}_0^c D_t^q x = G(x,v,t). \qquad (17)$$

Then the solution of state variables X is obtained through LCFD. For $q = 1$, the equation (17) reduces in the following standard methods

$${}_0^c D_t x(t) = \frac{d}{dt}x(t) = G(x,v,t); \qquad (18)$$

The component $\frac{d}{dt}S_h$ should be equal to the first relation of the system of the equations (9), meaning that

$$\frac{d}{dt}S_h = \lambda_h - (1-v_1)b\beta_h S_h S_{N_h} I_m - \mu_h S_h + \gamma_{k\tau} R_h,$$

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Similarly, we can get the others from the relation (18) and we have

$$\begin{cases} \frac{d}{dt}S_h = \lambda_h - (1-v_1)b\beta_h S_h S_{N_h} I_m - \mu_h S_h + \gamma_{k\tau} R_h, \\ \frac{d}{dt}E_h = (1-v_1)b\beta_h S_h S_{N_h} I_m - (\mu_h + \eta_h)E_h, \\ \frac{d}{dt}I_h = \eta_h E_h - (\mu_h + \delta_h + \rho_h + \phi_3 v_3)I_h, \\ \frac{d}{dt}R_h = (\rho_h + \phi_3 v_3)I_h - (\mu_h + \gamma_{k\tau})R_h, \\ \frac{d}{dt}S_m = \lambda_m - (1-v_1)b\beta_m S_m S_{N_m} I_h - (\mu_m + \phi_1 v_1 + \phi_2 v_2)S_m, \\ \frac{d}{dt}E_m = (1-v_1)b\beta_m S_m S_{N_m} I_h - (\mu_m + \eta_m + \phi_1 v_1 + \phi_2 v_2)E_m \\ \frac{d}{dt}I_m = \eta_m E_m - (\mu_m + \phi_1 v_1 + \phi_2 v_2)I_m. \end{cases}$$

From the system (16), the second relation contains RCFD which is

$$ {}_t^c D_T^q k = \frac{\partial L}{\partial x} + k^T \frac{\partial G}{\partial x}, \qquad (19)$$

Then, the solution of adjoint variables k is obtained through RCFD. For $q = 1$, the equation (19) reduces in the following standard methods

$$ {}_t^c D_T k = -\frac{d}{dt}k = \frac{\partial L}{\partial x} + k^T \frac{\partial G}{\partial x}. \qquad (20)$$

Therefore, in (20) we have that

$$\tfrac{d}{dt}k = (\tfrac{d}{dt}k_1, \tfrac{d}{dt}k_2, \tfrac{d}{dt}k_3, \tfrac{d}{dt}k_4, \tfrac{d}{dt}k_5, \tfrac{d}{dt}k_6, \tfrac{d}{dt}k_7)^T,$$

with simplification the adjoint variables can be written as

$$\begin{cases} -\frac{d}{dt}k_1 = (k_2 - k_1)(1-v_1)b\beta_h S_{N_h} I_m - k_1\mu_h, \\ -\frac{d}{dt}k_2 = A + (k_3 - k_2)\eta_h - k_2\mu_h, \\ -\frac{d}{dt}k_3 = B + (k_4 - k_3)(\rho_h + \phi_3 v_3) + (k_6 - k_5)(1-v_1)b\beta_m S_m \alpha_1 S_{N_m} S_m - k_3(\delta_h + \mu_h), \\ -\frac{d}{dt}k_4 = (k_1 - k_4)\gamma_{k\tau} - k_4\mu_h, \\ -\frac{d}{dt}k_5 = C + (k_6 - k_5)(1-v_1)b\beta_m S_{N_m} I_h - k_5(\mu_m + \phi_1 v_1 + \phi_2 v_2), \\ -\frac{d}{dt}k_6 = C + (k_7 - k_6)\eta_m - k_6(\mu_m + \phi_1 v_1 + \phi_2 v_2), \\ -\frac{d}{dt}k_7 = C + (k_2 - k_1)(1-v_1)b\beta_h S_h \alpha_1 S_{N_h} - k_7(\mu_m + \phi_1 v_1 + \phi_2 v_2). \end{cases}$$

In (16), the third relation can be written as

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$$\begin{bmatrix} \frac{\partial L}{\partial v_1} + k^T \frac{\partial G}{\partial v_1} \\ \frac{\partial L}{\partial v_2} + k^T \frac{\partial G}{\partial v_2} \\ \frac{\partial L}{\partial v_3} + k^T \frac{\partial G}{\partial v_3}. \end{bmatrix} = 0. \qquad (21)$$

After the simplification, the controls are obtained as follow

$$\begin{cases} v_1 = \dfrac{(k_2 - k_1) b\beta_h S_h S_{N_h} I_m + (k_6 - k_5) b\beta_m S_m S_{N_m} I_h + (k_5 S_m + k_6 E_m + k_7 I_m)\phi_1}{2D}, \\ v_2 = \dfrac{k_5 \lambda_m + k_5 \phi_2 S_m + (k_6 E_m + k_7 I_m)\phi_2}{2E}, \\ v_3 = \dfrac{(k_3 - k_4)\phi_3 I_h}{2F}. \end{cases} \qquad (22)$$

The solution of optimal control v_i^* should be ranged in $[0,1]$ because its control component v_i is bounded in $[0,1]$. From (22), we deduce the optimal control v_i^* as follow;

$$v_i^* = \begin{cases} 0 & \text{if} \quad v_i \le 0, \\ v_i & \text{if} \quad 0 < v_i < 1, \\ 1 & \text{if} \quad v_i \ge 1, \end{cases} \quad \text{with } i = 1, 2, 3.$$

5. Estimation of parameters

Let $s_h = \dfrac{S_h(t)}{N_h}, e_h = \dfrac{E_h(t)}{N_h}, i_h = \dfrac{I_h(t)}{N_h}, r_h = \dfrac{R_h(t)}{N_h}, s_m = \dfrac{S_m(t)}{N_m}, e_m = \dfrac{E_m(t)}{N_m}, i_h = \dfrac{I_m(t)}{N_m}.$ Therefore, the system (1) becomes,

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$$\begin{cases} \frac{ds_h}{dt} = \lambda_h - b\beta_h s_h S_{N_h} i_m(t) - \mu_h s_h + \gamma_{k\tau} r_h, \\ \frac{de_h}{dt} = b\beta_h s_h S_{N_h} i_m(t) - \left(\mu_h + \eta_h\right) e_h, \\ \frac{di_h}{dt} = \eta_h e_h - \left(\mu_h + \delta_h + \rho_h\right) i_h, \\ \frac{dr_h}{dt} = \rho_h i_h - \left(\mu_h + \gamma_{k\tau}\right) r_h, \\ \frac{ds_m}{dt} = \lambda_m - b\beta_m s_m S_{N_m} i_h(t) - \mu_m s_m, \\ \frac{de_m}{dt} = b\beta_m s_m S_{N_m} i_h(t) - \left(\mu_m + \eta_m\right) e_m, \\ \frac{di_m}{dt} = \eta_m e_m - \mu_m i_m, \end{cases} \tag{23}$$

Let set

$$\frac{dx}{dt} \approx \frac{x_j - x_{j-1}}{\Delta t}, 0 \le t \le T_{\max}, j = 1,\ldots,N,$$

where $x_j = x(t_j)$ and $\Delta t = \frac{T_{\max}}{N}$ with N indicates the total number of discretization intervals such that $x_j = x_{j-1} + \Delta t$. Therefore, the discrete system becomes

$$\begin{cases} s_h^{n+1} = (1 - \Delta t\mu_h) s_h^n + \Delta t\left(\lambda_h - b\beta_h s_h^n S_{N_h} i_m^n + \gamma_{k\tau} r_h^n\right), \\ e_h^{n+1} = (1 - \Delta t\left(\mu_h + \eta_h\right)) e_h^n + \Delta t b\beta_h s_h^n S_{N_h} i_m^n(t), \\ {}_h^{n+1} = (1 - \Delta t\left(\mu_h + \delta_h + \rho_h\right)) i_h^n + \Delta t e_h^n \eta_h e_h^n, \\ r_h^{n+1} = \left(1 - \Delta t\left(\mu_h + \gamma_{k\tau}\right)\right) r_h^n + \Delta t\rho_h i_h^n, \\ s_m^{n+1} = \left(1 - \Delta t\mu_m\right) s_m^n + \Delta t\left(\lambda_m - b\beta_m s_m^n S_{N_m} i_h^n\right), \\ e_m^{n+1} = (1 - \Delta t\left(\mu_m + \eta_m\right)) e_m^n + \Delta t b\beta_m s_m^n S_{N_m} i_h^n, \\ i_m^{n+1} = (1 - \Delta t\mu_m) i_m^n + \Delta t\eta_m e_m^n. \end{cases} \tag{24}$$

To estimate the model parameter, let us consider

$$\underline{i_h}^{\mu} = (i_h^{\mu}(t_1),\ldots,i_h^{\mu}(t_N))^T, \underline{i_m}^{\mu} = (i_m^{\mu}(t_1),\ldots,i_m^{\mu}(t_N))^T,$$

where μ denotes the perturbation parameter which is caused by some imprecision on measured

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data. The optimal control problem is formulated as follows.

Find

$$\underline{u} = (\lambda_h, \beta_h, \mu_h, \eta_h, \delta_h, \rho_h, \lambda_m, \beta_m, \mu_m, \eta_m, \alpha, \upsilon, k, \tau)^t,$$

solution of

$$J(\underline{u}) = \min_{\underline{u}} J(\underline{u}) \qquad (25)$$

subject to (24) where

$$J(\underline{u}) = \left\| \underline{i_h}^{\mu} - i_h^{\mu} \right\|^2 + \left\| \underline{i_m^{\mu}} - i_m^{\mu} \right\|^2.$$

Using MATLAB, fminicom is used in numerical simulation to identify the parameters in the mathematical model are illustrated in Figures 2 and 3.

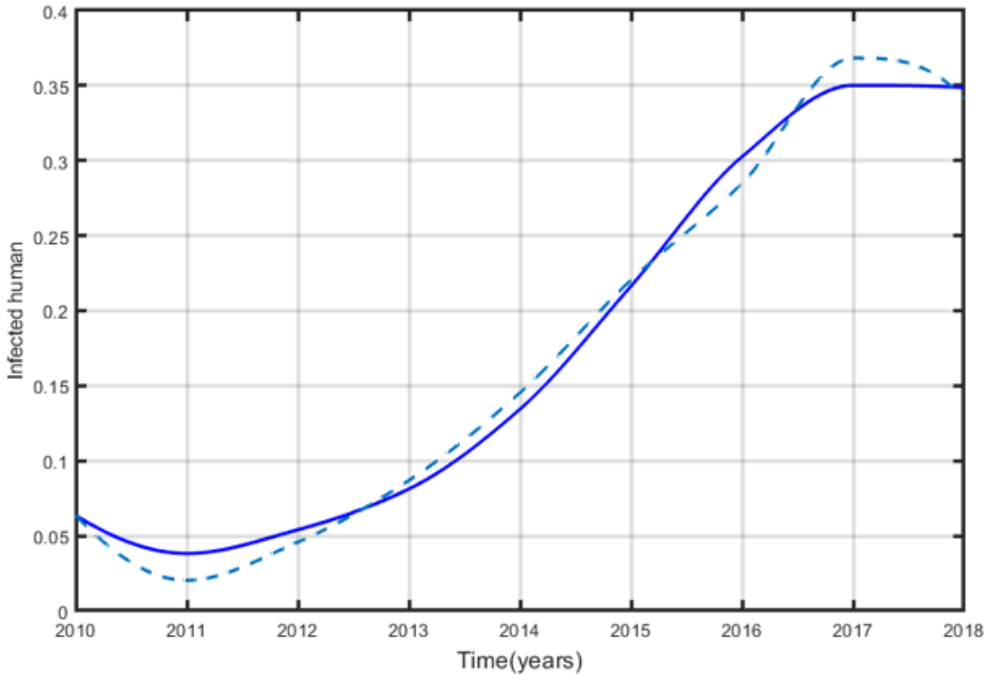

Fig. 2: Trend of infected humans. It shows that the solutions of the mathematical model (23) (Solid lines) are close to observed data (dashed lines) for infected human

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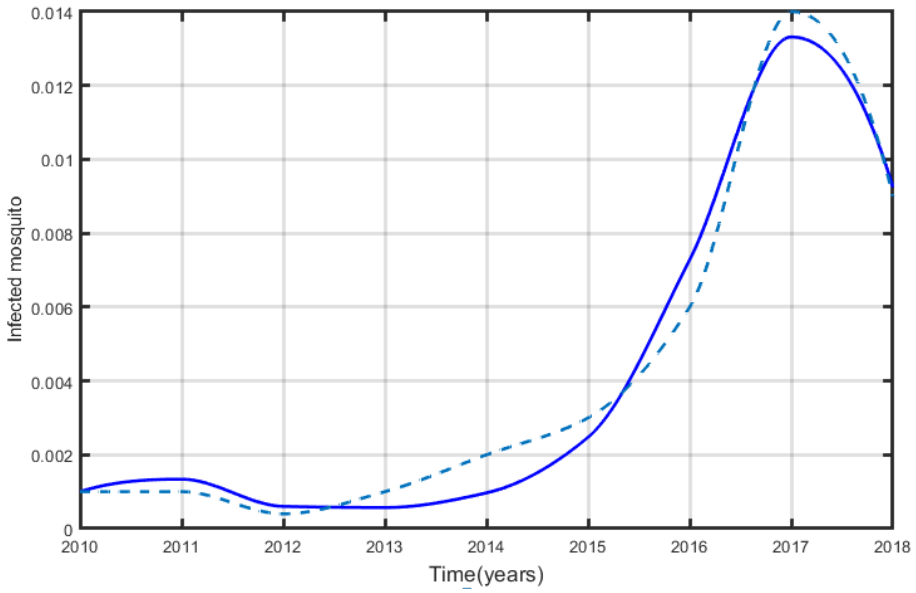

Fig. 3: Trend of infected mosquitoes.

It shows that the solutions of the mathematical model (23) (Solid lines) are close to observed data (dashed lines) for infected mosquitoes

Table 1 The estimate for the mathematical model parameters

Parameter	**Value**	**Parameter**	**Value**	**Parameter**	**Value**
λ_h	29.3285	B	39.4232	β_h	0.9802
δ_h	5.9195	ρ_h	6.0048	υ	14.0843
λ_m	17.6182	β_m	0.9517	μ_m	4.9498
μ_h	0.8636	η_h	46.9972	k	26.4648
τ	26.4639	η_m	0.8227	α	28.6799

6. Numerical test

Basing on the value of parameters and without intervention strategies on malaria transmission in Rwanda, we get a basic reproduction number $R_0 = 1.3250$. This result shows that new infection population produced by one typical infective is greater than one and the size of infective class is increased. Thus, disease will spread in the population of the country.

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The numerical simulations of optimal control problem are done using MaTlaB packages with solving the optimal control problem with cost function (13) subject to (10) basing on different cases of control impact. The results of some methods of malaria prevention are illustrated in figures where the dashed lines denote the use of controls while solid lines are related to not using control strategy.

The method of malaria prevention using one control like treated bed net $(v_1(t) \neq 0)$ and consider $(v_2(t) = v_3(t) = 0)$. The Figure 4 illustrate the results of numerical simulations.

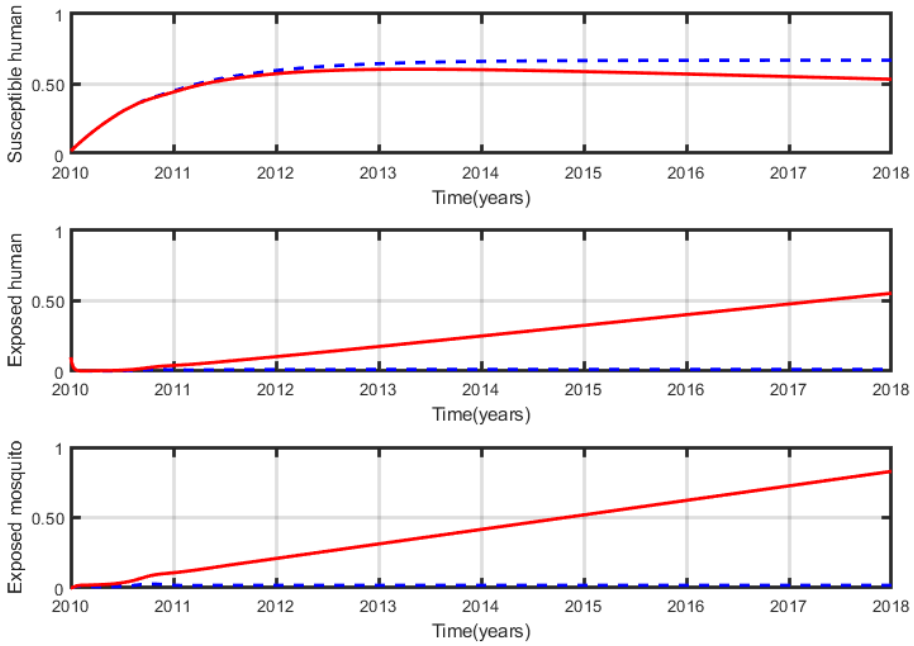

Fig. 4: Impact of using treated bed net on the variation of susceptible, exposed human and exposed mosquito.

It is clear that with the use of ITNs; the calculation shows that the reproduction number $R_0 = 1.0769$. This result shows that a typical infected population produced more than one infected population. This control is not enough for eradicating the disease due to the persistence of infected population.

The method malaria prevention using two controls such as insecticide treated bed nets $(v_1(t) \neq 0)$ together with Artemisinin based Combination Therapiest $(v_3(t) \neq 0)$ are used and $(v_2(t) = 0)$. Numerical simulations results are shown in the Figures 5 and 6.

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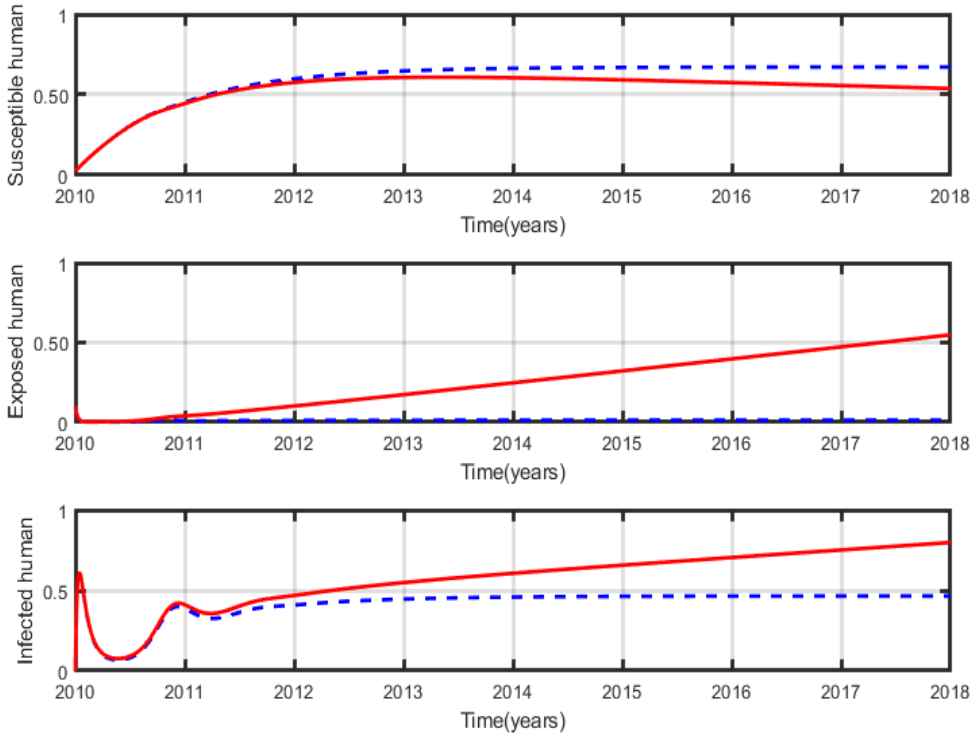

Fig. 5: Impact of using insecticide treated bed nets and Artemisinin based Combination Therapies on the variation of susceptible, exposed and infected human.

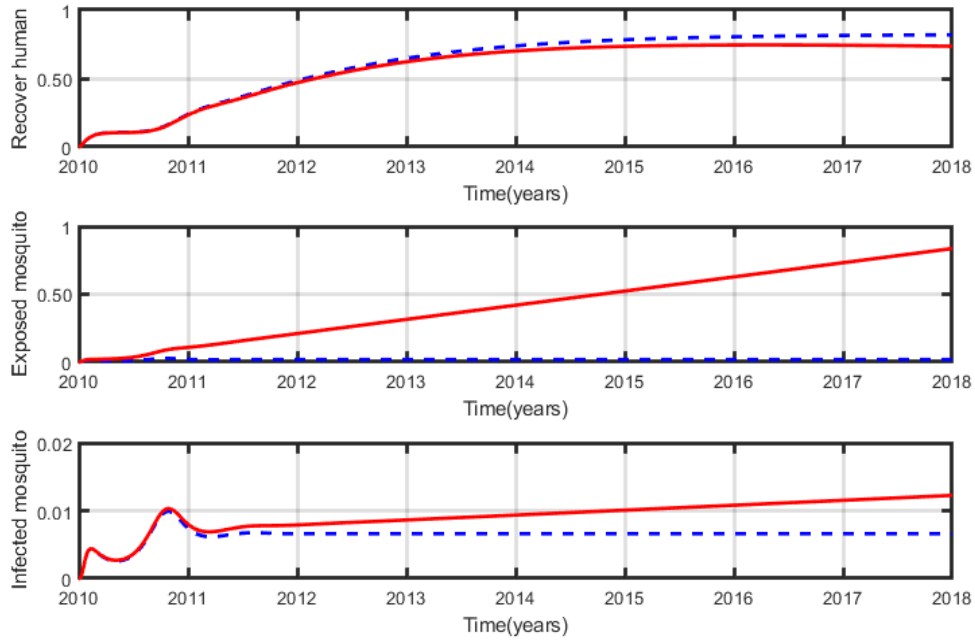

Fig. 6: Impact of using insecticide treated bed nets and Artemisinin based Combination Therapies on the variation of recover human, exposed and infected mosquito.

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Using ITNs and ACTs as controls; the calculation shows that the reproduction number $R_0 = 1.0299$. This result shows that a typical infected population produced around one infected population. This control can stabilize the disease.

The method of malaria prevention using three controls such as the combination of insecticide treated bed nets $(v_1(t) \neq 0)$, indoor residual spray $(v_2(t) \neq 0)$ and Artemisinin based Combination Therapies $(v_3(t) \neq 0)$ as controls are used. We get the Figures 7 and 8

that illustrated the results of numerical simulations.

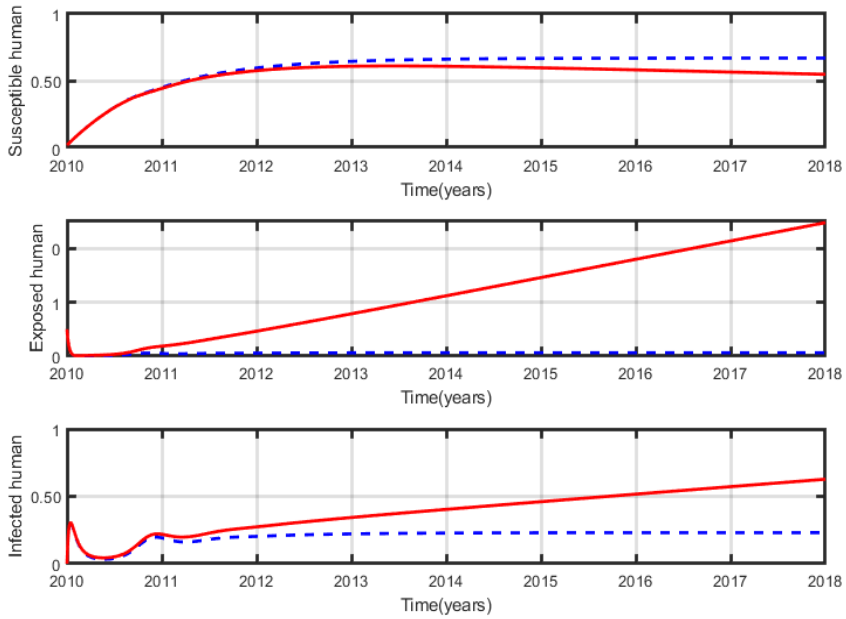

Fig. 7: Impact of using ITNs, IRS and ACTs on the variation of susceptible, exposed and infected human.

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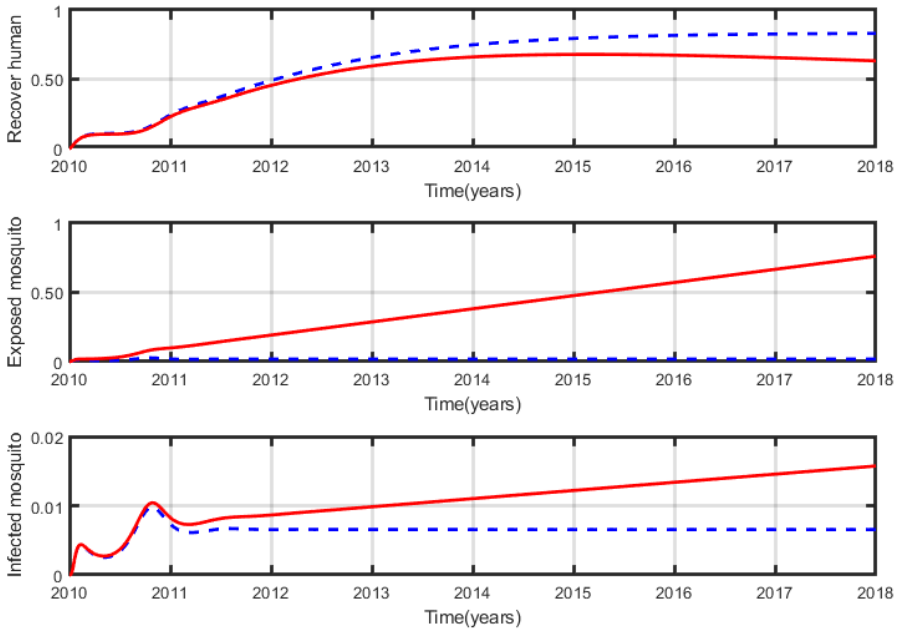

Fig. 8: Impact of using ITNs, IRS and ACTs on the variation of mosquitoes.

Using the combination of ITNs, IRS and ACTs as controls; the calculation shows that the reproduction number $R_0 = 0.9699$. This result shows that one infected population produced less than one infected population. Thus, the disease will die out in the population. However, it will take longer to eradicate it.

The Figure 4 shows that the highest impact of using ITNs is increasing susceptible humans and decreasing exposed humans and mosquitoes. Thus, this control is not enough for eradicating the disease due to the persistence of infected population. The results from Figure 5 and Figure 6 show that the highest impact achieved is lowering exposed and infected population and increasing susceptible humans. The results from Figure 7 and 8 show that the highest impact of this combination is increasing the susceptible humans and human recovery and lowering the infected human and mosquitoes at a good level. Therefore, the Figure 4, Figure 5 with Figure 6 and Figure 7 with 8 showed that the combination of ITNs, IRS and ACTs is better in prevention of malaria.

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7. Conclusion

In this work, we did the formulation and analysis of the SEIR-SEI mathematical model with seven ordinary differential equations describing the dynamics of malaria transmission in the host and vector populations, with incidence forces of infections which are nonlinear for human and mosquito populations. The formulation and analysis of the model were concluded by control strategies which are ITNs, IRS and ACTs. The existence of DFE and EE, and reproduction number R_0 were investigated. The optimal control of this malaria model using the Caputo fraction derivative were also considered to find the optimal control parameters which minimize the spreading of malaria in Rwanda. The mathematical model including the optimal controls (1) was solved and numerical simulation showed that the method of using three controls ITNs, IRS and ACTs together in endemic region are more effective to the society in minimizing the number of infected human and infected mosquito while the recovery humans are increased in coming years. In this perspective, the simulation showed that whenever the method of using the combination of three controls, ITNs, IRS and ACTs is well followed and implemented, it can effectively minimize the rate of malaria transmission in Rwanda. Finally, the malaria will die out in our society.

References

[1] Jean-Pierre Bizimana, Emmanuel Twarabamenye, and Stefan Kienberger (2015) *Assessing the social vulnerability to malaria in Rwanda*, Malaria Journal, 14(2), Article number: 2, http://www.malariajournal.com/content/14/1/2.

[2] James Kant KAMUHANDA (2016) *Review of Malaria Epidemiology in Rwanda, Environmental Studies*, Imperial Journal of Interdisciplinary Research (IJIR)

[3] Macdonald, G. (1957) *The epidemiology and control of malaria.* The Epidemiology and Control of Malaria

[4] Mojeeb AL-Rahman EL-Nor Osman, Cuihong Yang & Isaac Kwasi Adu (2019) *Mathematical Model of Malaria Transmission with Optimal Control in Democratic Republic of the Congo*. Global Journals, Volume 19 Issue 1 Version 1.0, pp 1-23, Online ISSN: 2249-4626 & Print ISSN: 0975-5896.

https://dx.doi.org/10.4314/rjeste.v4i1.9

[5] Mojeeb AL-Rahman EL-Nor Osman and Isaac Kwasi Adu (2017) *Simple Mathematical Model for Malaria Transmission*. Journal of Advances in Mathematics and Computer Science, Volume 25(6), pp. 1-24, Article no. JAMCS.37843, ISSN: 2456-9968, Past ISSN: 2231-0851.

[6] Mpeshe, S. C., Haario, H., & Tchuenche, J. M. (2011) *A mathematical model of Rift Valley fever with human host.* Acta biotheoretica, 59(3-4), pp. 231-250, DOI 10.1007/s10441-011-9132-2.

[7] OKELLO GABRIEL OTIENO (2016) *Optimal Control Strategies for Minimizing Malaria Transmission in Kenya*, PhD thesis, Moi University, Kenya.

[8] Olaniyi S., Obabiyi O.S. (2013) *Mathematical Model for Malaria Transmission Dynamics in Human and Mosquito Populations with Nonlinear Forces of Infection*. International Journal of Pure and Applied Mathematics, Volume 88 No. 1, pp. 125-156, doi: http://dx.doi.org/10.12732/ijpam.v88i1.10, ISSN: 1311-8080 (printed version); ISSN: 1314-3395 (on-line version).

[9] Ross, R. (2011) *The prevention of malaria.* London, John Murray.

[10] Roy, P., Upadhyay, R. K., & Caur, J. (2020). Modeling Zika transmission dynamics: Prevention and control. *Journal of Biological Systems*, *28*(03), 719-749.

[11] Rwanda 2014 National Human Development Report Decentralization and Human Development (2015) *Accelerating socio-economic transformation and sustaining accountable governance*, Final Report.

[12] Smith, D. L., McKenzie, F. E., Snow, R. W., & Hay, S. I. (2007) *Revisiting the basic reproductive number for malaria and its implications for malaria control.* PLoS biology, 5(3).

[13] U.S. President'sMalaria Initiative Vector Link Project. Rwanda (2018) *2018 Entomological Monitoring*, July 2017–June 2018.. Final Report. Kigali, Rwanda: AIRS Project, Abt Associates Inc. Contract: AID-OAA-I-17-00008, Task Order: AID-OAA-TO-17-00027, Submitted to: United States Agency for International Development/PMI.

[14] USAID, 2019, President's malaria initiative Rwanda (2019) *Malaria Operational Plan FY, 2019*.

[15] World malaria report (2019) *World malaria report 2019.*Geneva: World Health Organization; 2019. ISBN 978-92-4-156572-1, https://www.who.int/malaria).

https://dx.doi.org/10.4314/rjeste.v4i1.9