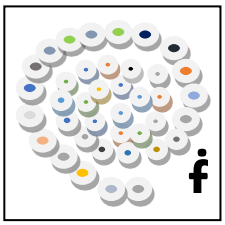

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Optimal control analysis of Onchocerciasis transmission model

I.O. Onwubuya[*], G.N. Nkem[†], N. Tindi[‡], and C.E. Madubueze[‡]

Abstract

A deterministic model for the transmission dynamics of Onchocerciasis is developed and analyzed in this study. The model consists of two populations, namely, human and vector (blackfly) populations. The basic reproduction number is derived and used to establish the stability of the disease-free equilibrium state. The sensitivity analysis is carried out using Partial Rank Correlation Coefficient (PRCC), which the result is used in formulating the optimal control model with three control strategies. Pontryagin's Maximum Principle is employed in the optimal control model to determine the optimality system for controlling onchocerciasis disease. This is further solved numerically to show the impact of the control strategies on the transmission of the disease.

Keywords: Onchocerciasis; basic reproduction number; sensitivity analysis; optimal control

1 Introduction

Onchocerciasis is a parasitic infection that results in blindness and painful skin sores. There are thirty-seven(37) nations where the disease is present, with thirty(30) of those countries being in Africa, six(6) in the Americas, and one(1) in the Arabian Peninsula [7,16]. With an estimated incidence of $500,000$ for people with a visual impairment and $270,000$ for people who are blind, onchocerciasis is the second most common preventable cause of blindness after trachoma in sub-Saharan Africa [12] & [24]. Small Simulium blackflies, which spawn in swiftly moving, highly oxygenated rivers and streams, are the carriers of the parasite, Onchocerca volvulus [12]. When an infected blackfly consumes blood from an uninfected human, it discharges one or more Onchocerca volvulus larvae into the human host. Within a year, these larvae become fully grown adult worms. They frequently group together to form fibrous nodules under the skin, usually over bony prominences [7], [12].

Over the last three decades, significant progress has been made in controlling onchocerciasis in both Africa and the Americas, owing mainly to international public-private partnerships, sustained funding by relevant agencies and stakeholders, and the development of new tools and technology as well as regional programs shifting from eradicating the illness to, whenever possible, eradicating the infection [7], [8] & [31]. Onchocerciasis is currently controlled mostly in Africa through annual mass drug administration (MDA) with ivermectin [31], [2] & [12]. Depending on the coverage, duration, and frequency of MDA, periodic community-wide mass drug administration (MDA) with ivermectin (Mectizan, Merck) can stop the spread of infection and prevent eye and skin illness [11,24]. However, with the recent onchocerciasis endemic situation in Africa, the MDA approach may not be enough to halt the further transmission of the disease even in regions where vector control has achieved success, as the disease may be reimported from infected persons that are remigrating in that region [12], [25]. The ability to fully understand the mechanisms governing the control of parasite population in the vertebrate

[*]Corresponding author. Department of Mathematics, Airforce Institute of Technology Kaduna, Kaduna, Nigeria; Email: isaacobiajulu@gmail.com

[†]Modelling, Simulation and Data Science Network, Africa, Department of Mathematics, Federal University Oye-Ekiti, Ekiti, Nigeria

[‡]Department of Mathematics, Joseph Sarwuan Tarkaa Univeristy, Makurdi, Nigeria

host has been impeded by the lack of animal models in which the entire life cycle of Onchocerca volvulus may be successfully reproduced [5], [18]. Mathematical frameworks have been devised to investigate how these mechanisms affect parasite population dynamics and how control measures affect them. The assumptions about the adult female worm's reproductive life duration and the distribution of its survival times at the longest-living parasite stage are critical to all frameworks because they significantly impact post-control forecasts [5]. Creating a rational foundation for regulations intended to stop the spread of a disease is one of the goals of modelling epidemics [26], [23]. The evaluation of the public health authorities' intervention is made possible by including realistic optimal solutions in models. In an epidemic, decisions must be made on how much of the population should be treated to reduce both the spread of infection and the implementation costs of the treatment. Optimal control is a potent mathematical technique for making decisions that entail using the right tactics to eliminate infections from the populace [23].

In this study, we develop a mathematical model for onchocerciasis disease transmission and prevention measures. The objective is to learn more about the most effective intervention for reducing and ultimately eliminating onchocerciasis from the population. The intervention strategies included in the model include public health education measures, improved treatment against black flies, and insecticide spraying. Our model serves as a better framework to assist the ongoing control, elimination and eradication efforts of onchocerciasis disease in that it reveals the optimal control strategies with effectively reduced cost of implementation.

The arrangement of this paper is as follows: Section 2 is the model formulation for the onchocerciasis disease, and the model analysis is presented in Section 3. The optimal control of the formulated model is discussed in Section 4, while Section 5 displays the numerical simulations and their discussions. Section 6 is the conclusion.

2 Model Formulation

In this section, we formulate a deterministic onchocerciasis model that describes the transmission dynamics in the human population and vector (Blackfly) population at any time t with $N_H(t)$ and $N_V(t)$ as the total human population and total vector population respectively. The human population, $N_H(t)$ and the vector population, $N_V(t)$, are compartmentalized into epidemiological classes as displayed in Figure 1. As shown in Figure 1, the human population is subdivided into Susceptible human $(S_h(t))$, Exposed human $(E_h(t))$, Infected human $(I_h(t))$ and Recovered human $(R_h(t))$, whereas, the vector (blackfly) population is subdivided into Susceptible blackflies $(S_v(t))$, Exposed blackflies $(E_v(t))$ and Infected blackflies $(I_v(t))$.

The recruitment of humans into the susceptible human population, $(S_h(t))$, is through birth or immigration at a constant rate, Λ_h. It is increased due to recovered humans who lose immunity at the rate, ω. Susceptible humans get infected with onchocerciasis when bitten by infected blackflies at a force of infection λ_h and become exposed. The force of infection is given by $\lambda_h = \dfrac{m_h \beta_h I_v}{N_h}$, with m_h and β_h as the biting rate of blackflies and the human transmission rate, respectively. It decreases by the natural death rate, μ_h, which is assumed for all human compartments. The exposed human population, $(E_h(t))$, is decreased by the progression rate from exposed humans to infected human class $(I_h(t))$ at a rate, σ_h. The infected human population, $(I_h(t))$, undergoes treatment at the rate,$(I_h(t))$ and progresses to the Recovered human class, $(R_h(t))$, while those that recovered become susceptible again due to loss of drug-induced immunity at the rate, ω.

Susceptible blackfly population $(S_v(t))$ are generated via birth or immigration of blackflies into the population at the rate Λ_v. It is further decreased by force of infection, $\lambda_v = \dfrac{m_v \beta_v I_h}{N_h}$ of the contact between the susceptible blackfly and infected blackfly. Exposed vector $(E_v(t))$ is decreased at the rate, σ_v and the natural death at rate μ_v. The infected vector $(I_v(t))$ is generated from the exposed blackfly $(E_v(t)))$ that feeds on infectious blood meals and similarly diminishes at the rate, μ_v. Based on the flow diagram (Fig. 1), we described the model mathematically with the following system of ordinary

differential equations:

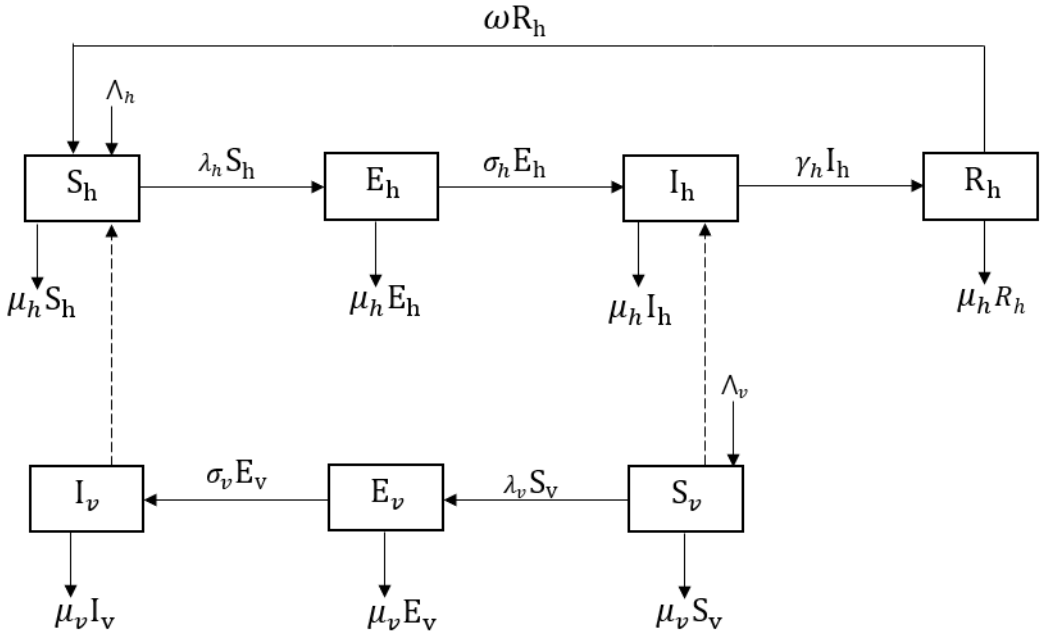

Figure 1: Flow diagram for transmission dynamics of onchocerciasis model.

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - \frac{m_h\,\beta_h\,I_v\,S_h}{N_h} + \omega\,R_h - \mu_h S_h,\\
\frac{dE_h}{dt} &= \frac{m_h\,\beta_h\,Iv\,S_h}{N_h} - (\mu_h + \sigma_h)\,E_h,\\
\frac{dI_h}{dt} &= \sigma_h E_h - (\gamma_h + \mu_h)\,I_h,\\
\frac{dR_h}{dt} &= \gamma_h I_h - (\omega + \mu_h)\,R_h,\\
\frac{dS_v}{dt} &= \Lambda_v - \frac{m_v\,\beta_v\,I_h\,S_v}{N_h} - \mu_v S_v,\\
\frac{dE_v}{dt} &= \frac{m_v\,\beta_v\,I_h\,S_v}{N_h} - (\sigma_v + \mu_v)E_v,\\
\frac{dI_v}{dt} &= \sigma_v E_v - \mu_v I_v
\end{aligned} \tag{1}$$

with initial conditions $S_h(0) > 0, E_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0, S_v(0) > 0, E_v(0) \geq 0$, $I_y(0) \geq 0$ and the parameters of the model assumed positive.

3 Model Analysis

The total human population is determined by

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$$

Table 1: Description of State Variables

Parameters	Description	Initial Value	Source
$S_h(t)$	Susceptible Individuals at risk of infection at time, t	$20,000$	Assumed
$E_h(t)$	Exposed individuals but not infectious at time, t	1500	Assumed
$I_h(t)$	Infected individuals with larva worm at time, t	150	Assumed
$R_h(t)$	Recovered individuals at time, t	10	Assumed
$S_v(t)$	Susceptible blackfly population at time, t	2500	Assumed
$E_v(t)$	Exposed blackfly but not infectious at time, t	250	Assumed
$I_v(t)$	Infected blackfly at time, t	10	Assumed

Table 2: Parameter Estimation for Numerical Simulation

Parameters	Description	Value, Year^{-1}	Source
Λ_h	Recruitment rate of susceptible individuals	$3,449,679$	[3]
ω	Progression rate from infected to recovery human	0.019	[3]
m_h	Number of bites rate by infected blackflies	0.8	[10]
β_h	Transmission rate for human population	2.12	[22]
μ_h	Human natural death rate	0.0000391 - 0.0000548(0.000052)	[23]
σ_h	Progression rate from exposed to infectious	0.00137 - 0.00363(0.00139)	[13, 17]
γ_h	Recovery rate	0.067	[34]
Λ_v	Recruitment rate of susceptible Vector (blackfly)	$361,028.57$	[3]
β_v	Transmission rate for vector population	0.758	[10]
μ_v	Human natural death rate	0.0118 - 0.0714(0.068)	[13, 23]
σ_v	Progression rate from exposed to infectious blackfly	0.0714 - 0.1667(0.078)	[13]
m_v	Biting rate of the blackfly	0.8	[10]

while the total vector population is given by

$$N_v(t) = S_v(t) + E_v(t) + I_v(t).$$

So adding the first, second and third equations of the model (1), we obtain

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h. \tag{2}$$

Again, adding the fourth, fifth and sixth equations of (1), we get

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v. \tag{3}$$

3.1 Model Well-Posedness

In this section, we prove the invariant region and well-posedness of the model (1). This is done by proving the positivity, boundedness, existence and uniqueness of the solutions of the model (1) for all time, $t > 0$.

Lemma 3.1.1 (Positivity) Given the initial solution to be $(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), E_v(0), I_v(0)) \geq 0 \in \Phi$. The solution set $(S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t))$ of the onchocerciasis model (1) is non-negative for all time $t > 0$.

Proof. With the assumption of the initial solution set $(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), E_v(0), I_v(0)) \geq 0$, the first equation of model (1) is given as

$$\frac{dS_h}{dt} \geq \Lambda_h - \beta_h(t) S_h$$

where $\beta_h(t) = \dfrac{m_h \beta_h I_v}{N_h} + \mu_h$ so that the solution will be

$$S_h(t) \geq S_h(0) \exp\left(\int_0^t -\beta_h(s)ds\right) + \exp\left(\int_0^t -\beta_h(s)ds\right) \times \int_0^t \Lambda_h \exp\left(\int_0^u \beta_h(\tau)d\tau\right) \geq 0.$$

Hence, $S_h(t) \geq 0,\ \forall,\ t \geq 0$. In the same way, the other remaining state variables are obtained such that $\forall,\ t > 0$,

$$\begin{gathered}
E_h(t) \geq E_h(0) \exp\left[-\left(\sigma_h + \mu_h\right)\right] \geq 0, \\
I_h(t) \geq I_h(0) \exp\left[-\mu_h\right] \geq 0, \\
R_h(t) \geq R_h(0) \exp\left[-\left(\omega + \mu_h\right)\right] \geq 0, \\
S_v(t) \geq S_v(0) \exp\left[\int_0^t -\beta_v(s)ds\right] + \left[\int_0^t -\beta_v(s)ds\right] \times \int_0^t \Lambda_v \exp\left[\int_0^u \beta_v(\tau)d\tau\right] \geq 0, \\
E_v(t) \geq E_v(0) \exp\left[-\left(\sigma_v + \mu_v\right)\right] \geq 0, \\
I_v(0) \geq I_v(0) \exp\left[-\mu_v\right] \geq 0
\end{gathered}$$

where $\beta_v(t) = \dfrac{\mathrm{m}_v \beta_v I_h}{N_h} + \mu_v$.

Lemma 3.1.2 (Boundedness) Assuming that the initial conditions for the human and vector population sizes of model (1) satisfy $N_h(0) = \dfrac{\Lambda_h}{\mu_h}$ and $N_v(0) = \dfrac{\Lambda_v}{\mu_v}$ respectively, then whenever the solution exists on an interval I, it satisfies the following boundeness, $N_h(t) = \dfrac{\Lambda_h}{\mu_h},\ N_v(t) = \dfrac{\Lambda_v}{\mu_v}$.

Proof. We have from equation (2) that

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h.$$

This gives by integrating factor method that

$$N_h(t) = \frac{\Lambda_h}{\mu_h} + \left(N_h(0) - \frac{\Lambda_h}{\mu_h}\right) \exp(-\mu_h t).$$

Whenever $N_h(0) = \dfrac{\Lambda_h}{\mu_h}$, we have $N_h(t) = \dfrac{\Lambda_h}{\mu_h}$. Similarly, we have from equation (3) that $\dfrac{dN_v}{dt} = \Lambda_v - \mu_v N_v$. This gives

$$N_v(t) = \frac{\Lambda_v}{\mu_v} + \left(N_v(0) - \frac{\Lambda_v}{\mu_v}\right) \exp(-\mu_v t)$$

The bound for $N_v(0)$ is given as $N_v(0) = \dfrac{\Lambda_v}{\mu_v}$, we have $N_v(t) = \dfrac{\Lambda_v}{\mu_v}$.

Theorem 3.1.1 (Picard-Lindelof): Let $n \in N, n = (n_i), i = 1, 2, \ldots n$ and $x_0 \in \mathbb{R}^n$. Assume the function $f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n$ is locally Lipschitz with respect to x and continuous with respect to t, x. Then, there exist $t^* > 0$ and a unique function $x : [0, t^*] \to \mathbb{R}^n$ satisfying $x'(t) = f(x(t), t)$ for every $t \in [0, t^*]$ and initial condition $x(0) = x_0$.

Theorem 3.1.2 (Existence and uniqueness)Let $t^* > 0$, if the initial conditions satisfy

$$(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), E_v(0), I_v(0) \geq 0.$$

Then $\forall,\ t \in \mathbb{R}$, the solution set $(S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t))$ exist in $\mathbb{R}_+^7$ and is unique.

Proof. Model (1) is rewrite as

$$X(t) = \begin{bmatrix} S_h(t) \\ E_h(t) \\ I_h(t) \\ R_h(t) \\ S_v(t) \\ E_v(t) \\ I_v(t) \end{bmatrix} \quad \text{and} \quad f(x) = \begin{bmatrix} \Lambda_h - \dfrac{\mathrm{m_h}\beta_h S_h I_v}{N_h} + \omega R_h - \mu_h S_h \\ \dfrac{\mathrm{m_h}\beta_h S_h I_v}{N_h} - (\sigma_h + \mu_h) E_h \\ \sigma_h E_h - (\gamma_h + \mu_h) I_h \\ \gamma_h I_h - (\omega + \mu_h) R_h \\ \Lambda_v - \dfrac{\mathrm{m_v}\beta_v S_v I_h}{N_h} - \mu_v S_v \\ \dfrac{\mathrm{m_v}\beta_v S_v I_h}{N_h} - (\sigma_v + \mu_v) E_v \\ \sigma_v E_v - \mu_v I_v \end{bmatrix}.$$

The vector matrix, $f(x)$ is continuous and locally Lipschitz in $\mathbb{R}^7_+$. Hence by the Picard-Lindelof theorem and the Lemmas proved on positivity and boundedness of solutions, there exists $t^* > 0$ such that the solutions of the model (1) exist locally at least on an interval $[0, t^*]$ and is unique. Hence, the solution set $(S_h(t),\ E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t))$ of the model (1) exists and is unique $\forall,\ t \in \mathbb{R}$. So based on the proof of positivity, boundedness and existence and uniqueness of the solution, we state the following theorem for the mathematical well-posed and biological validity of the model (1). Hence, the model (1) is well-posed and validity in the set

$$\Omega = \left\{ (S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t)) \in \mathbb{R}^7_+, N_h(t) = \frac{\Lambda_h}{\mu_h}, N_v(t) = \frac{\Lambda_v}{\mu_v} \right\}.$$

3.2 Existence of Equilibrium State and Basic Reproduction Number, R_0

We analyze in this section the existence and stability of the disease-free equilibrium state of the model.

3.2.1 Disease-free Equilibrium State, E_0

The disease-free equilibrium (DFE), E_0, is established in the absence of the disease, that is, when $E_h = I_h = E_v = I_v = 0$. This is obtained by solving the model equations (1) simultaneously at the equilibrium state to give the DFE, E_0. as

$$E_0 = (S_h(0), E_h(0), I_h(0), S_v(0), E_v 0, I_v(0)) = \left[\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right]. \tag{4}$$

3.2.2 Basic Reproduction Number, R_0

In order to prove the stability of the disease-free equilibrium state, we first compute the basic reproduction number, R_0, a threshold quantity used to determine whether the disease will remain or die out in the population as time progresses. The basic reproduction number, R_0, is computed using the next-generation approach described by Van de Driessche and Watmough (2002). It is the spectral radius of the characteristics equation $|FV^{-1} - \lambda I| = 0$, where F is the Jacobian matrix at DFE for the rate of new infections in the population, V is the Jacobian matrix at DFE for the transition between the population by other means, λ is the associated eigenvalue, while I is the identity matrix of the same order with F and V. We partition the infected compartments of the model as follows;

$$G = \begin{bmatrix} \dfrac{m_h \beta_h I_v S_h}{N_h} \\ 0 \\ \dfrac{m_v \beta_v I_h S_v}{N_h} \\ 0 \end{bmatrix} \quad \text{and} \quad U = \begin{bmatrix} (\mu_h + \sigma_h) E_h \\ -\sigma_h E_h + (\mu_h + \gamma_h) I_h \\ (\sigma_v + \mu_v) E_v \\ -\sigma_v E_v + \mu_v I_v \end{bmatrix}.$$

Taking the partial derivative of G and U with respect to E_h, I_h, E_v and I_v at the DFE, E_0, we obtained the following matrices;

$$F = \begin{bmatrix} 0 & 0 & 0 & m_h\beta_h \\ 0 & 0 & 0 & 0 \\ 0 & \frac{m_v\beta_v S_{vo}}{N_{ho}} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} (\mu_h+\sigma_h) & 0 & 0 & 0 \\ -\sigma_h & (\mu_h+\gamma_h) & 0 & 0 \\ 0 & 0 & (\sigma_v+\mu_v) & 0 \\ 0 & 0 & -\sigma_v & \mu_v \end{bmatrix}$$

with $S_{v0} = \frac{\Lambda_v}{\mu_v}$, $N_{h0} = \frac{\Lambda_h}{\mu_h}$. Evaluating the characteristics equation, $\left|FV^{-1} - \lambda I\right| = 0$ yields the largest eigenvalue as basic reproduction number, R_0 and is given by

$$R_0^2 = R_{ov}R_{0h} = \frac{m_v\beta_v\sigma_v s_{vo}}{\mu_v(\sigma_v+\mu_v)}\frac{m_h\beta_h\sigma_h}{(\mu_h+\gamma_h)N_{ho}(\sigma_h+\mu_h)} = \frac{m_h m_v\beta_h\beta_v\sigma_h\sigma_v\Lambda_v\mu_h}{\Lambda_h(\mu_h+\gamma_h)\mu_v^2(\sigma_v+\mu_v)(\sigma_h+\mu_h)}. \tag{5}$$

Here, $R_{0v} = \frac{m_v\beta_v\sigma_v S_{v0}}{\mu_v(\sigma_v+\mu_v)}$ is the vector reproduction number and $R_{0h} = \frac{m_h\beta_h\sigma_h}{(\mu_h+\gamma_h)N_{h0}(\sigma_h+\mu_h)}$ is the human reproduction number.

With the approach of the next-generation method by Van de Driessche and Watmough (2002), we state the following theorem for the stability of disease-free equilibrium state, E_0.

Theorem 3.2.2.1 The DFE, E_0, of the model (1) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

3.3 Sensitivity Analysis

Sensitivity analysis is performed to ascertain each model parameter's relative role and influence on the transmission dynamics of onchocerciasis. This analysis enables us to verify and identify those parameters with a high impact on R_0, which relevant stakeholders and intervention strategies should target. It indicates how crucial each model parameter is in the transmission dynamics of onchocerciasis in human and blackfly populations. We employ the approach used by [27], [6], and [15] to investigate the degree of involvement of each model parameter in the onchocerciasis transmission.

Following the approach in [27], [6], [15], the Partial Rank Correlation Coefficients (PRCCs) of the parameters of R_0 are presented in Fig. 2 and Table 3. The PRCCs of the parameters $(\beta_h, \beta_v, m_h, m_v, \sigma_v)$ with significant positive signs (TRUE) indicate that an increase in their values results in a corresponding increase in the value of R_0, which in turn leads to the persistence of the onchocerciasis disease in both human and blackfly populations. Whereas, the PRCCs of the parameters $(\mu_v$ and $\gamma_h)$ with negative signs imply that an increase in their values leads to a decrease in the value of R_0, meaning that the disease can be eradicated in both populations.

Thus, the result of our sensitivity analysis implies that reducing the number of bites by the infected blackflies, recruitment rate of blackflies, progression rate from the exposed vector (blackfly) to the infected vector, effective contact rate between the susceptible human and infected blackfly and effective contact rate between the susceptible blackfly and infected human will eradicate onchocerciasis in both populations. Also, increasing the recovery rate of the infected humans via treatment and increasing the blackfly death rate via insecticides such as larvicides and adulticides will go a long way in reducing the number of infected humans, as this will reduce the vector (blackfly) population drastically.

4 Optimal Control Analysis of Onchocerciasis

This section applies optimal control theory to the onchocerciasis transmission model (1). The basis for applying optimal control to infectious disease epidemics is to single out the best and most effective strategies that will decrease the disease infection rate to the lowest level with optimized cost of implementation [[35]].

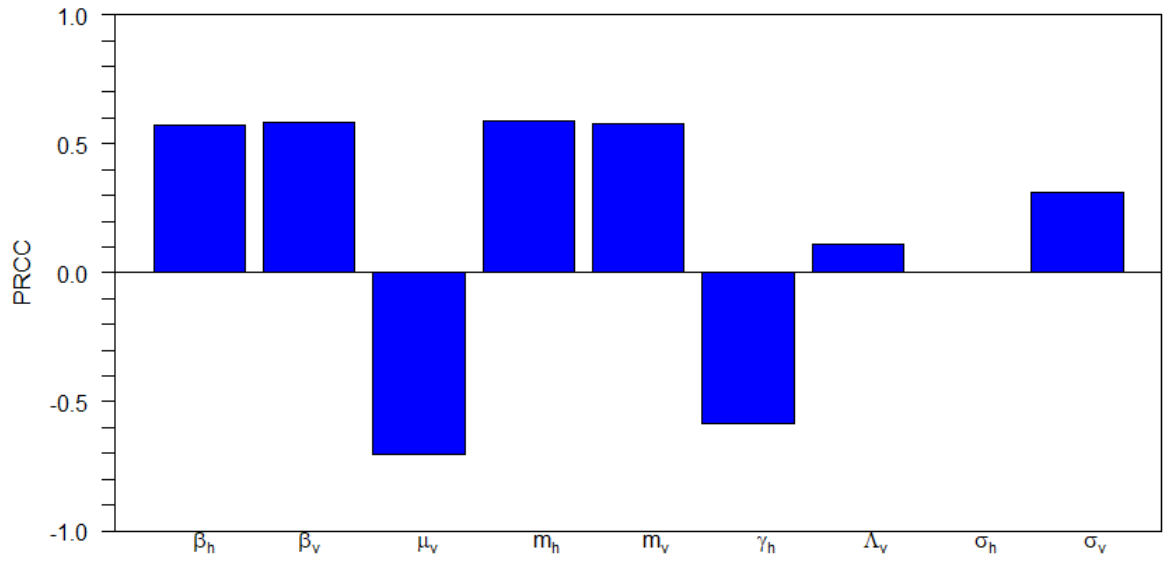

Figure 2: Tornado plot of PRCCs for some model parameters of R_0. Parameter values used are given in Table 2.

Table 3: Parameter PRCC significance (unadjusted p-values)

Variable	PRCC	p-value	Keep
β_h	0.5730809118	0.000000	TRUE
β_v	0.5857611824	0.000000	TRUE
μ_v	-0.703129617	0.000000	TRUE
m_h	0.5876046634	0.000000	TRUE
m_v	0.5793744542	0.000000	TRUE
γ_h	-0.5835942125	0.000000	TRUE
Λ_v	0.1125637169	0.000378	TRUE
σ_h	0.0001702512	0.995700	FALSE
σ_v	0.3098972117	0.000000	TRUE

From the result of our sensitivity analysis, we develop an optimal control method with time-dependent control functions (control variables) $u_1(t), u_2(t), u_3(t)$ where $u_1(t)$ is public health education control, $u_2(t)$ is the treatment control (that is the early treatment for infected human with larva worms and treatment with droxyline for infected human with adult worms) and $u_3(t)$ is the use of insecticides (insecticides spray). Public health education creates awareness about the importance of wearing insect repellents, permethrin-treated clothing, protective coats and long sleeves. It also educates people (the human population) about the transmission of onchocerciasis and how to prevent it via media such as radio, television and social media platforms. The insecticide spray, which includes larvicide and adulticide, will ensure that the breeding sites of the blackflies are minimized and brought

under control. Therefore, the optimal control model of the model (1) is given by;

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_{\mathrm{h}} - \frac{(1-\mathrm{u_1(t)})\,\mathrm{m_h}\beta_{\mathrm{h}}\mathrm{I_v}\mathrm{S_h}}{\mathrm{N_h}} + \omega R_h - \mu_{\mathrm{h}}\mathrm{S_h},\\
\frac{dE_h}{dt} &= \frac{(1-\mathrm{u_1(t)})\,\mathrm{m_h}\beta_{\mathrm{h}}\mathrm{l_v}\mathrm{s_h}}{\mathrm{N_h}} - (\mu_{\mathrm{h}}+\sigma_{\mathrm{h}})\,\mathrm{E_h},\\
\frac{dI_h}{dt} &= \sigma_h E_h - (\gamma_h + \tau \mathrm{u_2(t)} + \mu_h)\, I_h,\\
\frac{dR_h}{dt} &= (\gamma_h + \tau \mathrm{u_2(t)})\, I_h - (\omega + \mu_H)\, R_h,\\
\frac{dS_v}{dt} &= \Lambda_v - \frac{(1-\mathrm{u_1(t)})\,\mathrm{m_v}\beta_{\mathrm{v}}\mathrm{I_h}\mathrm{S_v}}{\mathrm{N_h}} - (\mu_v + \varepsilon \mathrm{u_3(t)})\,\mathrm{S_v},\\
\frac{dE_v}{dt} &= \frac{(1-\mathrm{u_1(t)})\,\mathrm{m_V}\beta_{\mathrm{v}}\mathrm{I_h}\mathrm{S_V}}{\mathrm{N}_h} - (\sigma_v + \mu_v + \varepsilon \mathrm{u_3(t)})\, E_v,\\
\frac{dI_v}{dt} &= \sigma_v E_v - (\mu_v + \varepsilon \mathrm{u_3(t)})\, I_v,
\end{aligned} \tag{6}$$

where τ is the constant rate for the use of treatment control effort and ϵ is the constant rate for the use of insecticide spray control.

Our goal is to minimize the number of exposed humans and the infected human population and increase the number of susceptible humans with the optimal cost of implementation. With regards to onchocerciasis disease, the objective (cost) function to be minimized is given by

$$\mathrm{J}\,(u_1, u_2, u_3) = \int_0^T \left(A_1 I_h + A_2 I_v + \frac{\mathrm{c_1}}{2}\mathrm{u_1^2} + \frac{\mathrm{c_2}}{2}\mathrm{u_2^2} + \frac{\mathrm{c_3}}{2}\mathrm{u_3^2} \right) dt \tag{7}$$

subject to equation (6) with initial conditions of model system (1) on the interval $[0, T]$.

From equation (7), A_1 and A_2 are weighing constants for the onchocerciasis prevention effects on infected human and infected blackfly populations, respectively, T is the final time to implement the controls. Also, the parameters c_1, c_2 and c_3 are the relative costs for implementing the associate control measures, $u_1(t)$, $u_2(t)$ and $u_3(t)$ respectively at the due time. The terms $c_1 u_1^2, c_2 u_2^2$ and $c_3 u_3^2$ depict the costs correlated with the onchocerciasis prevention and control for infected humans and infected blackfly populations. In addition, greater values of c_1, c_2 and c_3 will indicate higher implementation costs for preventing and controlling onchocerciasis for infected humans and blackfly populations.
Thus, we seek an optimal control for $\mathrm{u_1^*}$, $\mathrm{u_2^*}$ and $\mathrm{u_3^*}$, such that

$$\mathrm{J}\,(\mathrm{u_1^*}, \mathrm{u_2^*}, \mathrm{u_3^*}) = \min_{\Omega} \{J\,(\mathrm{u_1}, \mathrm{u_2}, \mathrm{u_3})\} \tag{8}$$

where $\Omega = \{(u_1, u_2, u_3)\,; 0 \le u_i \le 1, i = 1, 2, 3\}$. It is worth noting that in this region, whenever the value of a control is zero, it implies that no investment is made to control the disease, whereas whenever the value of a control is one, it implies that a control effort has been carried-out maximally. To obtain the necessary conditions that an optimal control must satisfy, we employed Pontryagin's Maximum Principle by [12, 15 - 20] to model the system (6) and equation (7). This principle converts model system (6) and equation (7) into a problem of minimizing pointwise a Hamiltonian function, H, with respect to (u_1, u_2, u_3), given as

$$H = I_h + I_v + \frac{c_1}{2}u_1^2 + \frac{c_2}{2}u_2^2 + \frac{c_3}{2}u_3^2 + \sum_{i=1}^{7} \lambda_i\, f_1 \tag{9}$$

where f_i denote the right-hand side of model system (6) and λ_i for $i = 1, 2, \ldots, 7$ denote the associated adjoint variables for the state variables, $S_h, E_h, I_h, R_h, S_v, E_v, I_v$.
We derived the system of adjoint variables by taking the partial derivative of H with respect to each of their corresponding state variable, which gives

$$\frac{\partial \lambda_1}{dt} = -\frac{\partial H}{\partial S_h} = (\lambda_1 - \lambda_2)\frac{(1-u_1(t))m_h\beta_h I_v}{N_h}\left(1 - \frac{S_h}{N_h}\right) + (\lambda_6 - \lambda_5)\frac{(1-u_1(t))\,m_v\beta_v I_h S_v}{N_h^2} + \mu_h\lambda_1,$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E_h} = (\lambda_2 - \lambda_1)\frac{(1-u_1(t))\,m_h\beta_h I_v S_h}{N_h^2} + (\lambda_6 - \lambda_s)\frac{(1-u_1(t))\,m_v\beta_v I_h S_v}{N_h^2} + u_h\lambda_2 + (\lambda_2 - \lambda_3)\,\sigma_h,$$

$$\begin{aligned}\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I_h} &= (\lambda_2 - \lambda_1)\frac{(1-u_1(t))\,m_h\beta_h I_v S_h}{N_h^2} + \mu_h\lambda_3 + (\lambda_3 - \lambda_4)\,(\gamma_h + \tau u_2(t)) \\ &+ (\lambda_5 - \lambda_6)\left(1 - \frac{I_h}{N_h}\right)\frac{(1-u_1(t)m_v\beta_v S_v}{N_h} - A_1,\end{aligned}$$

$$\frac{\partial \lambda_4}{dt} = -\frac{\partial H}{\partial R_h} = (\lambda_2 - \lambda_1)\frac{(1-u_1(t))\,m_h\,\beta_h\,I_v\,S_h}{N_h^2} + (\lambda_6 - \lambda_5)\frac{(1-u_1(t))\,m_v\,\beta_v\,I_h\,S_v}{N_h^2} + \mu_h\,\lambda_4 + (\lambda_4 - \lambda_1)\omega,$$

$$\frac{\partial \lambda_5}{dt} = -\frac{\partial H}{\partial S_v} = (\lambda_5 - \lambda_6)\frac{(1-u_1(t))\,m_v\,\beta_v\,I_h}{N_h} + (\mu_v + \epsilon\,u_3(t))\lambda_5,$$

$$\frac{\partial \lambda_6}{dt} = -\frac{\partial H}{\partial E_v} = \sigma_v(\lambda_6 - \lambda_7) + (\mu_v + \epsilon\,u_3(t))\lambda_6,$$

$$\frac{\partial \lambda_7}{dt} = -\frac{\partial H}{\partial I_v} = (\lambda_1 - \lambda_2)\frac{(1-u_1(t))\,m_h\,\beta_h\,S_h}{N_h} + (\mu_v + \epsilon\,u_3(t))\lambda_7 - A_2 \tag{10}$$

with the transversality conditions, $\lambda_i(t) = 0, i = 1, 2, \ldots, 7$.

The optimal controls, u_1^*, u_2^*, u_3^* are obtained by solving these equations

$$\frac{\partial H}{\partial u_1} = 0,\ \frac{\partial H}{\partial u_2} = 0,\ \frac{\partial H}{\partial u_3} = 0$$

to obtain

$$u_1^* = \frac{1}{c_1}\left[(\lambda_2 - \lambda_1)\frac{m_h\beta_h I_v S_h}{N_h} + \frac{(\lambda_6 - \lambda_5)\,m_v\beta_v I_h S_v}{N_h}\right],\ \ u_2^* = \frac{1}{c_2}\left[(\lambda_3 - \lambda_4)\,\tau I_h\right],$$

and

$$u_3^* = \frac{1}{c_3}\left[\epsilon(\lambda_5\,S_v + \lambda_6\,E_v + \lambda_7\,I_v)\right]$$

and this can be written in compact form as

$$u_1^* = \begin{cases} 0 & \text{for } u_1 \le 0 \\ \dfrac{1}{c_1}\left[(\lambda_2 - \lambda_1)\dfrac{m_h\beta_h I_v S_h}{N_h} + \dfrac{(\lambda_6 - \lambda_5)\,m_v\beta_v I_h S_v}{N_h}\right] & \text{for } 0 < u_1 < 1 \\ 1 & \text{for } u_1 \ge 1 \end{cases}$$

$$u_2^* = \begin{cases} 0 & \text{for } u_2 \leq 0 \\ \dfrac{1}{c_2}\left[(\lambda_3 - \lambda_4)\,\tau I_h\right] & \text{for } 0 < u_2 < 1 \\ 1 & \text{for } u_2 \geq 1 \end{cases}$$

and

$$u_3^* = \begin{cases} 0 & \text{for } u_3 \leq 0 \\ \dfrac{1}{c_3}\left[\epsilon(\lambda_5\, S_v + \lambda_6\, E_v + \lambda_7\, I_v)\right] & \text{for } 0 < u_3 < 1 \\ 1 & \text{for } u_3 \geq 1 \end{cases}$$

Thus, the optimality conditions for the control efforts u_1^*, u_2^* and u_3^* are given in the following theorem.

Theorem 4.1 The optimal control set (u_1^*, u_2^*, u_3^*) that is minimizing the cost function $J\,(u_1^*, u_2^*, u_3^*)$ on Ω is given as follows

$$\left.\begin{aligned} u_1^* &= \max\left\{0, \min\left(1, \frac{1}{c_1}\left[(\lambda_2 - \lambda_1)\,\frac{m_h\beta_h I_v S_h}{N_h} + \frac{(\lambda_6 - \lambda_5)\,m_v\beta_v I_h S_v}{N_h}\right]\right)\right\}, \\ u_2^* &= \max\left\{0, \min\left(1, \frac{\tau\,(\lambda_s - \lambda_4)\,I_h}{c_2}\right)\right\}, \\ u_3^* &= \max\left\{0, \min\left(1, \frac{(\lambda_5 S_v + \lambda_6 E_v + \lambda_7 I_v)}{c_3}\right)\right\}. \end{aligned}\right\} \tag{11}$$

The optimality system comprises of equations (6), (10), (11) and the initial conditions of the model (1). The uniqueness of the solutions of the optimality system is obtained for the time interval $[0, T]$, and the bounded solutions to the optimality system are all unique for $t \in [0, T]$ based on literature [23] [1]. After then, the optimality system will be solved numerically to show the impact of the control strategies.

5 Numerical Simulation

Here, the numerical simulations are implemented using the forward and backward Runge-Kutta method, which is coded in MatLab software. The parameter values in Tables 1 and 2 are used for simulations to determine and propose the best control method for preventing and treating onchocerciasis in both populations. The following strategies are considered for the simulations

1. Single control strategy, that is only public health education $(u_1(t) \neq 0,\ u_2(t) = 0,\ u_3(t) = 0)$, only early treatment $(u_1(t) = 0,\ u_2(t) \neq 0,\ u_3(t) = 0)$, use of insecticides $(u_1(t) = 0,\ u_2(t) = 0,\ u_3(t) \neq 0)$ and it is showing in Figure 3 with its control profile,

2. Double control strategy, that is public health education and early treatment $(u_1(t) \neq 0,\ u_2(t) \neq 0,\ u_3(t) = 0)$, public health education and use of insecticides $(u_1(t) \neq 0,\ u_2(t) = 0,\ u_3(t) \neq 0)$, and early treatment and use of insecticides $(u_1(t) = 0,\ u_2(t) \neq 0,\ u_3(t) \neq 0)$ which is displayed in Figure 4 with its control profile,

3. Triple control strategy that is, public health education, early treatment and use of insecticides, $u_1(t) \neq 0, u_2(t) \neq 0, u_3(t) \neq 0$ and is presented graphically in Figure 5 with control profile.

5.1 Discussion

5.1.1 Single control strategy

Figure 3 displays the effect of implementing single control. From Figure 3(a), we notice that treating only the infectious humans (u_2) decreases the number of infected human compartments more than applying only any of the other control strategies. Figure 3(b) shows the importance of using insecticide spray on vector (blackfly) breeding sites. It reveals that the number of infected vectors diminishes drastically to almost extinction within 10 weeks, implying that applying insecticide spray on the blackfly's breeding site will help reduce the burden of onchocerciasis disease. Figure 3(c) depicts the evolution of the control profile over time. We observed from Figure 3(c) that the upper bounds for implementing only u_1, only u_2 and only u_3 are $100\%, 65\%, 85\%$ respectively and over time they decrease to the lower bound in the final time, 100 weeks. This means that 65% implementation of only prompt treatment for the infected persons will reduce the number of infected persons, but it does not remove the endemicity of the onchocerciasis disease in both host populations, as we notice no effect on infected vectors in Figure 3b. Meanwhile, 85% application of insecticide spray in the breeding site of the blackfly has a significant impact on both populations as it reduces the number of infected humans and infected vectors. This shows the importance of insecticide spray on onchocerciasis disease and aligns with results in [23] and [10].

5.1.2 Double control strategy

Figure 4 depicts the combined implementation of a double control strategy. From Figure $4(a)$, the combined implementation of prompt treatment for the infected humans, (u_2) and any one of public health education, (u_1) or application of insecticide spray, (u_3) decreases the number of infected human in the population than the implementation of public health education and application of insecticide spray in the blackfly breeding sites. While, Figure $4(b)$ shows that within ten weeks, the combined control strategy, applying insecticide spray (u_3) to the onchocerciasis endemic area with any of public health education (u_1) or early treatment for the infected human (u_2) reduces the infect blackflies in the population than any other combination of double strategy. For the alliance of u_1 and u_2, it takes about 90% upper bound of u_1 and 65% of u_2, which u_1 declines gradually to its lower bound at the final time of implementation while u_2 maintain it's upper bound till about 95 weeks before declining to its lower bound (see Figure 4(c)). The combined implementation of u_2 and u_3 requires the upper bound of u_2 and u_3 to be 65% and 58%, respectively, before both decline at 95 weeks to the lower bound. The control profile for simultaneous implementation of public health education, u_1, and applying insecticide spray, u_3 is presented in Figure 4(b). It shows that 38% and 75% upper bounds for u_1 and u_3 gradually decline to their lower bounds at the final implementation time (see Figure 4(b)). We notice from Figure 4 that implementing the double control strategy, such as early treatment for the infected human and applying insecticide spray in the breeding site of blackflies, will have more impact on both host populations than any other double control strategy implementation.

5.1.3 Triple control strategy

Figure 5 shows the population dynamics of the infected human population, $I_h(t)$, infected blackfly population, $I_v(t)$ with triple control strategy, without control strategy, and the control profile. As shown in Figure $5(a-b)$, with the implementation of triple control strategy, the number of infected humans (Figure 5(a)) and infected blackflies (Figure 5(b)) reduced drastically, leaving a small number of infected humans in the population and almost zero infected blackfly population after ten weeks. Whereas without control strategy reveals the endemicity of the onchocerciasis infection in both host populations, with the infected blackfly population decreasing to almost zero after 95 weeks. Figure $5(c)$ displays the control profile for achieving the results in Figure 5(a-b). The combine triple control strategy requires about 17%, 65% and 58% upper bounds for u_1, u_2 and u_3 respectively. The numerical simulation results agree with the sensitivity analysis result in Subsection (3.3). This reveals that

combined implementation of control strategies will help to prevent the further spread of onchocerciasis disease in both human and blackfly populations and, thus, provides the health practitioners and relevant stakeholders with the best intervention strategies, which in tune with WHO onchocerciasis prevention and control guidelines [34].

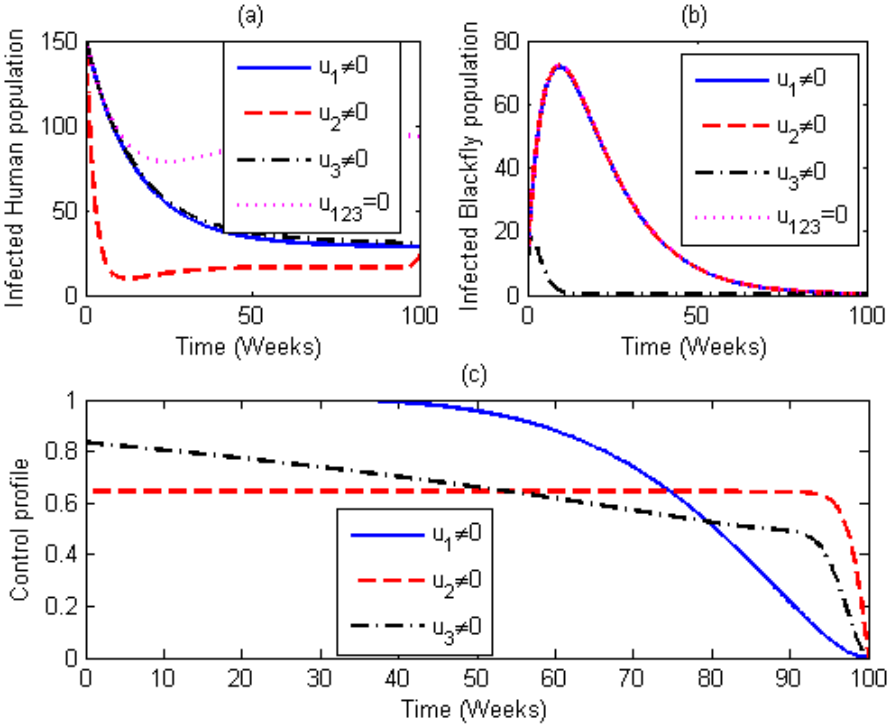

Figure 3: Simulation plots showing implementation of any single control strategy (a) for the infected human population, $I_h(t)$, (b) for infected blackfly population, $I_v(t)$, (c) the control profile for $(u_1 \neq 0,\ u_2 = 0,\ u_3 = 0)$, $(u_1 = 0, u_2 \neq 0,\ u_3 = 0)$, and $(u_1 = 0,\ u_2 = 0,\ u_3 \neq 0)$. The parameter values and initial population values used are given in Tables 1 and 2 with $A_1 = 0,\ A_2 = 1, C_1 = 100$, $C_2 = 300$, $C_3 = 200$, $\tau = 0.5$, $\epsilon = 0.5$.

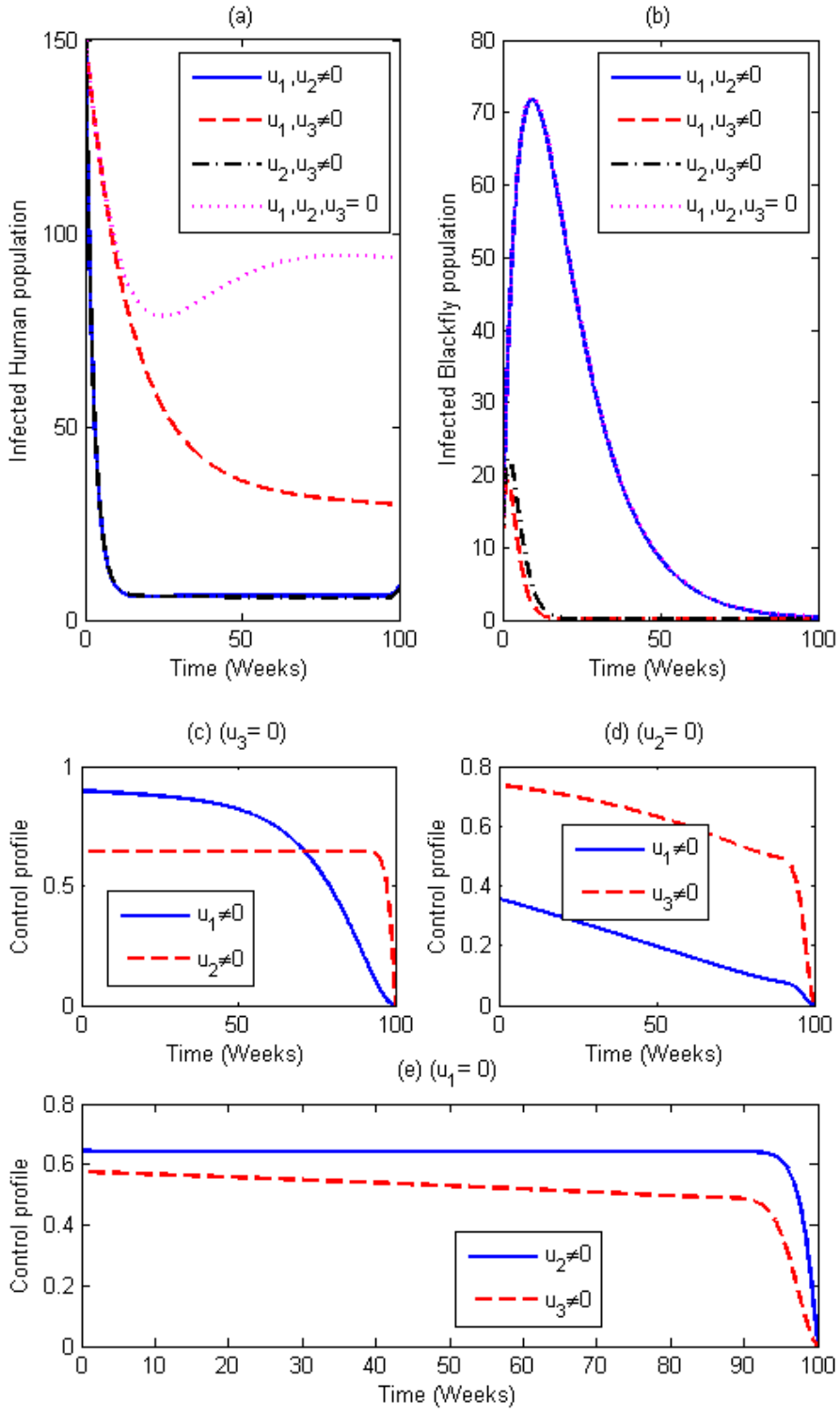

Figure 4: Simulation plots showing implementation of any double control strategies for (a) infected human population, $I_h(t)$, (b) infected blackfly population, $I_v(t)$, (c) the control profile for $u_1 \neq 0$, $u_2 \neq 0$, $u_3 = 0$, (d) control profile for $u_1 \neq 0$, $u_2 = 0$, $u_3 \neq 0$ and (e) control profile for $u_1 = 0$, $u_2 \neq 0$, $u_3 \neq 0$. The parameter values and initial population values used are given in Tables 1 and 2 with $A_1 = 0$, $A_2 = 1$, $C_1 = 100$, $C_2 = 300$, $C_3 = 200$, $\tau = 0.5$, $\epsilon = 0.5$.

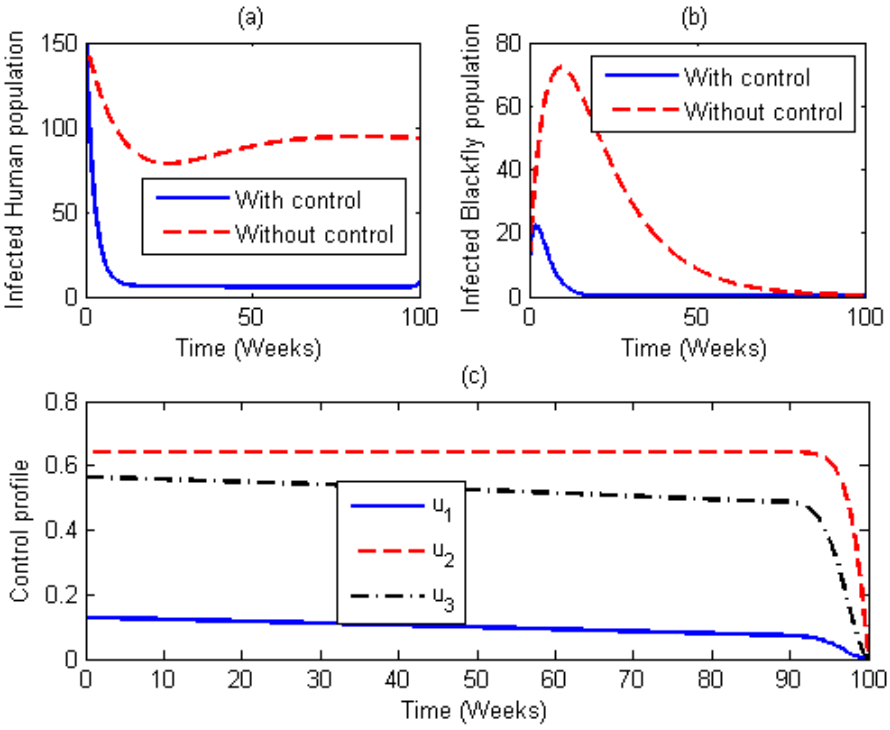

Figure 5: Simulation plots showing implementation of all the triple control strategies and without control strategy for (a) infected human population, $I_h(t)$, (b) infected blackfly population, $I_v(t)$, (c) the control profile for $u_1 \neq 0$, $u_2 \neq 0$, $u_3 \neq 0$. The parameter values and initial population values used are given in Tables 1 and 2 with $A_1 = 0$, $A_2 = 1$, $C_1 = 100$, $C_2 = 300$, $C_3 = 200$, $\tau = 0.5$, $\epsilon = 0.5$.

6 Conclusion

A mathematical model for the dynamics of onchocerciasis is formulated in this work. First, the fundamental properties of the model, such as positivity, boundedness and the existence and uniqueness of the solutions of the model, are proven. The threshold quantity, the basic reproduction number, is derived and used to establish the stability of the disease-free equilibrium. The sensitivity analysis is conducted to determine the influence of each model parameter of basic reproduction number on onchocerciasis transmission. The result revealed that reducing the number of bites by the infected blackflies, blackfly recruitment rate, blackfly progression rate, effective contact rates for both populations and increasing human recovery rate and the blackfly death rate will eradicate onchocerciasis in both populations. Based on the sensitivity analysis result, an optimal control model is developed and applied Pontryagin's maximum principle to obtain the optimality system that is solved numerically. The numerical results revealed that when public health education, early treatment, and insecticide use are implemented together, the optimal level of control and containment of Onchocerciasis is achieved. The findings of this study can serve as a valuable reference for the Onchocerciasis Local National Control Program, as well as the foundation for the planning and design of the best intervention strategies to eradicate Onchocerciasis by relevant stakeholders.

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