Sensitivity Analysis of Onchocerciasis Transmission Dynamics

Chinwendu E. Madubueze, Isaac O. Onwubuya, Godwin N. Nkem, Adedeji D. Gbadebo and E. James

ABSTRACT - To prevent the further transmission of onchocerciasis, a deterministic model of onchocerciasis disease transmission incorporating vector control (Larvicides) and public health education as intervention measures has been developed and evaluated. The equilibrium states (disease-free and endemic equilibria) and the model's reproduction number, R_0, have also been established. The Latin Hypercube Sampling (LHS) and the Partial Rank Correlation Coefficient (PRCC) techniques are applied to the parameters of R_0, to assess the influence of each model parameter on the transmission of the disease. Our sensitivity analysis shows that larvicides and public health awareness considerably impact onchocerciasis transmission. This is also supported by the simulation results.

Index Terms - Onchocerciasis, Sensitivity analysis, Equilibrium state, Basic reproduction number, Larvicides, Public health education.

I. INTRODUCTION

Onchocerciasis, a primary cause of blindness and skin lesion, is a filarial infection as well as a vector borne parasite disease. It is transmitted by repeated bites from an infected blackfly (Simulium damnosum) to human [5]. Onchocerciasis is one of the 'neglected' tropical diseases and the world's second leading infectious cause of blindness in humans after trachoma. The disease is common in tropical areas where residents are living near an oxygen-rich running streams and rivers, which encourages the environmental survival of Simulium damnosum's aquatic nature and the spread of the disease [6]. This also explains the adoption of the popular term, 'river blindness disease' [27]. The presence of riverine breeding grounds for blackflies has a significant impact on the frequency of onchocerciasis infection in a community as the disease burden is higher in areas near rivers. The prevalence of the disease is highest among people age 30 years. Furthermore, there are geographical and gender-specific changes in the pattern of onchocerciasis infection; the morbidity rate is higher in men than in women [7].

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C. E. Madubueze is a Senior Lecturer at the Federal University of Agriculture, Makurdi, Nigeria (corresponding author phone: +2348039523389; e-mail: ce.madubueze@gmail.com).

I. O. Onwubuya is a PhD candidate at the Federal University of Agriculture, Makurdi, Nigeria. (e-mail: isaacobiajulu@gmail.com).

G. N. Nkem is a Research Associate at the Walter Sisulu University, Mthatha, Eastern Cape, South Africa. (e-mail: nkemgodwin1@gmail.com).

A. D. Gbadebo is a Research Fellow at the Walter Sisulu University, Mthatha, Eastern Cape, South Africa. (e-mail: gbadebo.adedejidaniel@gmail.com).

E. James is an undergraduate student of the Federal University of Agriculture, Makurdi, Nigeria. (e-mail: jamesenemona34@gmail.com).

According to [8], about 90% of onchocerciasis cases are found in Africa, primarily in West Africa.

Onchocerca volvulus is a parasite that lodges in the eye and skin of an infected person. It is the foremost cause of eye and skin diseases which microfilariae are the symptom's causation and move in the subcutaneous tissue of the human body [8, 9]. Some people that are infected experience severe itching and different skin abnormalities, while others experience eye lesions which could result in irreversible blindness or visual loss. Typically, nodules grow beneath the skin around the adult worms [9].

The WHO recommends ivermectin (mectizan)® as the standard medicine for the treatment of onchocerciasis, worldwide [9], and this has been deployed over the years. Onchocerciasis is common in Africa, particularly, in Nigeria where it continues to pose a serious public health risk [3]. South American countries such as Colombia, Ecuador, Mexico, and Guatemala have been declared onchocerciasis-free by the WHO. They implemented mass ivermectin administration bi-annually for years. However, it is still an endemic problem in the African sub-region, two Latin American countries (Brazil and Venezuela), and Yemen in the Arabian Peninsula [8, 9], and this can be traced to issues such as the lack of political will, political instabilities, and cultural and environmental factors. As a result, additional interventions are needed in these regions to stop the further transmission of onchocerciasis infection.

The fumigation of streams and riverine areas and the public health education for citizens are some of the interventions recommended by [8, 9]. These strategies would supplement mass ivermectin administration [12]. The public health education strategy focuses on sharing adequate knowledge of the epidemiology of onchocerciasis, whereas, fumigation is the act or process of disinfecting an area with the fumes of many chemicals (larvicides) for the purpose of eliminating disease-causing pathogens.

Several authors have developed mathematical models of onchocerciasis [1,2,5,6,13,14,15,17,18,19,20,22]. Various strategies have also been used to analyze these models within controlled environments and without control. [14] developed a compartmental model to describe the transmission process of the onchocerciasis disease, [1] investigated the stability of a deterministic model of the disease, and [20] modelled onchocerciasis spread and its management in tropical nations using Nigeria as a case study. Onchocerciasis was discussed by [17] using a deterministic model on CDTI prospects, while a specific ivermectin medication for onchocerciasis disease was modeled in [18]. A mathematical model with multiple intervention options was established in [19]. According to [2],

ivermectin use alone might not be sufficient to eradicate onchocerciasis in the population. With that, [4] examined the impact of larvicide application on the control of blackflies in West Africa.

From the aforementioned authors, none studied the potential of implementing public health education and fumigation alongside mass ivermectin administration (mectizan)® to eradicate onchocerciasis using mathematical model approach. Thus, this study will evaluate the impact of these three controls on onchocerciasis's transmission dynamics by formulating a compartmental model of onchocerciasis infection with control measures. The sensitivity analysis of the model will be performed using LHS and PRCCs techniques on reproduction number in order to assess how each parameter affects onchocerciasis disease transmission.

The rest of the paper is organised as follows: Section 2 is the model formulation for the onchocerciasis with control strategies. The model analysis for the onchocerciasis is discussed in Section 3. In Section 4, numerical simulation and discussion are carried out to verify some analytical results while Section 5 is the conclusion.

II. MODEL FORMULATION

In this section, a deterministic model that involves two populations is developed for onchocerciasis dynamics. The two populations are human and vector (blackfly) populations. The human population at any time, t is subdivided into five (5) populations namely: Susceptible human $(\mathrm{S_h}(t))$, Exposed human $(\mathrm{E_h}(t))$, Infected human without blindness $(\mathrm{I_h}(t))$, Infected human with blindness $(\mathrm{I_{hb}}(t))$, and the Recovered human $(\mathrm{R_h}(t))$. The blackfly population at any time, t, consists of three (3) components namely: the Susceptible blackflies $(\mathrm{S_v}(t))$, the Exposed blackflies $(E_v(t))$, and the Infected blackflies $(\mathrm{I}_v(t))$.

The dynamics of the susceptible human population is generated via birth/immigration at a rate, Λ_h. Susceptible human becomes infected when bitten by infected blackflies at a force of infection, $\lambda_\mathrm{h} = \frac{\mathrm{m_b}(1-\varepsilon)\beta_h I_v}{N_h}$, and becomes exposed in latent periods. Here, ε (i. e. $0 < \varepsilon < 1$) is the public health education constant, $\mathrm{m_b}$ is the biting rate of blackflies and β_h is the human transmission rate. After a period of time, the exposed human $(\mathrm{E_h})$ progresses to infected human without blindness population $(\mathrm{I_h})$ at a rate, σ_h. A proportion, τ, of infected humans without blindness $(\mathrm{I_h})$, recovers due to early treatment at rate, γ_1 while the complementary proportion develops complications that resulted in blindness at a rate, ϕ. We assume that infected humans with blindness $(\mathrm{I_{hb}})$ recover from onchocerciasis at rate, γ_2 with treatment spite of their blindness. Those who recovered from the disease lose drug induced immunity at a rate, ω. For the population of humans, the natural mortality rate is assumed to be at rate, μ_h.

For blackfly population, we have a recruitment rate, Λ_v, that occurs via birth/immigration in the population. This creates the susceptible blackfly population (S_v) that decreases by the application of larvicides at a rate, ρ_1 where ρ_1 is larvicides' application. Susceptible blackfly population (S_v) is also reduced by force of infection, $\lambda_\mathrm{v} = \frac{m_b(1-\varepsilon)(\beta_{v1}I_h+\beta_{v2}I_{hb})}{N_h}$ of the susceptible blackfly which feeds on infectious human blood meals and becomes exposed blackfly. Here, β_{v1} is the blackfly transmission rate from $\mathrm{I_h}(t)$ and β_{v2} as the blackfly transmission rate from $\mathrm{I_{hb}}(t)$. Exposed vector (E_v) decreases by progression rate, σ_v and becomes an infected blackfly $(\mathrm{I_v})$. Apart from the public health education control and the application of larvicides, the blackfly population is also reduced by predation by other animals at rate, ρ_2. The blackflies natural mortality rate is considered to be rate, μ_v. The schematic flow diagram illustrating the dynamics of the system is represented in Fig 1.

With the flow diagram and the model description, we obtain the following system of ordinary differential equations for the onchocerciasis dynamics;

$$\left.\begin{aligned}
\tfrac{dS_h}{dt} &= \Lambda_h + \omega R - \lambda_h S_h - \mu_h S_h,\\
\tfrac{dE_h}{dt} &= \lambda_h S_h - (\sigma_\mathrm{h} + \mu_\mathrm{h})E_h,\\
\tfrac{dI_h}{dt} &= \sigma_h E_h - (\tau\gamma_1 + (1-\tau)\phi + \mu_\mathrm{h})I_h,\\
\tfrac{dI_{hb}}{dt} &= (1-\tau)\phi I_h - (\gamma_2 + \mu_\mathrm{h})I_{hb},\\
\tfrac{dR_h}{dt} &= \tau\gamma_1 I_h + \gamma_2 I_{hb} - (\omega + \mu_\mathrm{h})R_h,\\
\tfrac{dS_v}{dt} &= \Lambda_v(1-\rho_1) - \lambda_v S_v - (\mu_\mathrm{v} + \rho_1 + \rho_2)S_v,\\
\tfrac{dE_v}{dt} &= \lambda_v S_v - (\mu_\mathrm{v} + \sigma_\mathrm{v} + \rho_1 + \rho_2)E_v,\\
\tfrac{dI_v}{dt} &= \sigma_v E_v - (\mu_\mathrm{v} + \rho_1 + \rho_2)I_v\,,
\end{aligned}\right\} \quad (1)$$

where $\lambda_\mathrm{h} = \frac{\mathrm{m_b}(1-\varepsilon)\beta_h I_v}{N_h}$ and $\lambda_\mathrm{v} = \frac{m_b(1-\varepsilon)(\beta_{v1}I_h+\beta_{v2}I_{hb})}{N_h}$ with initial data, $S_h(0) = S_{h0}$, $E_h(0) = E_{h0}$, $I_h(0) = I_{h0}$, $I_{hb}(0) = I_{hb0}$, $R_h(0) = R_{h0}$, $S_v(0) = S_{v0}$, $E_v(0) = E_{v0}$, $I_v(0) = I_{v0}$.

With $N_h(t) = S_h(t) + E_h(t) + I_h(t) + I_{hb}(t) + R_h(t)$ and $N_v(t) = S_v(t) + E_v(t) + I_v(t)$, this implies that

$$\left.\begin{aligned}
\tfrac{d\mathrm{N_h(t)}}{dt} &= \Lambda_h - \mu_h \mathrm{N_h(t)},\\
\tfrac{d\mathrm{N_v(t)}}{dt} &= \Lambda_v(1-\rho_1) - (\mu_v + \rho_1 + \rho_2)\mathrm{N_v(t)}.
\end{aligned}\right\} \quad (2)$$

III. MODEL ANALYSIS

A. Positivity of Solutions

We established that all system (1) solutions with non-negative initial data are non-negative for all $t > 0$.

Theorem 1. If the initial data of system (1) are non-negative, then the solutions $\{S_h, E_h, I_h, I_{hb}, R_h, S_v, E_v, I_v\}$ of the system (1) remain non-negative for all time $t \geq 0$.

Proof. From the first equation of (1), we have

$$\frac{dS_h}{dt} = \Lambda_h + \omega R_h - \lambda_h S_h - \mu_h S_h \;\geq -(\lambda_h + \mu_h)S_h$$

from which $S_h(t) \geq S_h(0)\exp\{\int_0^t -(\lambda_h + \mu_h)\,d\tau\} \geq 0$.

This implies that $S_h(t) \geq 0$ for all time $t \geq 0$.

The same idea can be used to show the positivity of other state variables for all $t > 0$. Thus, the solutions of the model equation (1) remain positive for all $t \geq 0$ since they are exponential functions.

B. Invariant Region

Lemma 1. Given the solutions $(\mathrm{S_h}, \mathrm{E_h}, \mathrm{I_h}, \mathrm{I_{hb}}, \mathrm{R_h}, \mathrm{S_v}, \mathrm{E_v}, \mathrm{I_v})$ of the system (1) with positive initial conditions, the region given by the set $\Omega = \Omega_h \times \Omega_v$ where $\Omega_h = \left\{(S_h, E_h, I_h, I_{hb}, R_h) \epsilon R_+^5 : N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$, $\Omega_v = \left\{(S_v, E_v, I_v) \epsilon R_+^3 : N_v \leq \frac{\Lambda_v(1-\rho_1)}{(\mu_v+\rho_1+\rho_2)}\right\}$ is positive invariant region for the model system (1).

Proof. From equation (2), it can be shown by differential inequality that

$$\underset{t\to\infty}{limsup} N_h \leq \frac{\Lambda_h}{\mu_h} \text{ and } \underset{t\to\infty}{limsup} N_v \leq \frac{\Lambda_v(1-\rho_1)}{(\mu_v+\rho_1+\rho_2)}.$$

Hence, the set Ω is positively invariant, that is, all the solutions in Ω remain in Ω for $t > 0$.

C. Disease-Free Equilibrium State

At equilibrium state, the model (1) is not changing with time. This implies equating to zero the right-hand side of equation (1) and solve simultaneously to obtained the disease-free equilibrium state (DFE) when $E_h = 0$. This is given by

$$E_0 = (S_h^0, E_h^0, I_h^0, I_{hb}^0, R_h^0, S_v^0, E_v^0, I_v^0) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, \frac{\Lambda_v(1-\rho_1)}{k_5}, 0, 0\right) \quad (3)$$

with $N_h^0 = S_h^0 = \frac{\Lambda_h}{\mu_h}$ and $\mathrm{k_5} = \mu_\mathrm{v} + \rho_1 + \rho_2$.

D. Basic Reproduction Number

One of the most fundamental threshold quantities in epidemiology is the basic reproduction number, $\mathrm{R_0}$. It measures an infectious disease's maximum reproductive potential. The basic reproduction number is the average number of secondary cases arising from a primary infected case introduced in an entirely susceptible population [11]. It is derived using the next generation approach to find the spectral radius of matrix, $\mathcal{F}V^{-1}$ where F is the appearance of new infections matrix and V is the matrix of infection transfer by other means. Both matrices are Jacobian matrices of column vectors, F_i and V_i respectively such that F_i and V_i are presented as

$$F_i = \begin{pmatrix} \frac{\mathrm{m_b}(1-\varepsilon)I_v S_h \beta_h}{N_h} \\ 0 \\ 0 \\ \frac{m_b(1-\varepsilon)(\beta_{v1} I_h + \beta_{v2} I_{hb}) S_v}{N_h} \\ 0 \end{pmatrix},$$

$$\mathrm{V_i} = \begin{pmatrix} \mathrm{k_1 E_h} \\ -\sigma_\mathrm{h} \mathrm{E_h} + \mathrm{k_2 I_h} \\ -(1-\tau)\phi \mathrm{I_h} + \mathrm{k_3 I_{hb}} \\ \mathrm{k_6 E_v} \\ -\sigma_\mathrm{v} \mathrm{E_v} + \mathrm{k_5 I_v} \end{pmatrix}$$

where

$$\left.\begin{array}{l} \mathrm{k_1} = \sigma_\mathrm{h} + \mu_\mathrm{h},\ \mathrm{k_2} = \tau\gamma_1 + (1-\tau)\phi + \mu_\mathrm{h}, \\ \mathrm{k_3} = \gamma_2 + \mu_\mathrm{h},\ \mathrm{k_4} = \omega + \mu_\mathrm{h}, \mathrm{k_5} = \mu_\mathrm{v} + \rho_1 + \rho_2, \\ \mathrm{k_6} = \mu_\mathrm{v} + \rho_1 + \rho_2 + \sigma_\mathrm{v}\,. \end{array}\right\} \quad (4)$$

Taking the partial derivatives of F_i and V_i at DFE, E_0, we obtained

$$\mathcal{F} = \begin{pmatrix} 0 & 0 & 0 & 0 & \frac{\mathrm{m_b}(1-\varepsilon)S_h^0\beta_h}{N_h^0} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\mathrm{m_b}(1-\varepsilon)\beta_{v1}S_v^0}{N_h^0} & \frac{\mathrm{m_b}(1-\varepsilon)\beta_{v2}S_v^0}{N_h^0} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mathrm{k_1} & 0 & 0 & 0 & 0 \\ -\sigma_\mathrm{h} & \mathrm{k_2} & 0 & 0 & 0 \\ 0 & -(1-\tau)\phi & \mathrm{k_3} & 0 & 0 \\ 0 & 0 & 0 & \mathrm{k_6} & 0 \\ 0 & 0 & 0 & -\sigma_\mathrm{v} & \mathrm{k_5} \end{pmatrix}.$$

The basic reproduction number, $\mathrm{R_0}$, which is the dominant eigenvalue of the matrix $F\mathrm{V}^{-1}$ is given by

$$\mathrm{R_0} = \sqrt{\frac{\mathrm{m_b}(1-\varepsilon)^2(1-\rho_1)\sigma_\mathrm{v}\sigma_\mathrm{h}\Lambda_v\mu_h\beta_\mathrm{h}(\beta_{\mathrm{v}1}\mathrm{k_3}+\beta_{\mathrm{v}2}(1-\tau)\phi)}{\mathrm{k_1 k_2 k_3 k_5^2 k_6}\Lambda_h}} \quad (5)$$

with $\mathrm{k}_1, \mathrm{k}_2, \mathrm{k}_3, \mathrm{k}_5, \mathrm{k}_6$ defined in Eq. (4).

The application of next-generation method implies the following stability theorem.

Theorem 2. The disease-free equilibrium, $\mathrm{E_0}$, is locally asymptomatically stable provided $\mathrm{R_0} < 1$ otherwise it is unstable when $\mathrm{R_0} > 1$.

Theorem 2 means that onchocerciasis disease will be eradicated in the community if $\mathrm{R_0} < 1$ while it remains in the population when $\mathrm{R_0} > 1$.

E. Existence of Endemic Equilibrium

The endemic equilibrium state is solved when $E_h \neq 0$. We have the endemic equilibrium as follows:

$E^* = (S_h^*, E_h^*, I_h^*, I_{hb}^*, R_h^*, S_v^*, E_v^*, I_v^*)$

where

$S_h^* = \frac{\Lambda_h k_2 k_3 k_4 - A E_h^*}{\mu_h k_2 k_3 k_4},\ I_h^* = \frac{\sigma_h E_h^*}{k_2},\ I_{hb}^* = \frac{(1-\tau)\phi I_h^*}{k_3},$

$R_h^* = \frac{\tau\gamma_1 I_h^* + \gamma_2 I_{hb}^*}{k_4},\ E_v^* = \frac{k_5 I_v^*}{\sigma_v},\ S_v^* = \frac{\Lambda_v(1-\rho_1)\sigma_v - k_5 k_6 I_v^*}{\sigma_v k_5},$

$I_v^* = \frac{\Lambda_v(1-\rho_1)\sigma_h\sigma_v D E_h^*}{k_5 k_6 (N_h^* k_2 k_3 k_5 + \sigma_h D E_h^*)}$

and E_h^* serves as the positive solution of the quadratic equation

$$PE_h^{*2} + QE_h^* - R = 0$$

such that

$P = Ak_1k_4k_5k_6\mu_h\sigma_h D + A^2k_1k_5^2k_6$,

$Q = A\Lambda_h k_1k_2k_3k_4k_5^2k_6\left(2 - \frac{\sigma_h R_0^2\omega}{A}\left((1-\tau)\phi\gamma_2 + \tau k_3\gamma_1\right)\right) + k_1k_2k_3\mu_h\sigma_h Dk_4^2(\Lambda_h k_5k_6 + m_{b2}(1-\varepsilon)\beta_h\Lambda_v(1 - \alpha\rho_1)\sigma_v)$,

$R = \Lambda_h^2k_1k_2^2k_3^2k_4^2k_5^2k_6(R_0^2 - 1)$,

with

$A = k_1k_2k_3k_4 - (1-\tau)\phi\omega\gamma_2\sigma_h - \omega\tau\gamma_1k_3\sigma_h > 0$,

$D = m_b(1-\varepsilon)(\beta_{v1}k_3 + \beta_{v2}(1-\tau)\phi)$,

$N_h^* = \frac{(k_2k_3k_4\mu_h + \sigma_hk_3\mu_h(k_4+\gamma_1) + \sigma_h(1-\tau)\phi\mu_h(k_4+\gamma_2) - A) + k_2k_3k_4\Lambda_h}{k_2k_3k_4\mu_h}$.

This implies that $E_h^* = \frac{-Q+\sqrt{Q^2+4PR}}{2P} > 0$ provides that $R_0 > 1$. Thus, the endemic equilibrium, $E^* = (S_h^*, E_h^*, I_h^*, I_{hb}^*, R_h^*, S_v^*, E_v^*, I_v^*)$ exists whenever $R_0 > 1$.

F. Sensitivity Analysis

Sensitivity analysis is used in disease modelling to identify how influential the model parameters are on the basic reproduction number [16]. The Latin Hypercube Sampling (LHS) scheme and Partial Rank Correlation Coefficients (PRCCs) technique are employed to investigate the biological contributions of each model parameter on the basic reproduction number [32]. For the sensitivity analysis, the parameters of R_0 will be sampled by LHS scheme and then computed using PRCCs. The impact of each model parameters on R_0 is investigated by performing 1000 simulations for per run. The PRCCs' signs enabled us to ascertain the strength of relationship between the model parameters and R_0. Thus, an increase in the model parameters with positive (negative) PRCCs will result in an increase (decrease) in R_0.

The PRCCs' outcome for each model parameter with respect to R_0 are shown in Figures 2 and 3. The tornado plot (Fig. 2) and scatter plots (Fig. 3) demonstrate the degree at which each parameter influences R_0. Fig. 2 shows that of all the eleven parameters of R_0, the human transmission rate (β_h), the biting rate of blackflies (m_b), the natural death rate of the blackfly (μ_v), the public health education constant (ε) and the larvicides application (ρ_1) have great effects on R_0 which make them inclusive in formulating policy for the control of onchocerciasis infection. Furthermore, Monte Carlo results are demonstrated in Fig. 3 for five parameters with large PRCCs values. It is evident in Fig 3 that an increase in the model parameters μ_v, ε, ρ_1 and decrease in the parameters β_h and m_b will result to a decrease in R_0 which supports the PRCCs in Fig. 2 and Table II.

Some important parameters with p-values less than 0.05 in Table II are shown in Tables III and IV along with the pairwise PRCCs' comparisons for unadjusted and false discovery rate (FDR) adjusted p-values. The purpose is to identify any discrepancy in the processes characterising the compared parameters. When the compared pair parameters have a p-value less than 0.05, it implies that the paired parameters are different (TRUE), otherwise, it is not different (FALSE) for p-values greater than 0.05. With the exception of the pairs $\beta_h - m_b$, $\mu_v - \rho_1$, $\Lambda_v - \phi$, every other pair of PRCC parameters are significantly different, as seen in Table V. The paired parameters, $\beta_h - m_b$ and $\mu_v - \rho_1$ are not different as they behave similarly whereas the paired parameters, $\Lambda_v - \phi$, are not among the most sensitivity parameters. This demonstrates that these five parameters $(\beta_h, m_b, \mu_v, \varepsilon, \rho_1)$ have the greater influence and superior force in the transmission of onchocerciasis disease. Thus, efforts should be geared towards these parameters in other to halt the onchocerciasis from spreading more in the two populations.

Furthermore, the effect of the control parameters, ε and ρ_1, is demonstrated in Fig. 4 as contour lines and 3D plot. Fig. 4a shows that the basic reproduction number R_0 is less than one when the application of larvicides is between the range 0.1 – 0.3 ($\rho_1 = 0.1 - 0.3$) and the public health education is high ($\varepsilon = 0.8$ and above). Fig. 4(b) illustrates that the basic reproduction number, R_0 decreases drastically when ε and ρ_1 increase and vice versa. This implies that raising public awareness of onchocerciasis disease and the application of larvicides in the breeding sites of the blackfly will reduce onchocerciasis disease in human and blackfly populations.

IV. NUMERICAL RESULTS

The numerical results of the model (1) is demonstrated in this section. The 4th Order Runge-Kutta scheme which is imbedded in MatLab R2007b is used. The parameters values in the Table II and the Initial data, $S_h(0) = 20000, E_h(0) = 1500, I_h(0) = 100, I_{hb}(0) = 50, R_h(0) = 10,\ S_v(0) = 2500, E_v(0) = 250, I_v(0) = 10$ are employed for the numerical results.

G. Discussion

Fig. 5 shows the effect of the application of larvicides only, ρ_1, public health education only, ε , and the simultaneous application of larvicides and public health education, (ρ_1, ε) , on the transmission of onchocerciasis in the population. The results in Fig. 5 reveal that public health education alone ($\varepsilon = 0.5$) has no significant impact in controlling the disease (see Fig 5(a-d)) and $R_0 > 1$. Whereas, the application of larvicides alone ($\rho_1 = 0.5$) results to a significant reduction in the infected vectors population (see Fig. 5(d)), which in turn results to a reduction in the infected humans population (see Figs. 5(a-b)), and $R_0 < 1$. The results are better with the simultaneous application of larvicides and public health education when compared to that of the application of larvicides only. Although, the application of larvicides only can stop the further spread of

disease but the simultaneous application of larvicides and public health education is advocated because the public health education will address the challenges of lack of political will, political instabilities and cultural factors that perpetuate the disease.

Fig. 6(a-d) demonstrates the importance of larvicides application on onchocerciasis disease when the public health education control is 0.5 . It is observed that when the rate of applying larvicides is low ($\rho_1 = 0.1$), the disease spreads and becomes endemic in the population in spite of the simultaneous application of public health education. However, when the rate of larvicide application is increased from $\rho_1 = 0.3$, the endemicity of the onchocerciasis disease drastically declines and is brought under control. This suggests that extensive and consistent fumigation of the environment alongside onchocerciasis-related public health education will control the burden of onchocerciasis disease in the population.

Fig. 7(a-d) depicts the impact of the rate of public health education on the spread of the onchocerciasis illness while the application of larvicides is kept constant at a concentration of 0.5. Fig. 7(a, b, d) reveals that with more public health education, the infected humans (see Fig. 7[a-b]) and infected blackflies (Fig. 7d) populations will reduce drastically. It also shows that with a 70% implementation of public health education, the number of infected humans without blindness (Fig. 7a) and infected blackflies (Fig, 7d) reduces to almost zero after 250 days and 300 days, respectively. The increase in susceptible blackflies occurs because of constant larvicide application ($\rho_1 = 0.5$) in the environment but it is still less in number when compared with Fig. 6(c). The phase portraits for sub-populations of the model when $R_0 < 1$ and $R_0 > 1$ are presented in Figs. 8 and 9. When $R_0 < 1$, the model solutions tend to the disease-free equilibrium (see Fig. 8[a-d]), implying that the onchocerciasis disease will be eliminated in the population with time. Whereas, in Fig. 9 for $R_0 > 1$, the solutions tend to endemic equilibrium, indicating an increase in the degree of infectivity in the population.

V. CONCLUSION

This study examined a mathematical model for the dynamics of onchocerciasis transmission taking into account vector control (larvicides application) and public health awareness as control interventions. The model is subdivided into two populations, human and vector (blackfly) populations. The disease-free equilibrium and the basic reproduction number of the model are obtained. Sensitivity analysis is analyzed to find out how crucial the parameters of the basic reproduction number are in eradicating the disease. The result showed that the applying larvicides in the affected area, increasing the blackfly death rate, creating more public health education awareness, and reducing blackfly biting rates will help in curtailing the disease. This is because the more people became knowledgeable about the transmission of onchocerciasis disease, the more they are likely to take measures to prevent being bitten by blackflies. In essence, this reduced the spread of the disease.

In addition, regular larvicide application to the environment led to the death of blackflies and reduced the transmission of the disease. Therefore, the result of this study shows that the joint implementation of larvicide application, public health education and mass ivermectin administration will reduce the transmission of onchocerciasis in endemic countries where mass ivermectin administration alone have failed to stop the disease spread. This finding is in line with WHO recommendations. In view of this, we recommend simultaneous implementations of public health education programs and larvicides application alongside mass ivermectin administration for controlling and preventing the spread of onchocerciasis disease.

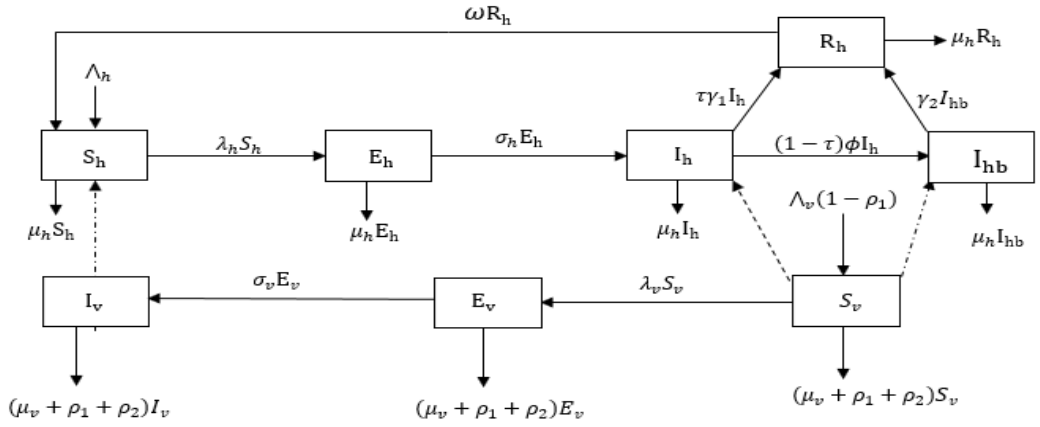

Fig 1. Schematic diagram for the transmission dynamics of onchocerciasis.

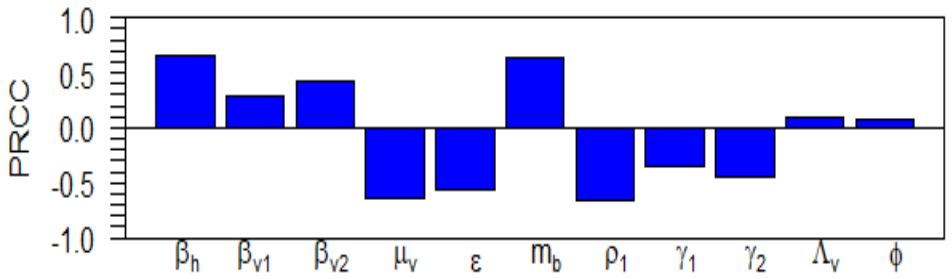

Fig 2. Tornado plots displaying the PRCCs of the parameters of R_0. The parameter values and ranges used are in Tables I and II.

TABLE I
PARAMETER VALUES AND THEIR SOURCES

Parameter	Nominal Value	Source	Parameter	Nominal Value	Source
β_h	2.12	[1]	ε	0 - 1	Varied
β_{v2}	2.5	[1]	m_b	0 - 1	Varied
β_{v1}	1.0	Assumed	ρ_1	0 – 1	Varied
γ_2	0.067	[24]	ρ_2	0.001	Assumed
γ_1	0.00167	Assumed	ϕ	0.01 – 0.5	Assumed
μ_h	0.000052	[23, 25]	Λ_h	2000	Assumed
μ_v	0.065	[27, 20]	Λ_v	2500 - 3500	Assumed
σ_h	0.023	[29, 30, 23]	φ	0.013	[31]
σ_v	0.074	[28, 29, 23]	τ	0.5	Assumed

TABLE II
PARAMETER PRCC SIGNIFICANCE (UNADJUSTED P-VALUE)

Parameter	Range	PRCC	p-value	Keep
β_h	$0.0004 - 2.3$	0.64657910	0.0000	TRUE
β_{v1}	$0.0003 - 2.5$	0.29695114	0.0000	TRUE
β_{v2}	$0.0003 - 1.0$	0.41806211	0.0000	TRUE
μ_v	$0.001 - 0.095$	-0.64165551	0.0000	TRUE
ε	$0.01 - 0.95$	-0.55735289	0.0000	TRUE
m_b	$0 - 1$	0.64028331	0.0000	TRUE
ρ_1	$0.001 - 0.1$	-0.65773654	0.0000	TRUE
γ_1	$0.0001 - 0.05$	-0.34518362	0.0000	TRUE
γ_2	$0.0001 - 0.5$	-0.45617737	0.0000	TRUE
Λ_v	$2500 - 3500$	0.09256759	0.00354	TRUE
ϕ	$0.01 - 0.5$	0.06902565	0.02986	TRUE

TABLE III
PAIRWISE PRCC COMPARISONS (UNADJUSTED P-VALUES)

	β_h	β_{v1}	β_{v2}	μ_v	ε	m_b	ρ_1	γ_1	γ_2	Λ_v	ϕ
β_h		0	$6.071E-13$	0	0	0.8114	0	0	0	0	0
β_{v1}			0.001991	0	0	0	0	0	0	$2.145E-06$	$1.396E-07$
β_{v2}				0	0	$3.398E-12$	0	0	0	$4.885E-15$	0
μ_v					0.0033€	0	0.5364	0	$2.448E-09$	0	0
ε						0	$3.844E-04$	$2.284E-09$	0.002425	0	0
m_b							0	0	0	0	0
ρ_1								0	$4.606E-11$	0	0
γ_1									0.003244	0	0
γ_2										0	0
Λ_v											0.5986
ϕ											

TABLE IV
PAIRWISE PRCC COMPARISONS (FDR ADJUSTED P-VALUES)

	β_h	β_{v1}	β_{v2}	μ_v	ε	m_b	ρ_1	γ_1	γ_2	Λ_v	ϕ
β_h		0	$8.144E-13$	0	0	0.8114	0	0	0	0	0
β_{v1}			0.002235	0	0	0	0	0	0	$2.51E-06$	$1.669E-07$
β_{v2}				0	0	$4.45E-12$	0	0	0	$6.717E-15$	0
μ_v					0.00355	0	0.5566	0	$2.992E-09$	0	0
ε						0	$4.405E-04$	$2.855E-09$	0.002668	0	0
m_b							0	0	0	0	0
ρ_1								0	$5.891E-11$	0	0
γ_1									0.003498	0	0
γ_2										0	0
Λ_v											0.6097
ϕ											

TABLE V
PARAMETERS DIFFERENT AFTER FDR ADJUSTMENT?

	β_h	β_{v1}	β_{v2}	μ_v	ε	m_b	ρ_1	γ_1	γ_2	Λ_v	ϕ
β_h		TRUE	TRUE	TRUE	TRUE	FALSE	TRUE	TRUE	TRUE	TRUE	TRUE
β_{v1}			TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE
β_{v2}				TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE
μ_v					TRUE	TRUE	FALSE	TRUE	TRUE	TRUE	TRUE
ε						TRUE	TRUE	TRUE	TRUE	TRUE	TRUE
m_b							TRUE	TRUE	TRUE	TRUE	TRUE
ρ_1								TRUE	TRUE	TRUE	TRUE
γ_1									TRUE	TRUE	TRUE
γ_2										TRUE	TRUE
Λ_v											FALSE
ϕ											

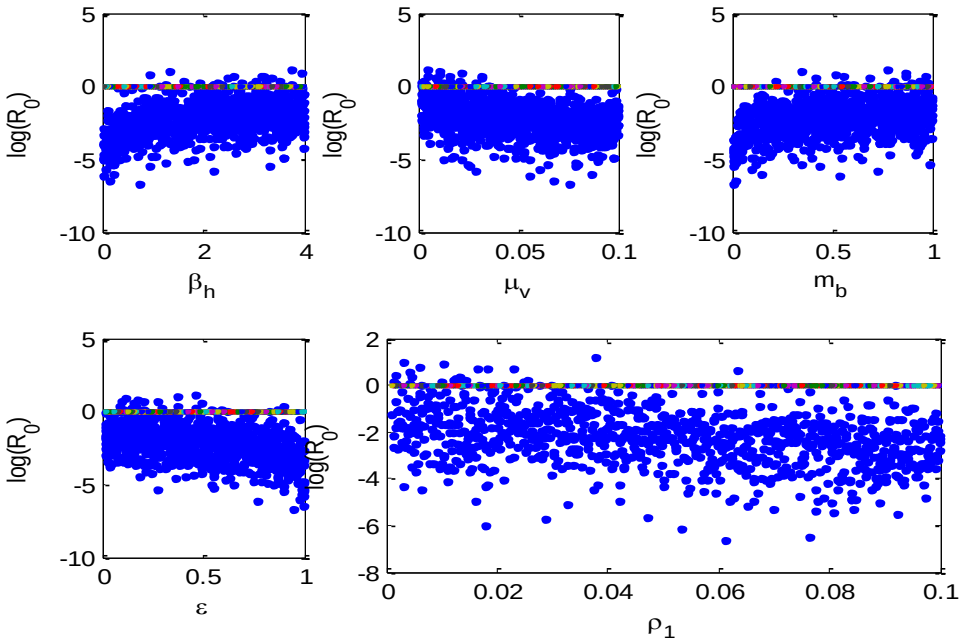

Fig 3. Monte Carlo simulations for the five most sensitive parameters (β_h, μ_v, m_b, ε, ρ_1) of R_0. The parameter ranges and values in Tables I and II are used with 1000 simulations per run.

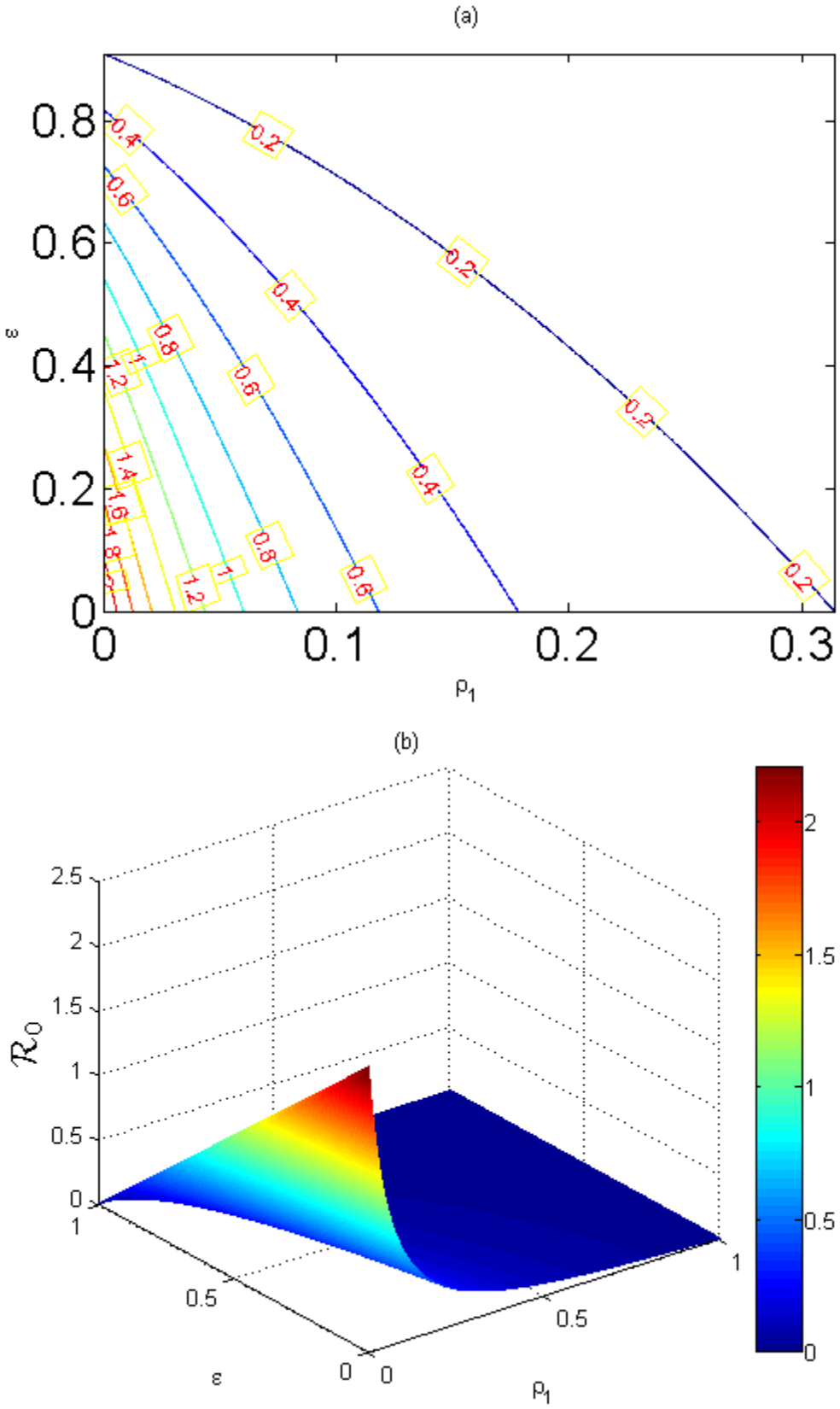

Fig 4. (a) The contour lines and (b) 3D plot displaying the impactt of public health education of the disease (ε) and application of larvacides (ρ_1) on R_0 . All the parameter values in Table I are used.

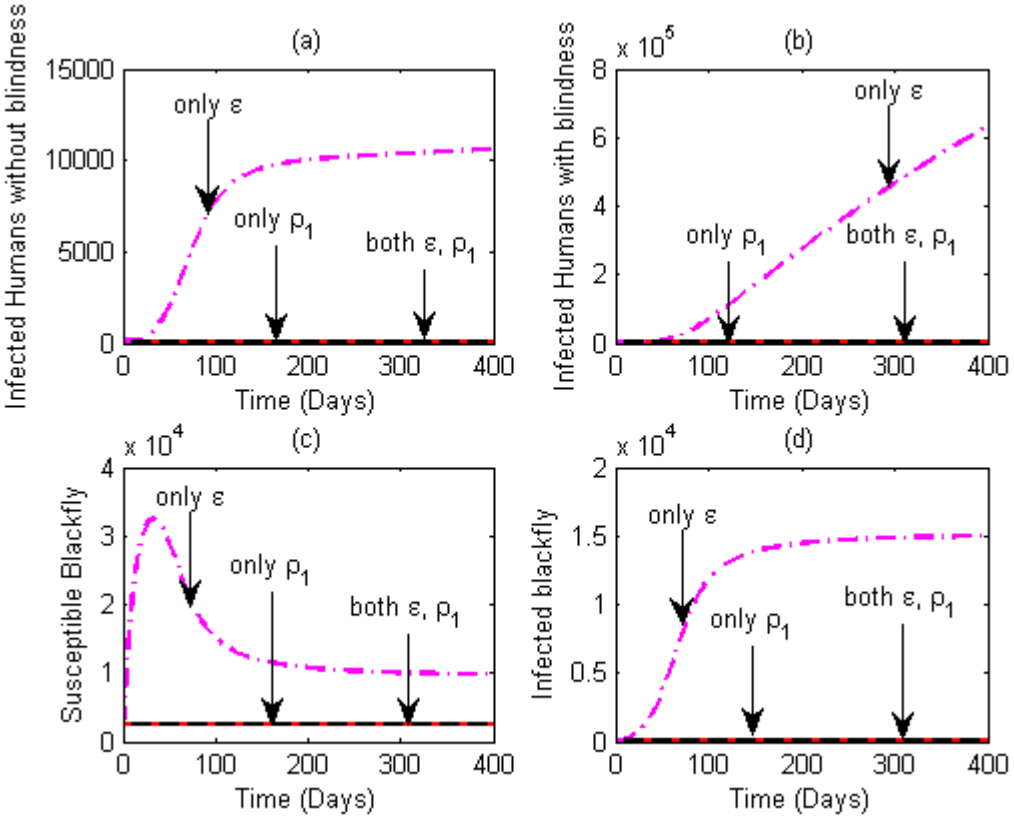

Fig 5. Dynamics Transmission of Onchocerciasis infection (a) infected human without blindness (b) infected human with blindness (c) susceptible blackfly, (d) infected blackfly when only larvicides ($\rho_1 = 0.5,\ \varepsilon = 0.0,\ R_0 = 0.1029$), only awareness control ($\rho_1 = 0.0, \varepsilon = 0.5,\ R_0 = 1.1645$) and both controls ($\rho_1 = 0.5, \varepsilon = 0.5, R_0 = 0.0515$) are applied. All the parameter values in Table I are used except where they are stated otherwise.

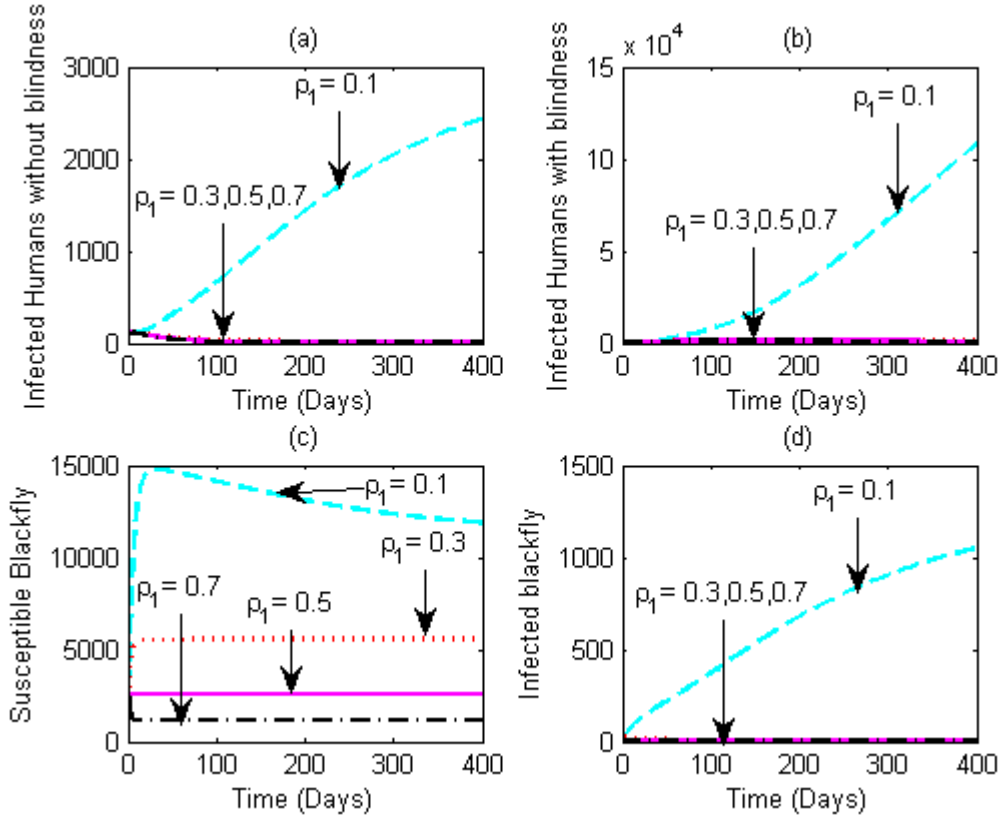

Fig 6. Dynamics Transmission of Onchocerciasis infection (a) infected human without blindness (b) infected human with blindness (c) susceptible blackfly, (d) infected blackfly when the rate of applying larvicides is increasing that is $\rho_1 = 0.1, 0.3, 0.5, 0.7$. All the parameter values in Table I are used.

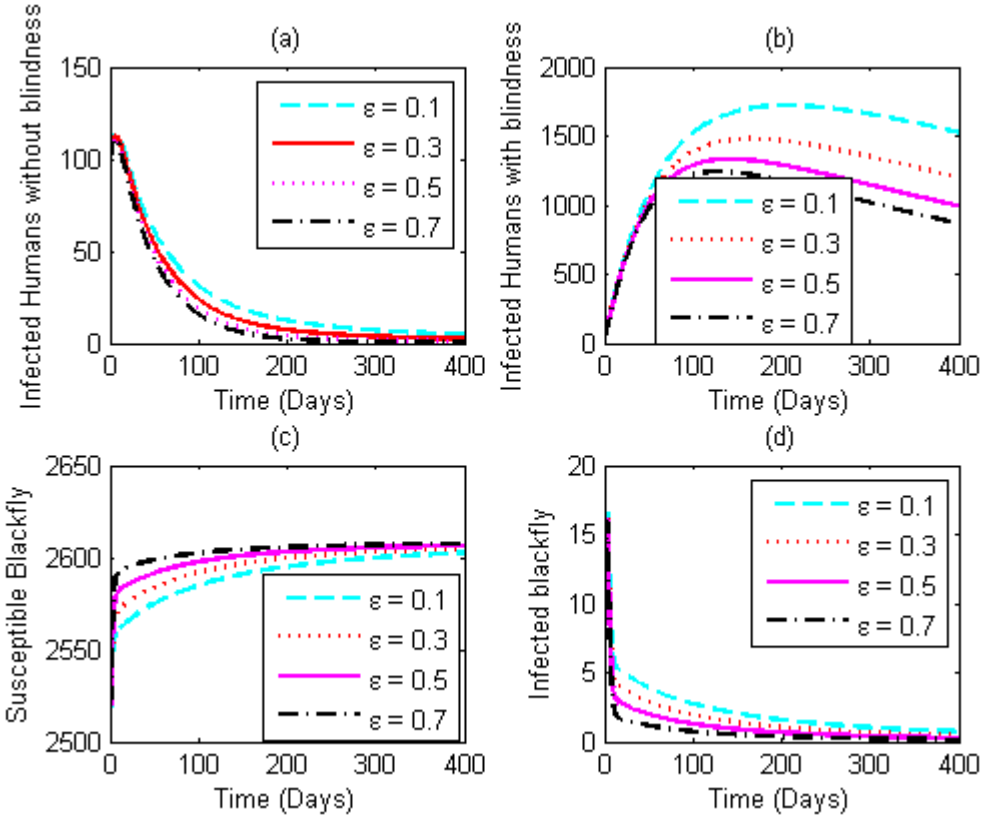

Fig 7. Dynamics Transmission of Onchocerciasis infection (a) infected human without blindness (b) infected human with blindness (c) susceptible blackfly, (d) infected blackfly when the rate of public health education of the infection is increasing that is $\varepsilon = 0.1, 0.3, 0.5, 0.7$. All the parameter values in Table I are used.

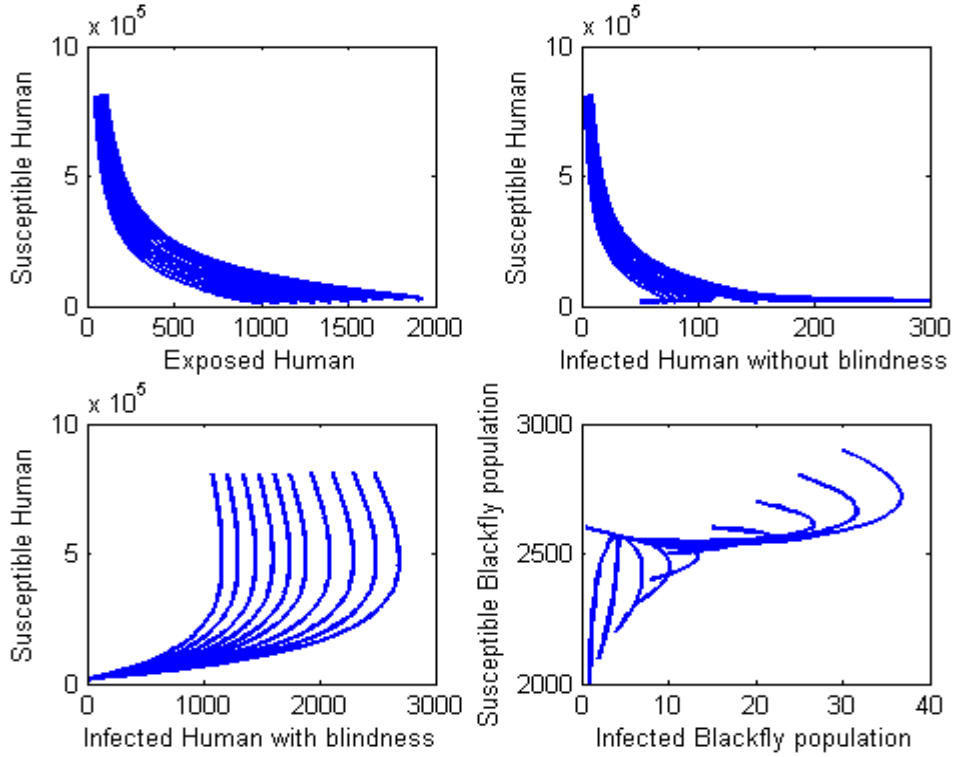

Fig 8. Phase portrait solutions for Onchocerciasis transmission when $R_0 < 1$. All the parameter values in Table 1 are used with $\varepsilon = 0$.

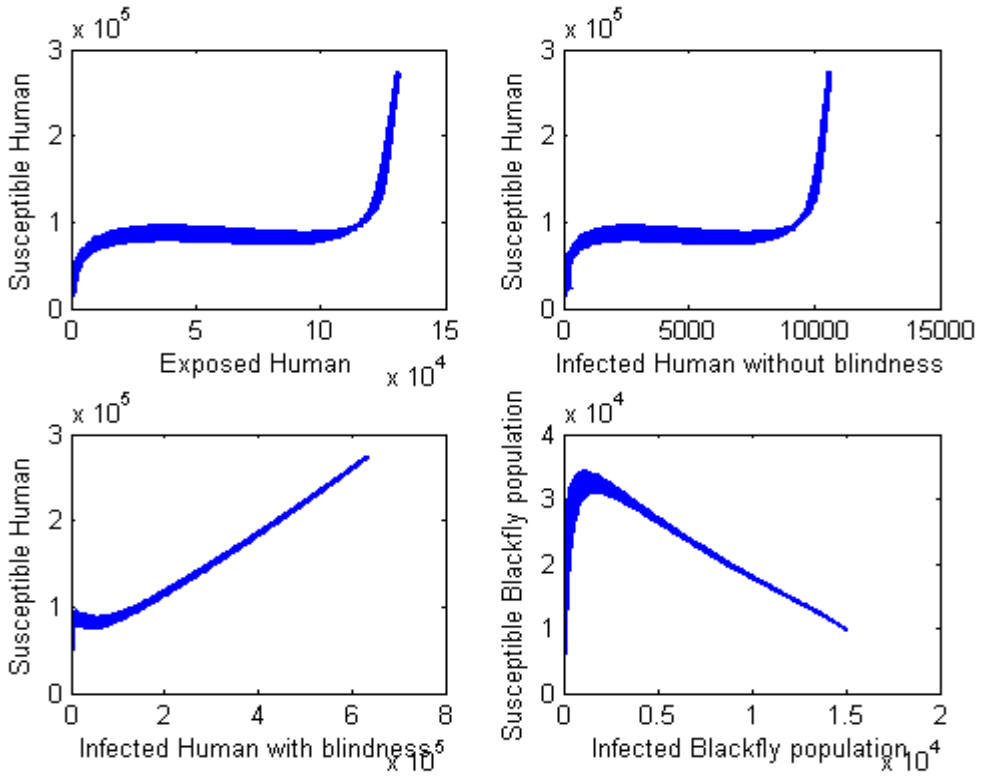

Fig 9. Phase portrait solutions for Onchocerciasis transmission when $R_0 > 1$. All the parameter values in Table 1 are used with $\rho_1 = 0$.

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