Modelling the impact of interventions against malaria-schistosomiasis co-infection dynamics

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Abstract. Sub-Saharan Africa is known to possess the greater part of the global burden of malaria and schistosomiasis infection. The co-endemicity of these two tropical diseases has initiated the investigation into the mechanisms of their co-infection due to the competing immunological responses associated with each disease in the recent time. It is known that malaria and schistosomiasis have similar epidemiological dispersal and cause challenges to public health and socio-economic development throughout the sub-Saharan region. There are very few works done on the application of optimal control theory to the dynamics of malaria-schistosomiasis co-infection to the best of our knowledge. Our aim here is to predict the impact of the present control interventions to provide necessary information for the policy makers against future control strategies. In this regard, we proposed a malaria-schistosomiasis co-infection model using a system of compartmental deterministic non-linear ordinary differential equations. Optimal control theory was applied to examine the best control strategies against malaria-schistosomiasis disease using insecticides treated bed nets (u_1), prevention by avoiding swimming or wading in freshwater (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), treatment of malaria-schistosomiasis (u_5), biological control (u_6) and insecticide spray, destruction of stagnant water and mosquito breeding sites (u_7) as control interventions in line with World Health Organisation (WHO) suggestion. Scenarios on various control strategies were developed using combinations of the seven control interventions either one at a time, combinations of two at a time or more than two at a time to minimize the transmission of malaria-schistosomiasis disease. Finally, the proposed model predicted that there were reductions in the transmission dynamics of malaria-schistosomiasis co-

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infection in the presence of at least two or more control interventions even in areas where there are limited resources.

Keywords: basic reproduction number, malaria-schistosomiasis, co-infection dynamics, non-linear ordinary differential equation, optimal control.

1. Introduction

The process by which the body of a host is affected by multiple pathogen species or by more than one disease concurrently is called *Co-infection*. It is known that co-infection with multiple infectious agent strains can be seen to be present in various diseases [34]. Co-infection with multiple pathogen strains can be seen to be present in several other diseases [34] and co-infection with multiple disease-carrying pathogen strains may be seen to be profound.Some widely common distributed combinations are HIV and tuberculosis, HIV and hepatitis, HIV and malaria and others [34]. The need to study the co-infection between two different diseases is beneficial and of great importance in that co-infection may have adverse and destructive effects on the health of the co-infected persons and also posed some public health challenges in a population [34].

The marriage between malaria and schistosomiasis can be traced to the two diseases sharing the same epidemiological distribution and due to the countering effects the Schistosoma *mansoni* parasites have on the immunological cytokines which may altar the balance between *Th1* and *Th2* type immune responses which lowers immunological control of malaria [19, 20, 47, 49, 54]. Studies have shown that the interaction between malaria and schistosomiasis may reduce the effectiveness of malaria treatment for inhibiting malaria transmission [40]. It is not yet explicit the mechanisms responsible for the increase in the severity of malaria and its symptoms in individuals infected with schistosomiasis [40]. Hence, malaria-schistosomiasis co-infection still poses great challenge to public health and socio-economic advancement in the whole of the sub-Saharan African countries [40].

It is established that Malaria is widespread, severe, and highly endemic vector borne disease which is found in various part of sub-Saharan Africa. There are about 85% of global malaria cases and 90% of malaria deaths at present in the sub-Saharan African countries [40]. Malaria is caused by parasites that are transmitted to people through the bites of infected mosquitoes [8, 62]. At present, malaria can be prevented and cured if the infected person obtain early treatment [1]. There are several studies on the mathematical modelling of malaria that has been carried out and analysed to integrate other real life issues [11, 12, 30, 37, 41, 43, 65].

In various developing countries which includes Africa, the Middle East, Asia and South America schistosomiasis continues to be a public health challenge till date [16]. It is known by estimation that 200 million people are infected with the parasite already where 85% resides in underdeveloped countries in Africa [26]. Schistosomiasis can be transmitted when there is a human contact with con-

taminated fresh water occupied by snails carrying the parasite [16, 45]. This disease can cause liver damage and anaemia, particularly among children [16]. Schistosomiasis is established as the most deadly Neglected Tropical Disease (NTD) which kills an estimated 280,000 person in a year [63, 16]. There are several studies already carried out on the dynamics of schistosomiasis so far [3, 10, 14, 15, 16, 25, 31, 36, 42, 64]. Other useful modelling studies can be found in [5, 9, 13, 21, 24, 27, 29, 32, 38, 39, 48, 52, 55, 56, 58].

To the best of our knowledge, there are few studies carried out so far on the malaria-schistosomiasis co-infection dynamics. Recently, [40] proposed a co-epidemic model of malaria and schistosomiasis transmission dynamics. In their work, they reported major epidemiological coupling between malaria and schistosomiasis in terms of worse malaria incidence and amid persons with Schistosoma *mansoni* intense egg output [6, 7] formulated and analysed a mathematical model of the co-interaction between malaria and schistosomiasis. They carried out qualitative, bifurcation analysis and comprehensive mathematical study of the co-infected model. They further investigated the impact of schistosomiasis and its treatment on malaria. Their results suggested that an increase in the schistosomiasis infected population with treatments may result in a decrease in malaria cases. The aim of this work is to predict the impact of potential intervention packages in order to provide proper guidance to public health and policymakers.

This paper is organised as follows; we present a malaria-schistosomiasis co-infection transmission model and the description of its current malaria-schistosomiasis control interventions in Section 2. In Section 3, we introduce the optimal control problem of the malaria-schistosomiasis co-infection model, existence of optimal control is shown, and Pontryagin's Maximum Principle is applied to find the necessary conditions for the optimal control. In Sections 4, we show our numerical experiments and results while in Section 5, we discussed our conclusion and recommendations.

2. Mathematical model and the description of its current Malaria-Schistosomiasis control interventions

In line with the World Health Organisation (WHO) guidelines [63] for all people at risk or infected with Malaria/Schistosomiasis. The control interventions for the reduction and/or elimination of the two combined disease should be multiple intervention [63]. We introduced multiple control interventions into our malaria-schistosomiasis co-infection model which are insecticides treated bed nets (u_1), prevention by avoiding swimming or wading in freshwater (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), treatment of malaria-schistosomiasis (u_5), biological control (u_6) and insecticide spray, destruction of stagnant water and mosquito breeding sites (u_7). Hence, the malaria-schistosomiasis co-infection model [6, 7] and the state variables (Table 1) with parameters in Table 2 yields

a non-autonomous co-infection model (1) below:

$$\begin{aligned}
\frac{dS_h}{dt} &= b_H + \gamma R_m + kR_{hs} + \varphi R_{ms} - (1-u_1(t))\beta_1\epsilon_h\sigma S_h I_v \\
&\quad - (1-u_2(t))\beta_2 S_h I_s - d_h S_h, \\
\frac{dI_m}{dt} &= (1-u_1(t))\beta_1\epsilon_h\sigma S_h I_v - (1-u_2(t))\beta_2 I_{hs} I_m \\
&\quad - (u_3(t)\omega + \theta + d_h + \tau_h) I_m, \\
\frac{dI_{hs}}{dt} &= (1-u_2(t))\beta_2 S_h I_s - (1-u_1(t))\beta_1\epsilon_h\sigma I_v I_{hs} \\
&\quad - \big(u_4(t)q_h + \rho_h + d_h + \tau_h\big) I_{hs}, \\
\frac{dV_{ms}}{dt} &= (1-u_1(t))\beta_1\epsilon_h\sigma I_v I_{hs} + (1-u_2(t))\beta_2 I_{hs} I_m \\
&\quad - \big(u_5(t)\alpha + r + m + d_h + \tau_h\big) V_{ms}, \\
\frac{dR_m}{dt} &= u_3(t)\omega I_m - (\gamma + d_h) R_m + \phi(1-\alpha u_5(t)) V_{ms}, \\
\frac{dR_s}{dt} &= u_4(t) q_h I_{hs} - (k + d_h) R_s + (1-\phi)(1-\alpha u_6(t)) V_{ms}, \\
\frac{dR_{ms}}{dt} &= \alpha u_5(t) V_{ms} - (\varphi + d_h) R_{ms}, \\
\frac{dS_s}{dt} &= b_s - (1-u_2(t))\beta_3(I_{hs} + \eta_1 V_{ms}) S_s - d_s S_s - u_6(t) S_s, \\
\frac{dI_s}{dt} &= (1-u_2(t))\beta_3(I_{hs} + \eta_1 V_{ms}) S_s - (d_s + \rho_s) I_s - u_6(t) I_s, \\
\frac{dS_v}{dt} &= b_v - (1-u_1(t))\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms}) S_v - d_v S_v - u_7(t) S_v, \\
\frac{dI_v}{dt} &= (1-u_1(t))\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms}) S_v - d_v I_v - u_7(t) I_v
\end{aligned}$$

subject to the initial conditions (2)

$$\begin{aligned}
&S_h(0) = S_{h,0}, I_m(0) = I_{m,0}, I_{hs}(0) = I_{hs,0}, \\
&V_{ms}(0) = V_{ms}(t,0), R_m(0) = R_{m,0}, R_{hs}(0) = R_{hs,0}, R_{ms}(0) = R_{ms,0}, \\
&S_s(0) = S_{s,0}, I_s(0) = I_{s,0}, S_v(0) = S_{v,0}, I_v(0) = I_{v,0}.
\end{aligned}$$

We provide the associated model variables and parameters in Tables 1 and 2.

3. Optimal control model of the Malaria-Schistosomiasis co-infection

In this section, we develop an optimal control model with the given dynamics and control constraint. We present from the model (1), time dependent controls such as the $0 \leq u_1 \leq 1$, $0 \leq u_2 \leq 1$,$0 \leq u_3 \leq 1$, $0 \leq u_4 \leq 1$, $0 \leq u_5 \leq 1$, $0 \leq u_6 \leq 1$ and $0 \leq u_7 \leq 1$ to inhibit the spread of malaria-schistosomiasis co-infection. The

Table 1: Variables used in the model

Variables	Description
S_H	Susceptible Human
I_m	Individuals infected with malaria only
I_{hs}	Individuals infected with schistosomiasis only
V_{ms}	Individuals infected with both malaria and schistosomiasis
R_m	Individuals who recovered from malaria only
R_{hs}	Individuals who recovered from schistosomiasis only
R_{ms}	Individuals who recovered from both malaria and schistosomiasis
S_s	Susceptible Snail
I_s	Snails infected with schistosomiasis
S_v	Susceptible Mosquito
I_v	Infected Mosquito with malaria

control variable $0 \leq u_1 \leq 1$ is the prevention by the use of insecticide treated bed nets, $0 \leq u_2 \leq 1$ is the prevention by avoiding swimming or wading in fresh water when you are in countries with high transmission of schistosomiasis, by drinking safe water, heating with water, and by vigorous towel drying after an accidental, very brief water exposure, the control $0 \leq u_3 \leq 1$ is the treatment of malaria with drug, the control $0 \leq u_4 \leq 1$ is the treatment of schistosomiasis with drug called praziquantel, $0 \leq u_5 \leq 1$ is the control on the treatment of co-infected person, $0 \leq u_6 \leq 1$ is the use of biological control by introducing a competitor into the snail natural habitat which can control the expansion of the snails population and eventually eliminate the snails from the breeding site while $0 \leq u_7 \leq 1$ is the use of insecticide and destruction of stagnant water and breeding sites. These controls are Lebesgue integrable and bounded.

3.1 Formulation of the optimal control model of Malaria-Schistosomiasis co-infection

The aim here is to find some controls $0 \leq u_1^*(t) \leq 1$, $0 \leq u_2^*(t) \leq 1$,$0 \leq u_3^*(t) \leq 1$,$0 \leq u_4^*(t) \leq 1$,$0 \leq u_5^*(t) \leq 1$,$0 \leq u_6^*(t) \leq 1$,$0 \leq u_7^*(t) \leq 1$ with $t \in [0, T]$ which minimises the cost functional. This implies that we want

$$\begin{aligned} &C\big(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t), u_6^*(t), u_7^*(t)\big) \\ &\leq C\big(u_1(t), u_2(t), u_3(t), u_4(t), u_5(t), u_6(t), u_7(t)\big), \end{aligned}$$

for all controls $(u_1, u_2, u_3, u_4, u_5, u_6, u_7) \in U$. Such that controls $u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t), u_6^*(t), u_7^*(t)$ are called *optimal*. $C(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t), u_6^*(t), u_7^*(t), I_m, I_{hs}, I_s, I_{ms}, I_v) = \int_0^T (w_1 I_m + w_2 I_{hs} + w_3 I_{ms} + w_4 I_s + w_5 I_v + w_6 u_1^2 + w_7 u_2^2 + w_8 u_3^2 + w_9 u_4^2 + w_{10} u_5^2 + w_{11} u_6^2 + w_{12} u_7^2) dt$ where $C : R^{n+m+1} \to R$ subject to the model equations of malaria-schistosomiasis co-infection (1) subject to the initial conditions (2). $S_H : [0, \infty) \to \mathbb{R}^n$, $I_m : [0, \infty) \to \mathbb{R}^n$, $I_{hs} : [0, \infty) \to \mathbb{R}^n$, $V_{ms} : [0, \infty) \to \mathbb{R}^n$, $R_m : [0, \infty) \to \mathbb{R}^n$, $R_{hs} : [0, \infty) \to \mathbb{R}^n$, $R_{ms} : [0, \infty) \to \mathbb{R}^n$, $S_s : [0, \infty) \to \mathbb{R}^n$, $I_s : [0, \infty) \to \mathbb{R}^n$, $S_v : [0, \infty) \to \mathbb{R}^n$, $I_v : [0, \infty) \to \mathbb{R}^n$. The

Table 2: Table showing parameters used in the malaria-schistosomiasis co-infection model

Parameter	Symbol
disease induced death rate due to malaria only	θ
probability of human getting infected with malaria	β_1
rate of acquiring schistosomiasis through contact with an infected snails	β_2
rate of acquiring schistosomiasis through contacts with infected humans	β_3
probability of mosquito getting infected by an infectious human	β_4
Malaria–schistosomiasis immunity waning rate	φ
Schistosomiasis induced death rate	r
malaria disease induced death rate	m
Co-infected who recovered from malaria only	ϕ
disease induced death rate of human due to schistosomiasis only	ρ_H
disease induced death rate of snails due to schistosomiasis only	ρ_s
human spontaneous recovery	ω
rate of loss of immunity to the schistosomiasis disease only	k
rate of loss of immunity to malaria and schistosomiasis disease	φ
human spontaneous recovery from schistosomiasis only	q_H
Recovery rate of co-infected individual	α
modification parameter	η_1
modification parameter	η_2
per capita birth rate of mosquitoes	b_v
per capita birth rate of snails	b_s
Natural death rate of humans	d_H
per capita biting rate of mosquitoes	ε_v
contact rate of vector per human per unit time	σ
per capita biting rate of humans	ε_h
Natural death rate of mosquitoes	d_v
Natural death rate of mosquitoes	d_s
rate of loss of immunity to the malaria disease only	γ
per capita birth rate of humans	b_h

aim of this work is to minimise the total number of infected human with malaria only, infected human with schistosomiasis only, infected human with schistosomiasis and malaria, infected mosquito and infected snails while at the same time minimising the associated cost of the use of insecticide treated bednets (u_1), use of prevention by avoiding swimming or wading in freshwater when one is in countries with high transmission of schistosomiasis (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), the treatment of malaria-schistosomiasis (u_5), use of biological control (u_6), and the use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7), of the population given the initial population sizes of all eleven compartments S_H, I_m, I_{hs}, V_{ms}, R_m, R_{hs},

R_{ms}, S_s, I_s, S_v, I_v. The first term in the cost functional $w_1 I_m(t)$ represents the total number of individuals infected with malaria only, $w_2 I_{hs}(t)$ stands for the total number of individuals infected with schistosomiasis only, $w_3 V_{ms}$ represents the total number of individuals infected with both malaria and schistosomiasis. The terms $w_4 I_s$ corresponds to the total number infected snails and $w_5 I_v$ denotes the total number of infected mosquitoes. The term $w_6 u_1^2$ denotes the cost associated with the use of insecticide treated bednets, $w_7 u_2^2$ denotes the cost associated with the use of preventive measures, while the term $w_8 u_3^2$ corresponds to the cost associated with the use of ACT drug for treatment of malaria. The term $w_9 u_4^2$ represents the cost associated with the use of treatment of malaria-schistosomiasis use of praziquantel for the treatment of schistosomiasis, $w_{10} u_5^2$ is the cost associated with the use of treatment of malaria-schistosomiasis, the term $w_{11} u_6^2$ is the cost associated with the use of biological control while the term $w_{12} u_7^2$ is the cost associated with the use of insecticide spray and destruction of stagnant water and mosquito breeding sites. The quadratic costs follows the nonlinear pattern of the cost of the controls and that was why it has been applied in this work. [59, 60, 61, 28, 23]. Therefore, the combined control functions $u_1(t)$, $u_2(t)$, $u_3(t)$, $u_4(t)$, $u_5(t)$, $u_6(t)$, and $u_7(t)$ are assumed to remain in an admissible class of measurable functions. Hence, we seek the optimal control $u_1^*(t)$,$u_2^*(t)$, $u_3^*(t)$, $u_4^*(t)$, $u_5^*(t)$, $u_6^*(t)$, $u_7^*(t)$ such that

$$C\big(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t), u_6^*(t), u_7^*(t)\big)$$
$$= \min\{C(u_1(t), u_2(t), u_3(t), u_4(t), u_5(t)u_6(t), u_7(t)) : u_1, u_2, u_3, u_4, u_5, u_6, u_7 \in U\};$$

where U is the control set defined above.

3.2 Existence of an optimal control model of malaria-schistosomiasis co-infection control model

In this section, we intend to state and proof that an optimal control pair $(S_h^*, I_m^*, I_{hs}^*, V_{ms}^*, R_m^*, R_s^*, R_{ms}^*, S_s^*, I_s^*, S_v^*, I_v^*, u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^*)$ exist for the malaria-schistosomiasis co-infection control model (1) employing the result from Filippov-Cesari Existence Theorem (1983) ([36]).

Theorem 3.1. *The optimal control problem* $C(u_1, u_2, u_3, u_4, u_5, u_6, u_7) = \min_{\{u_1,u_2,u_3,u_4,u_5,u_6,u_7\}} \int_0^T (w_1 I_m + w_2 I_{hs} + w_3 I_{ms} + w_4 I_s + w_5 I_v + w_6 u_1^2 + w_7 u_2^2 + w_8 u_3^2 + w_9 u_4^2 + w_{10} u_5^2 + w_{11} u_6^2 + w_{12} u_7^2)\, dt$ *where* $u = \{u_1, u_2, u_3, u_4, u_5, u_6, u_7 :$ u_i *measurable* $0 \le u_1(t) \le 1, 0 \le u_2(t) \le 1 t \in [t_0, t_f] \in \mathbb{R}^+ \quad for \quad i = 1, 2...\}$ *subject to the dynamic constraints of system equations* (1) *with initial conditions* (2) *has a solution.*

Proof. Suppose $B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t)) = \{g(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_1, u_2, u_3, u_4, u_5, u_6, u_7) + \zeta, f(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_1, u_2, u_3, u_4, u_5, u_6, u_7) : \zeta \le 0, u_1, u_2, u_3, u_4, u_5, u_6, u_7 \in U\}$.

Consider $z_1, z_2 \in B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$. To show that $B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$ is convex for each $(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$.

It will be shown that the line connecting z_1 and z_2 remains completely in $B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$. Thus, it is required to show that $\lambda Z_1 + (1-\lambda)z_2 \in B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$, $\forall\ \lambda \in [0,1]$.

The fact that $z_i \in B(t, S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t))$ indicates that there exist $\zeta_1 \leq 0$, $\zeta_2 \leq 0$, and control vectors $u_1, u_2 \in U$ such that $z_i = \big\{g\big(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_i\big)+\zeta_i, f(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_i)\big\}$ for $i = 1, 2$. Then, it yields $\lambda(g(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_1) + \zeta_1) + (1-\lambda)(g(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_2) + \zeta_2)$.

$\lambda(w_1 I_m + w_2 I_{hs} + w_3 I_{ms} + w_4 I_s + w_5 I_v + w_6 u_1^2) + (1-\lambda)(w_1 I_m + w_2 I_{hs} + w_3 I_{ms} + w_4 I_s + w_5 I_v + w_6 u_2^2) + \lambda(\zeta_1 + (1-\lambda)\zeta_2$.

Suppose $u_3 = \sqrt{\lambda u_1^2 + (1-\lambda)u_2^2}$ it is observed that $u_3 \in U$. Likewise, suppose $\zeta_3 = \lambda(\zeta_1 + (1-\lambda)\zeta_2$ it is observed that $\zeta_3 \leq 0$. Therefore, the first component of the convex combination belongs to $B\big(t, S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t)\big)$. Next, the second component is verified,
$\lambda(f(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_1)$
$+(1-\lambda)f(S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), u_2) = \lambda(\beta_3(I_{hs} + \eta_1 V_{ms})S_s - (d_s + \rho_s)I_s - u_1(t)I_s) + (1-\lambda)(\beta_3(I_{hs} + \eta_1 V_{ms})S_s - (d_s+\rho_s)I_s - u_1(t)I_s) = \lambda\beta_3(I_{hs}+\eta_1 V_{ms})S_s - \lambda(d_s+\rho_s)I_s - \lambda u_1(t)I_s + (1-\lambda)\beta_3(I_{hs}+\eta_1 V_{ms})S_s - (1-\lambda)u_2(t)I_s - (1-\lambda)(d_s+\rho_s)I_s = \lambda\beta_3(I_{hs}+\eta_1 V_{ms})S_s - \lambda(d_s+\rho_s)I_s + (1-\lambda)\beta_3(I_{hs}+\eta_1 V_{ms})S_s - (1-\lambda)(d_s+\rho_s)I_s - (\lambda u_1(t) + (1-\lambda)u_2(t))I_s$.
Suppose $u_4 = \lambda u_1 + (1-\lambda)u_2$, it is observed that $u_4 \in U$.In conclusion, the convex combination $\lambda(\zeta_1 + (1-\lambda)\zeta_2$ is in $B(t, S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t))$. Clearly, U is compact. Next, boundedness of the solution of (17) is shown. Indeed $\frac{dN_h}{dt} = b_H - d_h N_h - \psi I_h$, which implies $\frac{b_h}{d_h+\psi} \leq \liminf_{t\to\infty} N_h(t) \leq \limsup_{t\to\infty} N_h(t) \leq \frac{b_h}{d_h}$ and $b_v - d_v N_v(t) \leq \frac{dN_v(t)}{dt} \leq b_v - d_v N_v(t)$ denotes $\frac{b_v}{d_v} \leq \liminf_{t\to\infty} N_v(t) \leq \limsup_{t\to\infty} N_v(t) \leq \frac{b_v}{(d_v)}$ and $b_s - d_s N_s(t) \leq \frac{dN_s(t)}{dt} \leq b_s - d_s N_s(t)$ denotes $\frac{b_s}{d_s} \leq \liminf_{t\to\infty} N_s(t) \leq \limsup_{t\to\infty} N_s(t) \leq \frac{b_s}{(d_s)}$ Thus, $\sup N_h(t) \leq \frac{b_H}{d_h}$, $\sup N_v(t) \leq \frac{b_v}{d_v}$ and $\sup N_s(t) \leq \frac{b_s}{d_s}$. This complete the proof. □

3.3 Solution to the optimal control problem

To solve the optimal control problem, the Hamiltonian function is formulated for the optimal control problem, which is given by: $H(S_h(t), I_{hs}(t), I_m(t), V_{ms}(t), R_m(t), R_{hs}(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), \lambda_{S_h}(t), \lambda_{I_m}(t), \lambda_{I_{hs}}(t), \lambda_{V_{ms}}(t), \lambda_{R_m}(t), \lambda_{R_{hs}}(t), \lambda_{R_{ms}}(t), \lambda_{S_s}(t), \lambda_{I_s}(t), \lambda_{S_v}(t), \lambda_{I_v}(t), t) = w_1 I_m(t) + w_2 I_{hs}(t) +$

$w_3I_v(t)+w_4I_s(t)+w_5V_{ms}(t)+w_6u_1^2(t)+w_7u_2^2(t)+w_8u_3^2(t)+w_9u_4^2(t)+w_{10}u_5^2(t)+w_{11}u_6^2(t)+w_{12}u_7^2(t)+\lambda_{S_h}(t)\frac{dS_h}{dt}+\lambda_{I_m}(t)\frac{dI_m}{dt}+\lambda_{I_{hs}}(t)\frac{dI_{hs}}{dt}+\lambda_{V_{ms}}(t)\frac{dV_{ms}}{dt}+\lambda_{R_m}(t)\frac{dR_m}{dt}+\lambda_{R_s}(t)\frac{dR_s}{dt}+\lambda_{R_{ms}}(t)\frac{dR_{ms}}{dt}+\lambda_{S_s}(t)\frac{dS_s}{dt}+\lambda_{I_s}(t)\frac{dI_s}{dt}+\lambda_{S_v}(t)\frac{dS_v}{dt}+\lambda_{I_v}(t)\frac{dI_v}{dt} = w_1I_m(t)+w_2I_{hs}(t)+w_3I_v(t)+w_4I_s(t)+w_5V_{ms}(t)+w_6u_1^2(t)+w_7u_2^2(t)+w_8u_3^2(t)+w_9u_4^2(t)+w_{10}u_5^2(t)+w_{11}u_6^2(t)+w_{12}u_7^2(t)+\lambda_{S_h}(t)[b_H+\gamma R_m+kR_{hs}+\varphi R_{ms}-(1-u_1)\beta_1\epsilon_h\sigma S_hI_v-(1-u_2)\beta_2S_hI_s-d_hS_h]+\lambda_{I_m}(t)[(1-u_1)\beta_1\epsilon_h\sigma S_hI_v-(1-u_2)\beta_2I_sI_m-(u_3\omega+\theta+d_h+\tau_h)I_m]+\lambda_{I_{hs}}(t)[(1-u_2)\beta_2S_hI_s-(1-u_1)\beta_1\epsilon_h\sigma I_vI_{hs}-(u_4q_h+\rho_h+d_h+\tau_h)I_{hs}]+\lambda_{V_{ms}}(t)[(1-u_1)\beta_1\epsilon_h\sigma I_vI_{hs}+(1-u_2)\beta_2I_{hs}I_m-(u_5\alpha+r+m+d_H+\tau_h)V_{ms}]+\lambda_{R_m}(t)[u_3\omega I_m-(\gamma+d_h)R_m+\phi(1-\alpha u_5)V_{ms}]+\lambda_{R_s}(t)[u_4q_hI_{hs}-(k+d_h)R_s+(1-\phi)(1-\alpha u_6)V_{ms}]+\lambda_{R_{ms}}(t)[\alpha u_5V_{ms}-(\varphi+d_h)R_{ms}]+\lambda_{S_s}(t)[b_s-\beta_3(I_{hs}+\eta_1V_{ms})S_s-d_sS_s]+\lambda_{I_s}(t)[\beta_3(I_{hs}+\eta_1V_{ms})S_s-(d_s+\rho_s)I_s]+\lambda_{S_v}(t)[b_v-(1-u_1)\beta_4\epsilon_v\sigma(I_m+\eta_2V_{ms})S_v-d_vS_v-u_7S_v]+\lambda_{I_v}(t)[(1-u_1)\beta_4\epsilon_v\sigma(I_m+\eta_2V_{ms})S_v-d_vI_v-u_7I_v]$, where $\lambda_{S_h}(t)$,$\lambda_{I_m}(t)$, $\lambda_{I_{hs}}(t)$, $\lambda_{V_{ms}}(t)$, $\lambda_{R_m}(t)$, $\lambda_{R_{hs}}(t)$, $\lambda_{R_{ms}}(t)$, $\lambda_{S_s}(t)$, $\lambda_{I_s}(t)$, $\lambda_{S_v}(t)$, $\lambda_{I_v}(t)$ indicates the adjoint function to be determined.

The first and second order necessary condition with respect to the control are optimal conditions for u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^* if

$$H(S_H(t),I_{hs}(t),I_m(t),V_{ms}(t),R_m(t),R_{hs}(t),R_{ms}(t),S_s(t),I_s(t),S_v(t),I_v(t),\lambda_{S_h}(t),\lambda_{I_m}(t),\lambda_{I_{hs}}(t),\lambda_{V_{ms}}(t),\lambda_{R_m}(t),\lambda_{R_{hs}}(t),\lambda_{R_{ms}}(t),\lambda_{S_s}(t),\lambda_{I_s}(t),\lambda_{S_v}(t),\lambda_{I_v}(t),t)=H.$$

In order to shorten the notation let us denote $S_h(t), I_{hs}(t), ..., \lambda_{S_h}(t), ..., t$ by " $\odot$ ".

$$\nabla_{u_1}H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*}=\frac{\partial H}{\partial u_1}|_{u_1=u_1^*},$$

$2w_6u_1^*+\beta_1\epsilon_h\sigma S_hI_v\lambda_{S_h}(t)-\beta_1\epsilon_h\sigma S_hI_v\lambda_{I_m}(t)+\beta_1\epsilon_h\sigma I_vI_{hs}\lambda_{I_{hs}}(t)-\beta_1\epsilon_h\sigma I_vI_{hs}\lambda_{V_{ms}}(t)+\beta_4\epsilon_v\sigma(I_m+V_{ms})S_v\lambda_{S_v}(t)-\beta_4\epsilon_v\sigma(I_m+V_{ms})S_v\lambda_{I_v}(t)=0$

$$u_1^*=\frac{\begin{array}{l}\beta_1\epsilon_h\sigma S_hI_v(\lambda_{I_m}(t)-\lambda_{S_h}(t))\\ +\beta_1\epsilon_h\sigma I_vI_{hs}(\lambda_{V_{ms}}(t)-\lambda_{I_{hs}}(t))+\beta_4\epsilon_v\sigma(I_m+V_{ms})S_v(\lambda_{I_v}(t)-\lambda_{S_v}(t))\end{array}}{2w_6},$$

$$\nabla_{u_2}H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*}=\frac{\partial H}{\partial u_2}|_{u_2=u_2^*}$$

$2w_7u_2^*+\beta_2S_hI_s\lambda_{S_h}(t)+\beta_2I_{hs}I_m\lambda_{I_m}(t)-\beta_2S_hI_s\lambda_{I_{hs}}(t)-\beta_2I_{hs}I_m\lambda_{V_{ms}}(t)+\beta_3(I_{hs}+\eta_1V_{ms})S_s\lambda_{S_s}(t)-\beta_3(I_{hs}+\eta_1V_{ms})S_s\lambda_{S_v}(t)=0,$

$$u_2^*=\frac{\begin{array}{l}\beta_2S_hI_s(\lambda_{I_{hs}}(t)-\lambda_{S_h}(t))\\ +\beta_2I_{hs}I_m(\lambda_{V_{ms}}(t)-\lambda_{I_m}(t))+\beta_3(I_{hs}+\eta_1V_{ms})S_s(\lambda_{S_v}(t)-\lambda_{S_s}(t))\end{array}}{2w_7}.$$

$$\nabla_{u_3}H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*}=\frac{\partial H}{\partial u_3}|_{u_3=u_3^*},$$

$2w_3u_3^* - w\lambda_{I_m}(t) = 0,\ u_3^* = \frac{\lambda_{I_m}(t)wI_m}{2w_3}.$

$$\nabla_{u_4} H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*} = \frac{\partial H}{\partial u_4}|_{u_4=u_4^*}$$

$2w_9u_4^* - q_hI_{hs}\lambda_{I_{hs}}(t) = 0,\ u_4^* = \frac{{}_hI_{hs}\lambda_{I_{hs}}(t)}{2w_9}.$

$$\nabla_{u_5} H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*} = \frac{\partial H}{\partial u_5}|_{u_5=u_5^*}$$

$2w_{10}u_5^* - \alpha V_{ms}\lambda_{V_{ms}}(t) - \phi\alpha V_{ms}\lambda_{R_m}(t) - \alpha V_{ms}\lambda_{R_{hs}}(t) + \phi\alpha V_{ms}\lambda_{R_{hs}}(t)$
$+\alpha V_{ms}\lambda_{R_{ms}}(t) = 0;$
$u_5^* = \frac{\alpha V_{ms}\lambda_{V_{ms}}(t) - \phi\alpha V_{ms}\lambda_{R_m}(t) - \alpha V_{ms}\lambda_{R_{hs}}(t) + \phi\alpha V_{ms}\lambda_{R_{hs}}(t) + \alpha V_{ms}\lambda_{R_{ms}}(t)}{2w_{10}}.$

$$\nabla_{u_6} H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*} = \frac{\partial H}{\partial u_6}|_{u_6=u_6^*}$$

$2w_{11}u_6^* - \lambda_{S_s}(t)S_s - \lambda_{I_s}(t)I_s = 0,\ u_6^* = \frac{\lambda_{S_s}(t)S_s - \lambda_{I_s}(t)I_s}{2w_{11}}$

$$\nabla_{u_7} H(\odot)|_{u_1=u_1^*,u_1=u_1^*,u_2=u_2^*,u_3=u_3^*,u_4=u_4^*,u_5=u_5^*,u_6=u_6^*,u_7=u_7^*} = \frac{\partial H}{\partial u_7}|_{u_7=u_7^*}$$

$2w_{12}u_7^* - \lambda_{S_v}(t)S_v - \lambda_{I_v}(t)I_v = 0,\ u_7^* = \frac{\lambda_{S_v}(t)S_v - \lambda_{I_v}(t)I_v}{2w_{12}}.$
$\nabla_{u_1} H|_{u_1} = u_1^* = \frac{\partial^2 H}{\partial u_1^2} = 2w_6 > 0$
$\nabla_{u_2} H|_{u_2} = u_2^* = \frac{\partial^2 H}{\partial u_2^2} = 2w_7 > 0$
$\nabla_{u_3} H|_{u_3} = u_3^* = \frac{\partial^2 H}{\partial u_3^2} = 2w_8 > 0$
$\nabla_{u_4} H|_{u_4} = u_4^* = \frac{\partial^2 H}{\partial u_4^2} = 2w_9 > 0$
$\nabla_{u_5} H|_{u_5} = u_5^* = \frac{\partial^2 H}{\partial u_5^2} = 2w_{10} > 0$
$\nabla_{u_6} H|_{u_6} = u_6^* = \frac{\partial^2 H}{\partial u_6^2} = 2w_{11} > 0$
$\nabla_{u_7} H|_{u_7} = u_7^* = \frac{\partial^2 H}{\partial u_7^2} = 2w_{12} > 0.$

(i) If $\frac{\partial H}{\partial u_1} < 0$ i.e. $u_1^* = 0$, if
$$\frac{\beta_1\epsilon_h\sigma S_hI_v(\lambda_{I_m}(t) - \lambda_{S_h}(t)) + \beta_1\epsilon_h\sigma I_vI_{hs}(\lambda_{V_{ms}}(t) - \lambda_{I_{hs}}(t)) + \beta_4\epsilon_v\sigma(I_m + V_{ms})S_v(\lambda_{I_v}(t) - \lambda_{S_v}(t))}{2w_6} \le 0 \le u_1^* \le 1 \text{ if}$$
$\frac{\partial H}{\partial u_1} = 0$ i.e. $0 \le u_1 \le 1$ if
$$0 < \frac{\beta_1\epsilon_h\sigma S_hI_v(\lambda_{I_m}(t) - \lambda_{S_h}(t)) + \beta_1\epsilon_h\sigma I_vI_{hs}(\lambda_{V_{ms}}(t) - \lambda_{I_{hs}}(t)) + \beta_4\epsilon_v\sigma(I_m + V_{ms})S_v(\lambda_{I_v}(t) - \lambda_{S_v}(t))}{2w_6} \le 1$$
$u_1^*(t) = 1$, if $\frac{\partial H}{\partial u_1} > 0$ i.e. $u_1^* \ge 1$, if
$$\frac{\beta_1\epsilon_h\sigma S_hI_v(\lambda_{I_m}(t) - \lambda_{S_h}(t)) + \beta_1\epsilon_h\sigma I_vI_{hs}(\lambda_{V_{ms}}(t) - \lambda_{I_{hs}}(t)) + \beta_4\epsilon_v\sigma(I_m + V_{ms})S_v(\lambda_{I_v}(t) - \lambda_{S_v}(t))}{2w_6} > 0.$$

(ii) If $\frac{\partial H}{\partial u_2} < 0$ i.e. $u_2^* = 0$, if
$$\frac{\beta_2S_hI_s(\lambda_{I_{hs}}(t) - \lambda_{S_h}(t)) + \beta_2I_{hs}I_m(\lambda_{V_{ms}}(t) - \lambda_{I_m}(t)) + \beta_3(I_{hs} + \eta_1V_{ms})S_s(\lambda_{S_v}(t) - \lambda_{S_s}(t))}{2w_7} \le 0$$

$0 \leq u_2^* \leq 1$ if $\frac{\partial H}{\partial u_2} = 0$ i.e. $0 \leq u_2 \leq 1$ if
$0 < \frac{\beta_2 S_h I_s(\lambda_{I_{hs}}(t) - \lambda_{S_h}(t)) + \beta_2 I_{hs} I_m(\lambda_{V_{ms}}(t) - \lambda_{I_m}(t)) + \beta_3(I_{hs} + \eta_1 V_{ms}) S_s(\lambda_{S_v}(t) - \lambda_{S_s}(t))}{2w_7} \leq 1$
$u_2^*(t) = 1$, if $\frac{\partial H}{\partial u_2} > 0$ i.e. $u_2^* \geq 1$, if
$\frac{\beta_2 S_h I_s(\lambda_{I_{hs}}(t) - \lambda_{S_h}(t)) + \beta_2 I_{hs} I_m(\lambda_{V_{ms}}(t) - \lambda_{I_m}(t)) + \beta_3(I_{hs} + \eta_1 V_{ms}) S_s(\lambda_{S_v}(t) - \lambda_{S_s}(t))}{2w_7} > 0.$

(iii) If $\frac{\partial H}{\partial u_3} < 0$ i.e. $u_3^* = 0$, if $\frac{\lambda_{I_m}(t) w I_m}{2w_3} \leq 0$, $0 \leq u_3^* \leq 1$ if $\frac{\partial H}{\partial u_3} = 0$ i.e. $0 \leq u_3 \leq 1$ if
$0 < \frac{\lambda_{I_m}(t) w I_m}{2w_3} \leq 1$, $u_3^*(t) = 1$, if $\frac{\partial H}{\partial u_3} > 0$ i.e. $u_3^* \geq 1$, if $\frac{\lambda_{I_m}(t) w I_m}{2w_3} > 0$.

(iv) If $\frac{\partial H}{\partial u_4} < 0$ i.e. $u_4^* = 0$, if $\frac{q_h I_{hs} \lambda_{I_{hs}}(t)}{2w_9} \leq 0$, $0 \leq u_4^* \leq 1$ if $\frac{\partial H}{\partial u_4} = 0$ i.e. $0 \leq u_4 \leq 1$ if $0 < \frac{{}_h I_{hs} \lambda_{I_{hs}}(t)}{2w_9} \leq 1$, $u_4^*(t) = 1$, if $\frac{\partial H}{\partial u_4} > 0$ i.e. $u_4^* \geq 1$, if $\frac{q_h I_{hs} \lambda_{I_{hs}}(t)}{2w_9} > 0$.

(v) If $\frac{\partial H}{\partial u_5} < 0$ i.e. $u_5^* = 0$, if
$\frac{\alpha V_{ms} \lambda_{V_{ms}}(t) - \phi\alpha V_{ms} \lambda_{R_m}(t) - \alpha V_{ms} \lambda_{R_{hs}}(t) + \phi\alpha V_{ms} \lambda_{R_{hs}}(t) + \alpha V_{ms} \lambda_{R_{ms}}(t)}{2w_{10}} \leq 0$
$0 \leq u_5^* \leq 1$ if $\frac{\partial H}{\partial u_5} = 0$ i.e. $0 \leq u_5 \leq 1$ if
$0 < \frac{\alpha V_{ms} \lambda_{V_{ms}}(t) - \phi\alpha V_{ms} \lambda_{R_m}(t) - \alpha V_{ms} \lambda_{R_{hs}}(t) + \phi\alpha V_{ms} \lambda_{R_{hs}}(t) + \alpha V_{ms} \lambda_{R_{ms}}(t)}{2w_{10}} \geq 1$, if
$\frac{\alpha V_{ms} \lambda_{V_{ms}}(t) - \phi\alpha V_{ms} \lambda_{R_m}(t) - \alpha V_{ms} \lambda_{R_{hs}}(t) + \phi\alpha V_{ms} \lambda_{R_{hs}}(t) + \alpha V_{ms} \lambda_{R_{ms}}(t)}{2w_{10}} > 0.$

(vi) If $\frac{\partial H}{\partial u_6} < 0$ i.e. $u_6^* = 0$, if $\frac{\lambda_{S_s}(t) S_s - \lambda_{I_s}(t) I_s}{2w_{11}} \leq 0$ $0 \leq u_6^* \leq 1$ if $\frac{\partial H}{\partial u_6} = 0$, i.e. $0 \leq u_6 \leq 1$ if $0 < \frac{\lambda_{S_s}(t) S_s - \lambda_{I_s}(t) I_s}{2w_{11}} \geq 1$, if $\frac{\lambda_{S_s}(t) S_s - \lambda_{I_s}(t) I_s}{2w_{11}} > 0$.

(vii) If $\frac{\partial H}{\partial u_7} < 0$ i.e. $u_7^* = 0$, if $\frac{\lambda_{S_v}(t) S_v - \lambda_{I_v}(t) I_v}{2w_{12}} \leq 0$, $0 \leq u_7^* \leq 1$ if $\frac{\partial H}{\partial u_7} = 0$ i.e. $0 \leq u_7 \leq 1$ if $0 < \frac{\lambda_{S_v}(t) S_v - \lambda_{I_v}(t) I_v}{2w_{12}} \geq 1$, if $\frac{\lambda_{S_v}(t) S_v - \lambda_{I_v}(t) I_v}{2w_{12}} > 0$.

The costate system and transversality conditions (3) are

$$
\begin{aligned}
\lambda'_{S_H} &= (\lambda_{S_H} - \lambda_{I_m})(1-u_1)\beta_1\epsilon_h\sigma I_v + \lambda_{S_H}((1-u_2)\beta_2 I_s + d_h) \\
&\quad - \lambda_{I_{hs}}((1-u_2))\beta_2 I_s \\
\lambda'_{I_m} &= -w_1 + \lambda_{I_m}((1 - u_2\beta_2 I_s + 2u_3\omega + \theta + d_h + \tau_h)) \\
&\quad - \lambda_{V_{ms}}(1-u_2)\beta_2 I_s - \lambda_{R_m} u_3\omega + (\lambda_{S_v} - \lambda_{I_v})(1-u_1)\beta_4\epsilon_v\sigma S_v \\
\lambda'_{I_{hs}} &= -w_2 + (\lambda_{I_{hs}} - \lambda_{V_{ms}})(1-u_1)\beta_1\epsilon_h\sigma I_v + \lambda_{I_{hs}}(u_4 q_h + d_h + \rho_h + \tau_h) - \\
&\quad \lambda_{V_{ms}}(1-u_1)\beta_1\epsilon_h\sigma I_v - \lambda_{R_{hs}} u_4 q_h + \lambda_{S_s}(1-u_2)\beta_3 S_s - \lambda_{I_v}(1-u_2)\beta_3 S_s \\
\lambda'_{V_{ms}} &= -w_5 + \lambda_{V_{ms}}(\alpha u_5 + r + m + d_h + \tau_h) + \lambda_{R_m}\phi(\alpha u_5 - 1) \\
&\quad - \lambda_{R_{hs}}(1-\phi)(1-\alpha u_5) - \lambda_{R_{ms}}\alpha u_5 + \lambda_{S_s}(1-u_2)\beta_3\eta_1 S_s \\
&\quad - \lambda_{I_s}(1-u_2)\beta_3\eta_1 S_s + (\lambda_{S_v} - \lambda_{I_v})(1-u_1)\beta_4\epsilon_v\sigma\eta_2 S_v \\
\lambda'_{R_m} &= -\lambda_{S_H}\gamma + \lambda_{R_m}(\gamma + d_h) \\
\lambda'_{R_{hs}} &= -\lambda_{S_H} k + \lambda_{R_{hs}}(k + d_h) \\
\lambda'_{R_{ms}} &= -\lambda_{S_H}\varphi + \lambda_{R_{ms}}(\varphi + d_h)
\end{aligned}
$$

$$\begin{aligned}
\lambda'_{S_s} &= (\lambda_{S_s} - \lambda_{I_s})(1-u_2)\beta_3(V_{ms}\eta_1 + I_{hs}) - (d_s + u_6)\lambda_{S_s} \\
\lambda'_{I_s} &= -w_4 + (\lambda_{I_m} - \lambda_{V_{ms}})(1-u_2)\beta_2 * I_m \\
&\quad + (\lambda_{S_H} - \lambda_{I_{hs}})(1-u_2)\beta_2 S_H + \lambda_{I_s}(d_s + \rho_s + u_6) \\
\lambda'_{S_v} &= (\lambda_{S_v} - \lambda_{I_v})(1-u_1)\beta_4\epsilon_v\sigma(V_{ms}\eta_2 + I_m) + \lambda_{S_v}(d_v + u_7) \\
\lambda'_{I_v} &= -w_3 + (\lambda_{S_H} - \lambda_{I_m})(1-u_1)\beta_1\epsilon_h\sigma S_H + (\lambda_{I_{hs}} - \lambda_{V_{ms}})(1-u_1)\beta_1\epsilon_h\sigma I_{hs} \\
&\quad + \lambda_{I_v}(d_v + u_7)
\end{aligned}$$

with transversality condition $\lambda_{S_H}(T) = \lambda_{I_m}(T) = \lambda_{I_{hs}}(T) = \lambda_{V_{ms}}(T) = \lambda_{R_m}(T) = \lambda_{R_s}(T) = \lambda_{R_{ms}}(T) = \lambda_{S_s}(T) = \lambda_{I_s}(T) = \lambda_{S_v}(T) = \lambda_{I_v}(T)$. The optimal control problem above can be analysed using the Pontryagin's maximum principle (PMP) for the necessary condition of optimality.

Theorem 3.2. *Suppose* $u^*(t) = \{u_1, u_2, u_3, u_4, u_5, u_6, u_7\}$ *and a solution* $X^* = \{S_h(t), I_m(t), I_{hs}(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t)\}$ *of the corresponding state system (6) then there exist adjoint variables* $\lambda_{S_h}(t)$, $\lambda_{I_m}(t)$, $\lambda_{I_{hs}}(t)$, $\lambda_{V_{ms}}(t)$, $\lambda_{R_m}(t)$, $\lambda_{R_{hs}}(t)$, $\lambda_{R_{ms}}(t)$, $\lambda_{S_s}(t)$, $\lambda_{I_s}(t)$, $\lambda_{S_v}(t)$, $\lambda_{I_v}(t)$ *which satisfy the following:*

(*i*) *All the costate equations* $\lambda'_{S_h} = -\frac{\partial H}{\partial S_h}, ..., \lambda'_{S_s} = -\frac{\partial H}{\partial S_h}, ..., \lambda'_{I_v} = -\frac{\partial H}{\partial I_v}$ *with transversality conditions* $\lambda_{S_h(T)} = \lambda_{I_m(T)} = \lambda_{I_{hs}(T)} = \lambda_{V_{ms}(T)} = \lambda_{R_m(T)} = \lambda_{R_s(T)} = \lambda_{R_{ms}(T)} = \lambda_{S_s(T)} = \lambda_{I_s(T)} = \lambda_{S_v(T)} = \lambda_{I_v(T)}$. *Thus, we find the optimal control* u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^*.

$u_1^* = \max\{\min\{u_1, 1\}, 0\}$,$u_2^* = \max\{\min\{u_2, 1\}, 0\}$, $u_3^* = \max\{\min\{u_3, 1\}, 0\}$, $u_5^* = \max\{\min\{u_5, 1\}, 0\}$, $u_6^* = \max\{\min\{u_6, 1\}, 0\}$, $u_6^* = \max\{\min\{u_6, 1\}, 0\}$, $u_7^* = \max\{\min\{u_7, 1\}, 0\}$.

The optimal point is determined by solving the equation at the given optimal u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^*

$$\begin{aligned}
\frac{dS_h}{dt} &= b_H + \gamma R_m + kR_{hs} + \varphi R_{ms} - (1-u_1^*)\beta_1\epsilon_h\sigma S_h I_v - (1-u_2^*)\beta_2 S_h I_s \\
&\quad - d_h S_h, \\
\frac{dI_m}{dt} &= (1-u_1^*)\beta_1\epsilon_h\sigma S_h I_v - (1-u_2^*)\beta_2 I_s I_m - (u_3^*\omega + \theta + d_h + \tau_h)I_m, \\
\frac{dI_{hs}}{dt} &= (1-u_2^*)\beta_2 S_h I_s - (1-u_1)\beta_1\epsilon_h\sigma I_v I_{hs} - (u_4^* q_h + \rho_h + d_h + \tau_h)I_{hs}, \\
\frac{dV_{ms}}{dt} &= (1-u_1^*)\beta_1\epsilon_h\sigma I_v I_{hs} + (1-u_2^*)\beta_2 I_{hs} I_m - (u_5^*\alpha + r + m + d_h + \tau_h)V_{ms}, \\
\frac{dR_m}{dt} &= u_3^*\omega I_m - (\gamma + d_h)R_m + \phi(1-\alpha u_5^*)V_{ms},
\end{aligned}$$

$$\begin{aligned}
\frac{dR_s}{dt} &= u_4^* q_h I_{hs} - (k+d_h)R_s + (1-\phi)(1-\alpha u_6^*)V_{ms},\\
\frac{dR_{ms}}{dt} &= \alpha u_5^* V_{ms} - (\varphi + d_h)R_{ms},\\
\frac{dS_s}{dt} &= b_s - \beta_3(I_{hs} + \eta_1 V_{ms})S_s - d_s S_s,\\
\frac{dI_s}{dt} &= \beta_3(I_{hs} + \eta_1 V_{ms})S_s - (d_s + \rho_s)I_s,\\
\frac{dS_v}{dt} &= b_v - (1-u_1^*)\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms})S_v - d_v S_v - u_7^* S_v,\\
\frac{dI_v}{dt} &= (1-u_1^*)\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms})S_v - d_v I_v - u_7^* I_v
\end{aligned}$$

subject to the initial conditions (2), where the Hamiltonian H is defined by $H(S_h(t), I_{hs}(t), I_m(t), V_{ms}(t), R_m(t), R_s(t), R_{ms}(t), S_s(t), I_s(t), S_v(t), I_v(t), \lambda_{S_h}(t), \lambda_{I_m}(t), \lambda_{I_{hs}}(t), \lambda_{V_{ms}}(t), \lambda_{R_m}(t), \lambda_{R_{hs}}(t), \lambda_{R_{ms}}(t), \lambda_{S_s}(t), \lambda_{I_s}(t), \lambda_{S_v}(t), \lambda_{I_v}(t), t) = w_1 I_m(t) + w_2 I_{hs}(t) + w_3 I_v(t) + w_4 I_s(t) + w_5 V_{ms}(t) + w_6 u_1^{*2}(t) + w_7 u_2^{*2}(t) + w_8 u_3^{*2}(t) + w_9 u_4^{*2}(t) + w_{10} u_5^{*2}(t) + w_{11} u_6^{*2}(t) + w_{12} u_7^{*2}(t) + \lambda_{S_h}(t)\frac{dS_h}{dt} + \lambda_{I_m}(t)\frac{dI_m}{dt} + \lambda_{I_{hs}}(t)\frac{dI_{hs}}{dt} + \lambda_{V_{ms}}(t)\frac{dV_{ms}}{dt} + \lambda_{R_m}(t)\frac{dR_m}{dt} + \lambda_{R_{hs}}(t)\frac{dR_s}{dt} + \lambda_{R_{ms}}(t)\frac{dR_{ms}}{dt} + \lambda_{S_s}(t)\frac{dS_s}{dt} + \lambda_{I_s}(t)\frac{dI_s}{dt} + \lambda_{S_v}(t)\frac{dS_v}{dt} + \lambda_{I_v}(t)\frac{dI_v}{dt} = w_1 I_m(t) + w_2 I_{hs}(t) + w_3 I_v(t) + w_4 I_s(t) + w_5 V_{ms}(t) + w_6 u_1^{*2}(t) + w_7 u_2^{*2}(t) + w_8 u_3^{*2}(t) + w_9 u_4^{*2}(t) + w_{10} u_5^{*2}(t) + w_{11} u_6^{*2}(t) + w_{12} u_7^{*2}(t) + \lambda_{S_h}(t)[b_H + \gamma R_m + k R_{hs} + \varphi R_{ms} - (1-u_1^*)\beta_1\epsilon_h\sigma S_h I_v - (1-u_2^*)\beta_2 S_h I_s - d_h S_h] + \lambda_{I_m}(t)[(1-u_1^*)\beta_1\epsilon_h\sigma S_h I_v - (1-u_2^*)\beta_2 I_s I_m - (u_3^*\omega + \theta + d_h + \tau_h)I_m] + \lambda_{I_{hs}}(t)[(1-u_2^*)\beta_2 S_h I_s - (1-u_1^*)\beta_1\epsilon_h\sigma I_v I_{hs} - (u_4^* q_h + \rho_h + d_h + \tau_h)I_{hs}] + \lambda_{V_{ms}}(t)[(1-u_1^*)\beta_1\epsilon_h\sigma I_v I_{hs} + (1-u_2^*)\beta_2 I_{hs} I_m - (u_5^*\alpha + r + m + d_h + \tau_h)V_{ms}] + \lambda_{R_m}(t)[u_3^*\omega I_m - (\gamma + d_h)R_m + \phi(1-\alpha u_5^*)V_{ms}] + \lambda_{R_{hs}}(t)[u_4 q_h I_{hs} - (k+d_h)R_s + (1-\phi)(1-\alpha u_6^*)V_{ms}] + \lambda_{R_{ms}}(t)[\alpha u_5^* V_{ms} - (\varphi + d_h)R_{ms}] + \lambda_{S_s}(t)[b_s - \beta_3(I_{hs} + \eta_1 V_{ms})S_s - d_s S_s] + \lambda_{I_s}(t)[\beta_3(I_{hs} + \eta_1 V_{ms})S_s - (d_s + \rho_s)I_s] + \lambda_{S_v}(t)[b_v - (1-u_1^*)\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms})S_v - d_v S_v - u_7^* S_v] + \lambda_{I_v}(t)[(1-u_1^*)\beta_4\epsilon_v\sigma(I_m + \eta_2 V_{ms})S_v - d_v I_v - u_7^* I_v]$.

Hence, the resulting optimality system is given in the next section.

3.4 Optimality system

The optimality system consists of the system with initial condition (4) coupled with the adjoint system and the transversality condition (3) together with the characterization of the optimal control u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^* which is defined as $\frac{\partial H}{\partial u_1} = \frac{\partial H}{\partial u_2} = \frac{\partial H}{\partial u_3} = \frac{\partial H}{\partial u_4} = \frac{\partial H}{\partial u_5} = \frac{\partial H}{\partial u_6} = \frac{\partial H}{\partial u_7} = 0$ at u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*, u_7^*

$$u_1^* = \begin{cases} 0, & \text{if } \delta_1^* \le 0,\\ \delta_1^*, & \text{if } 0 < \delta_1^* < 1,\\ 1, & \text{if } \delta_1^* \ge 1 \end{cases}$$

where

$$\delta_1^* = \frac{\begin{array}{l}\beta_1\epsilon_h\sigma S_h I_v(\lambda_{I_m}(t) - \lambda_{S_h}(t))\\ \quad + \beta_1\epsilon_h\sigma I_v I_{hs}(\lambda_{V_{ms}}(t) - \lambda_{I_{hs}}(t)) + \beta_4\epsilon_v\sigma(I_m + V_{ms})S_v(\lambda_{I_v}(t) - \lambda_{S_v}(t))\end{array}}{2w_6}$$

$$u_2^* = \begin{cases} 0, & \text{if } \delta_2^* \leq 0, \\ \delta_2^*, & \text{if } 0 < \delta_1^* < 1, \\ 1, & \text{if } \delta_2^* \geq 1 \end{cases}$$

where

$$\delta_2^* = \frac{\beta_2 S_h I_s(\lambda_{I_{hs}}(t) - \lambda_{S_h}(t)) + \beta_2 I_{hs} I_m(\lambda_{V_{ms}}(t) - \lambda_{I_m}(t)) + \beta_3(I_{hs} + \eta_1 V_{ms}) S_s(\lambda_{S_v}(t) - \lambda_{S_s}(t))}{2w_7}.$$

$$u_3^* = \begin{cases} 0, & \text{if } \delta_3^* \leq 0, \\ \delta_3^*, & \text{if } 0 < \delta_3^* < 1, \\ 1, & \text{if } \delta_3^* \geq 1 \end{cases}$$

where

$$\delta_3^* = \frac{\lambda_{I_m}(t) w I_m}{2w_3}.$$

$$u_4^* = \begin{cases} 0, & \text{if } \delta_4^* \leq 0, \\ \delta_4^*, & \text{if } 0 < \delta_4^* < 1, \\ 1, & \text{if } \delta_4^* \geq 1 \end{cases}$$

where

$$\delta_4^* = \frac{{}_h I_{hs} \lambda_{I_{hs}}(t)}{2w_9}.$$

$$u_5^* = \begin{cases} 0, & \text{if } \delta_5^* \leq 0, \\ \delta_5^*, & \text{if } 0 < \delta_5^* < 1, \\ 1, & \text{if } \delta_5^* \geq 1 \end{cases}$$

where

$$\delta_5^* = \frac{\alpha V_{ms} \lambda_{V_{ms}}(t) - \phi\alpha V_{ms} \lambda_{R_m}(t) - \alpha V_{ms} \lambda_{R_{hs}}(t) + \phi\alpha V_{ms} \lambda_{R_{hs}}(t) + \alpha V_{ms} \lambda_{R_{ms}}(t)}{2w_{10}}.$$

$$u_6^* = \begin{cases} 0, & \text{if } \delta_6^* \leq 0, \\ \delta_6^*, & \text{if } 0 < \delta_6^* < 1, \\ 1, & \text{if } \delta_6^* \geq 1 \end{cases}$$

where

$$\delta_6^* = \frac{\lambda_{S_s}(t) S_s - \lambda_{I_s}(t) I_s}{2w_{11}}.$$

$$u_7^* = \begin{cases} 0, & \text{if } \delta_7^* \leq 0, \\ \delta_7^*, & \text{if } 0 < \delta_7^* < 1, \\ 1, & \text{if } \delta_7^* \geq 1 \end{cases}$$

where $\delta_7^* = \frac{\lambda_{S_v}(t) S_v - \lambda_{I_v}(t) I_v}{2w_{12}}$.

4. Numerical simulation and graphical illustration of the malaria-schistosomiasis co-infection model

The numerical solutions of the optimality system and the associate results of the optimal control were obtained by working out the optimality system which is made up of eleven ODE's from the state and adjoint systems. We employ an iterative scheme to solve the optimality system and start to solve the state equations with a guess for the controls over the simulated time using fourth order Runge Kutta scheme. The adjoint systems are solved through a backward sweep method, using the existing iterations solution of the state equations because of the transversality conditions. Using a convex combination of the earlier controls and the value from the characterisation of the controls were updated. We repeat the same process and iterations and they are stopped if the values of the preceding iterations are very close to the ones at the existing iterations [1]. We investigate the co-infection model with multiple control measures to study the impacts of control practices and the transmission dynamics of the malaria-schistosomiasis co-infection. By applying several combinations of the seven controls, one control at a time, two controls at a time, three controls at a time, four controls at a time, five controls at a time, six controls at a time and all the seven controls at a time, we examine and compare numerical results from simulations with the following circumstances:

1. using treatments of malaria with artemisinin combined therapy (u_3) only, no use of insecticide treated bednets ($u_1 = 0$), without the use of prevention by avoiding swimming ($u_2 = 0$), no treatment of schistosomiasis with praziquantel ($u_4 = 0$), without treatment of malaria-schistosomiasis ($u_5 = 0$), no use of biological control ($u_6 = 0$), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites ($u_7 = 0$);

2. using treatment of schistosomiasis with praziquantel (u_4) only, no use treatments of malaria with artemisinin combined therapy($u_3 = 0$),no use of insecticide treated bednets ($u_1 = 0$), without the use of prevention by avoiding swimming($u_2 = 0$), without treatment of malaria-schistosomiasis ($u_5 = 0$), no use of biological control ($u_6 = 0$), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites ($u_7 = 0$);

3. the use of insecticide treated bednets (u_1) and the use of prevention by avoiding swimming(u_2) only, no treatments of malaria with artemisinin combined therapy(u_3), no treatment of schistosomiasis with praziquantel (u_4), without treatment of malaria-schistosomiasis (u_5), no use of biological control (u_6), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7);

4. the use of prevention by avoiding swimming(u_2) and treatments of malaria with artemisinin combined therapy(u_3) only, no use of insecticide treated bednets (u_1), no treatment of schistosomiasis with praziquantel (u_4), without treatment of malaria-schistosomiasis (u_5), no use of biological control (u_6), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7);

5. using treatments of malaria with artemisinin combined therapy (u_3) and use of insecticide treated bednets (u_1) only, without the use of prevention by avoiding swimming (u_2), no treatment of schistosomiasis with praziquantel (u_4), without treatment of malaria-schistosomiasis (u_5), no use of biological control (u_6), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7);

6. using treatment of schistosomiasis with praziquantel (u_4) and use treatments of malaria with artemisinin combined therapy (u_3) only,no use of insecticide treated bednets (u_1), without the use of prevention by avoiding swimming (u_2), without treatment of malaria-schistosomiasis (u_5), no use of biological control (u_6), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7);

7. the use of insecticide treated bednets (u_1), the use of prevention by avoiding swimming (u_2), use treatments of malaria with artemisinin combined therapy (u_3), and using treatment of schistosomiasis with praziquantel (u_4) only, without treatment of malaria-schistosomiasis (u_5), no use of biological control (u_6), and no use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7);

8. the use of insecticide treated bednets (u_1), the use of prevention by avoiding swimming (u_2) and treatments of malaria with artemisinin combined therapy (u_3), using treatment of schistosomiasis with praziquantel (u_4), using treatment of malaria-schistosomiasis (u_5), use of biological control (u_6) and use of insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7).

Table 3 below gave the list of parameter values used in the numerical simulation of the model. We made use of the following weight constants in our numerical experiment $w_1 = 210$;$w_2 = 910$; $w_3 = 800$; $w_4 = 760$; $w_5 = 600$; $w_6 = 150$; $w_7 = 30$;$w_8 = 200$; $w_9 = 250$; $w_{10} = 310$;$w_{11} = 230$; $w_{12} = 200$; $b_h = 0.00011$; $b_v = 0.071$; $b_s = 0.06$; $\gamma = 0.00134$; $\beta_1 = 0.03$; $\beta_4 = 0.09$; $\sigma = 0.6$; $\epsilon_h = 0.2$; $\epsilon_v = 0.3$; $d_h = 0.00004$; $\theta = 0.005$; $d_v = 0.1429$; $k = 0.013$; $\tau_h = 0.0005$; $\varphi = 0.0005$; $\beta_2 = 0.406$; $\beta_3 = 0.004$; $q_H = 0.56$; $\alpha = 0.7$; $\eta_1 = 0.01$; $\eta_2 = 0.02$; $r = 0.02$; $m = 0.06$; $d_s = 0.003$; $\phi = 0.12$; $\omega = 0.05$; $\rho_h = 0.0039$; $\rho_s = 0.0004012$.

4.1 Optimal treatments of malaria with artemisinin combined therapy(u_3) only

Only the control (u_3) on treatment of malaria with artemisinin combined therapy is used to optimise the cost functional C, while the other controls u_1, u_2, u_4, u_5, u_6 and u_7 were set to zero. In Fig.1, the result showed a key difference in the I_m, I_{hs}, V_{ms}, I_s, and I_v with optimal strategy compared to I_m, I_{hs}, V_{ms}, I_s, and I_v without control. Specifically, it is observed that in Fig.1a, the control strategy lead to a decrease in the number of human infected with malaria only (I_m) as against the uncontrolled case. Similarly, in Fig.1b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategy led to an increase in the number of human with schistosomiasis only (I_{hs}) until it maintain a steady state. In Fig.1c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals.It was also observed that in Fig.1d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the present of the optimal control strategy. In Fig.1e, the population of infected snails increases with or without control strategies. The control profile is shown in Fig.1f, here it is observed that the optimal treatment control u_3 remains at the upper bound throughout the time period.

4.2 Optimal treatment of schistosomiasis with praziquantel (u_4) only

Only the control (u_4) on treatment of schistosomiasis with praziquantel is used to optimise the cost functional C, while the other controls u_1, u_2, u_3,u_5, u_6 and u_7 were set to zero. "In Fig.2, the result revealed major difference in the I_m, I_{hs}, V_{ms}, I_s, and I_v with optimal strategy compared to I_m, I_{hs}, V_{ms}, I_s, and I_v without control. It is observed that in Fig.2a, the control strategy reduced to zero at time $T = 90$ days in the number of human infected with malaria only (I_m) while I_m without control declined to zero at $T = 80$ days. Likewise, in Fig.2b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategy led to a swift decrease in the number of human with schistosomiasis only (I_{hs}) until it maintain a steady state. In Fig.2c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals. "It was also observed that in Fig.2d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the present of the optimal control strategy. In Fig.1e, the population of infected snails increases without control strategy but declines in the presence of optimal strategy. The control profile is shown in Fig.1f, here it is observed that the optimal treatment control u_4 remains at the upper bound throughout the time period.

Table 3: Table showing numerical values of parameters used in the model.

Parameter	Symbol	Value	Source
disease induced death rate due to malaria only	θ	0.005	[50]
probability of human getting infected with malaria	β_1	0.03	[1, 18, 49]
rate of acquiring schistosomiasis through contact with inf. snails	β_2	0.406	[53]
rate of acquiring schistosomiasis through contacts with inf. hum.	β_3	0.004	[ass]
probability of mosquito getting infected by an infectious hum.	β_4	0.09	[1, 18, 49]
Malaria–schistosomiasis immunity waning rate	φ	0.0005	[ass]
Schistosomiasis induced death rate	r	0.02	[ass]
malaria disease induced death rate	m	0.06	[ass]
Co-infected who recovered from malaria only	ϕ	0.12	[ass]
disease induced death rate of human due to schistosomiasis only	ρ_H	0.0039	[17]
disease induced death rate of snails due to schistosomiasis only	ρ_s	0.0004012	[2]
human spontaneous recovery	ω	0.05	[12]
rate of loss of immunity to the schistosomiasis disease only	k	0.013	[ass]
rate of loss of immunity to malaria and schistosomiasis disease	φ	0.0005	[ass]
human spontaneous recovery from schistosomiasis only	q_H	0.56	[ass]
modification parameter	η_1	0.01	[ass]
modification parameter	η_2	0.02	[ass]
per capita birth rate of mosquitoes	b_v	0.071	[1, 2, 18]
drug induced death rate	τ_h	0.0005	[ass]
per capita birth rate of snails	b_s	0.06	[16]
Natural death rate of humans	d_H	0.00004	[1, 63]
per capita biting rate of mosquitoes	ε_v	0.3	[22, 33, 51]
contact rate of vector per human per unit time	σ	0.502	[12]
per capita biting rate of humans	ε_h	0.2	[4, 22]
natural death rate of mosquitoes	d_v	0.1429	[18]
natural death rate of snails	d_s	0.003	[16]
rate of loss of immunity to the malaria disease only	γ	0.00134	[2, 18, 44]
per capita birth rate of humans	b_h	0.00011	[1, 57]

4.3 Optimal insecticide treated bednets (u_1) and prevention by avoiding swimming (u_2) only

The controls (u_1) and (u_2) were used to optimise the cost functional C, while the other controls u_3, u_4,u_5, u_6 and u_7 were set to zero. It is observed that in Fig.3a, the number of human infected with malaria only (I_m) declines to zero without control strategies while it decreases to a certain point with control strategies as against the uncontrolled case. Similarly, in Fig.3b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategies led to a decrease in the number of human with

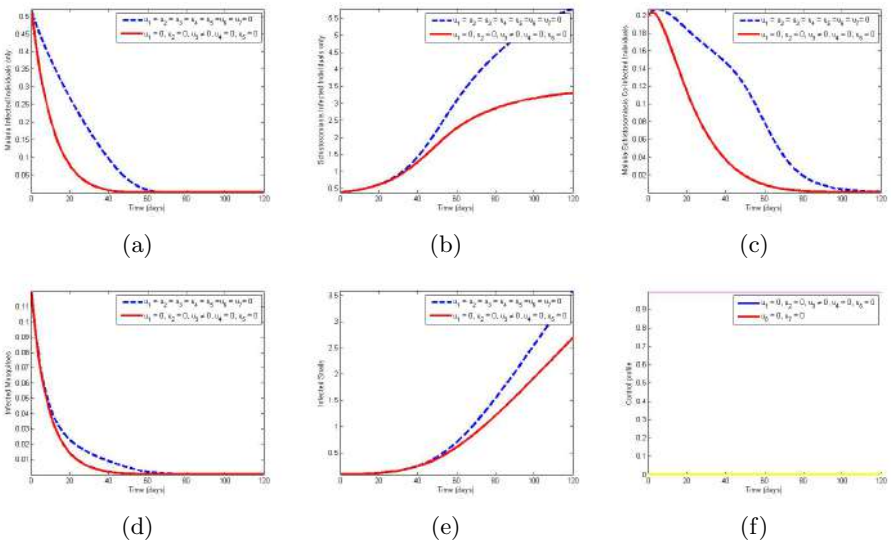


Figure 1: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.1a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.1b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.1c, Infected mosquitoes (I_v) in Fig.1d, Infected snails (I_s) in Fig.1e and control profile in Fig.1f

schistosomiasis only (I_{hs}). In Fig.3c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals.It was also observed that in Fig.3d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the present of the optimal control strategy. In Fig.3e, the population of infected snails increases without control strategies but decreases in the presence of the optimal strategies. The control profile is shown in Fig.3f, here it is observed that the optimal treated bednets control u_1 and prevention by avoiding swimming u_2 remains at the upper bound throughout the time period.

4.4 Optimal prevention by avoiding swimming (u_2) and treatments of malaria with artemisinin combined therapy (u_3) only

Here the controls (u_2) and (u_3) were used to optimise the cost functional C, while the other controls u_1, u_4, u_5, u_6 and u_7 were set to zero.It is observed that in Fig.4a, the number of human infected with malaria only (I_m) declines to zero without control strategies while it decreases to a certain point with control strategies as against the uncontrolled case. Similarly, in Fig.4b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategies led to a decrease in the number of human with

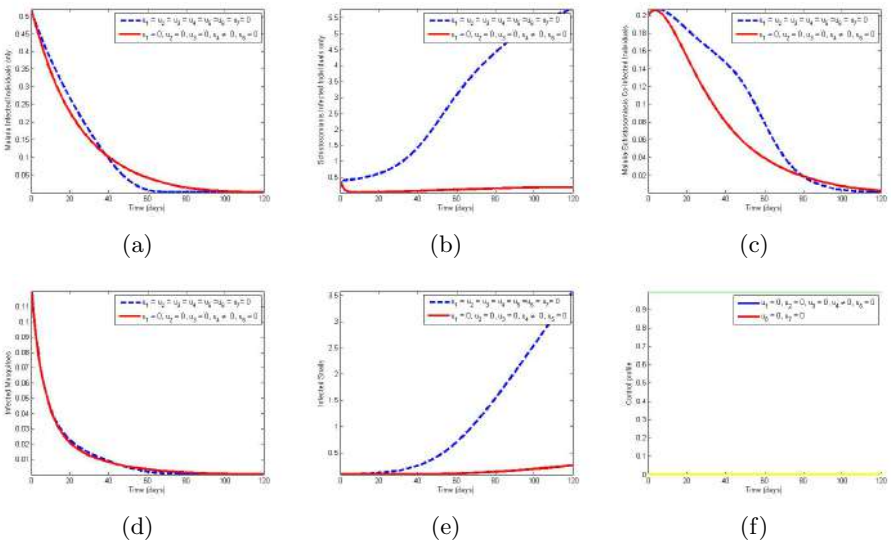


Figure 2: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.2a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.2b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.2c, Infected mosquitoes (I_v) in Fig.2d, Infected snails (I_s) in Fig.2e and control profile in Fig.2f.

schistosomiasis only (I_{hs}). In Fig.4c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals. It is also observed that in Fig. 4d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the presence of the optimal control strategy. In Fig.4e, the population of infected snails increases without control strategies but decreases in the presence of the optimal strategies. The control profile is shown in Fig.4f, here it is observed that the optimal prevention by avoiding swimming control u_2 and treatments of malaria with artemisinin combined therapy u_3 remains at the upper bound throughout the time period.

4.5 Optimal treatments of malaria with artemisinin combined therapy (u_3) and insecticide treated bednets (u_1) only

Here the controls (u_3) on treatment of malaria with artemisinin combined therapy and insecticide treated bednets u_1 were applied to optimise the cost functional C, while the other controls u_2, u_4,u_5, u_6 and u_7 were set to zero.Specifically, it is observed that in Fig.5a, the control strategy lead to a decrease in the number of human infected with malaria only (I_m) while the uncontrolled case decreases slowly. Similarly, in Fig.5b, the uncontrolled case resulted in the increased num-

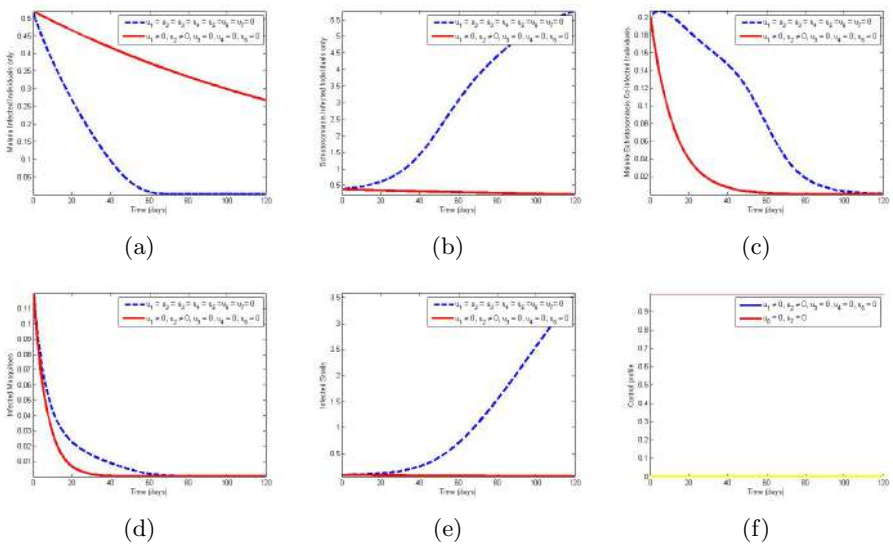


Figure 3: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.3a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.3b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.3c, Infected mosquitoes (I_v) in Fig.3d, Infected snails (I_s) in Fig.3e and control profile in Fig.3f

ber of human with schistosomiasis only (I_{hs}), while the control strategy led to an increase in the number of human with schistosomiasis only (I_{hs}) until it maintain a steady state. In Fig.5c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals.It is also observed that in Fig.5d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the present of the optimal control strategy. In Fig.5e, the population of infected snails increases with or without control strategies. The control profile is shown in Fig.5f, here it is observed that the Optimal treatments of malaria with artemisinin combined therapy(u_3) and insecticide treated bednets (u_1) remains at the upper bound throughout the time period.

4.6 Optimal treatment of schistosomiasis with praziquantel (u_4) and use treatments of malaria with artemisinin combined therapy(u_3) only

Here the controls (u_3) on treatment of malaria with artemisinin combined therapy and treatment of schistosomiasis with praziquantel u_4 were applied to optimise the cost functional C, while the other controls u_2, u_4, u_5, u_6 and u_7 were set to zero. It is observed that in Fig.6a, the control strategy lead to a decrease

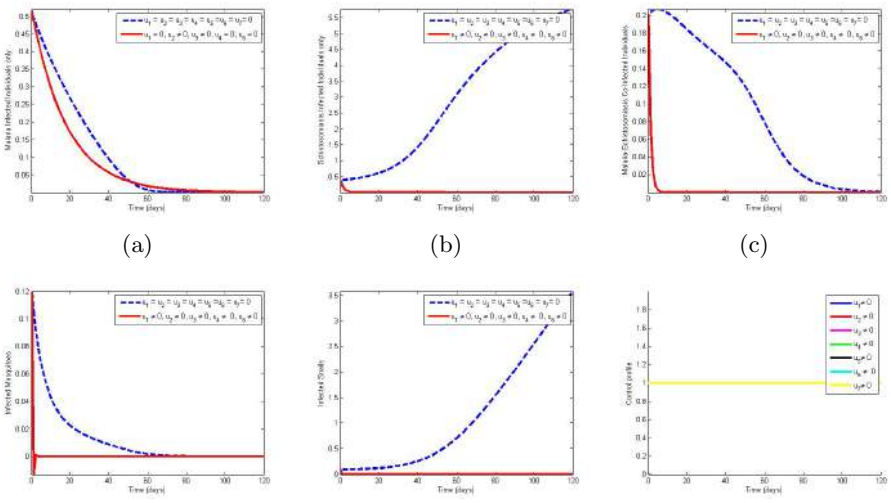


Figure 4: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.4a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.4b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.4c, Infected mosquitoes (I_v) in Fig.4d, Infected snails (I_s) in Fig.4e and control profile in Fig.4f

in the number of human infected with malaria only (I_m) while the uncontrolled case decreases slowly. Likewise, in Fig.6b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategy led to a decrease in the number of human with schistosomiasis only (I_{hs}). In Fig.6c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals. It was also observed that in Fig.6d, the population of infected mosquitoes decreases with or without control, but seems to fastly decline in the presence of the optimal control strategy. In Fig.6e, the population of infected snails increases without control strategies but decreases in the presence of optimal strategy. The control profile is shown in Fig.6f, here it is observed that the optimal treatments of malaria with artemisinin combined therapy(u_3) and treatment of schistosomiasis with praziquantel u_4 remains at the upper bound throughout the time period.

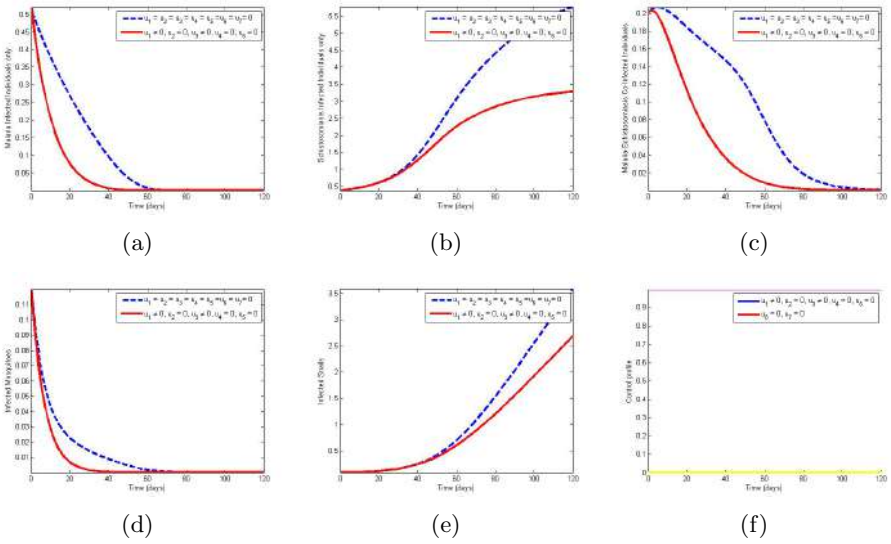
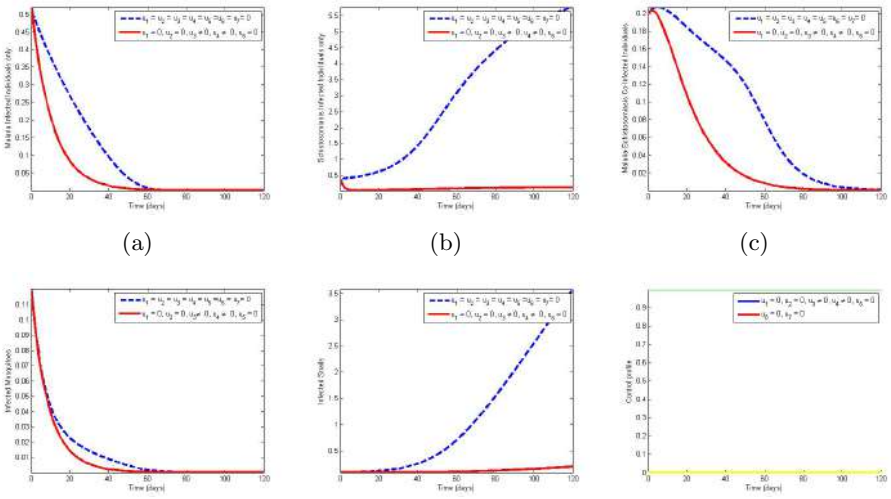


Figure 5: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.5a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.5b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.5c, Infected mosquitoes (I_v) in Fig. 5d, Infected snails (I_s) in Fig.5e and control profile in Fig.5f

4.7 Optimal insecticide treated bednets (u_1), prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy(u_3), and treatment of schistosomiasis with praziquantel (u_4) only

Here the controls (u_1) on insecticide treated bednets, prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy (u_3), and treatment of schistosomiasis with praziquantel (u_4) only were applied to optimise the cost functional C, while the other controls u_5, u_6 and u_7 were set to zero. Particularly, it is observed that in Fig.7a, the control strategy lead to a decrease in the number of human infected with malaria only (I_m) while the uncontrolled case declines slowly. Similarly, in Fig.7b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategy led to a decrease in the number of human with schistosomiasis only (I_{hs}) until it maintain a steady state. In Fig.7c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals. It was also observed that in Fig.7d, the population of infected mosquitoes decreases with or without control, but seems to swiftly decline in the present of the optimal control strategy. In Fig.7e, the population of infected snails increases without control



(a) (b) (c)

(d) (e) (f)

Figure 6: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.6a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.6b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.6c, Infected mosquitoes (I_v) in Fig.6d, Infected snails (I_s) in Fig.6e and control profile in Fig.6f.

strategy while it decreases in the presence of optimal strategy. The control profile is shown in Fig.7f, here it is observed that the optimal insecticide treated bednets (u_1), prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy (u_3), and treatment of schistosomiasis with praziquantel (u_4) remains at the upper bound throughout the time period.

4.8 Optimal insecticide treated bednets (u_1), prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), treatment of malaria-schistosomiasis (u_5), use of biological control (u_6) and insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7)

Here the all the seven controls that is optimal insecticide treated bednets (u_1), prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), treatment of malaria-schistosomiasis (u_5), use of biological control (u_6) and insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7) were applied to optimise the cost functional C. In particular, it is observed that in Fig.8a, the control strategy lead to a decrease in the number of human infected with malaria only (I_m) while the uncontrolled case decreases

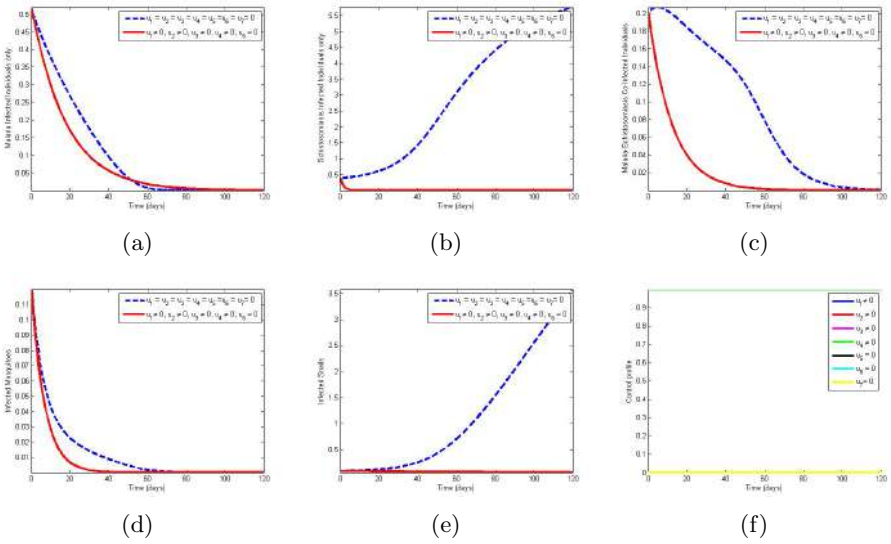
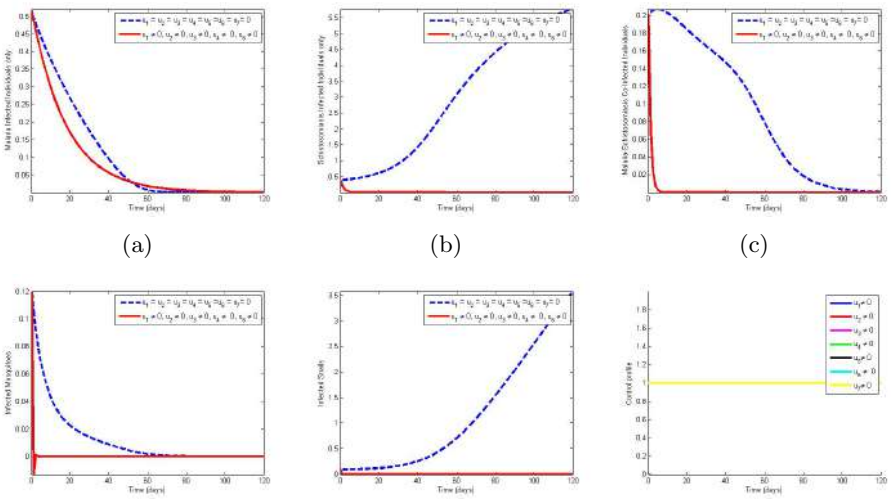


Figure 7: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.7a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.7b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.7c, Infected mosquitoes (I_v) in Fig.7d, Infected snails (I_s) in Fig.7e and control profile in Fig.7f.

slowly. Similarly, in Fig.8b, the uncontrolled case resulted in the increased number of human with schistosomiasis only (I_{hs}), while the control strategy led to a total decrease in the number of human with schistosomiasis only (I_{hs}) until it reaches zero. In Fig.8c, the uncontrolled case resulted in decrease number of co-infected human with both malaria-schistosomiasis (V_{ms}) slowly, while the control strategy led to faster declining in the malaria-schistosomiasis co-infected individuals completely to zero.It was also observed that in Fig.8d, the population of infected mosquitoes decreases without control slowly, but seems to swiftly decline in the presence of the optimal control strategy. In Fig.8e, the population of infected snails increases without control strategies but decreases drastically to zero as time goes on. The control profile is shown in Fig.8f, here it is observed that the optimal insecticide treated bednets (u_1), prevention by avoiding swimming (u_2), treatments of malaria with artemisinin combined therapy (u_3), treatment of schistosomiasis with praziquantel (u_4), treatment of malaria-schistosomiasis (u_5), use of biological control (u_6) and insecticide spray and destruction of stagnant water and mosquito breeding sites (u_7) remains at the upper bound throughout the time period.



(a) (b) (c)

(d) (e) (f)

Figure 8: Simulation showing the variation of Infected Human with malaria only (I_m) in Fig.8a, Infected Human with Schistosomiasis only (I_{hs}) in Fig.8b, Humans infected with both malaria and schistosomiasis (V_{ms}) in Fig.8c, Infected mosquitoes (I_v) in Fig.8d, Infected snails (I_s) in Fig.8e and control profile in Fig.8f.

5. Conclusion

In this paper, we developed and analysed a deterministic model for the transmission of malaria-schistosomiasis co-infection with control interventions using system of non linear ordinary differential equations. The optimal control problem was formulated, where we used one control intervention at a time, combinations of two, four, and seven control interventions at a time while we set others to zero to examine and compared the influence of the control strategies on malaria-schistosomiasis elimination. Our numerical results revealed that the combinations of seven control strategies at a time had the greatest impact on the reduction or stopping the transmission chain of the co-infected disease. This is followed by the combinations of four control strategies and lastly by the combination of two i.e. u_3 and u_4. In places where there are scarce or limited resources, it our suggestion that the combination of the two controls (u_3 and u_4) be adopted having observed their impact breaking the transmission chain of co-infection.Thus, we recommend that there should be many effective elimination programs both at local and national level on the control and elimination of malaria and schistosomiasis. The obtained results present a good framework for planning and designing cost-effective strategies for good interventions in dealing with malaria and malaria-schistosomiasis co-infection and provided guideline to

identify the most effective intervention packages by the national control bodies. This work can be extended by including the effects of the environment on the dynamics of malaria-schistosomiasis co-infection and also to incorporate some heterogeneities within and without, a community. Model validation and parameter estimation could also be essential aspect to explore by applying it to a particular malaria-schistosomiasis endemic region of the world in order to link available data with the model.

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