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OPTIMAL CONTROL ANALYSIS OF SCHISTOSOMIASIS DYNAMICS

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Abstract. This paper presents an extension of a deterministic epidemic model for schistosomiasis. The model is extended into an optimal control problem with the inclusion of three time-dependent optimal control measures. The optimal controls included are: early diagnosis and treatment of exposed humans; snail elimination using chemical molluscicide; and chlorination of water to eliminate free living cercariae. The existence of the optimal control solution is proven and the necessary conditions required for an optimal control with respect to the proposed model was established using Pontryagin's minimum principle. The forward-backward Runge Kutta scheme was used to carry out the numerical simulation. Seven control measures (S1–S7) were simulated using the three control strategies: $u_1(t)$, $u_2(t)$ and $u_3(t)$ and a combination of these controls. The results from the numerical simulation showed the effectiveness of each of the control strategies in controlling the prevalence of schistosomiasis. Based on the results, the most effective and swift control strategies are those involving snail elimination using chemical

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molluscicide. But due to the environmental implications of these control strategies, as it may lead to total extinction of the snails, it is highly recommended that no control involving snail elimination should be practiced. Thus, the best and also an effective control strategy will be a combination of treatment of infectious individuals and water treatment to eliminate cercariae by chlorination.

Keywords: Schistosomiasis; optimal control; Pontryagin's minimum principle; Runge Kutta method.

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1. INTRODUCTION

Schistosomiasis is a disease that is caused by a group of parasitic worms known as schistosomes. It affected about 290.8 million people in 2018 out of which only about 97.2 million people were treated, [32]. The mortality rate of the disease is about 4,400 to 200,000 per annum. The disease is endemic in Africa, Asia and South America. However, few cases have been reported in other continents. Species of schistosomes that cause illnesses in humans are: *schistosoma haematobium*, *schistosoma mansoni*, and *schistosoma japonicum*, [32]. These species of schistosomes are common in parts of Africa, Asia and South America, [33]. *Schistosoma mansoni* and *schistosoma japonicum* mainly cause diseases in the liver and bowels but *schistosoma haematobium* mostly affect the urinary and genital areas, [8]. Symptoms of schistosomiasis include but not limited to diarrhea, bloody stool, abdominal pain, liver damage, kidney failure etc. Fresh water with infected snails is the major means by which the disease is spread. Humans become infected when they come in contact with contaminated fresh water. Availability of clean water and reduction in the number of snails are two major effective strategies in controlling the disease, [32].

The prevalence of schistosomiasis in an endemic area could be reduced by the introduction of control strategies into a mathematical model, [36]. Zhang et al., [38] opined that schistosomiasis could be eliminated from an endemic area through multiple strategies targeted at different stages of development of schistosome parasite. The combination of the use of sanitary measures, hygiene education and treatment of infected individuals on large scale and vector control measures are the most effective strategy that can lead to the elimination of schistosomiasis.

The analysis of the optimal control of malaria and schistosomiasis co-infection model was carried out. The impact of the parameters on the spread of the disease was examined using

sensitivity analysis. Numerical simulation of the model showed that changes in the values of a parameter of the co-infection dynamics indicated a change in the stability of the equilibrium point, [3]. Furthermore, Okosun K.O. and Smith R., [29] developed a mathematical model for malaria and schistosomiasis co-infection to investigate the synergistic relationship between the two diseases in the presence of treatment. The results showed that schistosomiasis control has little effect on the prevalence of malaria. However, optimal control of schistosomiasis prevention and treatment has a moderate effect on reducing infected mosquitoes. This would lead to a reduction the malaria prevalence.

The results of the stability analysis performed on a schistosomiasis model showed that good public health education and latent period of infection could help to reduce the prevalence of schistosomiasis, [15]. A model comprising of four delay differential equations for the control of schistosoma japonicum was developed. The results suggested that the prevalence of schistosomiasis could be reduced by lengthening the pre-patent periods in humans through drug treatment, [37].

Elmojtaba Ibrahim M. and Adam Salma O.A., [13] used an SVCIRS model to study the effects of a vaccine on schistosomiasis disease in a human population and distinguished between the recovered with disabilities and the recovered without disabilities. The results showed that the disease could be controlled with high vaccine uptake. Similarly, since *S. mansoni* cercariae are very sensitive to chlorine, higher PH and CT values and lower temperature are required to significantly deactivate *S. mansoni* cercariae contaminated water. A regression model for the prediction of CT was obtained from the laboratory data,[5].

The total cost of treatment of infected individuals could be minimized by an optimal control technique by reducing the prevalence of the infected individuals. This could be achieved by increasing the treatment rate of infected individuals, [12]. Kalinda et al., [19] applied optimal control technique on a schistosomiasis model that depended on temperature by minimizing the cost of pre-patent and patent compartments. The results showed that schistosomiasis could be reduce by more than three-fold if the optimal control strategies were well implemented. The study also provided a cost-effective control strategies for schistosomiasis. Lo Nathan et al., [24] examined the cost-effectiveness of snail control implemented together with mass drug

administration (MDA) strategies to obtain the optimal epidemiological conditions that support previous control techniques. The results indicated that the method of snail control should be implemented in regions with high burden of schistosomiasis disease burden and recommended doses of the chemical should be used to avert negative ecological consequences.

Over the years, several other mathematical models have been developed for the transmission dynamics and control of schistosomiasis, [1], [7], [8], [11],[21], [31] [34] and others referenced herein.

This study is an extension of the deterministic epidemic model of Kanyi et al., [20]. The model studied the transmission dynamics of schistosomiasis based on the life cycle of the schistosome parasite. Two control strategies, treatment and WASH, were considered and analyzed numerically. Here, the model is extended into an optimal control problem with three time dependent optimal controls.

2. FORMULATION OF THE OPTIMAL CONTROL PROBLEM

The model is designed to study the transmission dynamics of schistosomiasis within the sub-populations of humans and snails alongside the dynamics of the free living miracidia and cercariae. Hence, the proposed model comprises of the Susceptible humans (S_h), Susceptible snails (S_s), Exposed humans (E_h), Exposed snails (E_s), Infected humans (I_h), Infected snails (I_s), Treated humans (T_h), the free living miracidia (N_m) and the free living cercariae (N_c). Moreover, an SEITS model for the human sub-population due to the fact that treated humans acquire no immunity and an SEI model for the snail sub-population on the assumption that infected snails do not recover are considered. The total human and the total snail sub-populations are denoted by N_h and N_s respectively. Thus, $N_h = S_h + E_h + I_h + T_h$ and $N_s = S_s + E_s + I_s$. Furthermore, this model incorporates three time dependent optimal control strategies. These controls are denoted by $u_1(t)$, $u_2(t)$ and $u_3(t)$, where:

$u_1(t)$ = early diagnosis and treatment of exposed humans;

$u_2(t)$ = snail elimination using chemical molluscicide, and

$u_3(t)$ = chlorination of water to eliminate free living cercariae.

The parameters used in this model, the descriptions and values are illustrated in table 1.

TABLE 1. A table showing description of the model parameters and their respective values

Parameter	Description	Value	Source
α_h	recruitment rate of humans	$254 d^{-1}$	Estimate, [20]
α_s	recruitment rate of snails	$3000 d^{-1}$	[38]
β_h	rate of transmission of humans from susceptible to exposed	$0.09753 Lcer^{-1} d^{-1}$	[19]
β_s	rate of transmission of snails from susceptible to exposed	$0.615 Lmir^{-1} d^{-1}$	[8], [10]
μ_h	natural death rate of humans	$0.00004379 d^{-1}$	Estimate, [20]
μ_s	natural death rate of snails	$0.000569 d^{-1}$	[8]
μ_m	natural death rate of miracidia	$0.9 d^{-1}$	[8]
μ_c	natural death rate of cercariae	$0.004 d^{-1}$	[8]
δ_h	death rate of humans due to infection	$0.000274 - 0.000913 d^{-1}$	Estimate, [20]
δ_s	death rate of snails due to infection	$0.0004012 d^{-1}$	[8]
σ_h	rate of transmission of humans from exposed to infected	$0.0238 - 0.0286 d^{-1}$	Estimate, [20]
σ_s	rate of transmission of snails from exposed to infected	$0.0286 - 0.0357 d^{-1}$	Estimate, [20]
γ_h	transmission rate of humans from infected to treated	$0.03 d^{-1}$	[10]
λ_1	rate individuals produce miracidia	$6.96 mir\ host^{-1} d^{-1}$	[23]
λ_2	rate snails produce cercariae	$2.6 cer\ host^{-1} d^{-1}$	[8]
ρ	treatment efficacy	0.8	Assumed, [20]
m_0	miracidia saturation constant	1×10^8	[8]
c_0	cercariae saturation constant	9×10^7	[8]
ε	limitation of the growth velocity	0.2	[8]

The optimal control problem is given by the following system of non-linear ordinary differential equations (1):

$$(1) \quad \begin{cases} \frac{dS_h}{dt} = \alpha_h + \rho T_h - \frac{\beta_h N_c S_h}{c_0 + \varepsilon N_c} - \mu_h S_h \\ \frac{dE_h}{dt} = \frac{\beta_h N_c S_h}{c_0 + \varepsilon N_c} - \sigma_h E_h - u_1 E_h - \mu_h E_h \\ \frac{dI_h}{dt} = \sigma_h E_h - \gamma_h I_h - \delta_h I_h - \mu_h I_h \\ \frac{dT_h}{dt} = u_1 E_h + \gamma_h I_h - \rho T_h - (1 - \rho)\delta T_h - \mu_h T_h \\ \frac{dN_m}{dt} = \lambda_1 I_h - \mu_m N_m \\ \frac{dS_s}{dt} = \alpha_s - \frac{\beta_s N_m S_s}{m_0 + \varepsilon N_m} - u_2 S_s - \mu_s S_s \\ \frac{dE_s}{dt} = \frac{\beta_s N_m S_s}{m_0 + \varepsilon N_m} - \sigma_s E_s - u_2 E_s - \delta_s E_s - \mu_s E_s \\ \frac{dI_s}{dt} = \sigma_s E_s - u_2 I_s - \delta_s I_s - \mu_s I_s \\ \frac{dN_c}{dt} = \lambda_2 I_s - u_3 N_c - \mu_c N_c \\ S_h(0) \geq 0, E_h(0) \geq 0, I_h(0) \geq 0, T_h(0) \geq 0, N_m(0) \geq 0, S_s(0) \geq 0, E_s(0) \geq 0, I_s(0) \geq 0, N_c(0) \geq 0. \end{cases}$$

3. ANALYSIS OF THE OPTIMAL CONTROL

Now, we define the objective functional that minimizes the control vector $u = (u_1, u_2, u_3)$ as

$$(2) \quad \mathcal{J}(u) = \int_0^{t_f} (v_1 E_h + v_2 N_s + v_3 N_c + v_4 u_1^2 + v_5 u_2^2 + v_6 u_3^2) dt$$

subject to the system of non-linear ordinary differential equations 1 with the weight constants denoted by the sequence $\{v_i\}$ for $i = 1, 2, \dots, 6$. The weight constants are essential for balancing the terms in the integral by preventing the dominance of one over another. Thus, they are called the *balancing cost factors*. The goal is to minimize the vector population (to reduce the production of cercariae) and the number of infective individuals alongside the cost of registering treatment (on exposed individuals) and the cost of applying chemical molluscicide and chlorination of water on snails and cercariae respectively. Hence, we attempt to obtain an optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ that can minimize the objective functional 2. That is,

$$(3) \quad \mathcal{J}(u^*) = \min_u \{ \mathcal{J}(u_1, u_2, u_3) | u_1, u_2, u_3 \in U \}$$

where

(4)

$$U = \{(u_1(t), u_2(t), u_3(t)) : 0 \leq u_1 \leq u_{1max} < 1, 0 \leq u_2 \leq u_{2max} < 1, 0 \leq u_3 \leq 1, 0 \leq t \leq t_f\}$$

is the control set, which is assumed to be Lebesgue measurable. The terms v_1, v_2 and v_3 represent the costs associated with the model variables E_h, N_s and N_c respectively, where $N_s = S_s + E_s + I_s$, denote the total snail sub-population. And the terms v_4, v_5 and v_6 represent the costs associated with each corresponding control u_j and because costs are mostly assumed to be non-linear in nature, consequently, each u_j , for $j = 1, 2, 3$, is taken to be quadratic.

3.1. Existence of the Optimal Controls. Here, we established the existence of an optimal control using the results presented in *Theorem 4.1* and its subsequent corollary, *corollary 4.1*, in Fleming and Rishel, [14]. These results are based on the satisfaction of the following properties:

- P1: the control set and its corresponding state variables are non-empty;
- P2: the control set is convex and closed;
- P3: the right-hand side of each of the equations in the state system is continuous and bounded above by a linear function in the state and control;
- P4: the integrand of the objective functional is convex on the control.
- P5: there are real numbers $a_1, a_2 > 0$ and $\omega > 1$ such that the integrand, L , of the objective functional satisfies

$$L \geq a_1 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\omega}{2}} - a_2.$$

Now, consider the following theorem:

Theorem 3.1. *Given an optimal control problem with respect to the system equation (1), then there is an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in U$ with the corresponding solution $(S_h^*, E_h^*, I_h^*, T_h^*, N_m^*, S_s^*, E_s^*, I_s^*, N_c^*)$ that can minimize $\mathcal{J}(u)$ over U .*

Proof. To prove this theorem, the above stated properties from Fleming and Rishel, [14] are considered. For property P1, the existence results found in *Theorem 9.2.1* of Lukes (1982), [25] for the system equation (1) is used. The boundedness of the coefficients shows that property P1 is satisfied. Property P2 also holds, since the control set U , by definition is both closed

and convex. The priori boundedness of the model's solutions shows that the right-hand side satisfies property P3. Moreover, Property P4 is satisfied because the integrand, L of the objective functional $\mathcal{J}(u)$ is clearly convex on the control set U . Finally, there are constants $a_1, a_2 > 0$ and $\omega > 1$ such that $L \geq a_1 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\omega}{2}} - a_2$, due to the fact that all the state variables are bounded and hence property P5 holds.

Accordingly, based on the results from Fleming and Rishel, [14], there exist an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in U$ that minimizes the objective functional $\mathcal{J}(u)$ over U . \square

3.2. Characterization of the Optimal Controls. The Pontryagin's minimum principle provide the necessary conditions that the optimal controls are required to fulfill. The Hamiltonian function is defined by incorporating a differentiable piece-wise vector-valued function $\Lambda(t) = [\Lambda_1(t), \Lambda_2(t), \Lambda_3(t), \Lambda_4(t), \Lambda_5(t), \Lambda_6(t), \Lambda_7(t), \Lambda_8(t), \Lambda_9(t)]$ where the Λ_k 's are the adjoint variables and each Λ_k corresponds to a state variable x_k with $x = (S_h, E_h, I_h, T_h, N_m, S_s, E_s, I_s, N_c)$. The Hamiltonian function is defined as

(5)

$$H(t, x, u, \Lambda) = L + \Lambda_1 \frac{dS_h}{dt} + \Lambda_2 \frac{dE_h}{dt} + \Lambda_3 \frac{dI_h}{dt} + \Lambda_4 \frac{dT_h}{dt} + \Lambda_5 \frac{dN_m}{dt} + \Lambda_6 \frac{dS_s}{dt} + \Lambda_7 \frac{dE_s}{dt} + \Lambda_8 \frac{dI_s}{dt} + \Lambda_9 \frac{dN_c}{dt}$$

where t denotes time, L the Lagrangian (the integrand in 2), the state variables are denoted by $x = (S_h, E_h, I_h, T_h, N_m, S_s, E_s, I_s, N_c)$, and the controls as $u = (u_1, u_2, u_3)$. The adjoint variables are denoted by $\Lambda = (\Lambda_1, \Lambda_2, \Lambda_3, \Lambda_4, \Lambda_5, \Lambda_6, \Lambda_7, \Lambda_8, \Lambda_9)$. Clearly, the Lagrangian

$$(6) \quad L = v_1 E_h + v_2 N_s + v_3 N_c + v_4 u_1^2 + v_5 u_2^2 + v_6 u_3^2$$

From the definition of the Hamiltonian function 5, we obtain:

$$\begin{aligned}
(7) \quad H(t, x, u, \Lambda) = & v_1 E_h + v_2 N_s + v_3 N_c + v_4 u_1^2 + v_5 u_2^2 + v_6 u_3^2 \\
& + \Lambda_1 \left(\alpha_h + \rho T_h - \frac{\beta_h N_c S_h}{c_0 + \varepsilon N_c} - \mu_h S_h \right) \\
& + \Lambda_2 \left(\frac{\beta_h N_c S_h}{c_0 + \varepsilon N_c} - \sigma_h E_h - u_1 E_h - \mu_h E_h \right) \\
& + \Lambda_3 \left(\sigma_h E_h - \gamma_h I_h - \delta_h I_h - \mu_h I_h \right) \\
& + \Lambda_4 \left(u_1 E_h + \gamma_h I_h - \rho T_h - (1 - \rho) \delta_h T_h - \mu_h T_h \right) \\
& + \Lambda_5 \left(\lambda_1 I_h - \mu_m N_m \right) \\
& + \Lambda_6 \left(\alpha_s - \frac{\beta_s N_m S_s}{m_0 + \varepsilon N_m} - u_2 S_s - \mu_s S_s \right) \\
& + \Lambda_7 \left(\frac{\beta_s N_m S_s}{m_0 + \varepsilon N_m} - \sigma_s E_s - u_2 E_s - \delta_s E_s - \mu_s E_s \right) \\
& + \Lambda_8 \left(\sigma_s E_s - u_2 I_s - \delta_s I_s - \mu_s I_s \right) \\
& + \Lambda_9 \left(\lambda_2 I_s - u_3 N_c - \mu_c N_c \right)
\end{aligned}$$

The adjoint system is given by

$$(8) \quad \frac{d\Lambda_k}{dt} = - \frac{\partial H}{\partial x_k(t)}$$

whose solution gives the adjoint or co-state variables. Moreover,

$$(9) \quad \left\{ \begin{aligned}
\frac{d\Lambda_1}{dt} &= - \frac{\partial H}{\partial S_h(t)} = (\Lambda_1 - \Lambda_2) \left(\frac{\beta_h N_c}{c_0 + \varepsilon N_c} \right) + \Lambda_1 \mu_h \\
\frac{d\Lambda_2}{dt} &= - \frac{\partial H}{\partial E_h(t)} = (\Lambda_2 - \Lambda_3) \sigma_h + (\Lambda_2 - \Lambda_4) u_1 + \Lambda_2 \mu_h - v_1 \\
\frac{d\Lambda_3}{dt} &= - \frac{\partial H}{\partial I_h(t)} = (\Lambda_3 - \Lambda_4) \gamma_h + \Lambda_3 (\delta_h + \mu_h) - \Lambda_5 \lambda_1 \\
\frac{d\Lambda_4}{dt} &= - \frac{\partial H}{\partial T_h(t)} = (\Lambda_4 - \Lambda_1) \rho + \Lambda_4 ((1 - \rho) \delta_h + \mu_h) \\
\frac{d\Lambda_5}{dt} &= - \frac{\partial H}{\partial N_m(t)} = (\Lambda_6 - \Lambda_7) \left(\frac{m_0 \beta_s S_s}{(m_0 + \varepsilon N_m)^2} \right) + \Lambda_5 \mu_m \\
\frac{d\Lambda_6}{dt} &= - \frac{\partial H}{\partial S_s(t)} = (\Lambda_6 - \Lambda_7) \left(\frac{\beta_s N_m}{m_0 + \varepsilon N_m} \right) + \Lambda_6 (u_2 + \mu_s) - v_2 \\
\frac{d\Lambda_7}{dt} &= - \frac{\partial H}{\partial E_s(t)} = (\Lambda_7 - \Lambda_8) \sigma_s + \Lambda_7 (u_2 + \delta_s + \mu_s) - v_2 \\
\frac{d\Lambda_8}{dt} &= - \frac{\partial H}{\partial I_s(t)} = \Lambda_8 (u_2 + \delta_s + \mu_s) - \Lambda_9 \lambda_2 - v_2 \\
\frac{d\Lambda_9}{dt} &= - \frac{\partial H}{\partial N_c(t)} = (\Lambda_1 - \Lambda_2) \left(\frac{c_0 \beta_h S_h}{(c_0 + \varepsilon N_c)^2} \right) + \Lambda_9 (u_3 + \mu_c) - v_3
\end{aligned} \right.$$

which satisfies the boundary condition $\Lambda_k(t_f) = 0, \quad \forall k = 1, 2, \dots, 9$.

We therefore formulate the following *theorem* based on the Pontryagin's Minimum Principle, [30] together with the existence properties from Corollary 4.1 of Fleming and Rishel, [14].

Theorem 3.2. *The optimal control triple (u_1^*, u_2^*, u_3^*) with corresponding states*

$(S_h^, E_h^*, I_h^*, T_h^*, N_m^*, S_s^*, E_s^*, I_s^*, N_c^*)$ to the state system 1 that minimizes the objective functional $\mathcal{J}(u)$ in equation (2) over U is given by*

$$(10) \quad \begin{cases} u_1^* = \min \left\{ \max \left(0, \frac{(\Lambda_2 - \Lambda_4)E_h}{2v_4} \right), u_{1max} \right\} \\ u_2^* = \min \left\{ \max \left(0, \frac{\Lambda_6 S_s + \Lambda_7 E_s + \Lambda_8 I_s}{2v_5} \right), u_{2max} \right\} \\ u_3^* = \min \left\{ \max \left(0, \frac{\Lambda_9 N_c}{2v_6} \right), 1 \right\}. \end{cases}$$

where the solution sequence (Λ_k) , for $k = 1, 2, \dots, 9$ satisfy equation (9).

Proof. Consider the existence results of optimal control from Fleming and Rishel, [14] which is based on the *Lipschitz* property of the model equations in relation to the model variables, the convexity of the integrand of the objective functional $\mathcal{J}(u)$ in relation to the controls u_1 , u_2 and u_3 , and that the solutions of the model variables are priori bounded. Clearly, the adjoint system (9) is obtained using the relation $\frac{d\Lambda_k}{dt} = -\frac{\partial H}{\partial x_k(t)}$, for $k = 1, 2, \dots, 9$, as previously stated. Additionally, the optimal controls (see [22]) is obtained by solving:

$$(11) \quad \frac{\partial H}{\partial \hat{u}_j} = 0$$

at $u_j = \hat{u}_j$ with $j = 1, 2, 3$. Thus,

$$(12) \quad \begin{cases} \frac{\partial H}{\partial u_1} = 2v_4 u_1 + (\Lambda_4 - \Lambda_2)E_h \\ \frac{\partial H}{\partial u_2} = 2v_5 u_2 - \Lambda_6 S_s - \Lambda_7 E_s - \Lambda_8 I_s \\ \frac{\partial H}{\partial u_3} = 2v_6 u_3 - \Lambda_9 N_c \end{cases}$$

and accordingly, at $u_j = \hat{u}_j$;

$$(13) \quad \begin{cases} \hat{u}_1 = \frac{(\Lambda_2 - \Lambda_4)E_h}{2v_4} \\ \hat{u}_2 = \frac{\Lambda_6 S_s + \Lambda_7 E_s + \Lambda_8 I_s}{2v_5} \\ \hat{u}_3 = \frac{\Lambda_9 N_c}{2v_6} \end{cases}$$

Hence, the optimal control vector which minimizes the objective functional, $\mathcal{J}(u)$ (2) denoted by $u^* = (u_1^*, u_2^*, u_3^*)$ is obtained as:

$$(14) \quad \begin{cases} u_1^* = \min \{ \max(0, \hat{u}_1), u_{1max} \} \\ u_2^* = \min \{ \max(0, \hat{u}_2), u_{2max} \} \\ u_3^* = \min \{ \max(0, \hat{u}_3), 1 \}. \end{cases}$$

Similarly, if we assign bounds to the control variable, then the optimality conditions are given by:

$$u_1^* = \begin{cases} 0, & \text{if } \hat{u}_1 < 0 \\ \hat{u}_1, & \text{if } 0 \leq \hat{u}_1 \leq u_{1max} \\ u_{1max}, & \text{if } \hat{u}_1 > u_{1max} \end{cases}, \quad u_2^* = \begin{cases} 0, & \text{if } \hat{u}_2 < 0 \\ \hat{u}_2, & \text{if } 0 \leq \hat{u}_2 \leq u_{2max} \\ u_{2max}, & \text{if } \hat{u}_2 > u_{2max} \end{cases}$$

and

$$(15) \quad u_3^* = \begin{cases} 0, & \text{if } \hat{u}_3 < 0 \\ \hat{u}_3, & \text{if } 0 \leq \hat{u}_3 \leq 1 \\ 1, & \text{if } \hat{u}_3 > 1 \end{cases}$$

The uniqueness for a small time interval is usual in "two-point" boundary value problems due to opposite time orientations, the state equations have initial conditions, and the adjoint equations have final time conditions. The optimal controls, u_1 , u_2 and u_3 are characterized in terms of the unique solution of the optimality system. \square

4. NUMERICAL SOLUTIONS

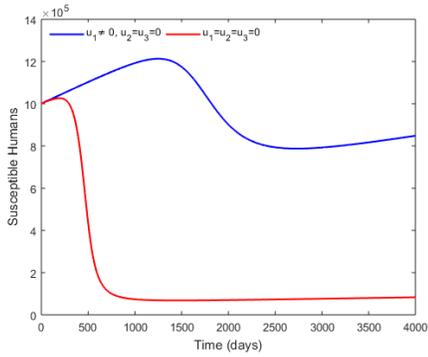
In this section, we carried out numerical simulation of the optimality system as characterized by the model equation (1) together with the adjoint system equation (9) using the forward-backward Runge Kutta fourth order scheme. Basically, we examined the effects of the following control strategies:

- S1: Optimal diagnosis and treatment of exposed individuals (u_1) only;
- S2: Optimal application of chemical mulluscicides on snails (u_2) only;
- S3: Optimal treatment of water by chlorination (u_3) only;

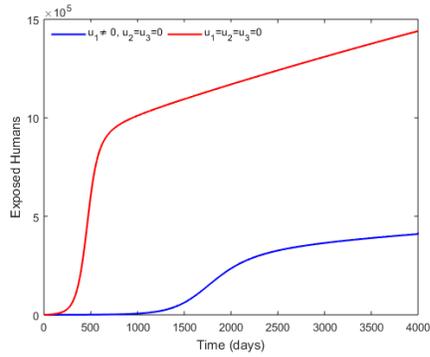
- S4: Optimal diagnosis and treatment of exposed individuals (u_1) and optimal application of chemical mulluscicides on snails (u_2);
- S5: Optimal diagnosis and treatment of exposed individuals (u_1) and optimal treatment of water by chlorination (u_3);
- S6: Optimal application of chemical mulluscicides on snails (u_2) and optimal treatment of water by chlorination (u_3) and
- S7: Optimal diagnosis and treatment of exposed individuals (u_1), optimal application of chemical mulluscicides on snails (u_2) and optimal treatment of water by chlorination (u_3).

The parameter values used in the numerical simulation are presented in table 1. These values are mainly obtained from existing literature and few others are estimated based on the population of and the disease dynamics in The Gambia. The weight constants were theoretically chosen and thus, it is assumed that let $v_1 = 0.6$, $v_2 = 0.3$, $v_3 = 0.4$, $v_4 = 0.9$, $v_5 = 0.1$ and $v_6 = 0.5$. Moreover, u_{1max} is taken as $u_{1max} = 0.8$ and $u_{2max} = 0.4$. Finally, the initial conditions used for the state variables are: $S_h(0) = 1000000$, $E_h(0) = 500$, $I_h(0) = 400$, $T_h(0) = 0$, $S_s(0) = 800000$, $E_s(0) = 400$, $I_s(0) = 200$, $N_m(0) = 200$ and $N_c(0) = 100$.

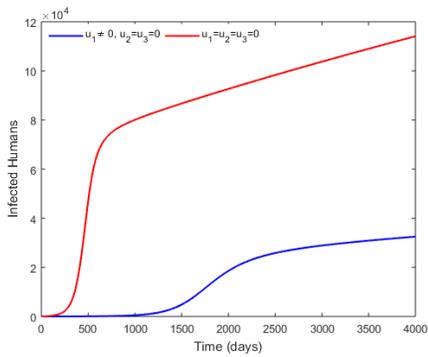
S1 - Optimal diagnosis and treatment of exposed individuals (u_1) only: Here, all the other two optimal controls were neglected i.e. $u_2 = u_3 = 0$, so as to examine the effects of optimal control u_1 . Results in figure 1, figure 2 and figure 3 showed the effects of this control strategy on the various compartments. It can be observed that early diagnosis and treatment of the exposed individuals only will actually slow the disease progression by reducing the rate of progression from exposed to infected individuals thereby mitigating the rate of production of miracidia by infected humans and hence, slowing down the number of snails contracting the disease. This means that the shedding of cercariae will also be drastically reduced. However, this control strategy alone is not sufficient enough to control entirely or in other words, eliminate the disease.



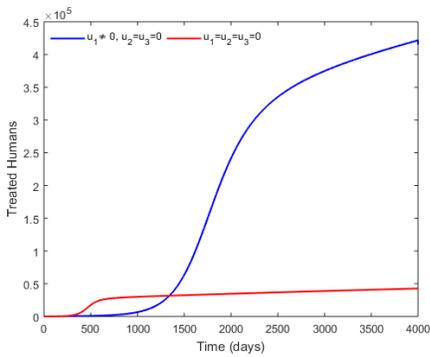
(A) Susceptible humans with u_1 only.



(B) Exposed humans with u_1 only.

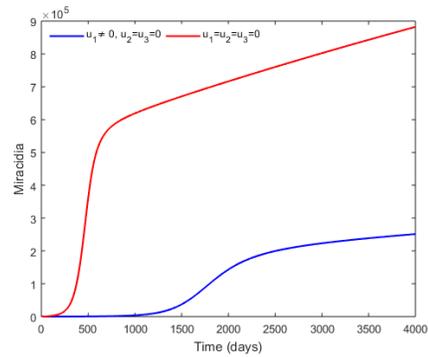


(C) Infected humans with u_1 only.

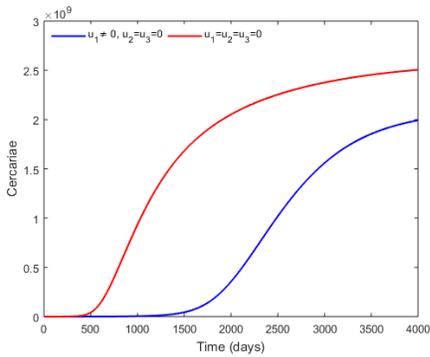


(D) Treated humans with u_1 only.

FIGURE 1. Evolution of the human sub-population with treatment of Exposed humans only

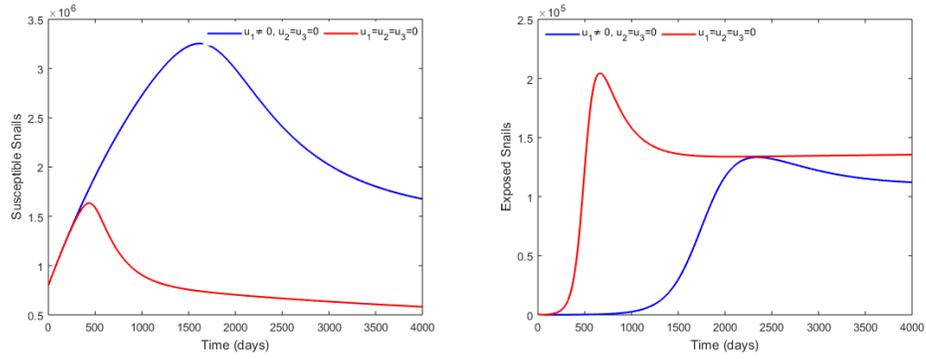


(A) Miracidia sub-population with u_1 only.



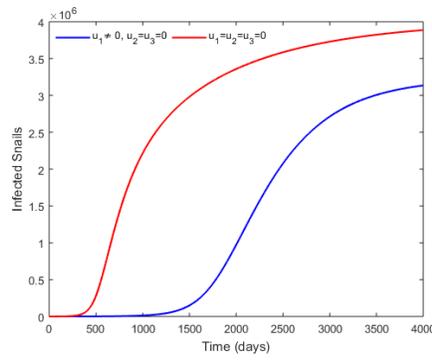
(B) Cercariae sub-population with u_1 only.

FIGURE 2. Evolution of the pathogen sub-population with treatment of Exposed humans only



(A) Susceptible snails with u_1 only.

(B) Exposed snails with u_1 only.



(C) Infected snails with u_1 only.

FIGURE 3. Evolution of the snail sub-population with treatment of Exposed humans only

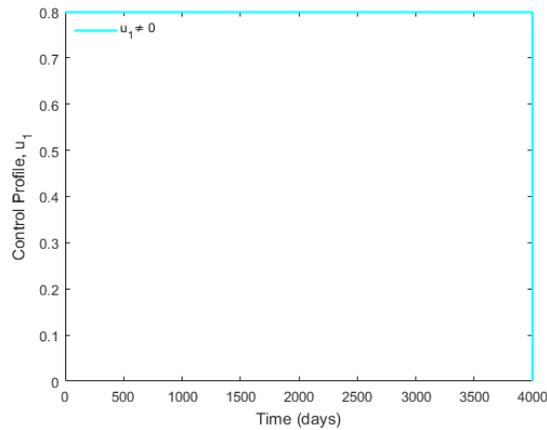


FIGURE 4. The optimal control profile with respect S1

S2 - Optimal application of chemical mulluscicide on snails (u_2) only: By this method, we considered $u_1 = u_3 = 0$ and then examine the influence of u_2 on the optimal control of the spread of the disease. Results in figure 5, figure 6 and figure 7 indicated the swiftness of this control mechanism in eradicating the disease. The strategy seek to stop the production of cercariae by killing the snails which are the intermediate hosts. However, from the figures, we can see the environmental consequences of the application of this control strategy as it may lead to the total extinction of the snail species. In other words, this control strategy is totally non-environmentally friendly, although, it still stand out as one of the quickest ways to eradicate the spread of schistosomiasis. These results are another indication that the spread of the disease is mainly ecological i.e. schistosomiasis spreads faster from snails to humans than from the humans to the snails.

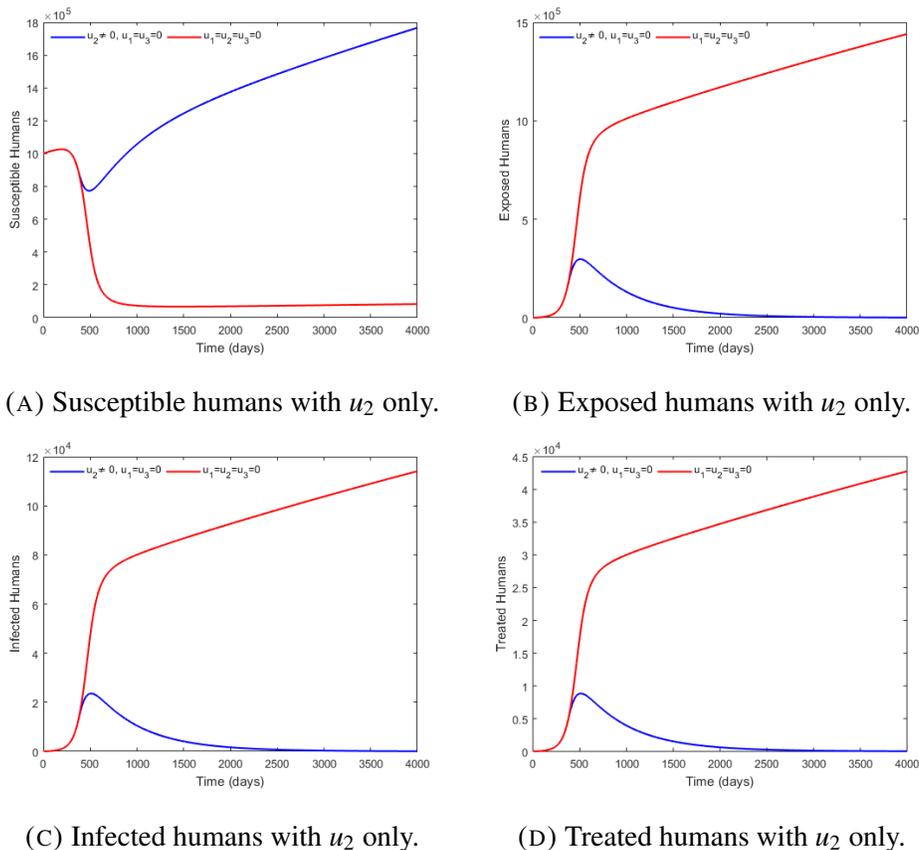
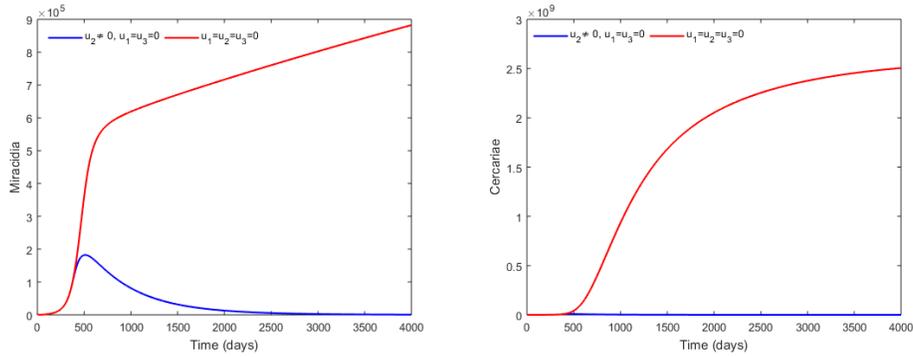
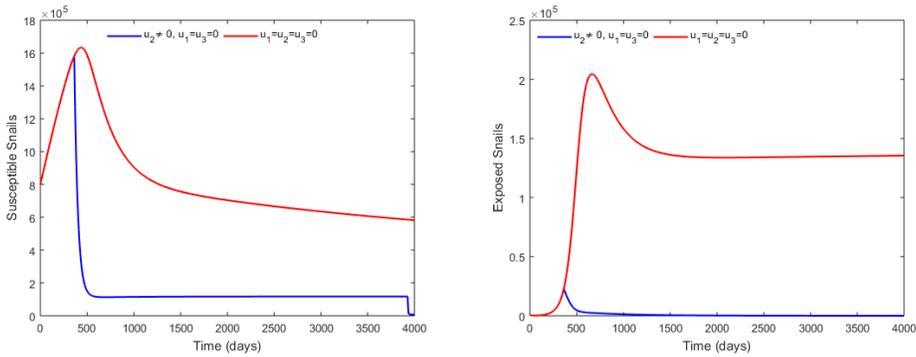


FIGURE 5. Evolution of the human sub-population with the use of chemical mulluscicide only

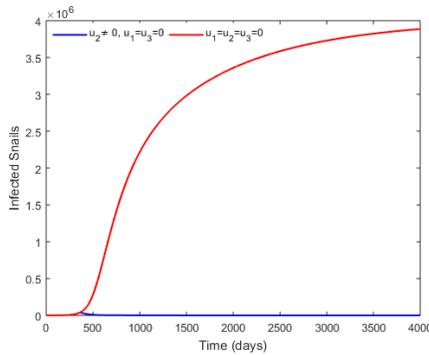


(A) Miracidia sub-population with u_2 only. (B) Cercariae sub-population with u_2 only.

FIGURE 6. Evolution of the pathogen sub-population with the use of chemical mulluscicide only



(A) Susceptible snails with u_2 only. (B) Exposed snails with u_2 only.



(C) Infected snails with u_2 only.

FIGURE 7. Evolution of the snail sub-population with the use of chemical mulluscicide only

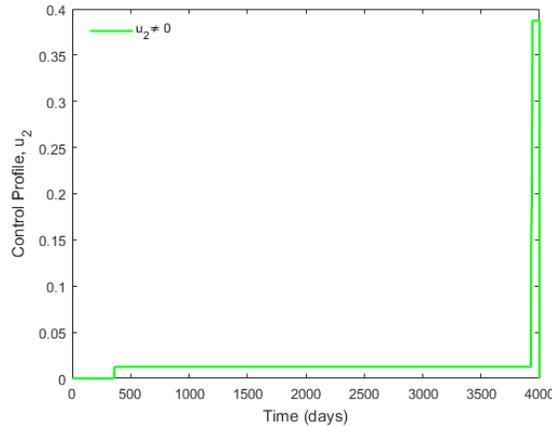


FIGURE 8. The optimal control profile with respect S2

S3 - Optimal treatment of water by chlorination (u_3) only: Here, we considered u_3 in the absence of both u_1 and u_2 . The aim is to investigate the effects of the optimal control u_3 on the progression of schistosomiasis. The graphical results presented in figure 9, figure 10 and figure 11 showed that u_3 is effective in slowing down the transmission of schistosomiasis within the human sub-population. But, since it only kill cercariae, the already exposed individuals will progress to the infected class and thus, join those already shedding eggs for the production of miracidia. This means that more snails (though at a slower rate) will continue to get infected and the production of cercariae will be a continuous process and as a consequence, the disease will possibly continue to spread although at a more slower rate.

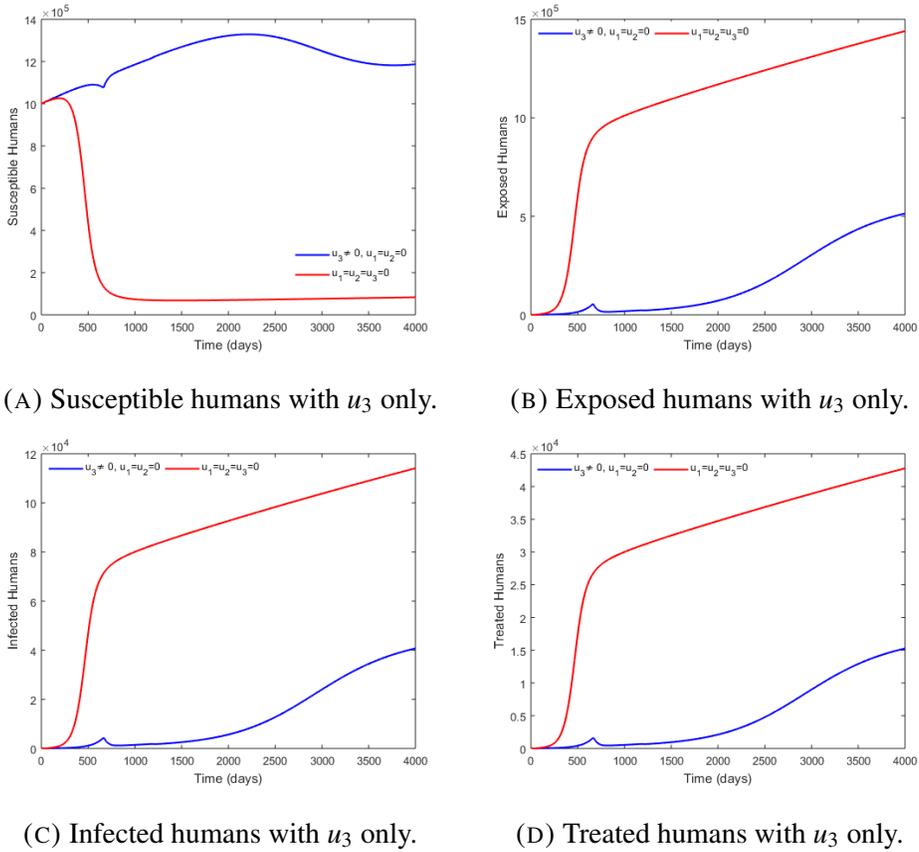


FIGURE 9. Evolution of the human sub-population with treatment of water by chlorination only

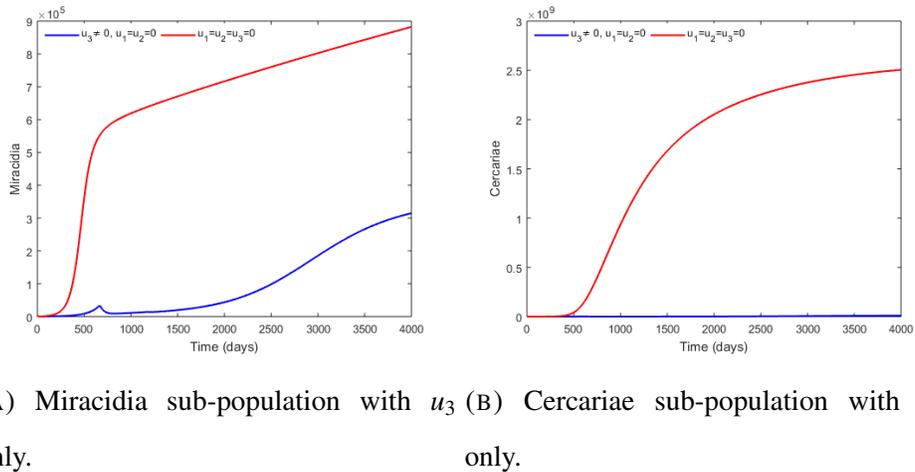
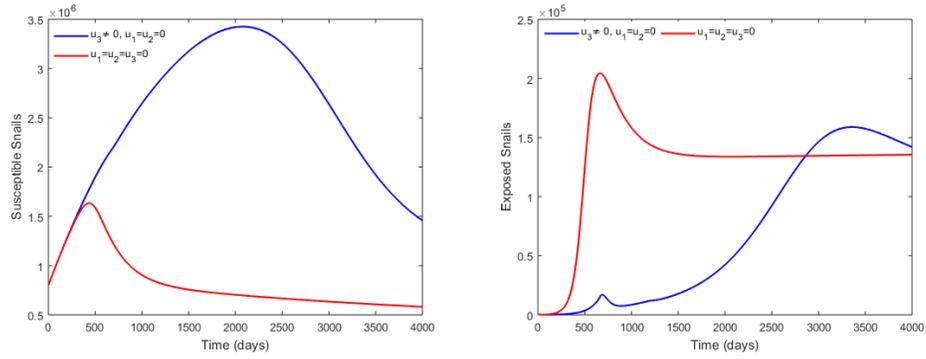
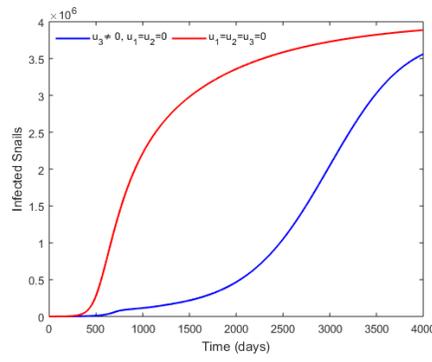


FIGURE 10. Evolution of the pathogen sub-population with treatment of water by chlorination only



(A) Susceptible snails with u_3 only.

(B) Exposed snails with u_3 only.



(C) Infected snails with u_3 only.

FIGURE 11. Evolution of the snail sub-population with treatment of water by chlorination only

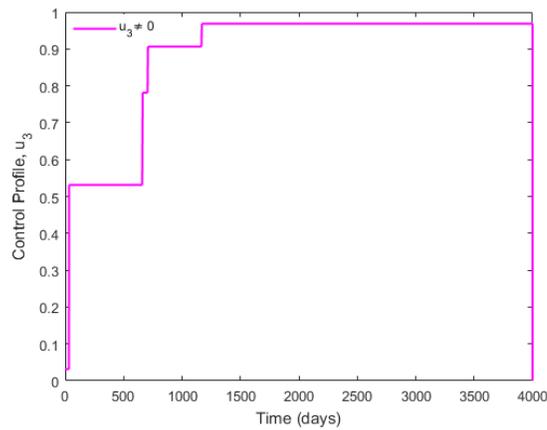
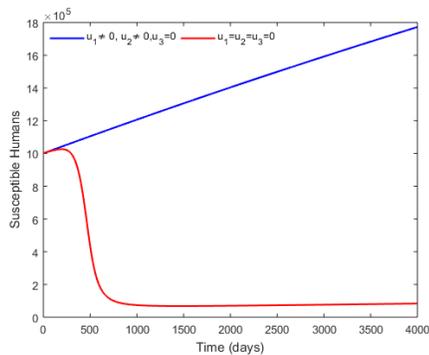


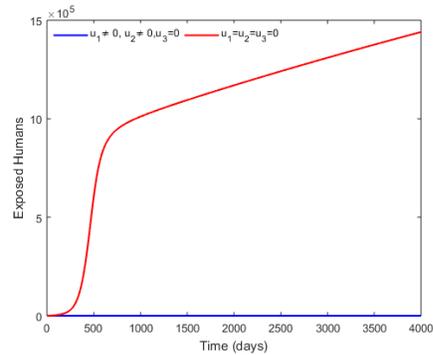
FIGURE 12. The optimal control profile with respect to S_3

S4 - Optimal diagnosis and treatment of exposed individuals (u_1) and optimal application of chemical mulluscicides on snails (u_2). This strategy implements optimal control by early diagnosis and treatment of exposed individuals (u_1) and optimal application of chemical mulluscicides on snails (u_2) only. The graphs in figure 13 , figure 14 and figure 15 show the effects of this optimal control strategy on the dynamics of the disease with respect to the dynamics of the human, snail and the free living miracidia and cercariae sub-populations. The results indicate that the control strategy require high cost (see figure 16) but can eventually lead to the eradication of the disease. Further, the strategy, like strategy S2, will lead to the total extermination of the snail species as shown in figure 15 .

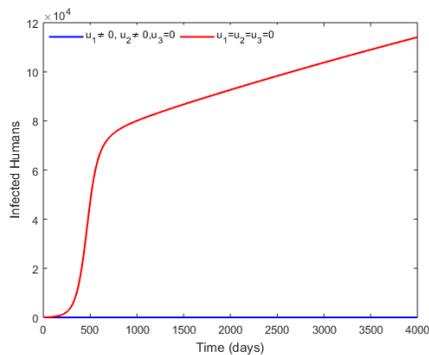


(A) Susceptible humans with u_1 and u_2

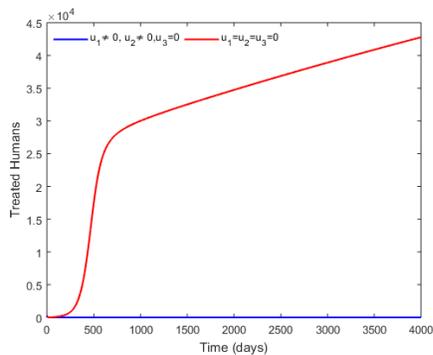
only.



(B) Exposed humans with u_1 and u_2 only.

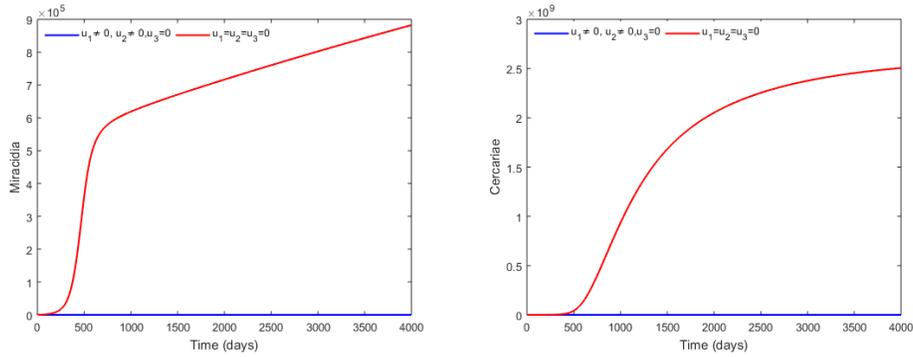


(C) Infected humans with u_1 and u_2 only.



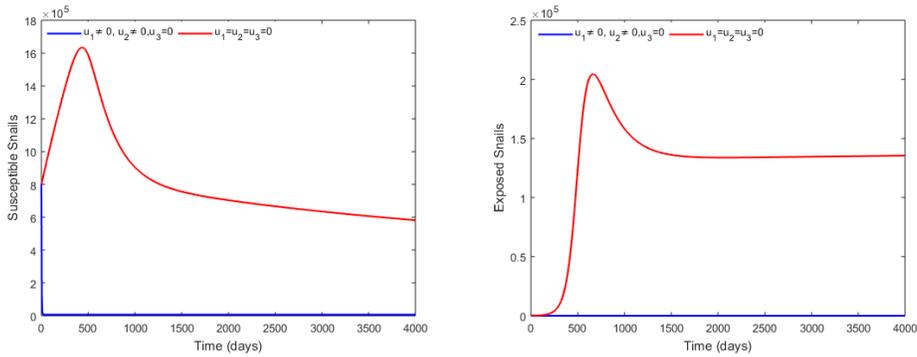
(D) Treated humans with u_1 and u_2 only.

FIGURE 13. Evolution of the human sub-population with treatment of the Exposed humans and use of chemical mulluscicide only.

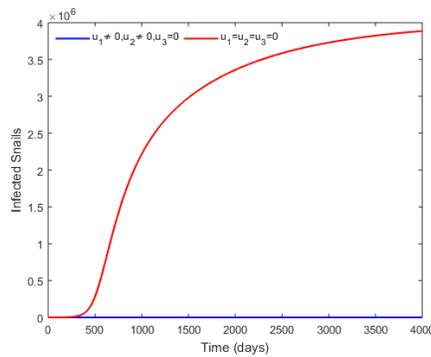


(A) Miracidia sub-population with u_1 and (B) Cercariae sub-population with u_1 and u_2 only.

FIGURE 14. Evolution of the pathogen sub-population with treatment of the Exposed humans and use of chemical mulluscicide only.



(A) Susceptible snails with u_1 and u_2 only. (B) Exposed snails with u_1 and u_2 only.



(C) Infected snails with u_1 and u_2 only.

FIGURE 15. Evolution of the snail sub-population with treatment of the Exposed humans and use of chemical mulluscicide only.

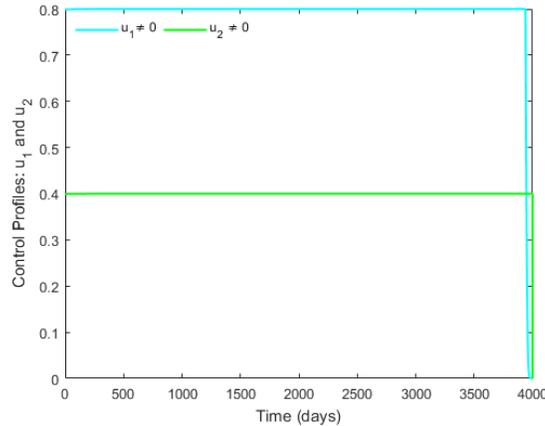
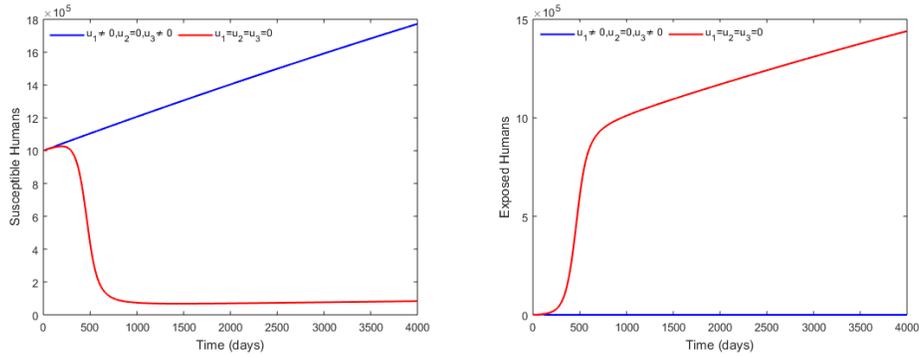
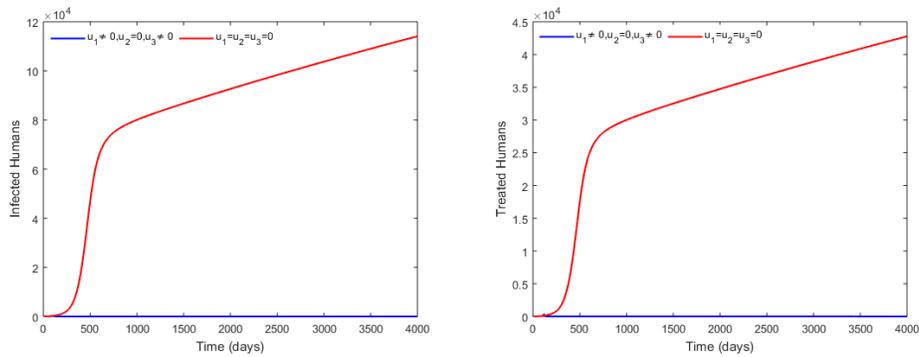


FIGURE 16. The optimal control profiles with respect to S4

S5 - Optimal diagnosis and treatment of exposed individuals (u_1) and optimal treatment of water by chlorination (u_3). This optimal control strategy employed u_1 and u_3 in the absence of the use of chemical molluscicide (u_2). The graphical results presented in figure 17, figure 18 and figure 19 indicate the effects that a combination of u_1 and u_3 will have on the dynamics of the human, snail and the free living miracidia and cercariae sub-populations. Figure 17 show a rapid fall in the infectious human compartments and a steady rise in the susceptible human compartment. Figure 18 show a sudden fall of the free living miracidia, figure 18a and the free living cercariae, figure 18b. Figure 19 equally shows a fall in the exposed and infected snail compartments which give way for a steady rise in the susceptible snail compartment. These results are an indication that implementation of this control strategy will not only eradicate the spread of schistosomiasis, it will, in fact, give way for a healthy snail population. Apparently, this combined optimal control strategy, is both effective and more environmentally friendly.

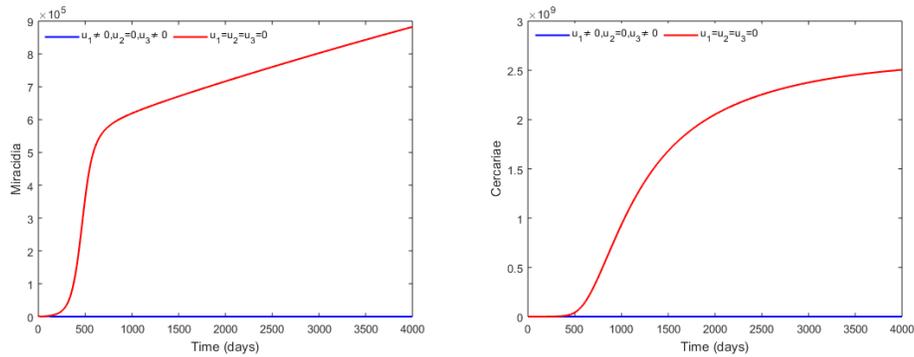


(A) Susceptible humans with u_1 and u_3 only. (B) Exposed humans with u_1 and u_3 only.



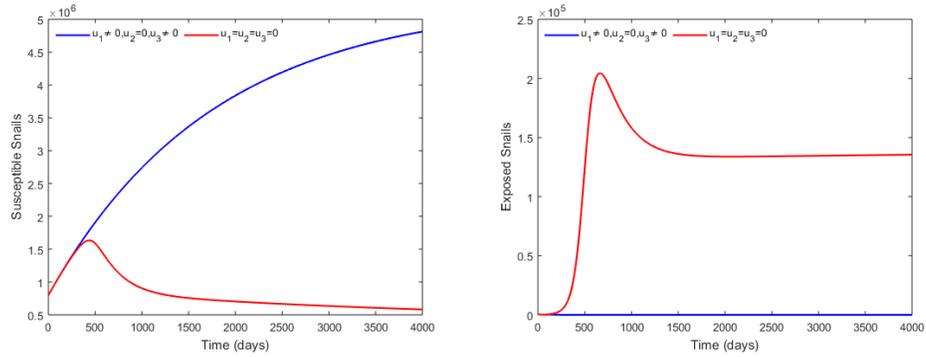
(C) Infected humans with u_1 and u_3 only. (D) Treated humans with u_1 and u_3 only.

FIGURE 17. Evolution of the human sub-population with treatment of the Exposed humans and water by chlorination only.

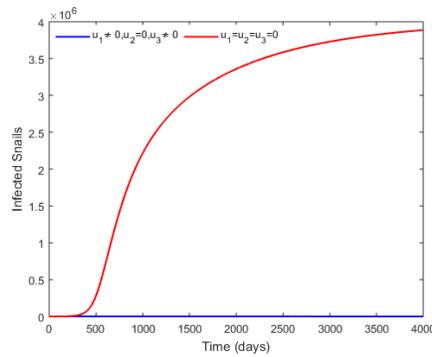


(A) Miracidia sub-population with u_1 and u_3 only. (B) Cercariae sub-population with u_1 and u_3 only.

FIGURE 18. Evolution of the pathogen sub-population with treatment of the Exposed humans and water by chlorination only.



(A) Susceptible snails with u_1 and u_3 only. (B) Exposed snails with u_1 and u_3 only.



(C) Infected snails with u_1 and u_3 only.

FIGURE 19. Evolution of the snail sub-population with treatment of the Exposed humans and water by chlorination only.

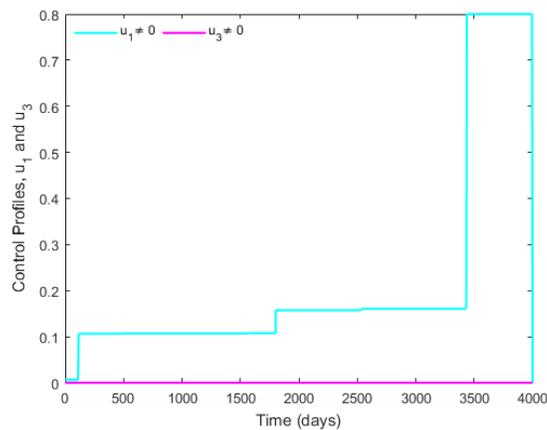
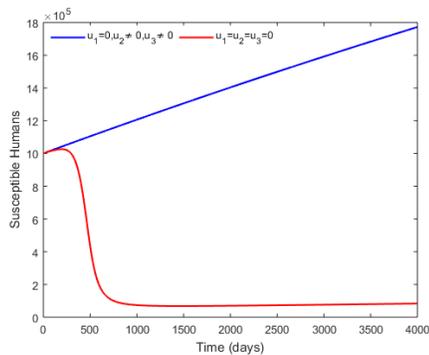
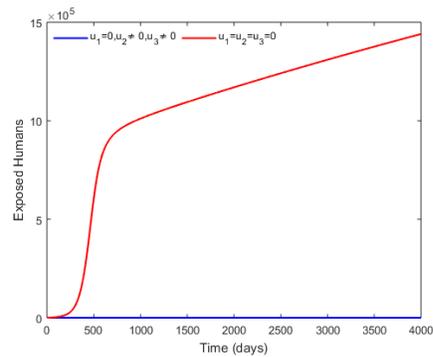


FIGURE 20. The optimal control profiles with respect to S5

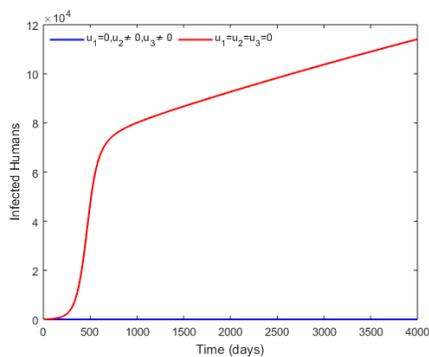
S6 - Optimal application of chemical molluscicides on snails (u_2) and optimal treatment of water by chlorination (u_3). With this strategy, the controls u_2 and u_3 are considered i.e. use of chemical molluscicides on snails and chlorination of water to kill cercariae. The results of this strategy as revealed in figure 21 , figure 22 and figure 23 showed a steady rise in susceptible human sub-population and a sudden fall in the infected human sub-population which indicated the eradication of the disease within the human sub-population, figure 21a and figure 21c. The pathogen sub-populations equally fall rapidly with the implementation of this control strategy, figure 22a and figure 22b. This shows how swift the control strategy can be in eliminating the disease. The results, however, further indicated that the process, similar to what is observed with strategies S2 and S4, will equally lead to the extinction of snails, see figure 23a , figure 23b and figure 23c.



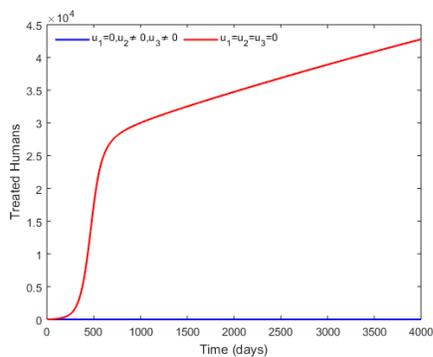
(A) Susceptible humans with u_2 and u_3



(B) Exposed humans with u_2 and u_3 only.

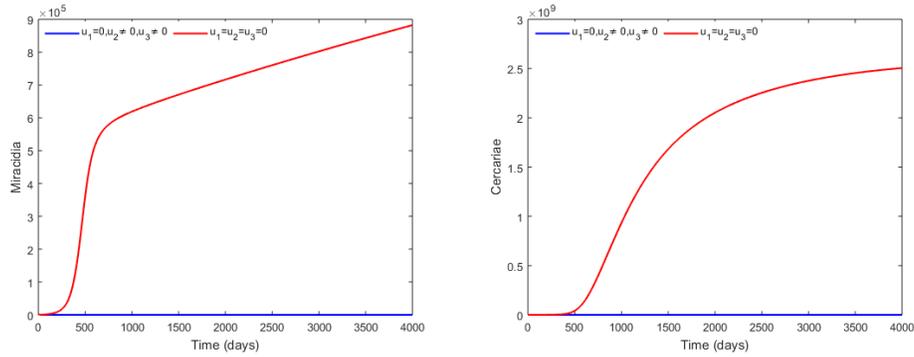


(C) Infected humans with u_2 and u_3 only.



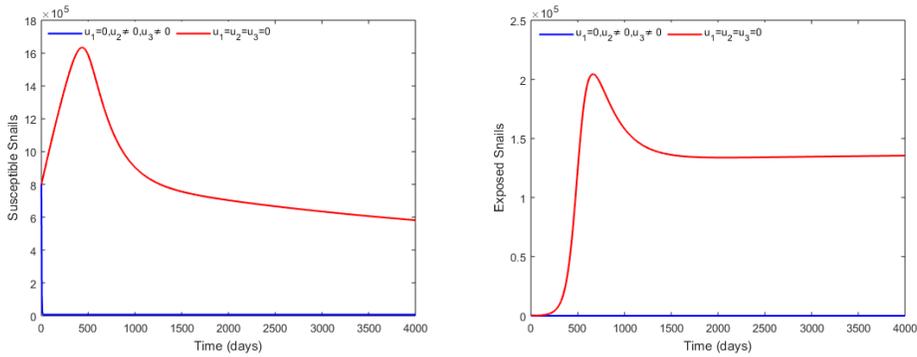
(D) Treated humans with u_2 and u_3 only.

FIGURE 21. Evolution of the human sub-population with the use of chemical molluscicide and treatment water by chlorination only.

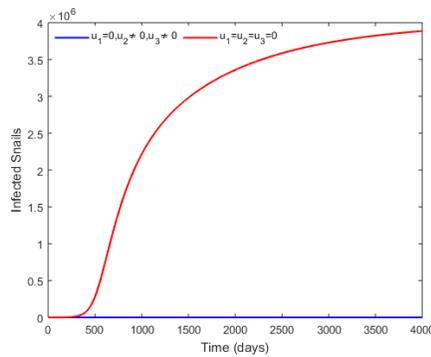


(A) Miracidia sub-population with u_2 and (B) Cercariae sub-population with u_2 and u_3 only.

FIGURE 22. Evolution of the pathogen sub-population the with use of chemical mulluscicide and treatment water by chlorination only.



(A) Susceptible snails with u_2 and u_3 only. (B) Exposed snails with u_2 and u_3 only.



(C) Infected snails with u_2 and u_3 only.

FIGURE 23. Evolution of the snail sub-population with the use of chemical mulluscicide and treatment water by chlorination only.

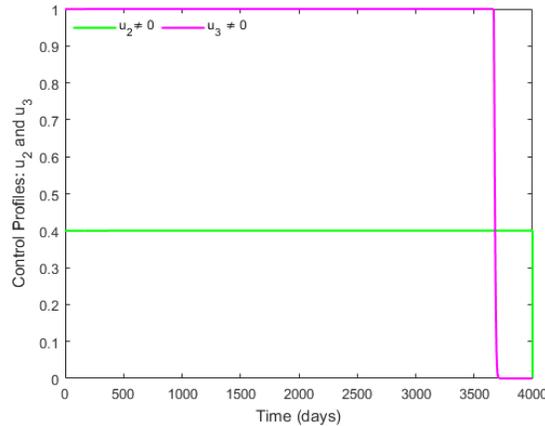
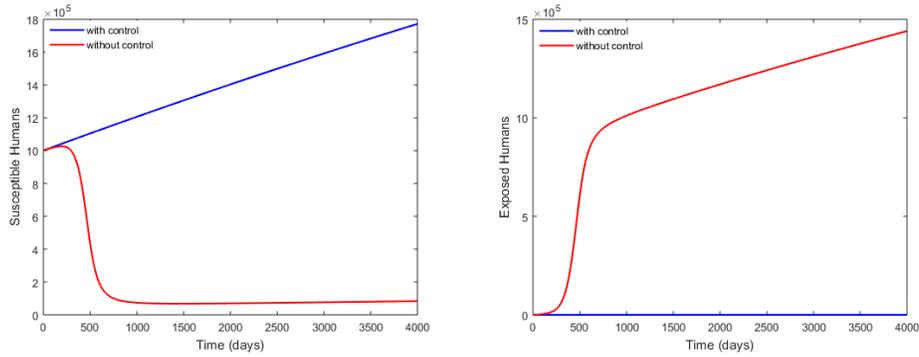


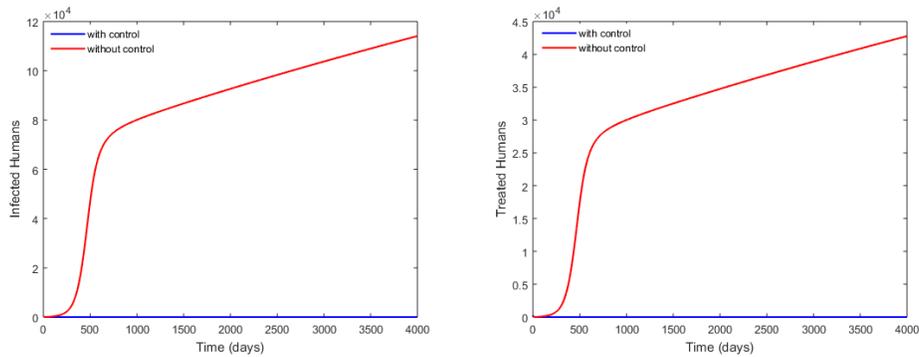
FIGURE 24. The optimal control profiles with respect to S6

S7 - Optimal diagnosis and treatment of exposed individuals (u_1), optimal application of chemical molluscicides on snails (u_2) and optimal treatment of water by chlorination (u_3).

This strategy combines all the three optimal control measures. The results of the implementation of these strategy are seen in figures 25 and 26. This measure is very effective in controlling the spread of schistosomiasis as it leads to the total eradication of the disease. However, the ecological impacts of the implementation of this strategy is highly negative. As observed in relation to strategies S2, S4 and S6, this strategy results in the extinction of snails, see figure 27 . Thus, in order to preserve the ecology by saving the snail species, this control strategy, although very effective, should not be implemented.

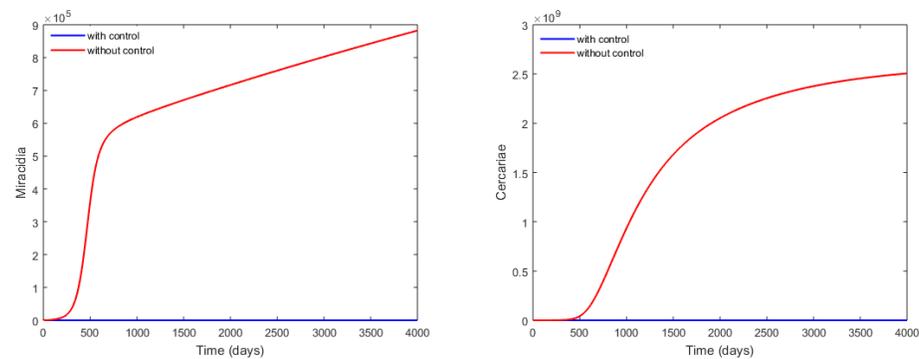


(A) Susceptible humans with optimal control. (B) Exposed humans with optimal control.



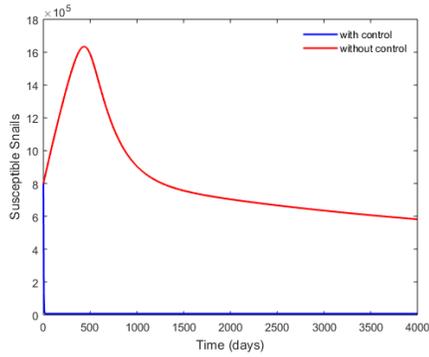
(C) Infected humans with optimal control. (D) Treated humans with optimal control.

FIGURE 25. Evolution of the human sub-population with optimal control.

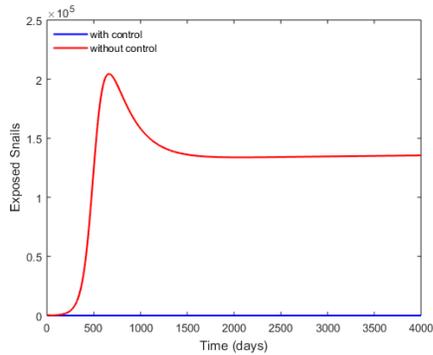


(A) Miracidia sub-population with optimal control. (B) Cercariae sub-population with optimal control.

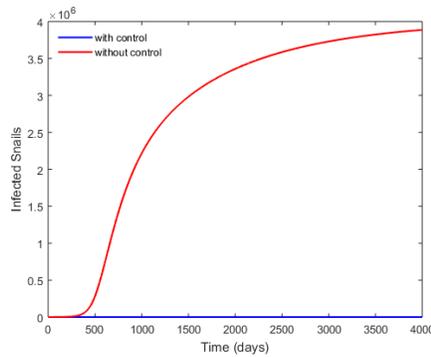
FIGURE 26. Evolution of the pathogen sub-population with optimal control.



(A) Susceptible snails with optimal control.



(B) Exposed snails with optimal control.



(C) Infected snails with optimal control.

FIGURE 27. Evolution of the snail sub-population with optimal control.

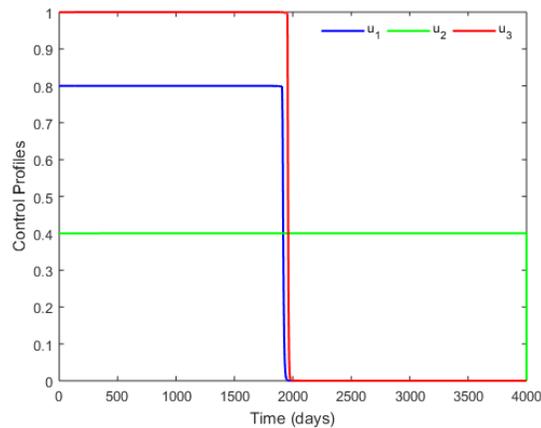


FIGURE 28. The optimal control profiles with respect to S_7

5. CONCLUSION

This paper presents an optimal control problem for the control of schistosomiasis with three time-dependent optimal control measures and a combination of these controls. The existence of the optimal control was established and the Hamiltonian and adjoint equations that characterize the optimal control problem based on the Pontryagin's minimum principle were derived. The optimal control problem was then solved numerically using the forward-backward Runge Kutta scheme. The results from the numerical simulation indicate that within the single control strategies, snail elimination using chemical molluscicide is the most effective control approach. However, the method is very damaging to the ecosystem as it may lead to the total extinction of the snail species. In fact, any control strategy involving using chemical molluscicide to kill snails are very effective but has a negative effect on the ecology as it leads to the extermination snails. This is an indication that the disease transmits faster from snails to humans than from humans to snails as observed in, [8], [9] and [10]. Consequently, we recommend the fifth control strategy (S5), a combination of early diagnosis and treatment of the exposed individuals and water treatment by chlorination. This optimal control strategy according to the results from the numerical simulations does not only eliminate the transmission of schistosomiasis, it also tend to preserve the ecosystem by giving rise to a schistosomiasis free human and snail sub-populations.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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