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APPLICATION OF OPTIMAL CONTROL STRATEGIES FOR THE DYNAMICS OF YELLOW FEVER

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Abstract. In this article, we present an application of optimal control theory to assess the effectiveness of control measures on the dynamics of YF. We formulate and analyse a deterministic mathematical model with personal protection, educational campaign and spray of insecticides as control variables using optimal control theory and Pontryagins Maximum Principle. The optimal controls are characterized in terms of optimality system, and solved numerically for several scenarios. The results show that multiple optimal control measures is most effective strategy to bring a stable disease-free situation compared to a single control. However, spray of insecticides alone was seen as not effective without personal protection, and optimal use of personal protection alone might be beneficial to minimize transmission of the infection to the community.

Keywords: Yellow fever; Optimal control; Personal protection; Educational campaign; Spray of insecticides.

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1. Introduction

Outbreaks of vector borne diseases like malaria, yellow fever (YF) and dengue that are transmitted to humans by blood-sucker mosquito have devastated several countries around the world [17]. Thus, modelling their dynamics and control has gained enormous attention.

Most infectious diseases could be eradicated, if adequate and timely steps (for example vaccination, treatment, educational and enlightenment campaign) are taken in the course of the epidemic. However, many of these diseases eventually become endemic in our societies due to lack of adequate policies and timely interventions to mitigate the spread of them.

YF, in particular, is a viral haemorrhagic fever caused by yellow fever virus (YFV) and is transmitted through the bite of an infected female yellow fever mosquito [25]. Humans and primates are the principle reservoirs for YF virus and the vector, female YF mosquito (*Aedes aegypti*) is the only transmitting agent of this virus.

The study of optimal control strategies in epidemiological models have been of much interest for informed decision-making. Over years, mathematical models of the spread of infectious diseases have been used to provide important insights into disease behaviour and optimal control strategies. For some diseases, medical treatments can be given to patients to cure the infection but there may not be vaccine to immunize susceptible individuals (e.g. in the case of Malaria). For a few other diseases, there is no cure but individuals can be vaccinated against getting infection (e.g. Polio, YF).

Optimal control theory have been applied to number of studies in mathematical models of vector-borne diseases like malaria [1],[22], chikungunya [18], dengue [26], rift valley fever [20], among others. Regarding to YF few studies have been done to address transmission dynamics like in [19],[2],[10], [27], but not addressing control strategies of the infection. In these studies theoretical and statistical models have been used.

Recently, [12] use a mathematical model in addressing YF transmission dynamics between primates and human being, into which model parameters and factors affecting diseases transmission were discussed. Nothing has been done to address control strategies of YF.

Thus, in this study we formulate an optimal control model for YF aiming at deriving optimal control strategies with minimum implementation cost. We extend the current model [12] by introducing time-dependent control efforts on prevention or personal protection, educational campaign and spray of insecticides efforts as controls to curtail the spread of YF. We use Pontryagins Maximum Principle in deriving the optimal control and Fleming and Rishel [7] and Lukes [15] in proving the existence of an optimal control.

2. Materials and Methods

2.1 Model Formulation

Control terms are added to the existing deterministic mathematical model for YF transmission dynamics by [12] as shown in Figure 1.

2.2 Model Flow Diagram and Description

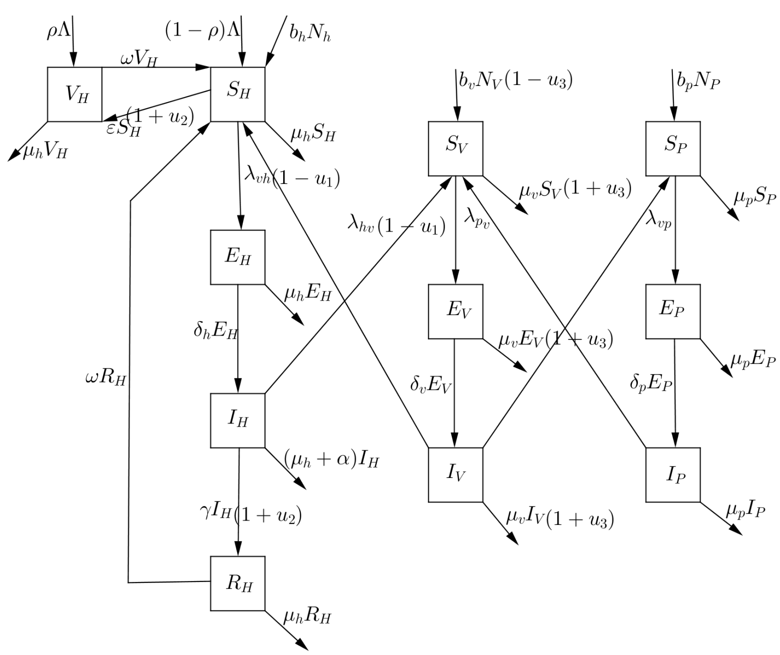

FIGURE 1. *Model flow diagram for transmission dynamics of YF under control measures.*

Three populations are considered in the model (humans, vector and primates) with the total population sizes at time t given by $N_h(t)$, $N_v(t)$ and $N_p(t)$ respectively. The populations are further compartmentalized into epidemiological classes whereby human population is divided into

5 classes: susceptible, S_h , vaccinated, V_h, exposed, E_h, infectious, I_h and recovered (immune), R_h.

Vector and primates population are divided into 3 classes each: susceptible, exposed, and infectious. They do not include the immune class as they never recover from the infection, that is their infective period ends with their death due to their relatively short life cycle compared to human.

We consider three control efforts, prevention or personal protection to human host, educational campaign to susceptible and infectious human hosts and spray of insecticides against the vector. We use the control mechanisms $u_i(t)$ in human host and vector populations, where $1-u_i(t)$ is the failure probability of the control mechanism $u_i(t)$ for i = 1; 2; 3. In the model the control mechanism $u_1(t)$ represents prevention or personal protection to human host, $u_2(t)$ represents educational campaign to susceptible and infectious human hosts and $u_3(t)$ represents spray of insecticides against the vector.

In the human population, prevention or personal protection includes, the use of mosquito treated bed-nets, use of mosquito coils, indoor residual spraying and the use of mosquito repellents. All these things are done in order to minimize or eliminate vector-human contacts. Thus, the associated force of infection to human from vector and vice versa is reduced by a factor of $1-u_1$.

Educational campaign is done to the human populations in such a way that upon its successful efforts, more susceptible human individuals will be motivated to vaccination before the occurrence of the disease making the vaccination rate, ε, to be increased by a factor $1+u_2$. Also, infectious human individuals will be encouraged and motivated to find treatment of the infections and use. That is to say a large number of infectious humans will be treated and hence the recovery rate, γ, will also be increased by a factor $1+u_2$.

Spray of insecticides against the vector is done to larvacide and adultcide and applied to those places where vector bleeding occurs in order to control vector population. It is assumed that application of insecticides will reduce the reproduction (birth) rate, b_vN_v, of the vector [3] by a factor $1-u_3$ and also will increase the death rate of vectors in each compartment at a rate proportional to $u_3(t)$. We take these rates to be $\mu_v(t)u_3(t)S_v(t)$, $\mu_v(t)u_3(t)E_v(t)$ and $\mu_v(t)u_3(t)I_v(t)$

for susceptible, exposed and infectious vector respectively. That is to say mortality rate of mosquito population, μ_v, is increased by a factor $1+u_3$. Thus, we construct the optimal model equations as follows:

2.3 Model Equations

Human:

$$
\begin{aligned}
\frac{dS_h(t)}{dt} &= b_hN_h+(1-\rho)\Lambda+\omega(V_h+R_h)-\lambda_{vh}(1-u_1)-\varepsilon(1+u_2)S_h-\mu_hS_h,\\
\frac{dV_h(t)}{dt} &= \rho\Lambda+\varepsilon(1+u_2)S_h-\omega V_h-\mu_hV_h,\\
\frac{dE_h(t)}{dt} &= \lambda_{vh}(1-u_1)-\delta_hE_h-\mu_hE_h,\\
\frac{dI_h(t)}{dt} &= \delta_hE_h-(\mu_h+\alpha)I_h-\gamma I_h(1+u_2),\\
\frac{dR_h(t)}{dt} &= \gamma I_h(1+u_2)-\omega R_h-\mu_hR_h,
\end{aligned} \tag{1}
$$

Vector:

$$
\begin{aligned}
\frac{dS_V(t)}{dt} &= b_vN_V(1-u_3)-\lambda_{hv}(1-u_1)-\lambda_{pv}-\mu_vS_V(1+u_3),\\
\frac{dE_V(t)}{dt} &= \lambda_{hv}(1-u_1)+\lambda_{pv}-\delta_vE_V-\mu_vE_V(1+u_3),\\
\frac{dI_V(t)}{dt} &= \delta_vE_V-\mu_vI_V(1+u_3),
\end{aligned} \tag{2}
$$

Primates:

$$
\begin{aligned}
\frac{dS_p(t)}{dt} &= b_pN_p-\lambda_{vp}-\mu_pS_p,\\
\frac{dE_p(t)}{dt} &= \lambda_{vp}-\delta_pE_p-\mu_pE_p,\\
\frac{dI_p(t)}{dt} &= \delta_pE_P-\mu_pI_p.
\end{aligned} \tag{3}
$$

where; $\lambda_{vh}=\frac{a\beta_1S_hI_v}{N_v}$, $\lambda_{hv}=\frac{a\beta_2S_vI_h}{N_h}$, $\lambda_{pv}=\frac{a\beta_3S_vI_p}{N_p}$ and $\lambda_{vp}=\frac{a\beta_4S_pI_p}{N_p}$.

In the model the term $\lambda_{vh}=\frac{a\beta_1S_hI_v}{N_v}$ denotes the rate at which susceptible human hosts S_h get infected by the infected vector I_v (force of infection from vector to human), $\lambda_{hv}=\frac{a\beta_2S_vI_h}{N_h}$ denotes the rate at which susceptible vector S_v get infected from the infected human host I_h (infection force from human host to vector), $\lambda_{pv}=\frac{a\beta_3S_vI_p}{N_p}$ denotes the rate at which the susceptible vector S_v get infected from the infected primate I_p (force of infection from primate to vector) and the term $\lambda_{vp} = \frac{a\beta_4 S_p I_v}{N_v}$ denotes the rate at which the susceptible primates S_p get infected from the infected vector I_v.

Thus, we define the total population sizes $N_h(t)$, $N_v(t)$ and $N_p(t)$ for human host, vector and primates respectively as:

$$
\begin{aligned}
N_h(t) &= S_h(t) + V_h(t) + E_h(t) + I_h(t) + R_h(t), \\
N_v(t) &= S_v(t) + E_v(t) + I_v(t), \\
N_p(t) &= S_p(t) + E_p(t) + I_p(t).
\end{aligned} \tag{4}
$$

Model systems (1), (2), (3) can be written together to form a single system of differential equations (5).

$$
\begin{aligned}
\frac{dS_h}{dt} &= b_h N_h + (1-\rho)\Lambda + \omega(V_h + R_h) - \frac{a\beta_1 S_h I_v}{N_v}(1-u_1) - \varepsilon(1+u_2)S_h - \mu_h S_h, \\
\frac{dV_h}{dt} &= \rho\Lambda + \varepsilon(1+u_2)S_h - \omega V_h - \mu_h V_h, \\
\frac{dE_h}{dt} &= \frac{a\beta_1 S_h I_v}{N_v}(1-u_1) - \delta_h E_h - \mu_h E_h, \\
\frac{dI_h}{dt} &= \delta_h E_h - (\mu_h + \alpha)I_h - \gamma(1+u_2)I_h, \\
\frac{dR_h}{dt} &= \gamma(1+u_2)I_h - \omega R_h - \mu_h R_h, \\
\frac{dS_v}{dt} &= b_v N_v(1-u_3) - \frac{a\beta_2 S_v I_h}{N_h}(1-u_1) - \frac{a\beta_3 S_v I_p}{N_p} - \mu_v S_v(1+u_3), \\
\frac{dE_v}{dt} &= \frac{a\beta_2 S_v I_h}{N_h}(1-u_1) + \frac{a\beta_3 S_v I_p}{N_p} - \delta_v E_v - \mu_v E_v(1+u_3), \\
\frac{dI_v}{dt} &= \delta_v E_v - \mu_v I_v(1+u_3), \\
\frac{dS_p}{dt} &= b_p N_p - \frac{a\beta_4 S_p I_v}{N_v} - \mu_p S_p, \\
\frac{dE_p}{dt} &= \frac{a\beta_4 S_p I_v}{N_v} - \delta_p E_p - \mu_p E_p, \\
\frac{dI_p}{dt} &= \delta_p E_p - \mu_p I_p.
\end{aligned} \tag{5}
$$

3. The Optimal Control Problem

In model system (5), we seek to minimize the number of exposed and infectious human with minimum implementation cost (that is the cost of applying control, u_1, u_2, u_3). Therefore for a

Parameters as they have been used in this study are described in Table 1:

TABLE 1. Description of parameters of the model system (5)

Symbol	Description	Value	Reference
β_1	Transmission probability of vector to human	0.8	[5], [2]
β_2	Transmission probability of human to vector	0.8	[21], [26]
β_3	Transmission probability of primate to vector	0.5	[12]
β_4	Transmission probability of vector to primate	0.9	estimate
δ_h	Progression rate from E_h to I_h	0.95 day^{-1}	[8], [6]
δ_v	Progression rate from E_v to I_v	0.95 day^{-1}	[2], [8]
δ_p	Progression rate from E_p to I_p	0.85 day^{-1}	[12]
b_h	Daily birth rate of human	0.0003	estimate
b_v	Daily birth rate of vector	0.002	estimate
b_p	Daily birth rate of primates	0.00004	estimate
a	Daily bitting rate	0.5	[5], [2]
γ	Recovery rate	0.005	[23], [4]
α	Death rate due to disease for human	0.001	[23], [4]
ω	rate of relapse of vaccinated and recovered human	0.05	[8]
ε	vaccination rate of susceptible human	0.5 day^{-1}	[12]
ρ	proportion of immigrant who are vaccinated	0.02 day^{-1}	[8]
Λ	arrival rate of immigrant per individual per time	70 day^{-1}	estimate
$\frac{1}{\mu_h}$	lifespan of human	60 years	[12], [20]
$\frac{1}{\mu_v}$	lifespan of vector	40 days	[18]
$\frac{1}{\mu_p}$	lifespan of primates	10 years	estimate

terminal time t_f, the aim is to minimise the cost of objective functional

$$J(u_1,u_2,u_3) = \int_0^{t_f} \left(A_1E_h + A_2I_h + B_1u_1^2 + B_2u_2^2 + B_3u_3^2\right) dt \tag{6}$$

where, A_1 and A_2 are positive weight constants of the exposed and infectious humans respectively; and B_1, B_2, B_3 are the positive weight constants for the control mechanisms u_1, u_2, u_3 respectively. However, with the idea of other researchers from the literature on epidemic controls ([22],[13],[1],[9],[16],[11]), we choose a quadratic cost function of the controls.

We also define $B_1u_1^2$ as the cost of the control mechanism in human associated with preventive measures like indoor residual spraying, use of mosquito treated bed nets, mosquito coils and mosquito repellents so as to minimize the vector human contacts; $B_2u_2^2$ is the cost of the control efforts on educational campaign to susceptible and infected human individuals and $B_3u_3^2$ is the cost of control mechanism in vectors associated with spraying of insecticide against vector to adulticide and larvacide, and those places where vector breeding occurs.

Thus, we seek to obtain an optimal control (u_1^*, u_2^*, u_3^*) such that;

$$J(u_1^*, u_2^*, u_3^*) = \min J(u_1, u_2, u_3 | u_1, u_2, u_3 \in \Gamma) \tag{7}$$

subject to system (5) where the control set is defined as $\Gamma = \{u_1, u_2, u_3 | u_i(t)$ is a piece wise continuous functions on $[0, t_f]$ and that $a_i \leq u_i \leq b_i$ for $i = 1, 2, 3\}$. Here a_i and b_i, are constants in [0,1].

In order to find an optimal solution, the basic framework of the problem is to state and prove the existence of optimal control for the model system (5) and then characterize the optimal control by deriving the optimality system.

3.1 Existence of an Optimal Control Problem

In this part, we state and prove the existence of optimal control using the existence results from [7] and [15]. We first state the following theorem;

Theorem 3.1.

Consider the optimal control problem with model system (5) as state equations. There exists an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in \Gamma$ such that

$$\min_{(u_1,u_2,u_3)\in\Gamma} J(u_1, u_2, u_3) = J(u_1^*, u_2^*, u_3^*)$$

Proof.

We note that the existence of an optimal control pair can be proved by using results from Fleming and Rishel [7] theorem 4.1 we first need to check the following properties:

1. The set of controls and corresponding state variables is non-empty.
2. The control set Γ is convex and closed.
3. The right hand side of the state system is bounded by a linear function in the state and control variables.

4. The integrand of the objective functional is convex.
5. There exist constants $c_1, c_2 > 0$, and $\alpha > 1$ such that the integrand of the objective functional is bounded below by $c_1 \left(|u_1|^2 + |u_2|^2 + |u_3|^2\right)^{\frac{\alpha}{2}} - c_2$.

Condition 1, is verified using results from Fleming and Rishel [7] Chapter III page 60, from them existence is assured by the state equations and control variables; which can also be seen in our ODE's model system (5). The control set Γ is bounded by definition; hence condition 2 is also satisfied. The RHS of the state system (5) satisfies condition 3 since the state solutions are bounded.
The integrand of our objective functional is

$$A_1 E_h + A_2 I_h + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2$$

It is clearly convex on control set Γ, which gives condition 4.
Finally, there are constants $c_1, c_2 > 0$ and $\alpha > 1$ satisfying

$$c_1 \left(|u_1|^2 + |u_2|^2 + |u_3|^2\right)^{\frac{\alpha}{2}} - c_2$$

because the state variables are bounded, which shows the existence of an optimal control solution.
Hence, we conclude that there exists an optimal control (u_1^*, u_2^*, u_3^*) that minimizes the objective functional $J(u_1, u_2, u_3)$ which follows from the existence results by [9].

3.2 Characterization of Optimal Control

With the existence of optimal control pair established, we now present the optimality system and derive the necessary conditions using the Pontryagin Maximum Principle [24]. The aim of this principle is to minimize the objective function. To accomplish this, we begin by defining a Lagrangian of our optimal control problem which is the Hamiltonian augmented with penalty multipliers for the control constraints. Thus, we define the Hamiltonian (H) for the control problem (5)-(6) as:

$$H = \mathscr{L}(E_h, I_h, u_1, u_2, u_3) + \sum_K \lambda_K f_K \tag{8}$$

where K is the set of state variables, that is $S_h, V_h, ..., I_p$; $\lambda_K, (K = 1, 2, ..., 11)$ is the adjoint functions of the K^{th} state variable, and f_K is the right hand side of the differential equation of the K^{th} state variable. This can be written as:

$$
\begin{aligned}
H \quad &= A_1E_h + A_2I_h + B_1u_1^2 + B_2u_2^2 + B_3u_3^2 + \lambda_1\frac{dS_h}{dt} + \lambda_2\frac{dV_h}{dt} + \lambda_3\frac{dE_h}{dt} + \lambda_4\frac{dI_h}{dt} \\
&+ \lambda_5\frac{dR_h}{dt} + \lambda_6\frac{dS_v}{dt} + \lambda_7\frac{dE_v}{dt} + \lambda_8\frac{dI_v}{dt} + \lambda_9\frac{dS_p}{dt} + \lambda_{10}\frac{dE_p}{dt} + \lambda_{11}\frac{dI_p}{dt}.
\end{aligned} \tag{9}
$$

Let Γ be set of controls, and Π be the set of adjoint variables, we define in more compact form the Lagrangian (augmented Hamiltonian) for our optimal problem as:

$$
\mathscr{L}(K, \Gamma, \Pi) = H - \sum_{i=1}^{3} w_{ij}(u_i(t) - a_i) - \sum_{i=1}^{3} w_{ij}(b_i - u_i(t)) \text{ for } j = 1, 2. \tag{10}
$$

where $w_{ij}(t) \geq 0$ are the penalty multipliers satisfying the following conditions

$$
w_{11}(t)(u_1(t) - a_1) = w_{12}(t)(b_1 - u_1(t)) = 0 \quad \text{at optimal control} \quad u_1^*,
$$

$$
w_{21}(t)(u_2(t) - a_2) = w_{22}(t)(b_2 - u_2(t)) = 0 \quad \text{at optimal control} \quad u_2^*,
$$

$$
w_{31}(t)(u_3(t) - a_3) = w_{32}(t)(b_3 - u_3(t)) = 0 \quad \text{at optimal control} \quad u_3^*.
$$

The Lagrangian can be extended as;

$$
\begin{aligned}
\mathscr{L}(K,\Gamma,\Pi) &= A_1E_h + A_2I_h + B_1u_1^2 + B_2u_2^2 + B_3u_3^2 \\
&+ \lambda_1[b_hN_h + (1-\rho)\Lambda + \omega(V_h+R_h) - \frac{a\beta_1S_hI_v}{N_v}(1-u_1) - \varepsilon(1+u_2)S_h - \mu_hS_h] \\
&+ \lambda_2[\rho\Lambda + \varepsilon(1+u_2)S_h - \omega V_h - \mu_hV_h] \\
&+ \lambda_3[\frac{a\beta_1S_hI_v}{N_v}(1-u_1) - \delta_hE_h - \mu_hE_h] \\
&+ \lambda_4[\delta_hE_h - (\mu_h+\alpha)I_h - \gamma(1+u_2)I_h] \\
&+ \lambda_5[\gamma(1+u_2)I_h - \omega R_h - \mu_hR_h] \\
&+ \lambda_6[b_vN_v(1-u_3) - \frac{a\beta_2S_vI_h}{N_h}(1-u_1) - \frac{a\beta_3S_vI_p}{N_p} - \mu_vS_v(1+u_3)] \\
&+ \lambda_7[\frac{a\beta_2S_vI_h}{N_h}(1-u_1) + \frac{a\beta_3S_vI_p}{N_p} - \delta_vE_v - \mu_vE_v(1+u_3)] \\
&+ \lambda_8[\delta_vE_v - \mu_vI_v(1+u_3)] \\
&+ \lambda_9[b_pN_p - \frac{a\beta_4S_pI_v}{N_v} - \mu_pS_p] \\
&+ \lambda_{10}[\frac{a\beta_4S_pI_v}{N_v} - \delta_pE_p - \mu_pE_p)] \\
&+ \lambda_{11}[\delta_pE_p - \mu_pI_p] \\
&- w_{11}(t)(u_1(t)-a_1) - w_{12}(t)(b_1-u_1(t)) - w_{21}(t)(u_2(t)-a_2) \\
&- w_{22}(t)(b_2-u_2(t)) - w_{31}(t)(u_3(t)-a_3) - w_{32}(t)(b_3-u_3(t)).
\end{aligned}
$$

where $\lambda_1, \lambda_2, ...\lambda_{11} = \lambda_K$ (for $K = s_h, v_h, ..., i_p$) are the adjoint variables or co-state variables. We seek for the minimal value of Lagrangian.

Theorem 3.2.

Given u_i^*, $(i = 1,2,3)$ be the set of optimal control, and K^* be the corresponding set of solutions of the state system that minimizes J over Γ then there exists adjoint variables λ_K such that

(11) $$\frac{d\lambda_K}{dt} = -\frac{\partial L}{\partial K} \quad \text{(adjoint condition)} \qquad \textit{and}$$

(12) $$\lambda_K(t_f) = 0 \quad \text{(transversality/final time condition)} \qquad furthermore$$

(13) $$\frac{\partial L}{\partial u} = 0 \quad \text{at} \quad (u_1, u_2, u_3 = 0) \quad \text{(optimality condition)}$$

Proof.

We differentiate partially the Lagrangian (Hamiltonian augmented with penalty multiplier) with respect to states variables to obtain the adjoint system. Thus, we have;

$$
(14)\quad
\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{\partial L}{\partial S_h} = \lambda_1\left[\frac{a\beta_1 I_v}{N_v}(1-u_1)+\varepsilon(1+u_2)+\mu_h\right]-\lambda_2\varepsilon(1+u_2)-\lambda_3\frac{a\beta_1 I_v}{Nv}(1-u_1),\\
\frac{d\lambda_2}{dt} &= -\frac{\partial L}{\partial V_h} = \lambda_2(\omega+\mu_h)-\lambda_1\omega,\\
\frac{d\lambda_3}{dt} &= -\frac{\partial L}{\partial E_h} = -A_1+\lambda_3(\delta_h+\mu_h)-\lambda_4\delta_h,\\
\frac{d\lambda_4}{dt} &= -\frac{\partial L}{\partial I_h} = -A_2+(\lambda_6-\lambda_7)\frac{a\beta_2 S_v}{N_h}(1-u_1)-\lambda_5\gamma(1+u_2)+\lambda_4[\mu_h+\alpha+\gamma(1+u_2)]\\
\frac{d\lambda_5}{dt} &= -\frac{\partial L}{\partial R_h} = \lambda_5(\mu_h+\omega)-\lambda_1\omega,\\
\frac{d\lambda_6}{dt} &= -\frac{\partial L}{\partial S_v} = (\lambda_6-\lambda_7)\left[\frac{a\beta_2 I_h}{N_h}(1-u_1)+\frac{a\beta_3 I_p}{N_p}\right]+\lambda_6\mu_v(1+u_3),\\
\frac{d\lambda_7}{dt} &= -\frac{\partial L}{\partial E_v} = \lambda_7(\delta_v+\mu_v)-\lambda_8\delta_v,\\
\frac{d\lambda_8}{dt} &= -\frac{\partial L}{\partial I_v} = (\lambda_1-\lambda_3)\frac{a\beta_1 S_h}{N_v}(1-u_1)+\lambda_8\mu_v(1+u_3)+(\lambda_9-\lambda_{10})\frac{a\beta_4 S_p}{Nv},\\
\frac{d\lambda_9}{dt} &= -\frac{\partial L}{\partial S_p} = (\lambda_9-\lambda_{10})\frac{a\beta_4 I_v}{Nv}+\lambda_9\mu_p,\\
\frac{d\lambda_{10}}{dt} &= -\frac{\partial L}{\partial E_p} = \lambda_{10}(\delta_p+\mu_p)+\lambda_{11}\delta_p,\\
\frac{d\lambda_{11}}{dt} &= -\frac{\partial L}{\partial i_p} = (\lambda_6-\lambda_7)\frac{a\beta_3 S_v}{N_p}+\lambda_{11}\mu_p.
\end{aligned}
$$

Now, to obtain the optimal control solution $u_i,(i=1,2,3)$, of our Lagrangian we differentiate partially the Lagrangian L, with respect to u_1,u_2,u_3 and set it to zero as follows:

$$
(15)\quad
\begin{aligned}
\frac{\partial L}{\partial u_1} &= 2B_1u_1+(\lambda_1-\lambda_3)\frac{a\beta_1 S_h I_v}{N_v}+(\lambda_6-\lambda_7)\frac{a\beta_2 S_v I_h}{Nh}-w_{11}+w_{12}\\
\frac{\partial L}{\partial u_2} &= 2B_2u_2+(\lambda_2-\lambda_1)\varepsilon S_h+(\lambda_5-\lambda_4)\gamma I_h-w_{21}+w_{22}\\
\frac{\partial L}{\partial u_3} &= 2B_3u_3-\lambda_6[b_vN_v+\mu_vS_v]-\lambda_7\mu_vE_v-\lambda_8\mu_vI_v-w_{31}+w_{32}
\end{aligned}
$$

Setting $\dfrac{\partial L}{\partial u_i}=0$ for $i=1,2,3$ and solving for the optimal control u_i, we obtain

$$
(16)\quad
\begin{aligned}
u_1^*(t) &= \frac{1}{2B_1}\left[(\lambda_3-\lambda_1)\frac{a\beta_1 S_h I_v}{N_v}+(\lambda_7-\lambda_6)\frac{a\beta_2 S_v I_h}{N_h}+w_{11}-w_{12}\right]\\
u_2^*(t) &= \frac{1}{2B_2}\left[(\lambda_1-\lambda_2)\varepsilon S_h+(\lambda_4-\lambda_5)\gamma I_h+w_{21}-w_{22}\right]\\
u_3^*(t) &= \frac{1}{2B_3}\left[\lambda_6(b_vN_v+\mu_vS_v)+\lambda_7\mu_vE_v+\lambda_8\mu_vI_v+w_{31}-w_{32}\right]
\end{aligned}
$$

To determine explicit expression for an optimal control without $w_{11},w_{12},w_{21},$ w_{22},w_{31},w_{32} we use a standard optimality technique involving the bounds of control. The following are three cases to be considered in each part.

Solving for $u_1^*(t)$

- On the set $\{t|a_1 < u_1^* < b_1\}$, we have

$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \implies w_{11} = w_{12} = 0$$

Hence the optimal control is

$$u_1^*(t) = \frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h}\right]$$

- On the set $\{t|u_1^* = b_1\}$, we have

$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \implies w_{11} = 0$$

Hence the optimal control is

$$b_1 = u_1^*(t) = \frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h} - w_{12}\right]$$

since $w_{12}(t) > 0$, therefore

$$\frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h}\right] \geq b_1$$

- On the set $\{t|u_1^* = a_1\}$, we have

$$w_{11}(u_1^* - a_1) = w_{12}(b_1 - u_1^*) = 0 \implies w_{12} = 0$$

Thus, the optimal control is

$$a_1 = u_1^*(t) = \frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h} + w_{11}\right]$$

Again since $w_{11}(t) > 0$, it shows that

$$a_1 \geq \frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h}\right]$$

We now represent $u_1^*(t)$ in compact form as

(17) $$u_1^*(t) = \min\{b_1, \max\{a_1, \frac{1}{2B_1}\left[(\lambda_3 - \lambda_1)\frac{a\beta_1 S_h I_v}{N_v} + (\lambda_7 - \lambda_6)\frac{a\beta_2 S_v I_h}{N_h}\right]\}\}$$

Solving for $u_2^*(t)$

- On the set $\{t|a_2 < u_2^* < b_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \implies w_{21} = w_{22} = 0$$

  Hence the optimal control is

$$u_2^*(t) = \frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h]$$

- On the set $\{t|u_2^* = b_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \implies w_{21} = 0$$

  Hence the optimal control is

$$b_2 = u_2^*(t) = \frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h - w_{22}]$$

  Since $w_{22}(t) > 0$, therefore

$$\frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h] \geq b_2$$

- On the set $\{t|u_2^* = a_2\}$, we have

$$w_{21}(u_2^* - a_2) = w_{22}(b_2 - u_2^*) = 0 \implies w_{22} = 0$$

  Thus, the optimal control is

$$a_2 = u_2^*(t) = \frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h + w_{21}]$$

  Again since $w_{21}(t) > 0$, therefore

$$a_2 \geq \frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h]$$

In compact form, we represent $u_2(t)$ as:

$$u_2^*(t) = \min\{b_2, \max\{a_2, \frac{1}{2B_2}[(\lambda_1 - \lambda_2)\varepsilon S_h + (\lambda_4 - \lambda_5)\gamma I_h]\}\} \tag{18}$$

Solving for $u_3^*(t)$

- On the set $\{t|a_3 < u_3^* < b_3\}$, we have

$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \implies w_{31} = w_{32} = 0$$

Hence the optimal control is

$$u_3^*(t) = \frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v]$$

- On the set $\{t|u_3^* = b_3\}$, we have

$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \implies w_{31} = 0$$

Hence the optimal control is

$$b_3 = u_3^*(t) = \frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v - w_{32}]$$

Since $w_{32}(t) > 0$, it shows that

$$\frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v] \geq b_3$$

- On the set $\{t|u_3^* = a_3\}$, we have

$$w_{31}(u_3^* - a_3) = w_{32}(b_3 - u_3^*) = 0 \implies w_{32} = 0$$

thus, the optimal control is

$$a_3 = u_3^*(t) = \frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v + w_{31}]$$

Again since $w_{31}(t) > 0$, we have

$$a_3 \geq \frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v]$$

Also we represent $u_3^*(t)$ in compact form as:

(19) $$u_3^*(t) = \min\{b_3, \max\{a_3, \frac{1}{2B_3}[\lambda_6(b_v N_v + \mu_v S_v) + \lambda_7 \mu_v E_v + \lambda_8 \mu_v I_v]\}\}$$

Thus, the optimality system comprise of the state system with adjoint system, the transversality (final time) and initial conditions as well as optimality conditions.

4. Numerical Results and Discussions

In this section, we present numerically the results of an optimal control strategies for the YF model. In order to obtain the optimal control, we solve the optimality system, consisting of model equations, adjoint equations and control mechanism variables by using iterative scheme of fourth order Runge-Kutta technique.

By using the initial conditions $S_h(0) = 3500$, $V_h(0) = 2500$, $E_h(0) = 1500$, $I_h(0) = 1500$, $R_h(0) = 1000$, $S_v(0) = 2500$, $E_v(0) = 1500$, $I_v(0) = 1500$, $S_p(0) = 2500$, $E_p(0) = 1500$, $I_p(0) = 1500$; we begin to solve the state system (model equations) using forward time Runge-Kutta method.

The adjoint equations are solved by a backward in time fourth order Runge-Kutta scheme using the current iterations solutions of the state equation and terminal conditions $\lambda_K(t_f) = 0$ where $t_f = 365$ days. By referring to [14], the process is repeated and iterations stopped if the values of the unknowns at the previous iterations are very very close to the ones at the present iterations.

We start by initial guess values of the weights in the objective function as $A_1 = A_2 = 1000$; $B_1 = 0.0001$, $B_2 = 1000$ and $B_3 = 0.01$. Again, we consider the controls to be bounded in the interval of [0,1]. In simulation we use values of parameters described in Table 1 and various combinations of the three controls at a time to investigate and compare their numerical results. To illustrate the effect of different optimal control strategies on the spread of YF in a population, we have considered the spread of YF in an endemic population and the entire time period T = 365 days.

4.1 Using Personal Protection Only

Personal protection u_1 is used to optimize the objective function J while we set educational campaign, u_2, and spray of insecticides against vector, u_3, to zero. As it is seen in Fig. 2 (A and B), due to personal protection the number of exposed and infectious humans hosts decreases to zero at time $t = 139$ days, while population of exposed and infectious human hosts increases for uncontrolled case.

The control profile shows that from $t = 0$ to $t = 139$ days there was no change observed with respect to control strategy may be individuals were thinking on how they can start implementing

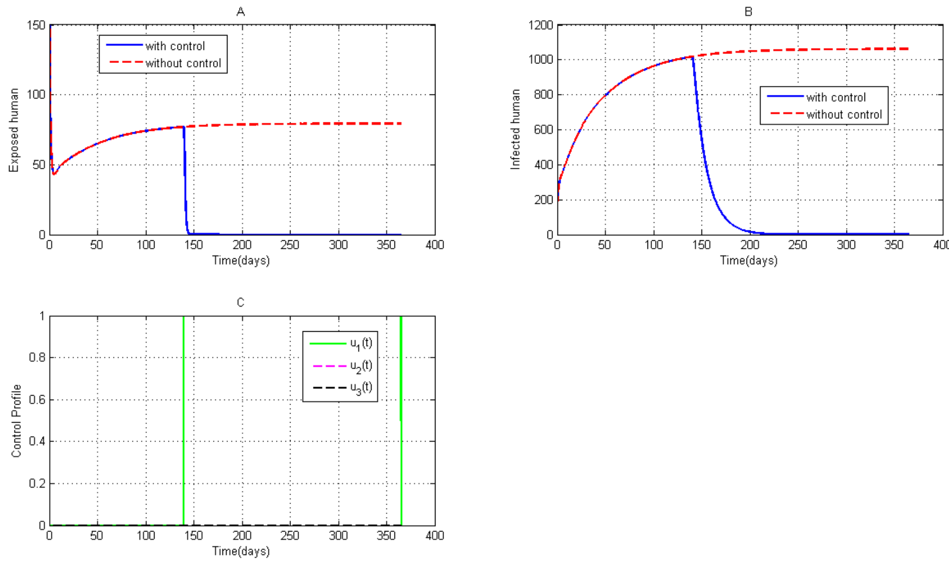

FIGURE 2. *Simulations of YF model showing the effect of personal protection on the spread of YF.*

the strategy, but after using preventive measures like indoor residual spraying, use of mosquito treated bed nets, mosquito coils and mosquito repellents; the exposed and infectious individuals reduces rapidly to zero.

This means that an effective use of personal protection can be beneficial to disease eradication even without the use of educational campaign and insecticides.

4.2 Using Educational Campaign Only

With this strategy, we optimize the objective function J using educational campaign, u_2, only while personal protection, u_1, and spray of insecticides, u_3, is set to zero. Fig. 3 (A and B) shows that there is a slight difference in the number of exposed and infectious human host with and without control although the exposed and infecteds are not reduced directly to zero. Thus, this strategy alone is not as good as the previous one, since we will have the exposed and infecteds in a years time.

4.3 Using Spray of Insecticides Only

The use of spray of insecticides against the vector, u_3, is used to optimize the objective function J while we set personal protection, u_1, and educational campaign, u_2, to zero, we

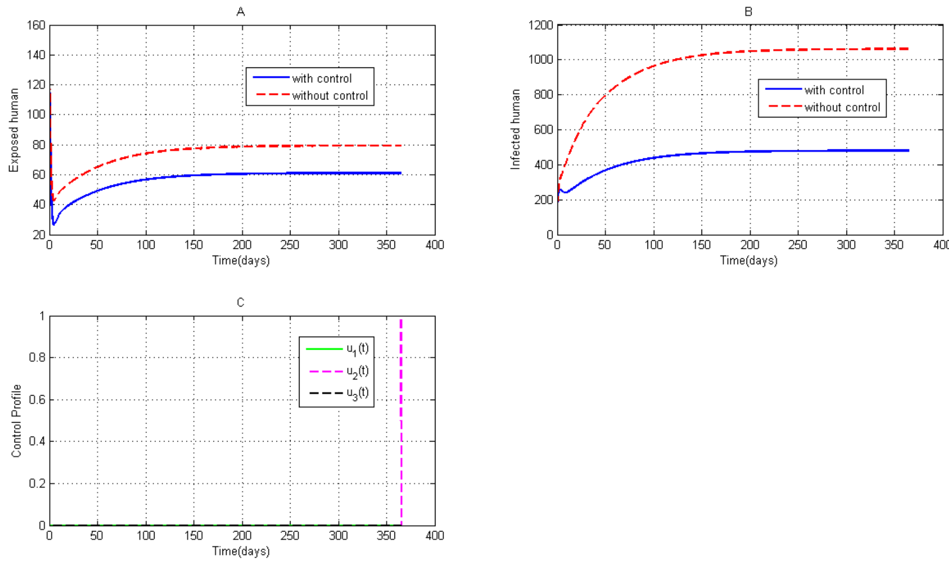

FIGURE 3. *Simulations of YF model showing the effect of educational campaign on the spread of YF.*

observe in Fig. 4 that there is no difference in the number of exposed and infectious individuals with and without control. This numerical results indicate that this strategy leaves more infecteds than it is in the first two strategies, hence, suggesting that optimal use of spray of insecticides alone is not effective for disease reduction as some of vectors will remain unaffected and cause the infection to both hosts.

4.4 Using Personal Protection and Educational Campaign

In this strategy, we use two controls personal protection, u_1, and educational campaign, u_2, to optimize the objective function J; while we set spray of insecticides, u_3, to zero. We observe in Fig. 5 (A and B) that due to combination of these two control strategies, there is a significant difference in the number of exposed and infecteds with and without control. However, the control u_1 is zero from $t = 0$ to $t = 149$ days, while the control u_2 is at its upper bound from $t = 0$ to $t = 190$ days before it drops to zero until its final time. The numerical results indicates that combination of these two strategies is good compared to using single strategy since the infecteds reduces to zero from time $t = 149$ to final time.

With this strategy, the control profiles suggests that control on personal protection, u_1, should be at its upper bound from $t = 149$ till the end of the intervention, while educational campaign,

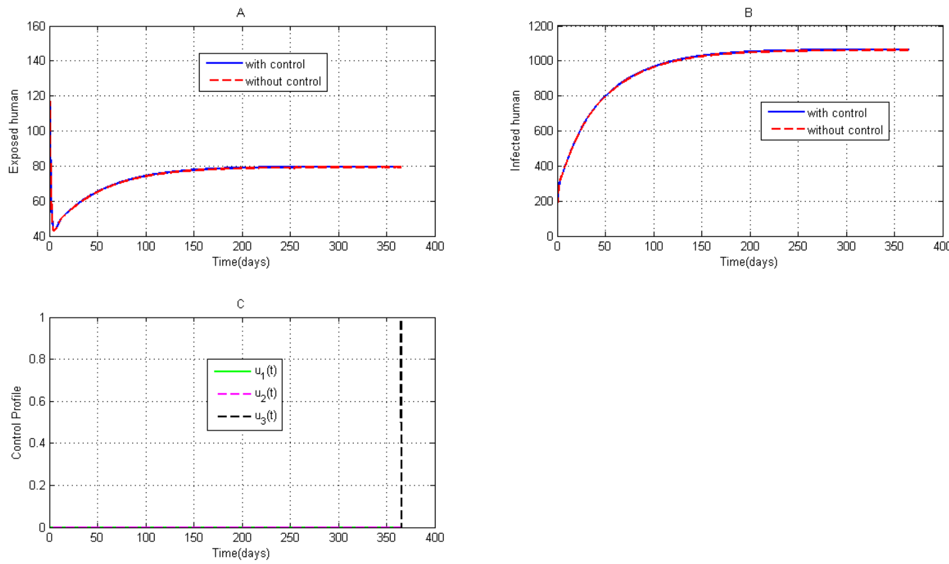

FIGURE 4. *Simulations of YF model showing the effect of spray of insecticides on the spread of YF.*

u_2, drops gradually from the upper bound to zero after $t = 190$ days. Hence, suggesting that optimal use of personal protection together with educational campaign is effective for reduction of disease transmission.

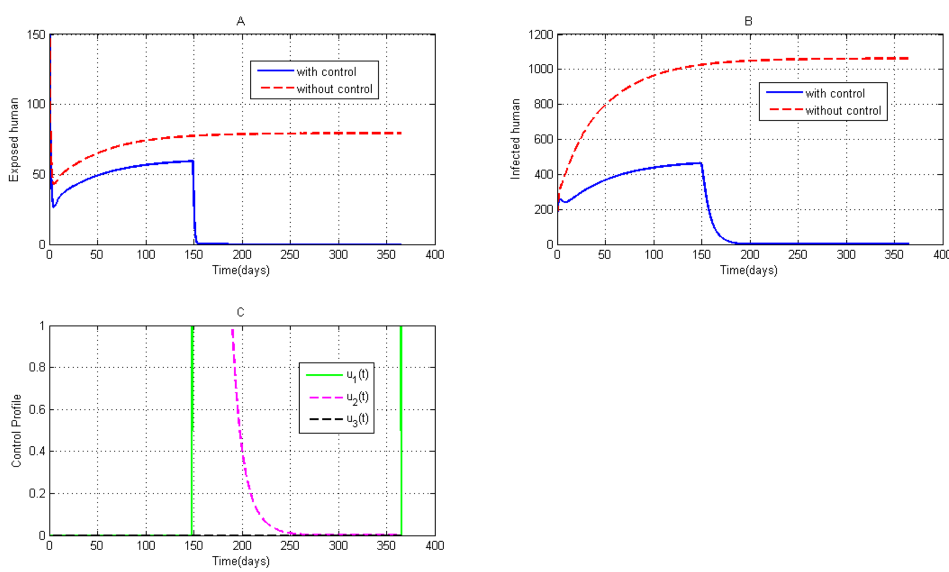

FIGURE 5. *The effect of personal protection and educational campaign on the spread of YF.*

4.5 Using Personal Protection and Spray of Insecticides

Combination of Personal protection, u_1, and spray of insecticides, u_3, is used to optimize the objective function J, while we set educational campaign, u_2 to zero. We observe in Fig. 6 (A and B) that no change has been effected from $t = 0$ to $t = 85$ days, meaning that the number of exposed and infected human were increasing to both cases with and without control. However, from $t = 88$ to $t = 312$ days the control u_3 is implemented with high cost which results to the decrease of the exposed and infecteds to zero, while the control u_1 is at its upper bound from $t = 88$ until the final time before it drops rapidly to zero. The numerical results indicates that combination of u_1 and u_3 is most effective compared to combination of u_1 and u_2.

This means that an effective and optimal use of personal protection and spray of insecticides against the vector may be beneficial even without the use of educational campaign, since the exposed and infecteds drops rapidly to zero earlier from $t = 88$ days till the final time.

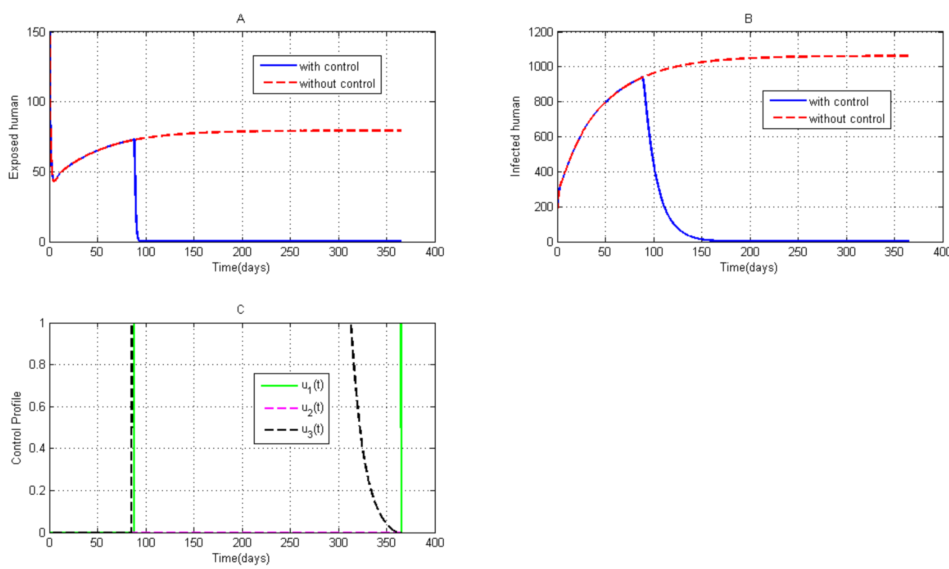

FIGURE 6. *The effect of personal protection and spray of insecticides on the spread of YF.*

4.6 Using Educational Campaign and Spray of Insecticides

With this strategy, the control educational campaign, u_2 to exposed and infectious human, and spray of insecticides on vector, u_3, are together used to optimise the objective function J; while personal protection, u_1, is set to zero. Fig. 7 (A and B) shows that the control u_3 is at its upper bound throughout the time before it rapidly fall down to zero at final time, while, the control u_2 is zero throughout the time. The numerical results indicates that using this strategy the infecteds and exposed individuals are not reduced directly to zero although there is a significant difference on using the control and without using the control. This result suggests that effective and optimal use of educational campaign and spray of insecticides could not be beneficial to disease transmission reduction without personal protection.

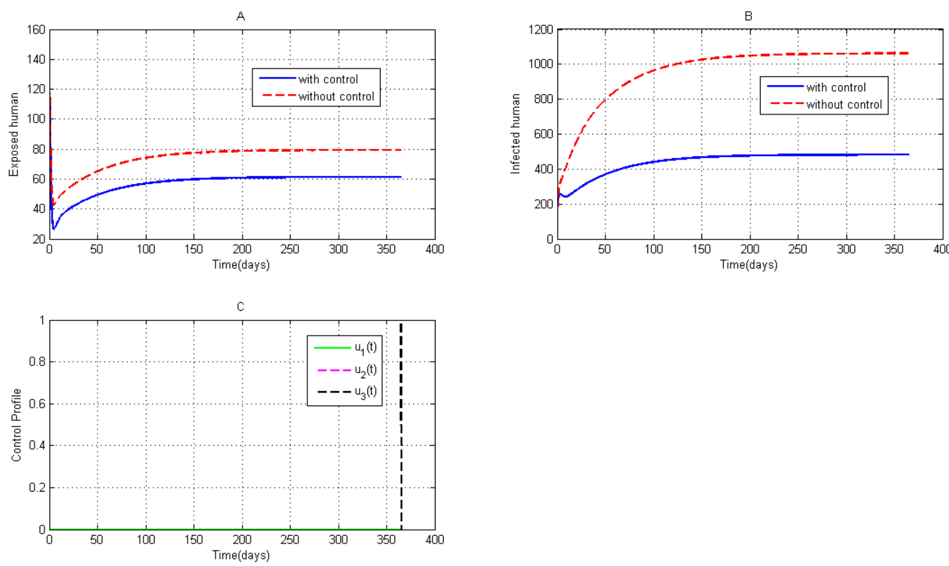

FIGURE 7. *The effect of educational campaign and spray of insecticides on the spread of YF.*

4.7 Personal Protection, Educational Campaign and Spray of Insecticides

Combination of all controls personal protection, u_1, educational campaign u_2 and spray of insecticides, u_3, is used to optimize the objective function J. We observe in Fig. 8 (A and B) that the control u_1 is at its upper bound from $t = 82$ days to final time before it fall rapidly to zero, the control u_2 is at its upper bound form $t = 0$ to $t = 124$ days before dropping gradually until the final time while the control u_3 is at its upper bound from $t = 80$ to $t = 298$ before dropping gradually to zero until the final time. Numerical results indicates that combination of all strategies u_1, u_2 and u_3 is most beneficial and effective compared to combination of two controls since the infected and exposed reduced to zero very early at $t = 80$ until the final time.

Also there is a strong significant difference on the number of infected and exposed with and without control.

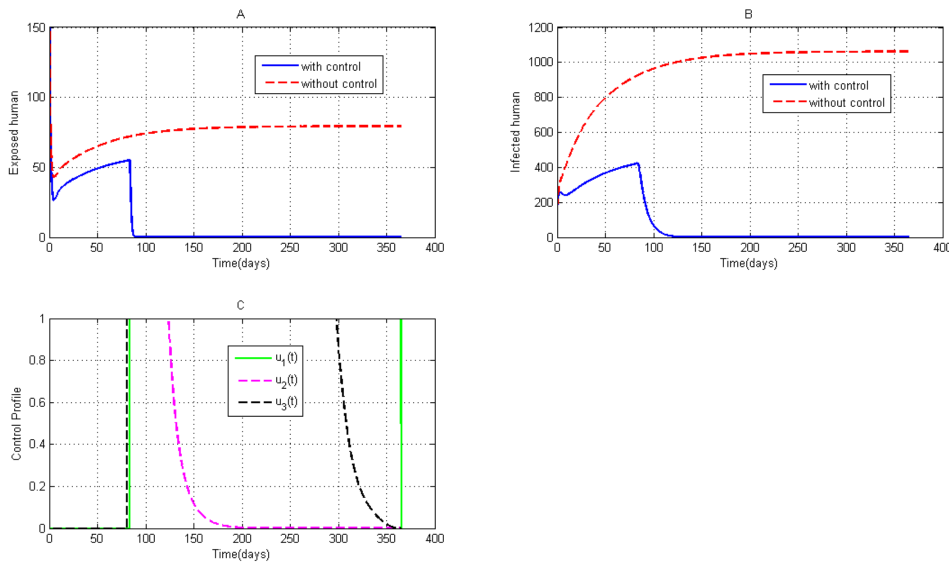

FIGURE 8. *The effect of all controls on the spread of YF.*

5. Conclusion

In this paper, we aimed at determining the control measures for eradicating the infection from the population. We derived and analyzed the necessary conditions for the optimal control model of YF disease in the presence of prevention or personal protection to human host which includes the use of mosquito treated bed-nets, use of mosquito coils, indoor residual spraying, use of mosquito repellents etc, educational campaign to susceptible and infectious human hosts and spray of insecticides against the vector.

We have identified optimal control strategies for several scenarios. The results show that using multiple optimal control measures is most effective strategy to bring a stable disease-free situation compared to a single control. However, spray of insecticides alone was seen as not effective without personal protection, and optimal use of personal protection alone might be beneficial to minimize transmission of the infection to the community.

Moreover, combination of three control measures was seen to be the most effective compared to combination of two control measures and single control. Thus control programs that follow three control strategies (personal protection, educational campaign and spray of insecticides) can effectively reduce the number of latent and infectious individuals and hence disease reduction.

Conflict of Interests

The authors declare that there is no conflict of interests.

Acknowledgments

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