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MODELING THE INFECTION DYNAMICS OF ONCHOCERCIASIS AND ITS TREATMENT

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Onchocerciasis is one of the neglected tropical diseases caused by *Onchocerca volvulus*. Ivermectin is known to be effective in the treatment of onchocerciasis because it suppresses the production of microfilariae by the adult female worms for a few months following treatment thus reducing transmission. In this study, a deterministic model is developed to assess the effect of mass treatment of onchocerciasis with ivermectin. The basic reproduction number, R_0, of the model system is determined and it is observed that the model exhibits backward bifurcation for some parameters implying the existence of multiple endemic equilibria when $R_0 < 1$. The existence of multiple equilibria emphasizes the fact that $R_0 < 1$ is not sufficient to eradicate the disease and the need is to lower R_0 much below one to make the disease-free equilibrium globally stable. Numerical simulations are done and conclusions drawn with respect to the known treatment protocols in endemic areas. The study results suggest that the mass treatment of the disease with ivermectin should cover a higher proportion of the population to control the disease and eventually eliminate it from the population.

Keywords: Onchocerciasis; Ivermectin; Microfilariae; Mathematical model; Simulations.

1. Introduction

Onchorcerciasis is a chronic vector-borne parasitic disease caused by *Onchocerca volvulus*.[1] The disease is transmitted by blood sucking black flies that belong to the

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genus *Simulium*. This disease is responsible for a skin disease with depigmentation and severe unrelenting itching.[2] It is prevalent in Africa, with more than 90% of the reported cases found in 31 Sub-Saharan countries that include Nigeria, Ghana, Sudan, Kenya, Cameroon amongst others. Cases of onchorcerciasis are also reported in South and Central America, for instance, in Brazil and Yemen in the Middle East.[3] The Ministry of Health in Ghana, for instance, estimated that 3.4 million of its population live in 66 endemic districts with an exclusion of the greater Accra region.[4] The highest rates of infections are found in communities living near fast flowing rivers thus the name river blindness.[5] Though not lethal, river blindness contributes to high economic loss in Sub-Saharan Africa.[6,7]

According to WHO, in 1995, it was estimated that 18 million people were affected by onchocerciasis. An estimated 270,000 were blind and 500,000 were severely visually impaired.[8] In 2004, African Programme for Onchorcerciasis Control (APOC) carried out Rapid Epidemiological Mapping of Onchocerciasis (REMO) in 19 endemic nations in Africa. It was estimated that 87 million people were at high risk of infection with onchercerciasis. These results also indicated that the mean infection rate was 38.2%. In order to curb the spread of onchocerciasis and its eradication from the population, APOC devised a strategy of elimination of infection by 15–17 years of annual mass distribution of ivermectin in the disease endemic areas. The WHO has also set the time frame for the elimination of onchocerciasis and other neglected tropical diseases by 2020–2025.[9] Since the inception of APOC in 1995, in 2013 about 26 endemic countries reported more than 100 million people on ivermectin treatment. Today, the strategy for the eradication of onchocerciasis in Africa is based on the community directed treatment with ivermectin. The success of this initiative has been seen in Mali and Nigeria. APOC has now shifted its attention from the elimination of onchocerciasis as a public health burden to entire elimination of infection in Africa by 2025.[9]

Ivermectin is an antimicrofilarial agent that acts as the secondary and primary form of prevention for individuals infected with onchocerciasis. It reduces the number of microfilariae picked up by the black fly during blood feeding.[10] However, new evidence suggests that it has no effect on oocyte production but the microfilariae inside the worm which are yet to be released are affected.[11] Ivermectin degenerates intrauterine microfilariae and thus suppresses the release of new microfilariae for up to 3–4 months after which it is still possible to continue producing microfilariae until it dies naturally.[11] More than 525 million tablets of ivermectin have been distributed since the establishment of the Mectizan™ Donation Program (MDP) by Merck and Co., Inc. The drugs are mainly distributed through Community Directed Treatment with Ivermectin (CDTI).[12] Ivermectin shows no or, if any, little macrofilaricidal effects in the killing of the adult worm.[13] This is an indicator that the drug does not kill adult worms to eliminate infections. Therefore, repeated mass treatment with ivermectin has to be administered in order to interrupt the transmission of the disease. For maximum success to be realized, ivermectin treatment should be

done for many years that correspond to the lifespan of an adult worm spanning 10–15 years. Quantitative estimates of onchocerciasis treatment with ivermectin have ranged from irreversible decline in microfilariae production of 30% after five-yearly treatments, a decline in the productivity index by 90% or more after 10 six-monthly treatments for six years and to containment of development at a single cell stage after four or five six-monthly treatment.[14] According to the report of the conference on the eradicability of onchocerciasis, the mass administration of ivermectin at six-month intervals in Gautemala can maintain the levels of microfilariae in the skin so low as to interrupt the transmission with a sufficient coverage of about 80% of the eligible individuals.[15] The report also indicates that in Ecuador, the transmission of *O. volvulus* was interrupted after five years of semi-annual ivermectin treatment.

The study of mass administration of ivermectin in the treatment of onchocerciasis is of great epidemiological importance. However, little mathematical modeling has been done on the potential long-term dynamics of the disease in the presence of treatment. Omade,[16] for instance, used SIR model with demography in modeling onchocerciasis. His work focused on the impact of vaccination on the disease and uses Euler method in providing numerical solutions to the model. Other models, pertinent to this work have also been proposed and analyzed, see for instance.[9,10] Turner *et al.*[17] used a previously developed EPIONCHO model to investigate the effect of vaccination and ivermectin. The model incorporated age and sex structure of the host population. Turner *et al.* then performed sensitivity analysis by varying the rate of decay (mean duration between 5 and 50 years) according to the range considered previously in the modeling of the Schistosomiasis vaccine as well as choosing a more modest 60% coverage of the vaccine. Turner *et al.*[18] explored the uncertainty in modeling projections of the long-term impact of ivermectin on *O. volvulus*. They established that biannual ivermectin treatment has a large additional benefit in both reducing microfilarial prevalence and intensity as compared to annual treatment. However, areas with high baseline endemicity and perennial transmission, 15 years of annual or biannual treatment with ivermectin may not be sufficient to bring infection levels below potential elimination thresholds.

In the current study, we develop a deterministic model to investigate the potential impact of mass administration of the drug ivermectin, that creates a class of individuals who are temporarily protected from infection in the first half of the year with the protection assumed to have completely waned in the second half of the year. This is done through the determination of the basic reproduction number that is used to assess the effect of treatment and analysis of stability of the steady state solutions of the deterministic model. Our work is innovative in that it creates temporary vaccinated classes that allows for the modeling of mass administration of a drug for all compartments. We use numerical simulations to predict the infection dynamics of the disease and draw more insightful epidemiological perspectives that result in recommendations aimed at disease eradication. We also compare our numerical results to previous work done on onchocerciasis treatment,

see for instance.[7] In order to gain more insight on the dynamics of onchocerciasis, we investigate the potential of increasing treatment frequency on the dynamics of the disease.

In this paper, our work has been organised as follows: in Sec. 2, a dynamic model is formulated and a brief discussion of the model properties is given and in Sec. 3, model analysis is carried out. In Sec. 4, we give the numerical simulations to support our project objectives as stated in Sec. 1. The paper is concluded in Sec. 5 with relevant discussions and recommendations.

2. Mathematical Model

In this section, we formulate a deterministic model that explores the infection dynamics of onchocerciasis and its treatment. Mass administration of ivermectin is the most common form of treatment for onchocerciasis. Initially, the strategy was to administer ivermectin annually. A change of strategy to six-monthly was implemented to increase the probability of eliminating the parasite.[18–20] The treatment in this model occurs in such a way that there is mass administration of ivermectin at the beginning of the first half of year and nothing in the second half of the year.

We define two functions that allow (i) movement through mass administration of ivermectin at the beginning of the first half of year and movement in the second half of the year after the drug wanes and (ii) infection only occurs in the second half of the year following waning of the drug. We model such a scenario using the following step functions:

$$p = \begin{cases} 0 & \text{if } i-1 \le t \le \dfrac{2i-1}{2} \\ 1 & \text{if } \dfrac{2i-1}{2} < t \le i \end{cases} \quad \text{and} \quad q = \begin{cases} 1 & \text{if } i-1 \le t \le \dfrac{2i-1}{2} \\ 0 & \text{if } \dfrac{2i-1}{2} < t \le i \end{cases} \tag{2.1}$$

for $i = 1, 2, 3, \ldots$. It is important to note that these are not the only functions that can be used to model such a scenario. It would be plausible to use an exponentially declining function or the Hill function over the defined intervals.

In order to investigate the possibility of increasing treatment frequency in our numerical simulations, we consider a case when the mass administration of ivermectin is done quarterly using the following function

$$p = \begin{cases} 0 & \text{if } i-1 \le t \le \dfrac{1+4(i-1)}{4} \\ 1 & \text{if } \dfrac{1+4(i-1)}{4} < t \le \dfrac{1+2(i-1)}{2} \\ 0 & \text{if } \dfrac{1+2(i-1)}{2} < t \le \dfrac{3+4(i-1)}{4} \\ 1 & \text{if } \dfrac{3+4(i-1)}{4} < t \le i \end{cases} \quad \text{and}$$

$$q = \begin{cases} 1 & \text{if } i-1 \le t \le \dfrac{1+4(i-1)}{4} \\ 0 & \text{if } \dfrac{1+4(i-1)}{4} < t \le \dfrac{1+2(i-1)}{2} \\ 1 & \text{if } \dfrac{1+2(i-1)}{2} < t \le \dfrac{3+4(i-1)}{4} \\ 0 & \text{if } \dfrac{3+4(i-1)}{4} < t \le i \end{cases}, \tag{2.2}$$

where $i = 1, 2, 3, \ldots$. We also investigate the case, where the mass administration of ivermectin is done continuously.

We consider a habitat with two interacting populations, humans (hosts) and the black flies (vectors). The human population $N_H(t)$ at time t is divided into eight compartments; susceptible human population $S_H(t)$, asymptomatic humans with onchocerciasis $E_H(t)$, symptomatic infectious humans $I_H(t)$, individuals with onchocerciasis in acute phase $A_H(t)$, susceptible individuals protected by ivermectin $S_T(t)$, asymptomatic humans with onchocerciasis on ivermectin $E_T(t)$, symptomatic infectious humans on ivermectin $I_T(t)$ and individuals with onchocerciasis in acute phase on ivermectin $A_T(t)$. The assumption is that every year, irrespective of one's infection status, every individual takes ivermectin. The vector population, N_v is divided into three compartments; susceptible vector $S_v(t)$, exposed vector $E_v(t)$ and infected vector $I_v(t)$. We consider a stage structured model that describes the stages of vector development. These include embryonic (E), larvae (L) and pupae (P) stages. The number of laid eggs is assumed to be proportional to the number of female black flies. The following differential equations describe the stage structured model of the aquatic phase in the vector development.

$$\left.\begin{aligned} \dot{E} &= r\left(1 - \frac{E}{K_e}\right)(S_v + E_v + I_v) - (\eta_1 + \mu_e)E, \\ \dot{L} &= \eta_1 E\left(1 - \frac{L}{K_l}\right) - (\eta_2 + \mu_l)L, \\ \dot{P} &= \eta_2 L - (b + \mu_p)P. \end{aligned}\right\} \tag{2.3}$$

Black flies breed exclusively in running water.[5] Large black fly populations indicate clean, healthy streams since most species do not tolerate organic pollution. Females lay their eggs on vegetation in streams. The eggs hatch in water and larvae attach to rocks, leaves, grass or any submerged objects.[21] The larvae feed by filtering water for tiny bits of organic matter. Mature larvae pupate underwater and emerging adults ride bubbles of air to the surface and are able to fly away. The adult black flies mate near the breeding site and females, that need a blood-meal to lay eggs, begin their search for blood. Once they have fed and digested, they lay eggs in a suitable stream habitat and the life cycle continues.[21] Since the eggs are laid in a contaminated free

habitat, it is reasonable to express the laying of eggs with a mathematical model which incorporates carrying capacity of the resources. This takes into account the availability of nutrients and the occupation of the available breeder sites by eggs or larvae. Thus, in the per capita recruitment term, we have $r\big(1-\frac{E}{K_e}\big)$, where K_e represents the availability of nutrients and space and r represents the rate at which the population would grow if they were unencumbered by environmental contamination. On the other hand, the transition rate from E to class L is η_1. However, when availability of food is not sufficient for class L, then the larvae can eat the young larvae to complete its development and we suppose that the death rate due to lack of food is proportional to the young larvae $\eta_1 E$ and to the coefficient $\frac{L}{K_l}$ that represents the availability of food for each larvae. Thus, the number of eggs that hatch and survive is given by $\eta_1 E\big(1-\frac{L}{K_l}\big)$. The transition rate from larvae to pupae is assumed to be η_2. It is assumed that the embryonic (E), larvae (L) and pupae (P) leave the dynamics through natural death rates μ_e, μ_l and μ_p, respectively. The pupae become female adults at the rate b.

The total human and vector populations at any given time, t, are, respectively, given by

$$N_H = S_H(t) + E_H(t) + I_H(t) + A_H(t) + S_T(t) + E_T(t) + I_T(t) + A_T(t) \quad \text{and}$$
$$N_v = S_v(t) + E_v(t) + I_v(t).$$

People are recruited to susceptible human class through birth at a constant rate Π. Susceptible individuals may become infected through contacts with infectious black flies. Here, it is assumed that only infectious black-flies can transmit infection to susceptible individuals during blood-meal. Infected individuals go through latent period during which they do not transmit infection. They progress from latent stage to the infectious stage at the rate γ. The infectious individuals progress to the individuals with acute infections at the rate δ. The constants θ and f represent ivermectin treatment and the efficacy of the treatment, respectively. It is assumed that during mass treatment with ivermectin, the susceptible individuals S_H, individuals in the latent stage E_H, infectious individuals I_H and individuals in acute phase A_H progress to susceptible individuals protected with ivermectin S_T, individuals in the latent stage protected with ivermectin E_T, infectious individuals protected with ivermectin I_T and individuals in acute phase protected with ivermectin A_T, respectively. It is further assumed that individuals protected with ivermectin relapse to their respective classes following the waning of the vaccine at the rate ω. In addition, we assume that individuals protected with ivermectin may acquire infection depending on the drug efficacy and progress to the subsequent protected classes with ivermectin. It is important to note that the progression of individuals in the latent stage protected with ivermectin to infectious individuals protected with ivermectin, and progression of infectious individuals protected with ivermectin to individuals in acute phase protected with ivermectin is reduced by factors $\alpha_2 \in [0,1]$ and $\alpha_3 \in [0,1]$, respectively.

The black flies are recruited into susceptible class from pupa stage at a rate b. It is assumed that the parasite enters the black fly through biting an infectious human. It is further assumed that only infectious humans in the classes I_H, A_H, I_T and A_T can transmit infections to the susceptible black flies through bites. Infected black flies go through a latent period during which they do not transmit infection. The infected black flies progress from latent stage to the infectious stage at the rate τ. We assume that the black flies leave the population through natural death. The movement of the host and vector populations is shown in the schematic diagram, Fig. 1.

Assuming that β be the black fly biting rate, that is, the average number of bites per black fly per unit time and ξ_1 be the probability that a bite by an infectious black fly on susceptible human leads to infection of the human. Thus, the rate of infection per susceptible human is given by

$$\lambda_h = \frac{\xi_1 p \beta I_v}{N_H}. \tag{2.4}$$

Individuals on ivermectin treatment in class S_T acquire infection at the rate $\alpha_1 \lambda_h$. Here, $\alpha_1 \in [0, 1]$, defines the reduced effect of infection of the susceptible individuals on ivermectin as a result of treatment. Similarly, assuming that ξ_2 is the transmission probability from infectious human to black flies, then the rate of infection per susceptible black fly is given by

$$\lambda_v = \frac{\xi_2 \beta (I_H + \kappa_1 A_H + \kappa_2 I_T + \kappa_3 A_T)}{N_H}, \tag{2.5}$$

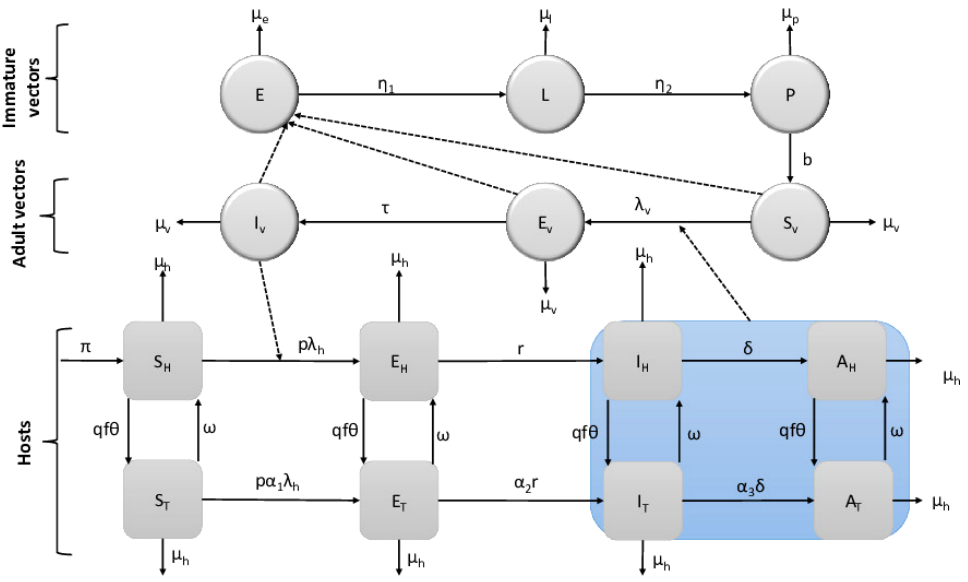


Fig. 1. A schematic diagram for the model.

where $\kappa_i \in [0,1]$ for $i = 1,2,3$, refers to the modification parameters that measures the reduced effect of infection relative to the infectious class I_H. We introduce $\beta_h = \xi_1\beta$ and $\beta_v = \xi_2\beta$ parameters to simplify the incidence terms.

With the above descriptions, the dynamics of onchocerciasis in the two interacting populations are described by the systems of nonlinear first order differential equations in (2.6).

$$\left.\begin{aligned}
\dot{S_H} &= \Pi + \omega S_T - \lambda_h S_H - Q_1 S_H,\\
\dot{E_H} &= \lambda_h S_H + \omega E_T - Q_2 E_H,\\
\dot{I_H} &= \gamma E_H + \omega I_T - Q_3 I_H,\\
\dot{A_H} &= \delta I_H + \omega A_T - Q_1 A_H,\\
\dot{S_T} &= qf\theta S_H - \alpha_1\lambda_h S_T - Q_4 S_T,\\
\dot{E_T} &= qf\theta E_H + \alpha_1\lambda_h S_T - Q_5 E_T,\\
\dot{I_T} &= qf\theta I_H + \alpha_2\gamma E_T - Q_6 I_T,\\
\dot{A_T} &= qf\theta A_H + \alpha_3\delta I_T - Q_4 A_T,\\
\dot{S_v} &= bP - \lambda_v S_v - \mu_v S_v,\\
\dot{E_v} &= \lambda_v S_v - Q_7 E_v,\\
\dot{I_v} &= \tau E_v - \mu_v I_v,\\
\dot{E} &= r\left(1 - \frac{E}{K_e}\right)(S_v + E_v + I_v) - Q_8 E,\\
\dot{L} &= \eta_1 E\left(1 - \frac{L}{K_l}\right) - Q_9 L,\\
\dot{P} &= \eta_2 L - Q_{10} P,
\end{aligned}\right\} \tag{2.6}$$

where

$$Q_1 = \mu_h + qf\theta, \quad Q_2 = \mu_h + \gamma + qf\theta, \quad Q_3 = \mu_h + \delta + qf\theta, \quad Q_4 = \mu_h + \omega,$$
$$Q_5 = \alpha_2\gamma + \mu_h + \omega, \quad Q_6 = \alpha_3\delta + \mu_h + \omega, \quad Q_7 = \tau + \mu_v, \quad Q_8 = \eta_1 + \mu_e,$$
$$Q_9 = \eta_2 + \mu_l \quad \text{and} \quad Q_{10} = b + \mu_p.$$

with initial conditions

$$S_H(0), E_H(0), I_H(0), A_H(0), S_T(0), E_T(0), I_T(0), A_T(0), S_v(0), E_v(0), I_v(0)$$
$$E(0), L(0) \quad \text{and} \quad P(0).$$

2.1. *Basic properties*

We present the general properties of our model system (2.6) with positive initial conditions. The model describes human (host) and black fly vector populations and thus, it is important to prove that all variables describing the dynamics of the populations are positive.

Theorem 2.1. *Suppose the initial conditions satisfy* $S_{H(0)} > 0$, $E_{H(0)} \geq 0$, $I_{H(0)} \geq 0$, $A_{H(0)} \geq 0$, $S_{T(0)} > 0$, $E_{T(0)} \geq 0$, $I_{T(0)} \geq 0$, $A_{T(0)} \geq 0$, $S_{v(0)} > 0$, $E_{v(0)} > 0$, $I_{v(0)} \geq 0, E(0) \geq 0, L(0) \geq 0$ *and* $P(0) \geq 0$ *and that the solutions to the system* (2.6) *exists on the interval* $[0, t_0]$ *for some* $t_0 > 0$, *then the functions* $S_H(t)$, $E_H(t)$, $I_H(t)$, $A_H(t)$, $S_T(t)$, $E_T(t)$, $I_T(t)$, $A_T(t)$, $S_v(t)$, $E_v(t)$ $I_v(t), E(t), L(t)$ *and* $P(t)$ *remain positive for all* $t \in [0, t_0]$.

The proof of this theorem follows the works in.[22]

Theorem 2.2. *The solutions of the model system in* (2.6) *with initial conditions given in* (2.6) *are bounded.*

Proof. The human and the vector populations evolve according to the following equations, respectively.

$$\frac{dN_H(t)}{dt} \leq \Pi - \mu_h N_H, \quad \frac{dN_v}{dt} \leq bP - \mu_v N_v,$$

so that

$$\lim_{t\to\infty} \sup(N_H(t)) \leq \frac{\Pi}{\mu_h}, \quad \lim_{t\to\infty} \sup(N_v(t)) \leq \frac{b\eta_2 K_l}{\mu_v Q_{10}} \quad \text{since } P \leq \frac{\eta_2 K_l}{Q_{10}}.$$

Thus, all feasible solutions of our model system (2.6) are positive and bounded and thus enter the invariant attracting region

$$\Omega = \left\{ (S_H, E_H, I_H, A_H, S_T, E_T, I_T, A_T, S_v, E_v, I_v, E, L, P) : N_H(t) \leq \frac{\Pi}{\mu_h}; E \leq K_e; \right.$$
$$\left. L \leq K_l; P \leq \frac{\eta_2 K_l}{Q_{10}}; N_v(t) \leq \frac{b\eta_2 K_l}{\mu_v Q_{10}} \right\}.$$

The set Ω is positively invariant and attracting. It is, therefore, sufficient to consider solutions of our model system (2.6) in Ω. The existence, uniqueness and subsequent results for our model system (2.6) hold in this region and all the solutions starting in Ω remain there for $t \geq 0$. Thus, the model system (2.6) is mathematically and epidemiologically well-posed, and it is, thus, sufficient to consider the dynamics generated by the model system in Ω. □

3. Model Analysis

3.1. *Basic reproduction number,* R_0

In the absence of disease in both the population, the model system (2.6) has two equilibria without disease; the trivial equilibrium (equilibrium without vector

and disease), $\mathcal{E}_0 = (S_H, 0, 0, 0, S_T, 0, 0, 0, 0, 0, 0, 0, 0, 0)$ and disease-free equilibrium (equilibrium with vector and without disease) given by $\mathcal{E}_1 = (S_H, 0, 0, 0, S_T, 0, 0, 0, S_v, 0, 0, E, L, P)$ with

$$S_H = \frac{\Pi}{Q_1(1-\Phi_1)}, \quad S_T = \frac{\Pi q f \theta}{Q_1 Q_4 (1-\Phi_1)}, \quad S_v = \frac{K_e K_l Q_8 Q_9 (N-1)}{r(K_e \eta_1 + K_l Q_9)},$$
$$E = \frac{K_e K_l Q_8 Q_9 Q_{10} \mu_v (N-1)}{\eta_1 (K_e Q_8 Q_{10} \mu_v + K_l br \eta_2)}, \quad L = \frac{K_e K_l Q_8 Q_9 Q_{10} \mu_v (N-1)}{br\eta_2 (K_e \eta_1 + K_l Q_9)},$$
$$P = \frac{K_e K_l Q_8 Q_9 \mu_v (N-1)}{br(K_e \eta_1 + K_l Q_9)}, \quad \Phi_1 = \frac{\omega q f \theta}{Q_1 Q_4}, \quad N = \frac{br\eta_1 \eta_2}{Q_8 Q_9 Q_{10} \mu_v}.$$

It is important to note that N is the net reproductive number.[21,23,24] We employ the next generation matrix method described in[25] to compute the basic reproduction number R_0 of the system (2.6). This is given by

$$R_0 = \sqrt{\mathcal{R}_0} = \sqrt{\frac{p\gamma\tau K_e K_l \beta_h \beta_v (\Phi_4 + \Phi_5 + \Phi_6) Q_8 Q_9 (N-1)}{Q_2 Q_3 Q_5 Q_6 Q_7 (Q_4 + fq\theta)^2 (1-\Phi_2)(1-\Phi_3)(K_e\eta_1 + K_l Q_9) r \Pi \mu_v}}. \tag{3.1}$$

The computation of the basic reproduction number is given in Appendix A. The square-root arises due to the fact that it takes two generations for infected hosts to produce new infected hosts.[26] In this paper, R_0 determines whether onchocerciasis dies out or persists in the population. The following results are established.

Theorem 3.1. *If*

(i) $N \leq 1$, *the trivial equilibrium* $\mathcal{E}_0$ *is locally asymptotically stable in* Ω.
(ii) $N > 1$, *the trivial equilibrium* $\mathcal{E}_0$ *is unstable and the disease-free equilibrium* $\mathcal{E}_1$ *is locally asymptotically stable in* Ω *whenever* $\mathcal{R}_0 < 1$.

Proof. The proof of Theorem 3.1 is given in Appendix B. □

The quantity R_0 is defined as the expected number of human/vector onchocerciasis infections generated by a single infected human/vector during the entire period of infectiousness when introduced in a completely susceptible human/vector population. The epidemiological implication of Theorem 3.1 is that, in general, when the basic reproduction number $\mathcal{R}_0$, is less than unity, on average each infected individual infects fewer than one individual and the disease dies out in time.[25]

3.2. *Endemic equilibrium,* $(\mathcal{E}_1)$

We define the nonzero steady state to be $S_H^*, E_H^*, I_H^*, A_H^*, S_T^*, E_T^*, I_T^*, A_T^*, S_V^*, E_V^*, I_V^*$ be nontrivial solutions to the endemic equilibrium points, see

Appendix C for computations. The theorem below summarizes the existence of the endemic equilibrium of the system (2.6).

Theorem 3.2. *When $N > 1$ then*

(i) *in the absence of infection in the treated human population, the system* (2.6) *has*

- *a unique endemic equilibrium whenever $\mathcal{R}_0 > 1$.*
- *no endemic equilibrium otherwise.*

(ii) *in the presence of infection in the treated human population, the system* (2.6) *has*

- *no endemic equilibrium if $\mathcal{R}_0 < R_0^c$, where R_0^c is a threshold value of $\mathcal{R}_0$.*
- *has at least one endemic equilibrium in Ω, if $\mathcal{R}_0 > 1$.*
- *has two endemic equilibria for some parameter values of $\mathcal{R}_0$ within the range $R_0^c < \mathcal{R}_0 < 1$ within this range, one endemic equilibrium and the disease-free equilibrium are locally stable.*
- *has no endemic equilibrium otherwise.*

Proposition 3.1. *The system* (2.6) *exhibits backward bifurcation for $\mathcal{R}_0 < 1$.*

From the results in Sec. 3.2, we have established that the system (2.6) has a backward bifurcation at $\mathcal{R}_0 = 1$ if and only if $\Gamma_1 < 0$ and $\Delta > 0$. The existence of backward bifurcation phenomenon indicates that the classical requirement for $\mathcal{R}_0 < 1$ is no longer sufficient for disease eradication.[27] In order to achieve a epidemiological goal of disease eradication, $\mathcal{R}_0$ must be brought below the critical value $\mathcal{R}_0^c$. To obtain the critical value $\mathcal{R}_0^c$, we set the discriminant Δ of the polynomial (C.5) to zero and make $\mathcal{R}_0$ the subject of the relation. Thus, we have

$$\mathcal{R}_0^c = 1 - \frac{\Gamma_1^2}{4\Gamma_2[r\Pi Q_1^2 Q_2 Q_3 Q_4^2 Q_5 Q_6 Q_7 Q_{10}\mu_v^2(K_l Q_9 + K_e\eta_1)]}. \tag{3.2}$$

We carry out bifurcation analysis to study the behavior of the system (2.6) using Centre Manifold Theorem (CMT) as described in.[28] A direct use CMT in,[28] can assist in determining the stability of the endemic equilibrium and the direction of bifurcation $\mathcal{R}_0 = 1$. We avoid duplicating the theorem and compute the values of **a** and **b**. Following the simplification made in Appendix C, we have the basic reproduction number given by

$$\mathcal{R}_0 = \frac{Q_8 Q_9 \tau\beta_h\mu_h^2 K_l K_e \beta_v \gamma(N-1)(\delta\kappa_1 + Q_1)}{\Pi Q_1^2 Q_2 Q_3 Q_7 r\mu_v(Q_9 K_l + \eta_1 K_e)}. \tag{3.3}$$

Suppose we let $\beta_h = \beta^*$ as the bifurcation parameter, so that at $\mathcal{R}_0 = 1$, we have

$$\beta^* = \frac{\Pi Q_1^2 Q_2 Q_3 Q_7 r\mu_v(Q_9 K_l + \eta_1 K_e)}{Q_8 Q_9 \tau\mu_h^2 K_l K_e \beta_v \gamma(N-1)(\delta\kappa_1 + Q_1)}. \tag{3.4}$$

Let x_i, for $i = 1, \ldots, 14$, represent $S_H, E_H, I_H, A_H, S_T, E_T, I_T, A_T, S_v, E_v, I_v E, L$ and P, respectively. So that our model system in (2.6) becomes

$$\left.\begin{aligned}
\dot{x_1} &= \Pi + \omega x_5 - x_1\left(\frac{p\beta_h x_{11}}{N_H}\right) - Q_1 x_1,\\
\dot{x_2} &= x_1\left(\frac{p\beta_h x_{11}}{N_H}\right) + \omega x_6 - Q_2 x_2,\\
\dot{x_3} &= \gamma x_2 + \omega x_7 - Q_3 x_3,\\
\dot{x_4} &= \delta x_3 + \omega x_8 - Q_1 x_4,\\
\dot{x_5} &= qf\theta x_1 - \alpha_1 x_5\left(\frac{p\beta_h x_{11}}{N_H}\right) - Q_4 x_5,\\
\dot{x_6} &= qf\theta x_2 + \alpha_1 x_5\left(\frac{p\beta_h x_{11}}{N_H}\right) - Q_5 x_6,\\
\dot{x_7} &= qf\theta x_3 + \alpha_2\gamma x_6 - Q_6 x_7,\\
\dot{x_8} &= qf\theta x_4 + \alpha_3\delta x_7 - Q_4 x_8,\\
\dot{x_9} &= bx_{14} - \beta_v x_9\left(\frac{x_3 + \kappa_1 x_4\kappa_2 x_7 + \kappa_3 x_8}{N_H}\right) - \mu_v x_9,\\
\dot{x_{10}} &= \beta_v x_9\left(\frac{x_3 + \kappa_1 x_4\kappa_2 x_7 + \kappa_3 x_8}{N_H}\right) - Q_7 x_{10},\\
\dot{x_{11}} &= \tau x_{10} - \mu_v x_{11},\\
\dot{x_{12}} &= r\left(1 - \frac{x_{12}}{K_e}\right)(x_9 + x_{10} + x_{11}) - Q_8 x_{12},\\
\dot{x_{13}} &= \eta_1 x_{12}\left(1 - \frac{x_{13}}{K_l}\right) - Q_9 x_{13},\\
\dot{x_{14}} &= \eta_2 x_{13} - Q_{10} x_{14}.
\end{aligned}\right\} \tag{3.5}$$

The linearisation matrix of system (3.5) around the disease-free equilibrium has a zero, simple eigenvalue. Therefore, a right eigenvector w associated with zero eigenvalue has components

$$w_1 = -\frac{\Pi r\mu_v(\gamma+\mu_h)(\delta+\mu_h)(\tau+\mu_v)(\eta_1 K_e + K_l(\eta_2+\mu_l))}{\gamma(N-1)\tau K_e\mu_h K_l\beta_v(\mu_e+\eta_1)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$

$$w_2 = \frac{\Pi r\mu_v(\gamma+\mu_h)(\delta+\mu_h)(\tau+\mu_v)(\eta_1 K_e + K_l(\eta_2+\mu_l))}{\gamma(N-1)\tau K_e K_l\beta_v(\mu_e+\eta_1)(\gamma+\mu_h)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$

$$w_3 = \frac{\Pi r\mu_v(\tau+\mu_v)(\eta_1 K_e + K_l(\eta_2+\mu_l))}{(N-1)\tau K_e K_l\beta_v(\mu_e+\eta_1)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$

$$w_4 = \frac{\delta\Pi r\mu_v(\tau+\mu_v)(\eta_1 K_e + K_l(\eta_2+\mu_l))}{(N-1)\tau K_e\mu_h K_l\beta_v(\mu_e+\eta_1)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$
$$w_5 = w_6 = w_7 = w_8 = w_{12} = w_{13} = w_{14} = 0,$$
$$w_9 = -\frac{\tau+\mu_v}{\tau}, \quad w_{10} = \frac{\mu_v}{\tau}, \quad w_{11} = 1.$$

The left eigenvector v is given by

$$v_1 = v_5 = v_9 = v_{12} = v_{13} = v_{14} = 0, \quad v_2 = 1, \quad v_3 = \frac{\gamma+\mu_h}{\gamma},$$
$$v_4 = \frac{\kappa_1(\gamma+\mu_h)(\delta+\mu_h)}{\gamma(\delta\kappa_1+\mu_h)},$$
$$v_6 = \frac{\delta\kappa_1\omega(\alpha_2(\gamma+\mu_h)(\alpha_3\mu_h+Q_6)+Q_4Q_6)+\phi_1}{Q_4Q_5Q_6(\delta\kappa_1+\mu_h)},$$
$$v_7 = \frac{(\gamma+\mu_h)(\mu_h(\alpha_3\delta(\kappa_3(\delta+\mu_h)+\kappa_1\omega)+Q_4(\kappa_2(\delta+\mu_h)+\omega))+\delta\kappa_1Q_6\omega)}{\gamma Q_4Q_6(\delta\kappa_1+\mu_h)},$$
$$v_8 = \frac{(\gamma+\mu_h)(\delta+\mu_h)(\kappa_3\mu_h+\kappa_1\omega)}{\gamma Q_4(\delta\kappa_1+\mu_h)},$$
$$v_{10} = \frac{\Pi r(\gamma+\mu_h)(\delta+\mu_h)(\eta_1K_e+K_l(\eta_2+\mu_l))}{\gamma(N-1)K_eK_l\beta_v(\mu_e+\eta_1)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$
$$v_{11} = \frac{\Pi r(\gamma+\mu_h)(\delta+\mu_h)(\tau+\mu_v)(\eta_1K_e+K_l(\eta_2+\mu_l))}{\gamma(N-1)\tau K_eK_l\beta_v(\mu_e+\eta_1)(\eta_2+\mu_l)(\delta\kappa_1+\mu_h)},$$

where

$$\phi_1 = \mu_h(\alpha_2(\gamma+\mu_h)(\alpha_3\delta\kappa_3(\delta+\mu_h)+Q_4(\kappa_2(\delta+\mu_h)+\omega))+Q_4Q_6\omega).$$

We then obtain the following nonzero second partial derivatives for the system in (3.5),

$$\frac{\partial^2 f_2}{\partial x_1\partial x_{11}} = \frac{\beta^*\mu_h}{\Pi}, \quad \frac{\partial^2 f_6}{\partial x_5\partial x_{11}} = \frac{\alpha_1\beta^*\mu_h}{\Pi}, \quad \frac{\partial^2 f_{11}}{\partial x_3\partial x_9} = \frac{\beta_v\mu_h}{\Pi},$$
$$\frac{\partial^2 f_{11}}{\partial x_4\partial x_9} = \frac{\kappa_1\beta_v\mu_h}{\Pi}, \quad \frac{\partial^2 f_{11}}{\partial x_7\partial x_9} = \frac{\kappa_2\beta_v\mu_h}{\Pi}, \quad \frac{\partial^2 f_{11}}{\partial x_8\partial x_9} = \frac{\kappa_3\beta_v\mu_h}{\Pi}, \quad \frac{\partial^2 f_2}{\partial x_{11}\partial\beta^*} = 1.$$

It, therefore, follows that the sign of **a** and **b** are given by

$$\mathbf{a} = v_2w_1w_{11}\frac{\partial^2 f_2}{\partial x_1\partial x_{11}} + v_{11}w_3w_9\frac{\partial^2 f_{11}}{\partial x_9\partial x_3} + v_{11}w_4w_9\frac{\partial^2 f_{11}}{\partial x_9\partial x_4} < 0,$$
$$\mathbf{b} = v_2w_{11}\frac{\partial^2 f_2}{\partial x_{11}\partial\beta^*} = 1 > 0.$$

We have **a** less than zero and **b** greater than zero, using the forth item of CMT in,[28] we conclude that when β^* changes from negative to positive, $\mathcal{E}_1$ changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium becomes positive and locally asymptotically stable.

From Theorem 3.2 item (ii), we have established that the infection in the treated human compartments may be the cause of the occurrence of the backward bifurcation phenomenon. Thus, it is important to show that backward bifurcation is caused by infection occurring along the treated human compartments. To achieve this, we consider the corresponding model without occurrence of infection in the treated human compartments. If there is no infection in the treated human compartments, it implies that ($\alpha_1 = \alpha_2 = \alpha_3 = 0$). The expressions for the endemic equilibrium of the resulting system in terms of λ_h^* and λ_v^*, are given by

$$S_H^* = \frac{\Pi}{Q_1(1-\Phi_1)+\lambda_h^*}, \quad E_H^* = \frac{\Pi\lambda_h^*}{Q_2(1-\Phi_7)(Q_1(1-\Phi_1)+\lambda_h^*)},$$

$$I_H^* = \frac{\Pi\gamma\lambda_h^*}{Q_2Q_3(1-\Phi_7)(1-\Phi_8)(Q_1(1-\Phi_1)+\lambda_h^*)},$$

$$A_H^* = \frac{\Pi\gamma\delta\lambda_h^*}{Q_1Q_2Q_3(1-\Phi_1)(1-\Phi_7)(1-\Phi_8)(Q_1(1-\Phi_1)+\lambda_h^*)},$$

$$S_T^* = \frac{qf\theta}{Q_4}S_H^*, \quad E_T^* = \frac{qf\theta}{Q_4}E_H^*, \quad I_T^* = \frac{qf\theta}{Q_4}I_H^*, \quad A_T^* = \frac{qf\theta}{Q_4}A_H^*,$$

$$S_v^* = \frac{bP^*}{\lambda_v^*+\mu_v}, \quad E_v^* = \frac{bP^*\lambda_v^*}{Q_7(\lambda_v^*+\mu_v)}, \quad I_v^* = \frac{b\tau P^*\lambda_v^*}{Q_7\mu_v(\lambda_v^*+\mu_v)},$$

$$E^* = \frac{bK_erP^*}{brP^*+K_eQ_8\mu_v}, \quad L^* = \frac{K_eK_lbr\eta_1P^*}{K_ebr\eta_1^*P^*+K_lQ_9(bP^*r+K_eQ_8\mu_v)},$$

$$P^* = \frac{K_eK_lQ_8Q_9\mu_v(N-1)}{br(K_e\eta_1+K_lQ_9)}.$$

Substituting the expressions for I_v^* into λ_h^* and I_H^*, A_H^*, I_T^* and A_T^* into λ_v^*, we get

$$\lambda_h^*(V_1\lambda_h^*+V_0)=0,$$

for

$$V_1 = -r\Pi Q_7(K_lQ_9+K_e\eta_1)(\gamma\delta\beta_v\mu_h(Q_4\kappa_1+fq\theta\kappa_3)+Q_1(1-\Phi_1)$$
$$(fq\gamma\theta\beta_v\kappa_2\mu_h - Q_4(1-\mathcal{R}_\alpha))),$$

$$V_0 = \Pi Q_1^2Q_2Q_3Q_4Q_7r\mu_v(1-\Phi_1)^2(1-\Phi_7)(1-\Phi_8)(\eta_1K_e+Q_9K_l)(\mathcal{R}_{0\alpha}-1),$$

where

$$R_{0\alpha} = \sqrt{\mathcal{R}_{0\alpha}} = \sqrt{\frac{\gamma(N-1)pQ_8Q_9\tau\beta_h\mu_h^2K_lK_e\beta_v(\Phi_9(1-\Phi_1))}{\Pi Q_1^2Q_2Q_3Q_4Q_7r\mu_v(1-\Phi_1)^2(1-\Phi_7)(1-\Phi_8)(Q_9K_l+\eta_1K_e)}},$$

and

$$\Phi_7 = \frac{\omega qf\theta}{Q_2Q_4}, \quad \Phi_8 = \frac{\omega qf\theta}{Q_3Q_4}, \quad \Phi_9 = \delta(Q_4\kappa_1+fq\theta\kappa_3)+Q_1(Q_4+fq\theta\kappa_2),$$

$$\mathcal{R}_\alpha = \frac{\gamma\beta_v\mu_h}{Q_3Q_4\mu_v(1-\Phi_7)(1-\Phi_8)}.$$

Note that the case $\lambda_h^* = 0$ corresponds to the disease-free equilibrium. Thus, the solution to the endemic equilibrium is obtained from the expression $V_1\lambda_h^* + V_0 = 0$. Here, $\lambda_h^* = \frac{V_0}{-V_1}$ such that the existence of endemic equilibrium is subject to $\mathcal{R}_{0\alpha} > 1$. Therefore, there exists a unique endemic equilibrium whenever $\mathcal{R}_{0\alpha} > 1$.

4. Numerical Simulation

4.1. *Parameter estimation*

In this section, we estimate the parameter values of the system (2.6). The parameter values presented in Table 1 are estimated from literature or randomly assumed to illustrate the theoretical results. Below are the explanations on how some parameters have been estimated.

(1) Human population recruitment rate Π is estimated based on the birth rate of between 30.5/1000 people to 40/1000 people per year in Sub-Sahara Africa.[29] For the purposes of illustration, a reasonable range of (30–40)per 1000 people is considered.
(2) The average life expectancy in Sub-Sahara Africa is estimated based on average life of 50–70 years.[29] The average life expectancy of black-fly is estimated based

Table 1. Estimated parameter values. The rates are given per month.

Parameter	Range	Point value	Source
Π	15–30	25	Estimated
μ_h	0.00118–0.0017	0.0014	Ref. 29
γ	0.0417–0.111	0.0982	Refs. 32 and 33
τ	2.172–5.071	2.21	Refs. 32 and 33
μ_v	0.3589–2.172	1.354	Refs. 32 and 33
f	0–1.0	0.85	Ref. 17
θ	0–1.0	0.65	Ref. 17
ω	0–1.0	0.08910	Ref. 17
α_1	0–1.0	0.025	Estimated
α_2	0–1.0	0.045	Estimated
α_3	0–1.0	0.065	Estimated
κ_1	0–1.0	0.085	Estimated
κ_2	0–1.0	0.055	Estimated
κ_3	0–1.0	0.025	Estimated
δ	0.000137–0.1874	0.0299	Estimated
r	2.51–5.62	4.72	Estimated
K_e	1000–100000	60000	Estimated
K_e	500–10000	6000	Estimated
η_1	1.014–7.605	3.41	Ref. 31
η_2	0.1667–1.014	0.8442	Ref. 31
b	4.346–7.605	7.241	Ref. 31
μ_e	1.014–7.605	1.04	Ref. 31
μ_l	0.1667–1.014	0.171	Ref. 31
μ_p	4.346–7.605	4.2	Ref. 31
β_h	0.0–0.1	0.08354	Estimated
β_v	0.0–0.1	0.07258	Estimated

on the average life span lasting for 2–3 weeks and sometimes can last up to 85 days.[30]

(3) The rate of laying of eggs r has been estimated to be between 2.5 and 5.6. The carrying charges K_e and K_l are estimated from the range 1000–100000 and 500–10000, respectively.

(4) The progression rates from eggs to larvae η_1 and from larvae to pupae η_2 as well as their mortality rates μ_e and μ_l have been estimated based on the 4–30 days and 1–6 months, respectively.[31]

(5) The rate at which the adults emerge from the pupae b has been estimated to be between 4–7 days.[31] The mortality rate of the pupae μ_p has been estimated to be between 4–7 days.

(6) The progression rate from latent class (infected individuals) to infectious class is estimated based on the duration $\frac{3}{4}$–2 years when the worm matures to release enough microfilariae that can be detectable in the skin.[32,33] On the other hand, the average incubation period in the black-fly is 1–2 weeks.[32,33]

(7) The progression rate from infectious individuals to individuals in acute phase is estimated based on the duration 1–3 years.[33]

(8) The mass administration rate θ, waning rate of the drug ω and drug efficacy f are estimated to be between 0% and 100%.[17]

For the purposes of illustration, the following initial conditions have been used.

$$S_H(0) = 5000, \quad E_H(0) = 300, \quad I_H(0) = 300, \quad A_H(0) = 100, \quad S_T(0) = 1000,$$
$$E_T(0) = 100, \quad I_T(0) = 100, \quad A_T(0) = 100, \quad S_V(0) = 3000, \quad E_V(0) = 400,$$
$$I_V(0) = 120, \quad E(0) = 10000, \quad L(0) = 5000, \quad P(0) = 3000.$$

4.2. *Sensitivity analysis*

In this section, we perform sensitivity analysis to ascertain the uncertainty of the parameters to the onchocerciasis model output. This is critical in enabling us identify the key input parameters that should be the center of focus for the disease to be contained. Sensitivity and uncertainty analysis are performed using the Latin hypercube sampling (LHS) scheme, a Monte-Carlo stratified sampling method that allows us to obtain an unbiased estimate of the model output for a given set of input parameter values.[34,35] The parameter space is simultaneously sampled without replacement as well as assuming statistical independence between the parameters. The selected sample is used to compute unbiased estimates of output values for disease threshold of the model. The computed partial rank correlation coefficients of the specific output threshold values are graphically presented in tornado plots, see Fig. 2. Parameters with positive PRCCs will increase R_0 when they are increased, whereas parameters with negative PRCCs will decrease R_0 when they are increased. The results in Fig. 2 show that β_h and β_v are the parameters with the greatest potential to worsen the onchocerciasis epidemics. This suggests that

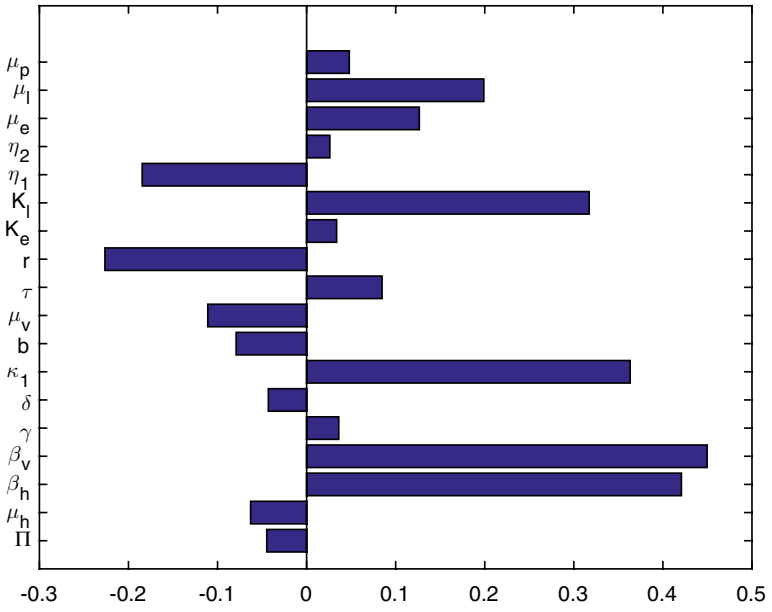


Fig. 2. Tornado plot showing PRCCs of the parameter values and the model reproduction number.

reducing contact rates between humans and the black flies may potentially be the most effective strategy to reduce $\mathcal{R}_0$, thus, controlling the spread of onchocerciasis. Other parameters with important effect on $\mathcal{R}_0$ are μ_v, r, κ_1, K_l.

4.3. *Numerical simulation results*

We now give the numerical results for the model system (2.6) starting with the both the case when $R_0 < 1$, that is, Fig. 3 and then for $R_0 > 1$, Fig. 4. The figures show how the various populations evolve. These results are comparable to the ones in[7,18] when one looks at the behavior of the solutions. We observe in Fig. 3 that when $R_0 < 1$, all trajectories initiating inside the region of attraction are approaching towards the disease-free state. We observe that the population of the infected individuals rises first and then declines and finally oscillates towards disease-free state. This behavior is also seen in both the infectious treated compartment. This indicates that the results of the simulations support the fact that the disease can be cleared from the population by ensuring that the basic reproduction number is kept at a level lower than one. It is, therefore, possible to eliminate the disease given the treatment with ivermectin for half of the year.

The simulation results of the population in Fig. 4 show the convergence of the disease epidemics to endemic equilibrium. We observe from the trajectories that the disease persistent state solutions predict a population that contains a larger number of individuals with acute phase infection of onchocerciasis. This prediction is as a

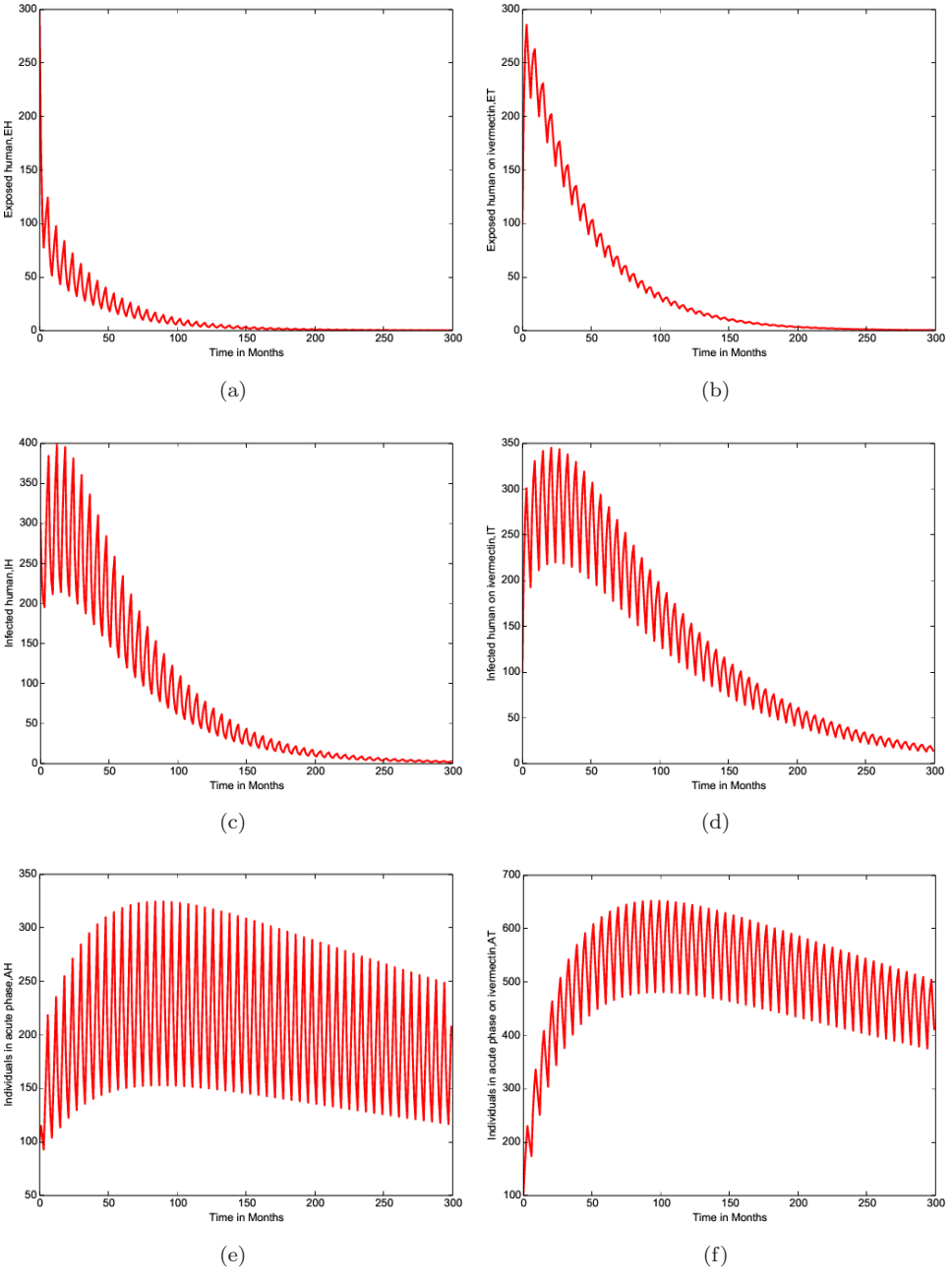
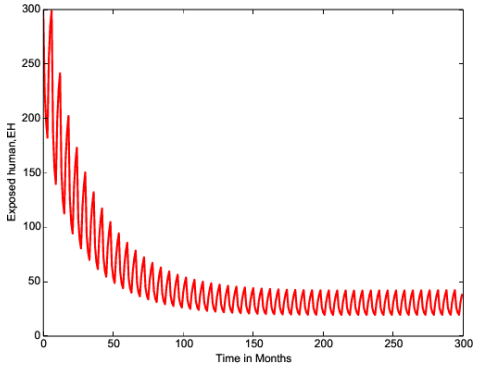
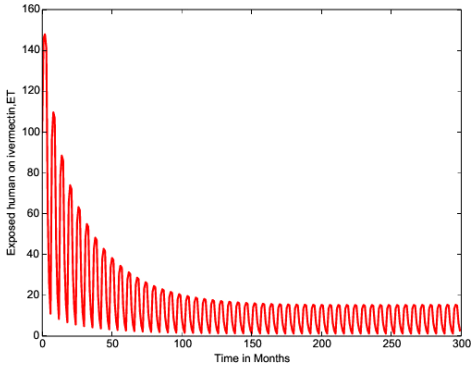


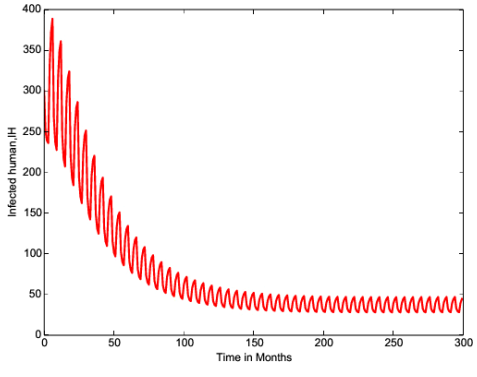
Fig. 3. (a), (c) and (e) show the human population dynamics of asymptomatic human (exposed individuals), symptomatic human (Infectious individuals) and individuals in the acute phase not on ivermectin while (b), (d) and (f) show the dynamics of the same individuals on ivermectin. The numerical solutions of model (2.6) when $R_0 = 0.5645$.



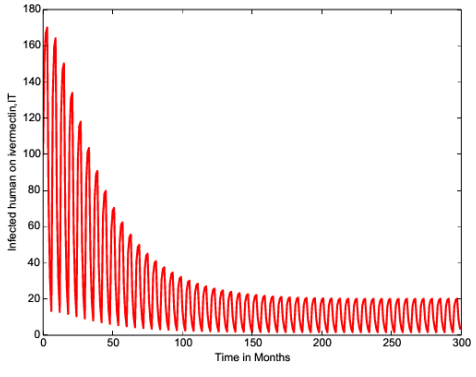
(a)



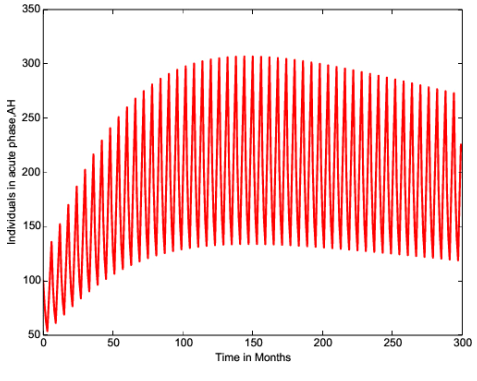
(b)



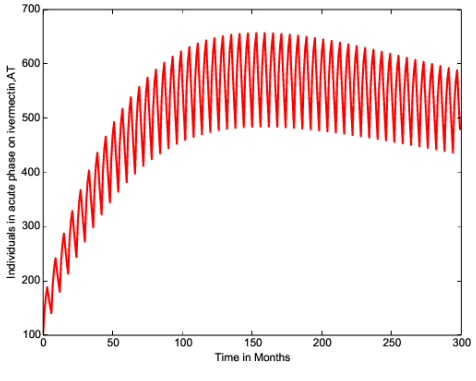
(c)



(d)



(e)



(f)

Fig. 4. (a), (c) and (e) show the human population dynamics of asymptomatic human (exposed individuals), symptomatic human (Infectious individuals) and individuals in the acute phase not on ivermectin while figures (b), (d) and (f) show the dynamics of the same individuals on ivermectin. The numerical solutions of model (2.6) when $R_0 = 1.8662$ with $\beta_h = 0.88354, \beta_v = 0.0.09458, \delta = 0.0847$ and all other parameters as given in Table 1.

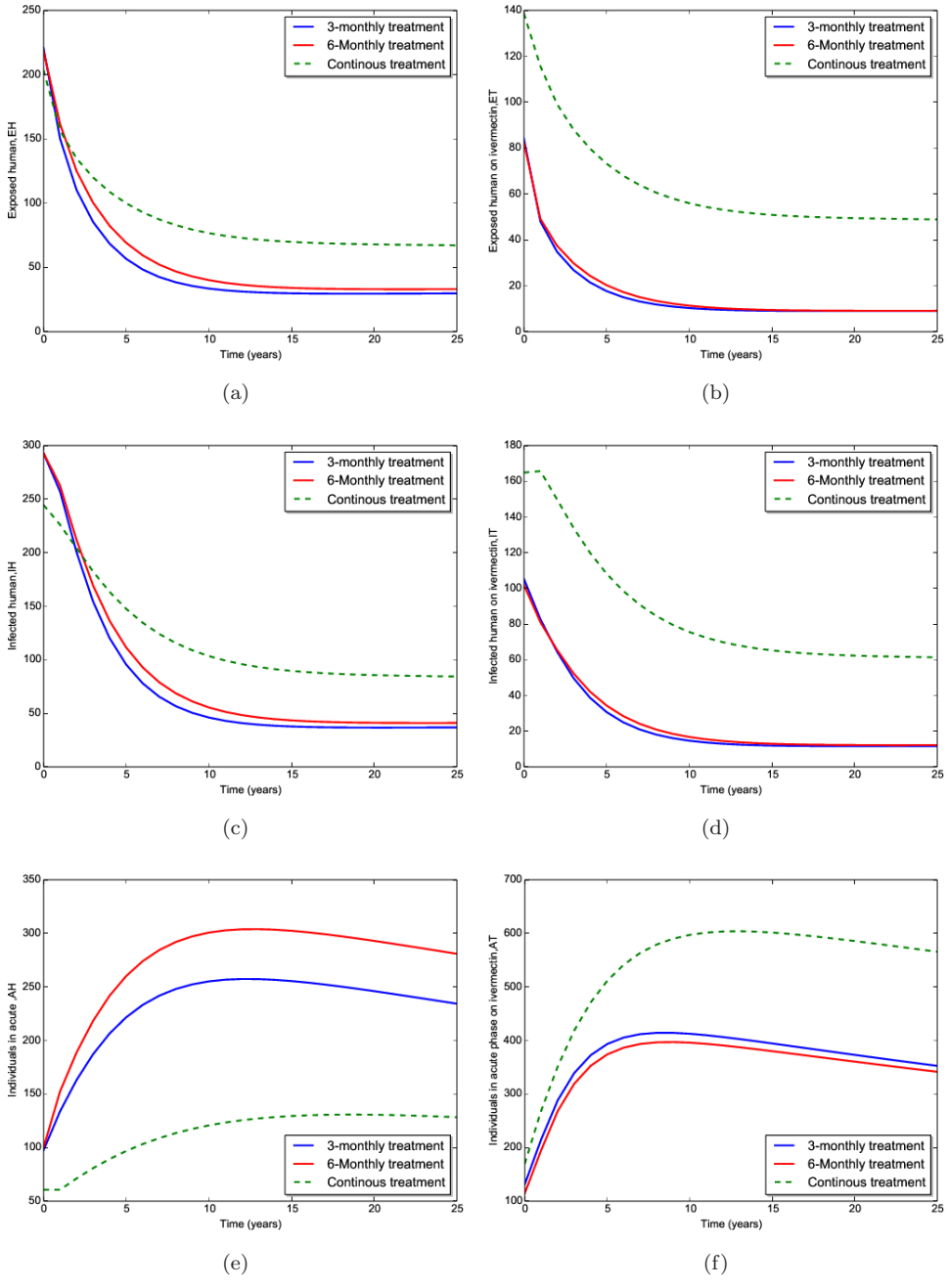


Fig. 5. Comparison on average the six-monthly, three-monthly and continuous treatment with ivermectin for the same parameters as used in Fig. 4.

result of the model design in which every infected individual ends up in the acute phase. For this to be avoided, there is a need to refine the model by introducing delays into the progression of individuals in the acute phase or reducing the rate of movement into the acute phase. This is consistent with the corresponding negative sensitivity index presented in Fig. 2 in which increasing in the progression rate of individuals from infectious class to acute phase decreases the basic reproduction number.

In order to gain more insight into eliminating the disease from the population, we ask the question; what is the potential impact of increasing the frequency of mass administration of ivermectin? In Fig. 5, we give comparative scenarios for the cases, where we have six-monthly mass administration of ivermectin, quarterly mass administration of ivermectin and continuous treatment. The functions used here are (2.1), (2.2) and then $p = q = 1$ for the continuous mass administration of ivermectin. The smooth continuous curves drawn here for comparisons sake are basically the yearly averages of the peaks of the oscillations. The study results in Fig. 5 show that the disease can easily be contained if continuous treatment with ivermectin is adopted. The figures show that continuous treatment is a better treatment strategy as compared to mass administration at regular intervals.

5. Discussion

In this study, we formulated a deterministic model that endeavors to capture the infection dynamics of onchorcerciasis and the mass treatment strategy that is currently in use. The model is used to show the likely outcomes if this treatment strategy is changed. We then look at the possibility of increasing the frequency to a quarterly treatment and a continuous treatment strategy. It is known that ivermectin treatment suppresses the production of microfilariae by the adult female worms for a few months following treatment, thus, reduces transmission. It, however, does not eliminate the infection but through a continuous treatment pressure, the disease will be eventually controlled. This study, therefore, provides a basic framework for assessing the impact of mass administration of ivermectin on the prevalence of onchocerciasis.

The basic reproduction number was determined using the next generation matrix method. The steady states of the model were determined and stability analysis was carried out. It is observed the system may exhibit backward bifurcation under some restrictions on parameters. This is demonstrated numerically. It is established that the death rate of the vector plays an important role in the occurrence of backward bifurcation. Increase in the vector death rate pushes R_0^c towards 1 leading to the disappearance of backward bifurcation. When there is no backward bifurcation, the system exhibits only forward bifurcation and in this case reducing R_0 below 1 becomes sufficient to eliminate the disease from the population.

Based on the numerical results and sensitivity analysis, onchocerciasis can be controlled and eventually eliminated by reducing the contact rates between human

and the black-flies, and increasing the removal of the black-flies. The numerical results reveal that an increase in the frequency of mass administration of ivermectin has a higher impact on reducing the infection dynamics of onchocerciasis. We observed that the continuous mass administration of ivermectin yields much better results as compared to the periodic mass administration of ivermectin. It suffices to deduce that a continuous mass administration of ivermectin can help achieve the WHO goal of onchocerciasis elimination much faster than the periodic treatments.

The model presented in this paper is by no means the best representation of onchocerciasis infection dynamics in which mass treatment is used as a control measure. First, the use of step functions to measure the waning of a ivermectin is an over estimation of the duration of protection by the treatment. Smoother functions, such as the Hill function or exponentially decaying functions, could probably be a better representation. The inclusion of the drug resistance and drug noncompliance to the model can aid predictions of treatment outcomes. Despite these short comings, the model presents some interesting results that are comparable to research done by others. Also, the results of the mathematical model are useful in assisting in the design of better treatment strategies that can lead to the eradication of onchocerciasis from the population.

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Appendix A. Computation of the Basic Reproduction Number, R_0

To compute the basic reproduction number, we assume that the net reproductive number $N > 1$. We use the next generation approach method to compute the basic reproduction number of the system (2.6). Thus, adopting the matrix notations in,[25] the matrices for new infections and transfers at disease-free equilibrium are given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{p\beta_h S_H}{N_H} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{p\alpha_1\beta_h S_T}{N_H} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_v S_v}{N_H} & \frac{\kappa_1\beta_v S_v}{N_H} & 0 & \frac{\kappa_2\beta_v S_v}{N_H} & \frac{\kappa_3\beta_v S_v}{N_H} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} Q_2 & 0 & 0 & -\omega & 0 & 0 & 0 & 0 \\ -\gamma & Q_3 & 0 & 0 & -\omega & 0 & 0 & 0 \\ 0 & -\delta & Q_1 & 0 & 0 & -\omega & 0 & 0 \\ -fq\theta & 0 & 0 & Q_5 & 0 & 0 & 0 & 0 \\ 0 & -fq\theta & 0 & -\gamma\alpha_2 & Q_6 & 0 & 0 & 0 \\ 0 & 0 & -fq\theta & 0 & -\delta\alpha_3 & Q_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & Q_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\tau & \mu_v \end{pmatrix}.$$

The spectral radius of FV^{-1} (dominant eigenvalue) gives the basic reproduction number

$$\begin{aligned} R_0 &= \sqrt{\mathcal{R}_0} \\ &= \sqrt{\frac{p\gamma\tau K_e K_l \beta_h \beta_v \mu_h^2 (\Phi_4 + \Phi_5 + \Phi_6) Q_8 Q_9 (N-1)}{Q_1^2 Q_2 Q_3 Q_4^2 Q_5 Q_6 Q_7 (1-\Phi_1)^2 (1-\Phi_2)(1-\Phi_3)(K_e\eta_1 + K_l Q_9) r \Pi \mu_v}}, \end{aligned} \tag{A.1}$$

where

$$\begin{aligned} \Phi_2 &= \frac{qf\theta\omega}{Q_2 Q_5}, \quad \Phi_3 = \frac{qf\theta\omega}{Q_3 Q_6}, \\ \Phi_4 &= Q_4^2((\delta\kappa_1 + Q_1)(\alpha_2 f\theta q\omega + Q_5 Q_6) + f\theta\kappa_2 q Q_1(\alpha_2 Q_3 + Q_5)), \\ \Phi_5 &= f\theta q Q_4(Q_1(\alpha_1(f\theta\kappa_2 q\omega + \alpha_2 Q_2(\kappa_2 Q_3 + \omega) + Q_6\omega) + \alpha_2\alpha_3\delta\kappa_3 Q_3) \\ &\quad + Q_5(-f\theta\kappa_2 q\omega + \alpha_3\delta(\kappa_1\omega + \kappa_3 Q_1) - Q_6(\omega - \delta\kappa_3)) + \omega(\alpha_2(-f\theta q(\omega - \delta\kappa_3) \\ &\quad - Q_3(f\theta\kappa_2 q - \alpha_3\delta\kappa_1) + \alpha_1\delta\kappa_1 Q_2) + \alpha_1\delta\kappa_1 Q_6)), \\ \Phi_6 &= \alpha_1 f\theta q(f\theta q\omega(\alpha_3\delta(\kappa_1\omega + \kappa_3 Q_1) \\ &\quad - f\theta\kappa_2 q\omega) + \alpha_2 Q_2(Q_3(\alpha_3\delta(\kappa_1\omega + \kappa_3 Q_1) - f\theta\kappa_2 q\omega) - f\theta q\omega(\omega - \delta\kappa_3)) \\ &\quad + f\theta q Q_6\omega(\delta\kappa_3 - \omega)). \end{aligned}$$

Appendix B. Local Stability of the Trivial Equilibrium, $\mathcal{E}_0$

Proof. $\mathcal{E}_0$ is said to be locally asymptotically stable if all the eigenvalues of the Jacobian matrix at $\mathcal{E}_0$ have negative real parts. The Jacobian matrix evaluated at the trivial equilibrium steady state $\left(S_H, 0, 0, 0, S_T, 0, 0, 0, 0, 0, 0, 0, 0, 0\right) = \left(\frac{\Pi}{Q_1(1-\Phi_1)}, 0, 0, 0, \frac{\Pi q f\theta}{Q_1 Q_4(1-\Phi_1)}, 0, 0, 0, 0, 0, 0, 0, 0, 0\right)$ is given by

$$J(\mathcal{E}_0) = \begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22} \end{pmatrix}, \tag{B.1}$$

where

$$A_{11} = \begin{pmatrix} -Q_1 & 0 & 0 & 0 & \omega & 0 & 0 & 0 & 0 \\ 0 & -Q_2 & 0 & 0 & 0 & \omega & 0 & 0 & 0 \\ 0 & \gamma & -Q_3 & 0 & 0 & 0 & \omega & 0 & 0 \\ 0 & 0 & \delta & -Q_1 & 0 & 0 & 0 & \omega & 0 \\ qf\theta & 0 & 0 & 0 & -Q_4 & 0 & 0 & 0 & 0 \\ 0 & qf\theta & 0 & 0 & 0 & -Q_5 & 0 & 0 & 0 \\ 0 & 0 & qf\theta & 0 & 0 & \alpha_2\gamma & -Q_6 & 0 & 0 \\ 0 & 0 & 0 & qf\theta & 0 & 0 & \alpha_3\delta & -Q_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_v \end{pmatrix},$$

$$A_{12} = \begin{pmatrix} 0 & -\dfrac{\Pi}{Q_1(1-\Phi_1)} & 0 & 0 & 0 \\ 0 & \dfrac{\Pi}{Q_1(1-\Phi_1)} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & -\dfrac{\alpha_1\Pi qf\theta}{Q_1Q_4(1-\Phi_1)} & 0 & 0 & 0 \\ 0 & \dfrac{\alpha_1\Pi qf\theta}{Q_1Q_4(1-\Phi_1)} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & b \end{pmatrix},$$

$$A_{21} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & r \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$A_{22} = \begin{pmatrix} -Q_7 & 0 & 0 & 0 & 0 \\ \tau & -\mu_v & 0 & 0 & 0 \\ r & r & -Q_8 & 0 & 0 \\ 0 & 0 & \eta_1 & -Q_9 & 0 \\ 0 & 0 & 0 & \eta_2 & -Q_{10} \end{pmatrix}.$$

The characteristic polynomial of $J(\mathcal{E}_0)$ is given by

$$p(\lambda) = (\lambda + Q_7)(\lambda + \mu_v)y_1(\lambda)y_2(\lambda)y_3(\lambda)y_4(\lambda), \tag{B.2}$$

where

$$\begin{aligned}
y_1(\lambda) &= (\lambda^2 + \lambda(Q_1 + Q_4) + Q_1Q_4(1 - \Phi_1))^2,\\
y_2(\lambda) &= (\lambda^2 + \lambda(Q_2 + Q_5) + Q_2Q_5(1 - \Phi_2)),\\
y_3(\lambda) &= (\lambda^2 + \lambda(Q_3 + Q_6) + Q_3Q_6(1 - \Phi_3)),\\
y_4(\lambda) &= \lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4,\\
a_1 &= Q_8 + Q_9 + Q_{10} + \mu_v,\\
a_2 &= (Q_{10}\mu_v + Q_9(Q_{10} + \mu_v) + Q_8(Q_9 + Q_{10} + \mu_v)),\\
a_3 &= (Q_8Q_9Q_{10} + \mu_v(Q_8Q_9 + (Q_{10}(Q_8 + Q_9)),\\
a_4 &= Q_8Q_9Q_{10}\mu_v(1 - N).
\end{aligned}$$

We can directly obtain $\lambda_1 = -Q_7$ and $\lambda_2 = -\mu_v$ as some of the roots of the polynomial (B.2). Other roots are the roots of $y_1(\lambda), y_2(\lambda), y_3(\lambda)$ and $y_4(\lambda)$. The roots of $y_1(\lambda), y_2(\lambda)$ and $y_3(\lambda)$ have negative real parts. It can easily be seen that all the coefficients of $y_4(\lambda)$ are positive since $N < 1$. We then use Routh–Hurwitz criterion to establish the necessary and sufficient conditions for all the roots of $y_4(\lambda)$ to have negative real parts. The Routh–Hurwitz criterion of stability of the trivial equilibrium $\mathcal{E}_0$ is given by

$$\begin{cases} H_1 > 0 \\ H_2 > 0 \\ H_3 > 0 \\ H_4 > 0 \end{cases} \Leftrightarrow \begin{cases} H_1 > 0 \\ H_2 > 0 \\ H_3 > 0 \\ H_4 > 0 \end{cases},$$

where

$$H_1 = a_1, \quad H_2 = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix}, \quad H_3 = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & a_4 & a_3 \end{vmatrix}, \quad H_4 = \begin{vmatrix} a_1 & 1 & 0 & 0 \\ a_3 & a_2 & a_1 & 1 \\ 0 & a_4 & a_3 & a_2 \\ 0 & 0 & 0 & a_4 \end{vmatrix}.$$

We then have

$$\begin{aligned}
H_1 &= a_1 = Q_8 + Q_9 + Q_{10} + \mu_v > 0,\\
H_2 &= a_1a_2 - a_3 = Q_8^2(Q_9 + Q_{10} + \mu_v) + Q_8(Q_9 + Q_{10} + \mu_v)^2 + (Q_9 + Q_{10})\\
&\quad (Q_9 + \mu_v)(Q_{10} + \mu_v) > 0,
\end{aligned}$$

$$
\begin{aligned}
H_3 = {} & a_1a_2a_3 - a_1^2a_4 - a_3^2 \\
& Q_8^2(b\eta_1\eta_2 r + (Q_9+Q_{10})(Q_9+\mu_v)(Q_{10}+\mu_v)(Q_9+Q_{10}+\mu_v)) \\
& + Q_8(2Q_9(b\eta_1\eta_2 r + Q_{10}\mu_v(Q_{10}+\mu_v)^2) + (Q_{10}+\mu_v)(2b\eta_1\eta_2 r + Q_{10}^2\mu_v^2) \\
& + Q_9^3(Q_{10}+\mu_v)^2 + Q_9^2(Q_{10}+\mu_v)(3Q_{10}\mu_v + Q_{10}^2 + \mu_v^2)) + b\eta_1\eta_2 r(Q_{10}+\mu_v)^2 \\
& + Q_9(Q_{10}+\mu_v)(2b\eta_1\eta_2 r + Q_{10}^2\mu_v^2) + Q_9^2(b\eta_1\eta_2 r + Q_{10}\mu_v(Q_{10}+\mu_v)^2) \\
& + (Q_9+Q_{10})Q_8^3(Q_9+\mu_v)(Q_{10}+\mu_v) + Q_9^3Q_{10}\mu_v(Q_{10}+\mu_v) > 0, \\
H_4 = {} & a_4H_3.
\end{aligned}
$$

The above result shows that we always have $H_1 > 0, H_2 > 0, H_3 > 0$ and $H_4 > 0$ if and only if $N < 1$. Therefore, we conclude that the trivial equilibrium $\mathcal{E}_0$ is locally asymptotically stable whenever $N < 1$. □

Appendix C. Existence of Endemic Equilibrium

From (2.4) and (2.5), we have

$$
\lambda_h^* = \frac{p\beta_h I_v^*}{N_H^*}, \quad \lambda_v^* = \frac{\beta_v(I_H^* + \kappa_1 A_H^* + \kappa_2 I_T^* + \kappa_3 A_T^*)}{N_H^*}, \tag{C.1}
$$

where $N_H^* = N_H^0 = \frac{\Pi}{\mu_h}$. Setting all the equations of the system (2.6) to zero and solving the state variables in terms of the forces of infections in (C.1), we have

$$
\begin{aligned}
S_H^* &= \frac{\Pi(\alpha_1\lambda_h^* + Q_4)}{Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*))}, \\
E_H^* &= \frac{\Pi\lambda_h^*(Q_5(\alpha_1\lambda_h^* + Q_4) + \alpha_1\omega \mathrm{qf}\theta)}{Q_2Q_5(1-\Phi_2)(Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*)))}, \\
I_H^* &= \frac{\gamma\Pi\lambda_h^*(\alpha_1(\alpha_2\omega q f\theta(\lambda_h^* + Q_2) + Q_6(Q_5\lambda_h^* + \omega q f\theta)) + Q_4(\alpha_2\omega q f\theta + Q_5Q_6))}{Q_2Q_3Q_5Q_6(1-\Phi_2)(1-\Phi_3)(Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*)))}, \\
A_H^* &= \frac{\lambda_h^*\Pi\gamma\delta(Q_4^2(Q_5Q_6 + \omega q f\theta\alpha_2) + \psi_1 + \psi_2)}{Q_1Q_2Q_3Q_4Q_5Q_6(1-\Phi_1)(1-\Phi_2)(1-\Phi_3)(Q_1Q_4(1-\Phi_1)} \\
&\quad + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*))) \\
S_T^* &= \frac{\Pi \mathrm{qf}\theta}{Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*))}, \\
E_T^* &= \frac{\Pi\lambda_h^* q f\theta(\alpha_1(\lambda_h^* + Q_2) + Q_4)}{Q_2Q_5(1-\Phi_2)(Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*)))}, \\
I_T^* &= \frac{\gamma\omega q f\theta\Pi\lambda_h^*(\alpha_1((\lambda_h^*(\alpha_2Q_3 + Q_5) + \omega q f\theta) + \alpha_2Q_2Q_3) + Q_4(\alpha_2Q_3 + Q_5))}{Q_2Q_3Q_5Q_6(1-\Phi_2)(1-\Phi_3)(Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1+\lambda_h^*)))},
\end{aligned}
$$

$$A_T^* = \frac{\Pi\lambda_h^*\gamma\delta fq\theta(Q_4(\alpha_2 f\theta q\omega + \alpha_3 Q_1(\alpha_2 Q_3 + Q_5) + Q_5Q_6) + \psi_3)}{Q_1Q_2Q_3Q_4Q_5Q_6(1-\Phi_1)(1-\Phi_2)(1-\Phi_3)(Q_1Q_4(1-\Phi_1) + \lambda_h^*(Q_4 + \alpha_1(Q_1 + \lambda_h^*)))},$$

$$S_v^* = \frac{bP^*}{\lambda_v^* + \mu_v}, \quad E_v^* = \frac{bP^*\lambda_v^*}{Q_7(\lambda_v^* + \mu_v)}, \quad I_v^* = \frac{b\tau P^*\lambda_v^*}{Q_7\mu_v(\lambda_v^* + \mu_v)},$$

$$E^* = \frac{bK_e rP^*}{brP^* + K_eQ_8\mu_v}, \quad L^* = \frac{K_eK_l br\eta_1 P^*}{K_e br\eta_1^* P^* + K_lQ_9(bP^* r + K_eQ_8\mu_v)}, \tag{C.2}$$

where

$$\psi_1 = Q_4(\alpha_1\lambda_h^*(\alpha_2 f\theta q\omega + Q_5Q_6) + \theta\omega(\alpha_3 fq(\alpha_2 Q_3 + Q_5) + \alpha_1 \mathrm{qf}(\alpha_2 Q_2 + Q_6))),$$

$$\psi_2 = \alpha_1\alpha_3\theta\omega(fq(\lambda_h^*(\alpha_2 Q_3 + Q_5) + \theta \mathrm{qf}\omega) + \alpha_2 Q_2 Q_3 \mathrm{qf}),$$

$$\psi_3 = \alpha_1(\lambda_h^*(\alpha_2 f\theta q\omega + \alpha_3 Q_1(\alpha_2 Q_3 + Q_5) + Q_5Q_6) + \alpha_3 Q_1(f\theta q\omega + \alpha_2 Q_2 Q_3) + \theta \mathrm{qf}\omega(\alpha_2 Q_2 + Q_6)).$$

The solution P^* takes the following form

$$f(P) = P[-brQ_{10}(K_lQ_9 + K_e\eta_1)P + K_eK_lQ_8Q_9Q_{10}\mu_v(N-1)] = 0. \tag{C.3}$$

Direct solution to (C.3) gives $P = 0$ or $P^* = \frac{K_eK_lQ_8Q_9\mu_v(N-1)}{br(K_e\eta_1 + K_lQ_9)}$. Note that the case $P = 0$ corresponds to the Note that the case $P = 0$ corresponds to the trivial equilibrium $\mathcal{E}_0$. We then consider the case $P > 0$, that is, $N > 1$. Substituting the values of I_v^* into the first expression in (C.1) and I_H^*, A_H^*, I_T^* and A_T^* into the second expression in (C.1) and simplifying, we obtain the following polynomial

$$g(\lambda_h^*) = \lambda_h^*(\lambda_h^{*2}\Gamma_2 + \lambda_h^*\Gamma_1 + \Gamma_0) = 0, \tag{C.4}$$

where

$$\Gamma_2 = -\alpha_1\Pi Q_7Q_{10}r\mu_v(\eta_1K_e + Q_9K_l)(Q_1(Q_4(Q_5(\Phi_1 - 1)(\gamma f\theta\kappa_2 q\mu_h\beta_v + Q_6(\gamma\mu_h\beta_v + Q_2Q_3(\Phi_2 - 1)(\Phi_3 - 1)\mu_v)) - \alpha_2\gamma f\theta q\mu_h\beta_v(\kappa_2 Q_3 + \omega)) - \alpha_3\gamma\delta f\theta\kappa_3 q\mu_h(\alpha_2 Q_3 + Q_5)\beta_v) + \gamma\mu_h\beta_v(\alpha_2 f\theta q\omega(f\theta q(\omega - \delta\kappa_3) + Q_3(f\theta\kappa_2 q - \alpha_3\delta\kappa_1) - \delta\kappa_1 Q_4) - \delta Q_5(f\theta q(\alpha_3\kappa_1\omega + \kappa_3 Q_6) + \kappa_1 Q_4 Q_6))),$$

$$\Gamma_1 = Q_{10}\mu_v((N-1)p\gamma\tau K_eK_lQ_8Q_9\alpha_1\beta_h\beta_v(-\delta Q_4Q_5Q_6\kappa_1 + fq\theta(\omega(\alpha_2(fq\theta\omega - \delta(Q_4 + Q_3\alpha_3)\kappa_1 + fq\theta Q_3\kappa_2) - \delta\alpha_3\kappa_1) - \delta(Q_5 + fq\theta\omega\alpha_2)\kappa_3) + Q_1(Q_4(Q_5Q_6(\Phi_1 - 1) - fq\theta(-\Phi_1\kappa_2 + \kappa_2 + \alpha_2(\omega + Q_3\kappa_2))) - fq\delta\theta(Q_3\alpha_2 + 1)\alpha_3\kappa_3))\mu_h^2 + r\Pi K_lQ_7Q_9((\gamma\beta_v((Q_5Q_6 + fq\theta\omega\alpha_2)(Q_1 + \delta\kappa_1)$$

$$
\begin{aligned}
&+ fq\theta Q_1(Q_5 + Q_3\alpha_2)\kappa_2)\mu_h + Q_1Q_2Q_3Q_5Q_6\mu_v(\Phi_2 - 1)(\Phi_3 - 1))Q_4^2\\
&+ (\gamma\theta Q_1\beta_v(\mathrm{qf}\alpha_1(\omega Q_6 + fq\theta\omega\kappa_2 + Q_2\alpha_2(\omega + Q_3\kappa_2)) + fq\delta Q_3\alpha_2\alpha_3\kappa_3)\mu_h\\
&+ fq\gamma\theta Q_5\beta_v(\delta(Q_6 + Q_1\alpha_3)\kappa_3 - \omega(Q_6 - \delta\alpha_3\kappa_1 + fq\theta\kappa_2))\mu_h\\
&+ \gamma\theta\omega\beta_v(\mathrm{qf}\delta Q_6\alpha_1\kappa_1 + \alpha_2(\mathrm{qf}\delta Q_2\alpha_1\kappa_1 + fq(Q_3(\delta\alpha_3\kappa_1 - fq\theta\kappa_2)\\
&+ fq\theta(\delta\kappa_3 - \omega))))\mu_h - Q_2Q_3Q_5Q_6(fq\theta\omega - Q_1^2\alpha_1)\mu_v(\Phi_2 - 1)(\Phi_3 - 1))Q_4\\
&+ \theta\alpha_1(-f^2q^2\theta Q_1Q_2Q_5\mu_v(\Phi_2 - 1)\omega^2 + fqQ_6(\mathrm{qf}\gamma\theta\beta_v(\delta\kappa_3 - \omega)\mu_h\\
&+ Q_1Q_2Q_3Q_5\mu_v(\Phi_2 - 1))\omega + \mathrm{qf}\gamma\beta_v(fq\theta\omega(\delta\alpha_3(\omega\kappa_1 + Q_1\kappa_3) - fq\theta\omega\kappa_2)\\
&+ Q_2\alpha_2(fq\theta\omega(\delta\kappa_3 - \omega) + Q_3(\delta\alpha_3(\omega\kappa_1 + Q_1\kappa_3) - fq\theta\omega\kappa_2)))\mu_h))\\
&+ r\Pi Q_7\eta_1((\gamma\beta_v((Q_5Q_6 + fq\theta\omega\alpha_2)(Q_1 + \delta\kappa_1) + fq\theta Q_1(Q_5 + Q_3\alpha_2)\kappa_2)\mu_h\\
&+ Q_1Q_2Q_3Q_5Q_6\mu_v(\Phi_2 - 1)(\Phi_3 - 1))Q_4^2 + (\gamma\theta Q_1\beta_v(\mathrm{qf}\alpha_1(\omega Q_6 + fq\theta\omega\kappa_2\\
&+ Q_2\alpha_2(\omega + Q_3\kappa_2)) + fq\delta Q_3\alpha_2\alpha_3\kappa_3)\mu_h + fq\gamma\theta Q_5\beta_v(\delta(Q_6 + Q_1\alpha_3)\kappa_3\\
&- \omega(Q_6 - \delta\alpha_3\kappa_1 + fq\theta\kappa_2))\mu_h + \gamma\theta\omega\beta_v(\mathrm{qf}\delta Q_6\alpha_1\kappa_1 + \alpha_2(\mathrm{qf}\delta Q_2\alpha_1\kappa_1\\
&+ fq(Q_3(\delta\alpha_3\kappa_1 - fq\theta\kappa_2) + fq\theta(\delta\kappa_3 - \omega))))\mu_h - Q_2Q_3Q_5Q_6(fq\theta\omega - Q_1^2\alpha_1)\\
&\times \mu_v(\Phi_2 - 1)(\Phi_3 - 1))Q_4 + \theta\alpha_1(-f^2q^2\theta Q_1Q_2Q_5\mu_v(\Phi_2 - 1)\omega^2\\
&+ fqQ_6(\mathrm{qf}\gamma\theta\beta_v(\delta\kappa_3 - \omega)\mu_h + Q_1Q_2Q_3Q_5\mu_v(\Phi_2 - 1))\omega\\
&+ \mathrm{qf}\gamma\beta_v(fq\theta\omega(\delta\alpha_3(\omega\kappa_1 + Q_1\kappa_3) - fq\theta\omega\kappa_2) + Q_2\alpha_2(fq\theta\omega(\delta\kappa_3 - \omega)\\
&+ Q_3(\delta\alpha_3(\omega\kappa_1 + Q_1\kappa_3) - fq\theta\omega\kappa_2)))\mu_h))),\\
\Gamma_0 = {}& Q_{10}\mu_v(K_e(\gamma(N-1)pQ_8Q_9\tau\beta_h\mu_h^2K_l\beta_v(Q_4^2((\delta\kappa_1 + Q_1)(-(\alpha_2f\theta qw + Q_5Q_6))\\
&- f\theta\kappa_2qQ_1(\alpha_2Q_3 + Q_5)) + \theta Q_4(fqQ_5(f\theta\kappa_2q\omega - \alpha_3\delta(\kappa_1\omega + \kappa_3Q_1)\\
&+ Q_6(\omega - \delta\kappa_3)) - Q_1(\alpha_2\alpha_3\delta f\kappa_3qQ_3 + \alpha_1\mathrm{qf}(f\theta\kappa_2q\omega + \alpha_2Q_2(\kappa_2Q_3 + \omega)\\
&+ Q_6\omega)) + \omega(\alpha_2(fq(f\theta q(\omega - \delta\kappa_3) + Q_3(f\theta\kappa_2q - \alpha_3\delta\kappa_1)) - \alpha_1\delta\kappa_1Q_2\mathrm{qf})\\
&- \alpha_1\delta\kappa_1Q_6\mathrm{qf})) + \alpha_1\theta\mathrm{qf}(f\theta q\omega(f\theta\kappa_2q\omega - \alpha_3\delta(\kappa_1\omega + \kappa_3Q_1))\\
&+ \alpha_2Q_2(f\theta q\omega(\omega - \delta\kappa_3) - Q_3(\alpha_3\delta(\kappa_1\omega + \kappa_3Q_1) - f\theta\kappa_2q\omega))\\
&+ f\theta qQ_6\omega(\omega - \delta\kappa_3))) + \eta_1\Pi Q_2Q_3Q_5Q_6Q_7r(\Phi_1 - 1)^2(\Phi_2 - 1)(\Phi_3 - 1)\mu_v)\\
&+ \Pi Q_2Q_3Q_5Q_6Q_7Q_9r(\Phi_2 - 1)(\Phi_3 - 1)(\Phi_1 - 1)^2K_l\mu_v).
\end{aligned}
$$

Note that the case when $\lambda_h^* = 0$, refers to the disease-free state treated earlier. The existence and the number of endemic equilibria for the system (2.6) is determined by the existence of, and the number of positive roots of the following quadratic equation

$$\lambda_h^{*2}\Gamma_2 + \lambda_h^*\Gamma_1 + \Gamma_0 = 0. \tag{C.5}$$

In order to reduce the complexity of the coefficients of Eq. (C.5), we consider the case $p = 1, q = 0$. Thus, the following coefficients are obtained.

$$\Gamma_2 = \alpha_1 \Pi Q_4 Q_5 Q_6 Q_7 Q_{10} r \mu_v (\eta_1 K_e + Q_9 K_l)(\gamma \mu_h \beta_v (\delta \kappa_1 + Q_1) + Q_1 Q_2 Q_3 \mu_v),$$

$$\begin{aligned}\Gamma_1 = {} & Q_4 Q_5 Q_6 (-\alpha_1 b \gamma \eta_1 \eta_2 r \tau K_e \beta_h \mu_h^2 K_l \beta_v (\delta \kappa_1 + Q_1) + \gamma Q_{10} \mu_h \beta_v \mu_v (\delta \kappa_1 + Q_1) \\ & \times (\alpha_1 Q_8 Q_9 \tau K_e \beta_h \mu_h K_l + \Pi Q_4 Q_7 r (\eta_1 K_e + Q_9 K_l)) + \Pi Q_1 Q_2 Q_3 Q_7 Q_{10} r \\ & \times (\alpha_1 Q_1 + Q_4) \mu_v^2 (\eta_1 K_e + Q_9 K_l)),\end{aligned}$$

$$\Gamma_0 = r \Pi Q_1^2 Q_2 Q_3 Q_4^2 Q_5 Q_6 Q_7 Q_{10} \mu_v^2 (K_l Q_9 + K_e \eta_1)(1 - \mathcal{R}_0).$$

$$\mathcal{R}_0 = \frac{Q_8 Q_9 \tau \beta_h \mu_h^2 K_l K_e \beta_v \gamma (N-1)(\delta \kappa_1 + Q_1)}{\Pi Q_1^2 Q_2 Q_3 Q_7 r \mu_v (Q_9 K_l + \eta_1 K_e)}.$$

The roots of the quadratic equation in (C.5) are given by

$$\lambda_h^* = \frac{-\Gamma_1 \pm \sqrt{\Gamma_1^2 - 4\Gamma_2 \Gamma_0}}{2\Gamma_2}$$

We notice that when $\mathcal{R}_0 > 1$ then $\Gamma_0 < 0$ which implies that the $\Delta = \Gamma_1^2 - 4\Gamma_2\Gamma_0 > 0$ and Eq. (C.5) has a unique positive solution thus the system (2.6) has a unique endemic equilibrium. If $\mathcal{R}_0 < 1$ then $\Gamma_0 > 0$ and by adding the conditions $\Gamma_1 < 0$ and $\Delta > 0$, we get two positive real equilibria. If $\mathcal{R}_0 = 1$, then $\Gamma_0 = 0$ and there is a unique nonzero solution of (C.5) which is positive if and only if $\Gamma_1 < 0$. The model system (2.6) in the absence of infection in the treated human population ($\alpha_1 = 0$), admits only one endemic equilibrium whenever $\mathcal{R}_0 > 1$.