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MODELLING AFRICAN TRYPANOSOMIASIS IN HUMAN WITH OPTIMAL CONTROL AND COST-EFFECTIVENESS ANALYSIS

HAMENYIMANA EMANUEL GERVAS*, ALFRED K. HUGO

Abstract. Human African Trypanosomiasis (HAT) also known as sleeping sickness, is a neglected tropical vector borne disease caused by trypanosome protozoa transmitted by bites of infected tsetse fly. The basic reproduction number, R_0 derived using the next generation matrix method which shows that the disease persists in the population if the value of $R_0 > 1$. The numerical simulations of optimal control model carried out to determine the control strategy that can combat HAT under the minimum cost. The results indicate that, the use of both education campaign, treatment and insecticides are more efficient and effective to eliminate HAT in African community but too costly. Furthermore, the cost-effectiveness of the control measures (education campaign, treatment and insecticides) were determined using incremental cost-effectiveness ratio (ICER) approach and the results show that, the use of education and treatment of infected people as the best cost effective strategy compared to other strategies.

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1. Introduction

Human African Trypanosomiasis (HAT) is a neglected vector borne disease caused by trypanosome protozoa transmitted by bites of infected tsetse fly; due to sleeping symptoms, the disease is also known as sleeping sickness. About thirty seven (37) sub-Saharan African Countries are reported to be affected by HAT where rural areas are highly affected by the disease due to presence of conducive environments for tsetse flies [15]. HAT is mainly caused by two species

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of protozoa which are Trypanosoma Brucei Gambiense (TBG), which causes the chronic form of HAT in central and western Africa while Trypanosoma Brucei Rhodesiense (TBR), which causes the acute form of the disease in Eastern and southern Africa [9, 31]. TBG is transmitted by riverine tsetse species while TBR is transmitted by savanna tsetse species [9, 31]. Rhodesiense HAT is an acute disease that can lead to death if not treated within 6 months while Gambiense HAT is a slow chronic progressive disease which causes death with an average duration of 3 years. The control of HAT started in $1960s$, however the intensive activities for describing HAT started in 20^{th} century where by many Africans lost their lives [11, 31].

Mathematical Models have been the corner stone to understand and analyze the transmission dynamics of the infectious diseases and suggest possible control measures [4]. Optimal Control model is one of the techniques which have been used by many researchers as a tool to understand the effect and evaluate the control strategies of infectious diseases where it is always aimed to reduce the number of infected individuals by using the control objective functional [21]. Cost effective analysis is also one of the techniques in economic evaluation which compares the costs and health effects of intervention to assess the extend to which it can be regarded as providing value for money; it helps decision makers to determine where to allocate limited health care resources thus is highly needed in cheap control of HAT especially riverine transmitted HAT [33, 34].

In 1988 Rogers, formulated a model to explain the mathematical frame work on transmission of HAT in multiple host populations [17]. Rogers' model was generalized by Hargrove [16], where the new parameter was introduced which allows the tsetse flies to feed off multiple hosts. The model also compared the effectiveness of insecticides treated cattle and trypanocide drugs methods used to treat cattle where it was concluded that insecticides treated cattle strategy is more effective and cheaper to control HAT than the use of trypanocide drugs. In 2013, Kajunguri [18] developed a model which considered a constant population in one of the villages in west Africa by fixing a number of domestic animals, human and tsetse flies, It was founded that, the cattle population contribute to about 92% of the total TBR transmission while the rest 8% is the contributed by human population. It was also observed that, the effective application of insecticides brings about a cost-effective method of control and eliminating the disease [34]

Although, the disease is still a threat to the lives of many sub-Saharan Africa dwellers, has neglected due to its low mortality rate and the poverty of its sufferers [31]. In this paper, we modify the Gervas et al model [31] by including the contact rate and contribution of environment in transmission of HAT. Since the cost-effectiveness analysis is very important in choosing the best control strategy with preference to the other we then analyze the cost-effectiveness of education, treatment and insecticides to obtain the most cheaper and effective strategy in elimination of HAT in Africa.

2. Model Formulation

In this section, mathematical model developed based on the effect of environment and contact rate in transmission of HAT in Africa; the system of differential equations that describes the HAT transmission dynamics is then derived. The modeled population includes human and vector populations. The susceptible human and vector populations are presented as S_H and S_V respectively. The exposed human and vector populations denoted by E_H and E_V respectively which represents the population with the disease however can not transmit to others. The infectious human and vector populations are denoted by I_H and I_V respectively while the variable R_H denotes the recovered human population. The population for both hosts and vectors are assumed to be constant, and tsetse fly cannot recover from the disease. It is also assumed that the transmission of HAT is enhanced by the tsetse biting rate a and effect of environment q, the carrying capacity for human and tsetse fly populations is denoted by k_1 and k_2 respectively. The intrinsic growth rate for human and vector populations is represented by r_1, r_2 respectively. In this model, the human and vector populations

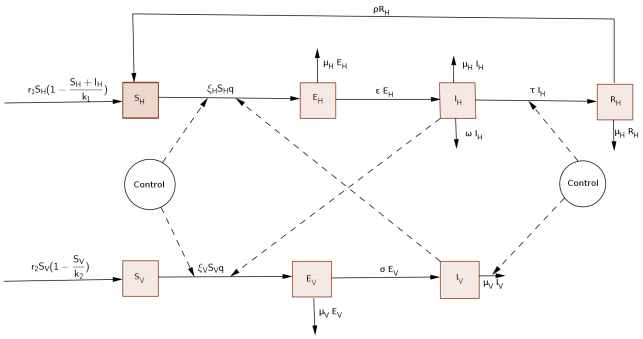

FIGURE 1. Compartmental model for the transmission of Human African Trypanosomiasis.

are assumed to decrease by the natural mortality rate μ_H and μ_V respectively. The parameter ω represents the disease induced death rate for humans while ξ_H and ξ_V are the infection rates for humans and vectors respectively. The parameter σ represents per capita rate of a vector becoming infectious, and the rest of the parameters are explained in Table 1. The rate of infection per susceptible human and tsetse-fly are respectively defined by

$$\xi_H = \frac{ap_H I_V(t)}{N_V(t)}, \qquad \xi_V = \frac{ap_V I_H(t)}{N_H(t)}.$$

Furthermore, the total human and vector populations are defined by $N_H = S_H + E_H + I_H + R_H$ and $N_V = S_V + E_V + I_V$. From the Figure (1) the following differential system is derived,

$$\begin{cases} \frac{dS_H}{dt} & = r_1 S_H(1 - \frac{S_H+I_H}{k_1}) + \rho R_H - \dfrac{ap_H I_V(t)}{N_V(t)} S_H q \\ \frac{dE_H}{dt} & = \dfrac{ap_H I_V(t)}{N_V(t)} S_H q - \varepsilon E_H - \mu_H E_H \\ \frac{dI_H}{dt} & = \varepsilon E_H - \mu_H I_H - \omega I_H - \tau I_H \\ \frac{dR_H}{dt} & = \tau I_H - \rho R_H - \mu_H R_H \\ \frac{dS_V}{dt} & = r_2 S_V(1 - \frac{S_V}{k_2}) - \dfrac{ap_V I_H(t)}{N_H(t)} S_V q \\ \frac{dE_V}{dt} & = \dfrac{ap_V I_H(t)}{N_H(t)} S_V - \mu_V E_V - \sigma E_V \\ \frac{dI_V}{dt} & = \sigma E_V - \mu_V I_V. \end{cases} \tag{1}$$

The system of differential equations (1) is then converted to the system of dimensionless differential equations (2) where the variables are denoted by $s_h = \dfrac{S_H}{N_H}$, $e_h = \dfrac{E_H}{N_H}$, $i_h = \dfrac{I_H}{N_H}$, $r_h = \dfrac{R_H}{N_H}$, $s_v = \dfrac{S_V}{N_V}$, $e_v = \dfrac{E_V}{N_V}$, $i_v = \dfrac{I_V}{N_V}$.
Thus, the model (1) becomes

$$\begin{cases} \frac{ds_h}{dt} & = r_1 s_h(1 - \frac{s_h+i_h}{k_1}) + \rho r_h - aqp_h i_v s_h \\ \frac{de_h}{dt} & = aqp_h i_v s_h - \varepsilon e_h - \mu_h e_h \\ \frac{di_h}{dt} & = \varepsilon e_h - \mu_h i_h - \omega i_h - \tau i_h \\ \frac{dr_h}{dt} & = \tau i_h - \rho r_h - \mu_h r_h \\ \frac{ds_v}{dt} & = r_2 s_v(1 - \frac{s_v}{k_2}) - aqp_v i_h s_v \\ \frac{de_v}{dt} & = aqp_v i_h s_v - \mu_v e_v - \sigma e_v \\ \frac{di_v}{dt} & = \sigma e_v - \mu_v i_v. \end{cases} \tag{2}$$

2.1. Positivity and Boundedness of the Solutions. In this subsection we show that system (2) is epidemiologically and mathematically well-defined in the positive invariant region;

$$R = \left\{ B \in \mathbb{R}^7_+ : n_h \leq r_1 s_h(0)(1 - \frac{s_h(0) + i_h(0)}{k_1}); n_v \leq r_2 s_v(0)(1 - \frac{s_v(0)}{k_2}) \right\}, \tag{3}$$

where $B = (s_h, e_h, i_h, r_h, s_v, e_v, i_v)$.

Theorem 2.1. *There exist a positive invariant region in which the solution $(s_h, e_h, i_h, r_h, s_v, e_v, i_v)$ is contained and bounded.*

Proof. The proof of this Theorem is as in [7, 31]. If we have the solution set $(s_h, e_h, i_h, r_h, s_v, e_v, i_v)$ with the positive initial conditions $(s_h(0), e_h(0), i_h(0),$

TABLE 1. The description of model variables and parameters

Variable	**Description**
s_h	Proportional of Susceptible human population
s_v	Proportional of Susceptible tsetse fly population
e_h,e_v	Proportional of Exposed human and tsetse fly population respectively
i_h,i_v	Proportional of Infectious human and tsetse population respectively
r_h	Proportional of Recovered human population
Parameter	**Description**
π_h	Recruitment rate for human population
π_v	Recruitment rate for tsetse fly population
p_h	Proportion of bites by the infectious vector on susceptible human population
p_v	Proportion of bites by susceptible vector on an Infectious human population
a	The biting rate of the tsetse flies
σ	Per capita rate of a vector becoming infectious
ε	Per capita rate of human becoming infectious
ω	Disease induced death rate
ρ	The rate at which the recovered human can become susceptible again
τ	Recovery rate
μ_h, μ_v	Human and tsetse fly natural death rates respectively
ξ_h	Force of infection for human population
ξ_v	Force of infection for tsetse flies
r	Contact rate
k	Carrying Capacity
q	The contribution of environment to the transmission of HAT

$r_h(0), s_v(0), e_v(0), i_v(0))$, we define

$$n_h(s_h, e_h, i_h, r_h) = s_h(t) + e_h(t) + i_h(t) + r_h(t) \text{ and}$$
$$n_v(s_v, e_v, i_v) = s_v(t) + e_v(t) + i_v(t).$$

The derivatives of n_h and n_v are taken with respect to time (t); we have:

$$\frac{dn_h}{dt} = \frac{ds_h}{dt} + \frac{de_h}{dt} + \frac{di_h}{dt} + \frac{dr_h}{dt},$$
$$= r_1 s_h(1 - \frac{s_h + i_h}{k_1}) - n_h\mu_h - \omega i_h.$$

It follows that

$$\frac{dn_h}{dt} \leq r_1 s_h(1 - \frac{s_h + i_h}{k_1}) - \mu_h n_h.$$

For n_v we get,

$$\begin{aligned}\frac{dn_v}{dt} &= \frac{ds_v}{dt} + \frac{de_v}{dt} + \frac{di_v}{dt}, \\ &= r_2 s_v(1 - \frac{s_v}{k_2}) - (e_v + i_v)\mu_v.\end{aligned}$$

Without loss of generality, it is assumed that

$$\frac{dn_v}{dt} \leq r_2 s_v(1 - \frac{s_v}{k_2}) - \mu_v n_v.$$

The solutions of these differential inequalities are obtained as below:

$$n_h \leq r_1 s_h(0)(1 - \frac{s_h(0) + i_h(0)}{k_1})\left(1 - \exp(-\mu_h t)\right),$$

and

$$n_v \leq r_2 s_v(0)(1 - \frac{s_v(0)}{k_2})(1 - \exp(-\mu_v t).$$

Thus as $t \longmapsto \infty$, we have

$$n_h \leq r_1 s_h(0)(1 - \frac{s_h(0) + i_h(0)}{k_1}) \text{ where } k_1 > 0$$

and

$$n_v \leq r_2 s_v(0)(1 - \frac{s_v(0)}{k_2}) \text{ where } k_2 > 0.$$

This means that the solution of population are bounded and positive implying that the invariant region exists and is defined by

$$R = \left\{ B \in \mathbb{R}^7_+ : n_h \leq r_1 s_h(0)(1 - \frac{s_h(0) + i_h(0)}{k_1}); n_v \leq r_2 s_v(0)(1 - \frac{s_v(0)}{k_2}) \right\}, \tag{4}$$

where $B = (s_h, e_h, i_h, r_h, s_v, e_v, i_v)$. □

3. Model Equilibria and Stability Analysis

3.1. Model Equilibria. The disease free equilibrium (E_0) and endemic equilibrium points (E_*) are respectively calculated as in [31], and are given by

$$E_0 = (k_1, 0, 0, 0, k_2, 0, 0)$$

and

$$E_* = (s_h^*, e_h^*, i_h^*, r_h^*, s_v^*, e_v^*, i_v^*).$$

where,

$$\begin{cases} s_h^* &= \dfrac{\mu_v(\varepsilon+\mu_h)(\mu_h+\omega+\tau)(\mu_v+\sigma)}{\varepsilon a^2 q^2 \sigma p_h p_v k_2 (r_2 - aqp_v i h^*)}, \\ e_h^* &= \dfrac{(\omega+\tau+\mu_h) i_h^*}{\varepsilon}, \\ r_h^* &= \dfrac{\tau i_h^*}{\mu_h+\rho}, \\ s_v^* &= \dfrac{k_2(r_2 - aqp_v i h^*)}{r_2}, \\ e_v^* &= \dfrac{aqp_v k_2 i_h^* (r_2 - aqp_v i h^*)}{\mu_v+\sigma}, \\ i_v^* &= \dfrac{aq\sigma p_v k_2 i_h^* (r_2 - aqp_v i h^*)}{\mu_v(\mu_v+\sigma)} \\ i_h^* &= \dfrac{\varepsilon e_h^*}{\mu_h+\omega+\tau} \end{cases} \tag{5}$$

3.2. Basic Reproduction Number, R_0. The basic reproduction number, R_0, is the number of secondary infections caused by one infected host or vector in a completely susceptible population [2, 31]. The *next generation matrix* approach as done by *Van den Driessche* and *Watmough* in [3, 4, 31] is used to determine the basic reproduction number. By setting

$$F = \begin{pmatrix} 0 & 0 & 0 & ap_h s_h q \\ 0 & 0 & 0 & 0 \\ 0 & ap_v s_v q & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ and}$$

$$V = \begin{pmatrix} \varepsilon+\mu_h & 0 & 0 & 0 \\ -\varepsilon & \mu_h+\omega+\tau & 0 & 0 \\ 0 & 0 & \mu_v+\delta & 0 \\ 0 & 0 & -\delta & \mu_v \end{pmatrix}.$$

The basic reproduction number is taken as the spectral radius of

$$FV^{-1} = \begin{pmatrix} 0 & 0 & \dfrac{aq\delta p_h}{\mu_v(-\delta+\mu_v)} & \dfrac{-aqp_h}{\mu_v} \\ 0 & \dfrac{aqp_v}{\mu_h+\tau+\omega} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Thus,

$$R_0 = \sqrt{\frac{a^2q^2\varepsilon p_h p_v \pi_h \pi_v \sigma}{\mu_v^2\mu_h(\varepsilon+\mu_h)(\sigma+\mu_v)(\mu_h+\tau+\omega)}}.$$

3.3. Stability Analysis. The disease free equilibrium (DFE) and endemic equilibrium (EE) defined by E_0 and E_* are proved to be both locally and globally asymptotically stable by the following theorems:

Theorem 3.1. *The DFE given by E_0 is locally asymptotically stable in the region defined by Equation* (3) *if $R_0 < 1$, otherwise is unstable.*

Proof. The DFE is said to be locally stable if the Jacobian matrix J_{E_0} has all its eigenvalues which are negative; this is possible if the trace of $J_{E_0} < 0$ and determinant of $J_{E_0} > 0$. From system (2), the following Jacobian matrix is obtained;

$$J_{E_0} = \begin{pmatrix} -\mu_h & 0 & 0 & \rho & 0 & 0 & -aqp_h s_h \\ 0 & -(\varepsilon+\mu_h) & 0 & 0 & 0 & 0 & aqp_h s_h \\ 0 & \varepsilon & -(\omega+\tau+\mu_h) & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau & -(\rho+\mu_h) & 0 & 0 & 0 \\ 0 & 0 & -aqp_v s_v & 0 & -\mu_v & 0 & 0 \\ 0 & 0 & aqp_v s_v & 0 & 0 & -(\sigma+\mu_v) & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma & -\mu_v \end{pmatrix}, \tag{6}$$

the trace (tr) of matrix is no doubt negative, that is

$$\begin{aligned} tr(J_{E_0}) &= -(\mu_h+\varepsilon+\mu_h+\mu_h+\omega+\tau+\rho+\mu_h+\mu_v+\sigma+\mu_v+\mu_v), \\ &= -(4\mu_h+3\mu_v+\varepsilon+\omega+\tau+\rho+\sigma) < 0. \end{aligned}$$

We now show if its determinant is greater that zero. The eigenvalues $\lambda_1 = -\mu_h$ and $\lambda_2 = -\mu_v$ of the matrix J_{E_0} are clearly have negative real parts; using the

basic properties of matrix algebra as in [24], the Jacobian matrix is reduced to

$$J_{E_1} = \begin{pmatrix} -(\varepsilon+\mu_h) & 0 & 0 & 0 & aqp_h s_h \\ \varepsilon & -(\omega+\tau+\mu_h) & 0 & 0 & 0 \\ 0 & \tau & -(\rho+\mu_h) & 0 & 0 \\ 0 & aqp_v s_v & 0 & -(\sigma+\mu_v) & 0 \\ 0 & 0 & 0 & \sigma & -\mu_v \end{pmatrix}. \quad (7)$$

From matrix J_{E_1} the eigenvalue $\lambda_3 = -(\rho+\mu_h)$ has negative real part; it is further reduced by using the same reduction techniques to;

$$J_{E_2} = \begin{pmatrix} -(\varepsilon+\mu_h) & 0 & 0 & aqp_h s_h \\ 0 & -(\omega+\tau+\mu_h) & 0 & \dfrac{aqp_h s_h \varepsilon}{\varepsilon+\mu_h} \\ 0 & aqp_v s_v & -(\sigma+\mu_v) & 0 \\ 0 & 0 & \sigma & -\mu_v \end{pmatrix}. \quad (8)$$

The matrix J_{E_2} has eigenvalue $-(\varepsilon+\mu_h)$ with negative real part. The matrix is finally reduced to a 2×2

$$J_{E_3} = \begin{pmatrix} -(\omega+\tau+\mu_h) & \dfrac{aqp_h s_h \varepsilon}{\varepsilon+\mu_h} \\ \dfrac{aqp_v s_v \sigma}{\sigma+\mu_v} & -\mu_v \end{pmatrix}. \quad (9)$$

The trace of matrix J_{E_3} is obvious negative and its determinant is,

$$\begin{aligned} Det(J_{E_3}) &= (\omega+\tau+\mu_h)\mu_v - \frac{aqp_h s_h \varepsilon}{\varepsilon+\mu_h} \times \frac{aqp_v s_v \sigma}{\sigma+\mu_v}, \\ &= (\omega+\tau+\mu_h)\mu_v \left[1 - \frac{a^2 q^2 \varepsilon p_h p_v \pi_h \pi_v \sigma}{\mu_v^2 \mu_h (\varepsilon+\mu_h)(\sigma+\mu_v)(\mu_h+\tau+\omega)}\right] \\ &= (\omega+\tau+\mu_h)\mu_v \left[1 - R_0^2\right] \end{aligned}$$

The determinant of matrix J_{E_3}, is positive if and only if $R_0 < 1$. Therefore the DFE is locally stable if $R_0 < 1$. □

Theorem 3.2. *The EE defined by E_* is globally asymptotically stable if $R_0 > 1$, it is unstable if $R_0 < 1$.*

Proof. The proof is provided based on the Lyapunov function as described in [4, 31]. The Lyapunov function that satisfies the system (2) is defined by,

$$L = N_1\left(s_h - s_h^* - s_h^* \ln\frac{s_h}{s_h^*}\right) + N_2\left(e_h - e_h^* - e_h^* \ln\frac{e_h}{e_h^*}\right) + N_3\left(i_h - i_h^* - i_h^* \ln\frac{i_h}{i_h^*}\right)$$

$$+ N_4\left(s_v - s_v^* - s_v^* \ln\frac{s_v}{s_v^*}\right) + N_5\left(e_v - e_v^* - e_v^* \ln\frac{e_v}{e_v^*}\right) + N_6\left(i_v - i_v^* - i_v^* \ln\frac{i_v}{i_v^*}\right)$$

with $N_i > 0$ to be determined. For all $(s_h, e_h, i_h, r_h, s_v, e_v, i_v) \neq (s_h^*, e_h^*, i_h^*, r_h^*, s_v^*, e_v^*, i_v^*)$ the function L is nonnegative and radially unbounded; thus, we prove that $L' \leq 0$ for all $(s_h, e_h, i_h, r_h, s_v, e_v, i_v) \neq (s_h^*, e_h^*, i_h^*, r_h^*, s_v^*, e_v^*, i_v^*)$. The r_h terms are ignored since if s_h, e_h, i_h are globally stable then $r_h \longrightarrow 0$ at any time t and EE is globally stable. The derivative of L with respect to time (t) is determined and replace the derivatives $s_h^{'}, e_h^{'}, i_h^{'}, r_h^{'}, s_v^{'}, e_v^{'}, i_v^{'}$ with system (2), then we have:

$$\begin{aligned}
L^{'} &= N_1\left(1-\frac{s_h^*}{s_h}\right)\left[r_1 s_h(1-\frac{s_h+i_h}{k_1}) - aqp_h i_v s_h\right] \\
&+ N_2\left(1-\frac{e_h^*}{e_h}\right)\left[aqp_h i_v s_h - (\mu_h+\varepsilon)e_h\right] \\
&+ N_3\left(1-\frac{i_h^*}{i_h}\right)\left[\varepsilon e_h - (\omega+\tau+u_h)i_h\right] \\
&+ N_4\left(1-\frac{s_v^*}{s_v}\right)\left[r_2 s_v(1-\frac{s_v}{k_2}) - aqp_v i_h s_v\right] \\
&+ N_5\left(1-\frac{e_v^*}{e_v}\right)\left[aqp_v i_h s_v - (\mu_v+\sigma)e_v\right] \\
&+ N_6\left(1-\frac{i_v^*}{i_v}\right)\left[\sigma e_v - u_v i_v\right].
\end{aligned}$$

By supposing $N_1 = N_2$ and $N_4 = N_5$, we have:

$$\begin{aligned}
L' &= N_1 r_1 s_h - N_1 r_1 s_h\frac{s_h+i_h}{k_1} - N_1 s_h^* r_1 + N_1 r_1 s_h^*\frac{s_h+i_h}{k_1} + N_1 s_h^* aqp_h i_v \\
&- N_2 e_h(\mu_h+\varepsilon) - N_2\frac{e_h^*}{e_h}aqp_h i_v s_h + N_2 e_h^*(\mu_h+\varepsilon) + N_3\varepsilon e_h - N_3(\omega+\tau+\mu_h)i_h \\
&- N_3\frac{i_h^*}{i_h}\varepsilon e_h + N_3 i_h^*(\omega+\tau+\mu_h) + N_4 r_2 s_v - N_4 r_2\frac{s_v^2}{k_2} - N_4 s_v^* r_2 + N_4 s_v^* r_2\frac{s_v}{k_2} \\
&+ N_4 s_v^* aqp_v i_h - N_5(\mu_v+\sigma)e_v - N_5\frac{e_v^*}{e_v}(aqp_v i_h s_v) + N_5 e_v^*(\mu_v+\sigma) + N_6\sigma e_v \\
&- \mu_v i_v N_6 - N_6\frac{i_v^*}{i_v}\sigma e_v + N_6\mu_v i_v^*.
\end{aligned}$$

At endemic equilibrium, we assume that $s_h = s_h^*, e_h = e_h^*, i_h = i_h^*, s_v = s_v^*, e_v = e_v^*$ and $i_v = i_v^*$ thus, the value of L' is indeed equal to zero.
Therefore, $L' = 0$ for all $(s_h, e_h, i_h, r_h, s_v, e_v, i_v) \neq (s_h^*, e_h^*, i_h^*, r_h^*, s_v^*, e_v^*, i_v^*)$ implying that the endemic equilibrium is globally asymptotically stable if $R_0 > 1$. □

4. Application of Optimal Control to HAT Model

In this section, the Pontryagin's Maximum Principle is used to determine conditions necessary to facilitate the existence of optimal control in human and tsetse fly populations in the transmission dynamics of HAT. Our objective is to

minimize the number of HAT infected individuals as well as tsetse fly in community at a minimal cost by applying preventive strategies. The control $u_1(t)$ is the preventive effort made to human population through education campaign; this intends to educate community members on proper preventive measures. The control $u_2(t)$ is the effort on curative measures which achieved by treating the infected people . The third control $u_3(t)$ applied is insecticides which intends to minimize tsetse flies in community. Following the above discussion, the system (2) is now converted to optimal control model defined by the system (10) as follows

$$\begin{cases} \frac{ds_h}{dt} &= r_1 s_h(1-\frac{s_h+i_h}{k_1}) + \rho r_h - (1-u_1)aqp_h i_v s_h \\ \frac{de_h}{dt} &= (1-u_1)aqp_h i_v s_h - \varepsilon e_h - \mu_h e_h \\ \frac{di_h}{dt} &= \varepsilon e_h - \mu_h i_h - \omega i_h - u_2 \tau i_h \\ \frac{dr_h}{dt} &= u_2 \tau i_h - \rho r_h - \mu_h r_h \\ \frac{ds_v}{dt} &= r_2 s_v(1-\frac{s_v}{k_2}) - (1-u_1)aqp_v i_h s_v \\ \frac{de_v}{dt} &= (1-u_1)aqp_v i_h s_v - \mu_v e_v - \sigma e_v \\ \frac{di_v}{dt} &= \sigma e_v - u_3 \mu_v i_v, \end{cases} \tag{10}$$

subject to the initial conditions $s_h \geq 0, e_h \geq 0, i_h \geq 0, r_h \geq 0, s_v \geq 0, e_v \geq 0, i_v \geq 0$. Thus, the control $u_1(t), u_2(t), u_3(t)$ are bounded Lebesgue measurable functions on the time horizon $[0,T]$, such that $U = u_i : 0 \leq u_i(t) \leq 1$, for $i = 1,2,3$. Mathematically, we analyze the optimal control problem whose objective function is defined over a fixed time horizon $[0,T]$ as,

$$\begin{aligned} &J(u_1,u_2,u_3) \\ &= \int_0^T \left(M_1 e_h + M_2 i_h + M_3 e_v + M_4 i_v + \frac{1}{2}b_1 u_1^2 + \frac{1}{2}b_2 u_2^2 + \frac{1}{2}b_3 u_3^2 \right) dt, \end{aligned} \tag{11}$$

subject to the state equations in system (10). The constants $M_1, M_2,$ and M_3, are positive relative weights of controlling exposed human, infected human, exposed vector and infected vector populations respectively while b_1, b_2, b_3 are positive relative weights for the regularization of optimal control. The quadratic nature of the cost function aids to clarify the nonlinear behavior of cost effectiveness application. The term $\frac{1}{2}b_1 u_1^2$ represents the control cost of education campaign to human population, $\frac{1}{2}b_2 u_2^2$ represents the control cost associated with infected human treatment and $\frac{1}{2}b_3 u_3^2$ presents the control cost associated with application of insecticides. Therefore, the optimal control (u_1^*, u_2^*, u_3^*) such that
$J(u_1^*, u_2^*, u_3^*) = \min_U J(u_1, u_2, u_3)$,
where $U = \{u_i$ is Lebesgue measurable on [0, T] and $0 \leq u_i \leq 1$ for $i = 1,2,3\}$.
The Pontryagin's maximum principle converts the control set U into a problem of minimizing the Hamiltonian H, point wise with respect to u_1, u_2, u_3. The

Hamiltonian function is therefore defined as

$$H = M_1 e_h + M_2 i_h + M_3 e_v + M_4 i_v + \frac{1}{2} b_1 u_1^2 + \frac{1}{2} b_2 u_2^2 + \frac{1}{2} b_3 u_3^2 + \lambda_{s_h} \frac{ds_h}{dt} + \lambda_{e_h} \frac{de_h}{dt} + \lambda_{i_h} \frac{di_h}{dt} + \lambda_{r_h} \frac{dr_h}{dt} + \lambda_{s_v} \frac{ds_v}{dt} + \lambda_{e_v} \frac{de_v}{dt} + \lambda_{i_v} \frac{di_v}{dt},$$

where $\lambda_{s_h}, \lambda_{e_h}, \lambda_{i_h}, \lambda_{r_h}, \lambda_{s_v}, \lambda_{e_v}, \lambda_{i_v}$ are co-state variables (adjoint variables).

4.1. Existence of an optimal control. The existence of an optimal control for the state system is checked by using the results obtained by Fleming and Rishel [38] through the following theorem.

Theorem 4.1. *Let the optimal control problem that minimizes the objective functional J be defined over a time horizon $[0, T]$. If the objective function is defined on a set of bounded and Lebesgue measurable control u and subjected to the dynamic constraint of some state equations, then there exists an optimal solution u^* such that $\mathbb{J}(u^*) = \min_U u$ provided that the following conditions hold:*

(i) The control set is convex and closed.

(ii) The right-hand side of the state system is bounded by a linear function in the state and control variable.

(iii) The state variables used in the system (10), together with their control variables are not empty.

(iv) There exist some constants $x_1, x_2 > 0$ and $y > 1$, for which the integrand of the objective function is convex and satisfies the boundary condition:

$$J(u) = x_1 \Big(\sum_{i=1}^{n} |u_i|^2 \Big)^{\frac{y}{2}} - x_2.$$

The reader is therefore advised to go through the proof of the theorem 4.1 from the book of Fleming and Rishel's [38] entitled Deterministic and Stochastic optimal control, pages 62, 69 and Lenhart [37]. Conversely, for the analysis of particular paper, the conditions that guarantees the existence of an optimal solution for the objective functional are verified.

Consider an optimal control problem described by Equation (11), which is subject to the state constraint given by system (10).

(1) By definition, the control variables u_1, u_2, u_3 are convex and closed.
(2) Clearly, the solutions of the state system are bounded since the state functions are linear with respect to the control variables. Hence, the second condition is satisfied.
(3) It is obvious that the state and our corresponding set of control variables U in the system (10) are presumed bounded and not empty.
(4) Since the state equations are bounded, we can find some positive constants $a_1, a_2 > 0$ and $b > 1$, for which the integrand of the objective functional is convex and satisfies

$$M_1 e_h + M_2 i_h + M_3 e_v + M_4 i_v + \frac{1}{2} b_1 u_1^2 + \frac{1}{2} b_2 u_2^2 + \frac{1}{2} b_3 u_3^2 \geq a_1 \Big(\sum_{i=1}^{3} |u_i|^2 \Big)^{\frac{b}{2}} - a_2.$$

Therefore, it worth to be concluded that there exists an optimal solution which lies between 0 and 1 that minimizes the objective functional articulated in (11).

4.2. Necessary Optimality Conditions. The optimality condition of the solution of the model, is established by the following theorem.

Theorem 4.2. *Let u_i be the set of optimal control and X_i be the corresponding solution of the set of equations that minimizes the objective function J over the set of controls, then there exist λ_i adjoint variables such that optimality system is*

$$\begin{cases} \dfrac{d\lambda_X(t)}{dt} = \dfrac{-\partial H}{dX} \\ \\ \lambda_X(T) = 0 \\ \\ \dfrac{\partial H}{\partial u} = 0. \end{cases}$$

By applying Pontryagin's maximum principle, the following adjoint system obtained with corresponding optimal solutions of the state equations:

$$\begin{cases} \frac{d\lambda_{s_h}}{dt} & = \left(r_1 \left(1 - \frac{s_h + i_h}{k_1} \right) - \frac{r_h s_h}{k_1} - (1 - u_1)\, aqp_h i_v \right) \lambda_{s_h} - (1 - u_1)\, aqp_h i_v\, \lambda_{e_h} \\ \frac{d\lambda_{e_h}}{dt} & = (\epsilon + \mu_h)\, \lambda_{e_h} - \epsilon\, \lambda_{i_h} - M_1 \\ \frac{d\lambda_{i_h}}{dt} & = \frac{r_h s_h\, \lambda_{s_h}}{k_1} + (\tau\, u_2 + \omega + \mu_h)\, \lambda_{i_h} - u_2 \tau\, \lambda_{r_h} + (1 - u_1)\, aqp_v s_v\, \lambda_{s_v} \\ & \quad - (1 - u_1)\, aqp_v s_v\, \lambda_{e_v} - M_2 \\ \frac{d\lambda_{r_h}}{dt} & = \rho\, \lambda_{s_h} + (\rho + \mu_h)\, \lambda_{r_h} \\ \frac{d\lambda_{s_v}}{dt} & = -\left(r_2 \left(1 - \frac{s_v}{k_2} \right) - \frac{r_2 s_v}{k_2} - (1 - u_1)\, aqp_v i_h \right) \lambda_{s_v} - (1 - u_1)\, aqp_v i_h\, \lambda_{e_v} \\ \frac{d\lambda_{e_v}}{dt} & = (\mu_v + \sigma)\, \lambda_{e_v} - \sigma\, \lambda_{i_v} - M_3 \\ \frac{d\lambda_{i_v}}{dt} & = (1 - u_1)\, aqp_h s_h\, \lambda_{s_h} - (1 - u_1)\, aqp_h s_h\, \lambda_{e_h} + u_3 \mu_v \lambda_{i_v} - M_4 \end{cases} \tag{12}$$

Through Pontryagin's maximum principle, the optimality system for the optimal control problem obtained. Further more, the optimality system involves the state equations of the system (10) including initial conditions $s_h \geq 0, e_h \geq 0, i_h \geq 0, r_h \geq 0, s_v \geq 0, e_v \geq 0, i_v \geq 0$, together with its adjoint (co-state) equations (12). Consequently, the adjoint system bounded by final values or transversality conditions as

$$\lambda s_h(T) = \lambda e_h(T) = \lambda i_h(T) = \lambda r_h(T) = \lambda s_v(T) = \lambda e_v(T) = \lambda i_v(T) = 0.$$

4.3. Characterization of the Optimal Control. The optimal solution for the Hamiltonian (H) is evaluated through the partial derivative of the Hamiltonian (H) with respect to the control (u_1, u_2, u_3). The optimal solution is obtained by solving $\frac{\partial H}{\partial u_i} = 0$ for $i = 1, 2, 3$ giving the following values

$$\begin{aligned} u_1 &= \frac{(\lambda_{e_h} - \lambda_{s_h})aqp_h i_v s_h + (\lambda_{e_v} - \lambda_{s_v})aqp_v i_h s_v}{k_1} \\ u_2 &= \frac{(\lambda_{i_h} - \lambda_{r_h})\tau i_h}{k_2} \\ u_3 &= \frac{\lambda_{s_v}\mu_v s_v + \lambda_{e_v}\mu_v e_v + \lambda_{i_v}\mu_v i_v}{k_3}. \end{aligned}$$

Therefore the solution is characterized as

$$\begin{aligned} u_1^* &= \min\{1, \max\{0, \frac{(\lambda_{e_h} - \lambda_{s_h})aqp_h i_v s_h + (\lambda_{e_v} - \lambda_{s_v})aqp_v i_h s_v}{k_1}\}\} \\ u_2^* &= \min\{1, \max\{0, \frac{(\lambda_{i_h} - \lambda_{r_h})\tau i_h}{k_2}\}\} \\ u_3^* &= \min\{1, \max\{0, \frac{\lambda_{s_v}\mu_v s_v + \lambda_{e_v}\mu_v e_v + \lambda_{i_v}\mu_v i_v}{k_3}\}\}. \end{aligned}$$

4.4. Uniqueness of the Optimal Control Solution. In this subsection, the uniqueness of the optimal control solution is evaluated following the method applied by Joshi et al [39]. Thus combining system (10) together with the optimality system results to;

$$\begin{cases} s_h = p_1(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ e_h = p_2(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ i_h = p_3(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ r_h = p_4(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ s_v = p_5(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ e_v = p_6(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ i_v = p_7(t, s_h, e_h, i_h, s_v, e_v, i_h) \\ s_h(0), e_h(0), i_h(0), r_h(0), s_v(0), e_v(0), i_v(0), \\ s_h(T), e_h(T), i_h(T), r_h(T), s_v(T), e_v(T), i_v(T) \text{ and } t \text{ is fixed.} \end{cases} \tag{13}$$

where $s_h \in R^{ni}, e_h \in R^{ni}, i_h \in R^{ni}, r_h \in R^{ni}, s_v \in R^{ni}, e_v \in R^{ni}, i_v \in R^{ni}$ for $i = 1, 2, 3, 4, 5, 6, 7$ as dimension of vector space R^{ni} and

$$\begin{cases} q_1 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n1} \\ q_2 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n2} \\ q_3 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n3} \\ q_4 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n4} \\ q_5 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n5} \\ q_6 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n6} \\ q_7 = R \times R^{n1} \times R^{n2} \times R^{n3} \times R^{n4} \times R^{n5} \times R^{n6} \times R^{n7} \longrightarrow R^{n7} \end{cases} \tag{14}$$

are continuous.

Theorem 4.3. *Given that $q_1, q_2, q_3, q_4, q_5, q_6, q_7$ are bounded, satisfying Lipschitz condition in relation to $s_h, e_h, i_h, s_v, e_v, i_v$ with constant $L > 0$ then the solution of 13 are unique if the final time, T is sufficiently small.*

Proof. Assume that the system (13) has two solutions;

$s_{h1}(t), e_{h1}(t), i_{h1}(t), s_{v1}(t), e_{v1}(t), i_{v1}(t)$ and $s_{h2}(t), e_{h2}(t), i_{h2}(t), s_{v2}(t), e_{v2}(t), i_{v2}(t)$. Using the approach of Maksimov [40] by applying Lipschitz condition for q_1 we obtain

$$\begin{aligned} &\|s_{h1}(t) - s_{h2}(t)\| \\ &\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\ &+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| \\ &+ \|i_{v1}(m) - i_{v2}(m)\|)dm \end{aligned}$$

Applying Lipschitz condition for q_2 we get

$$\begin{aligned} &\|e_{h1}(t) - e_{h2}(t)\| \\ &\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\ &+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| + \|i_{v1}(m) \\ &- i_{v2}(m)\|)dm \end{aligned}$$

Similarly applying Lipschitz condition for $q_3 - q_7$ we get

$$\begin{aligned} &\|i_{h1}(t) - i_{h2}(t)\| \\ &\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\ &+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| + \|i_{v1}(m) \\ &- i_{v2}(m)\|)dm \end{aligned}$$

$$\begin{aligned}
&\|r_{h1}(t) - r_{h2}(t)\| \\
&\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\
&+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| + \|i_{v1}(m) \\
&- i_{v2}(m)\|)dm
\end{aligned}$$

$$\begin{aligned}
&\|s_{v1}(t) - s_{v2}(t)\| \\
&\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\
&+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| \\
&+ \|i_{v1}(m) - i_{v2}(m)\|)dm
\end{aligned}$$

$$\begin{aligned}
&\|e_{v1}(t) - e_{v2}(t)\| \\
&\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\
&+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| \\
&+ \|i_{v1}(m) - i_{v2}(m)\|)dm
\end{aligned}$$

$$\begin{aligned}
&\|i_{v1}(t) - i_{v2}(t)\| \\
&\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\
&+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| \\
&+ \|i_{v1}(m) - i_{v2}(m)\|)dm
\end{aligned}$$

By adding the above equations, we have

$$\begin{aligned}
&\|s_{h1}(t) - s_{h2}(t)\| + \|e_{h1}(t) - e_{h2}(t)\| + \|i_{h1}(t) - i_{h2}(t)\| + \|r_{h1}(t) - r_{h2}(t)\| \\
&+ \|s_{v1}(t) - s_{v2}(t)\| + \|e_{v1}(t) - e_{v2}(t)\| + \|i_{v1}(t) - i_{v2}(t)\| \\
&\leq \int_0^T L(\|s_{h1}(m) - s_{h2}(m)\| + \|e_{h1}(m) - e_{h2}(m)\| + \|i_{h1}(m) - i_{h2}(m)\| \\
&+ \|r_{h1}(m) - r_{h2}(m)\| + \|s_{v1}(m) - s_{v2}(m)\| + \|e_{v1}(m) - e_{v2}(m)\| \\
&+ \|i_{v1}(m) - i_{v2}(m)\|)dm
\end{aligned}$$

According to the mean value theorem, $\exists c$ for $0 \leq c \leq T$ such that

$$\begin{aligned}
&\|s_{h1}(t) - s_{h2}(t)\| + \|e_{h1}(t) - e_{h2}(t)\| + \|i_{h1}(t) - i_{h2}(t)\| + \|r_{h1}(t) - r_{h2}(t)\| \\
&+ \|s_{v1}(t) - s_{v2}(t)\| + \|e_{v1}(t) - e_{v2}(t)\| + \|i_{v1}(t) - i_{v2}(t)\| \\
&\leq LT(\|s_{h1}(c) - s_{h2}(c)\| + \|e_{h1}(c) - e_{h2}(c)\| + \|i_{h1}(c) - i_{h2}(c)\| + \|r_{h1}(c) - r_{h2}(c)\| \\
&+ \|s_{v1}(c) - s_{v2}(c)\| + \|e_{v1}(c) - e_{v2}(c)\| + \|i_{v1}(c) - i_{v2}(c)\|)
\end{aligned}$$

For all $t \in [0, T]$. The proof will be complete if T is small enough such that $t < 1$ where T denote the final time. □

4.5. Optimal Control Numerical Results. In this subsection, we analyse and discuss the numerical effects of optimal control strategies. The numerical simulation of Optimal Control Model is done by using Octave programming language using the set of literature parameters as in Table 2; the following initial conditions were considered,

$$s_h(0) = 30, e_h(0) = 7, i_h(0) = 2, r_h(0) = 0, s_v(0) = 40, e_v(0) = 10, i_v(0) = 3,$$

and the weight constants were assumed to be

$$M_1 = 1, M_2 = 2, M_3 = 2, M_4 = 2, b_1 = 2, b_2 = 10, b_3 = 5.$$

TABLE 2. Parameters values used for simulations

Parameter	**Value**	**Reference**
π_h	0.000215/day	[7, 31]
π_v	0.07/day	[7, 31]
p_h	0.62	[17, 31]
p_v	0.065	[17, 31]
a	varying	Assumed
σ	0.001	Assumed
ε	0.083	[31, 27]
ω	0.004	[5, 31]
ρ	0.02	[17, 31]
τ	0.125	[5, 31]
μ_h	0.00044	Assumed
μ_v	0.034	[26, 31]
$r_1 = r_2$	0.62	[17]
q	0.2	Assumed
k_1, k_2	5000, 300000	Assumed.

The simulation was done by considering the effect contact rate and the contribution of environment on transmission of HAT. The control profiles at different values of u_1, u_2 and u_3 are represented by the Figures 2 and 3 where u_1, u_2, u_3 is represented by red (dashed), blue (solid) and green(dashed-dotted) line respectively. For the Figures 4, 5, 6, 7, blue line (solid) shows the impact on human or vector population when no any control is used while the red line (dashed) shows the impact of applying controls on the infectious populations.

Strategy I: The effects of applying treatment and insecticides only on infectious humans and vectors respectively. The figure 4 depicted that the use of treatment u_2 and insecticides u_3 only has a strong positive impact in reducing the number of infectious individuals implying that this strategy is effective to eliminate both infectious tsetse flies and human populations.

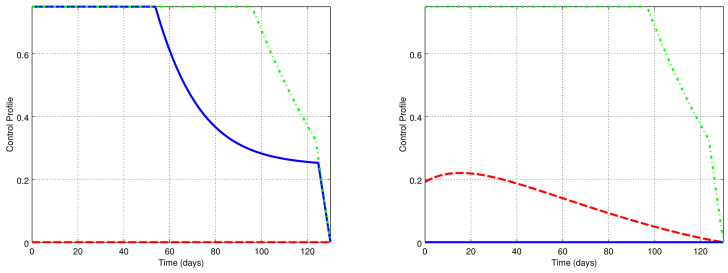

FIGURE 2. (a) Control Profile when $u_1 = 0$, $u_2 \neq 0$ and $u_3 \neq 0$. (b) Control profile when $u_1 \neq 0, u_2 = 0$ and $u_3 \neq 0$.

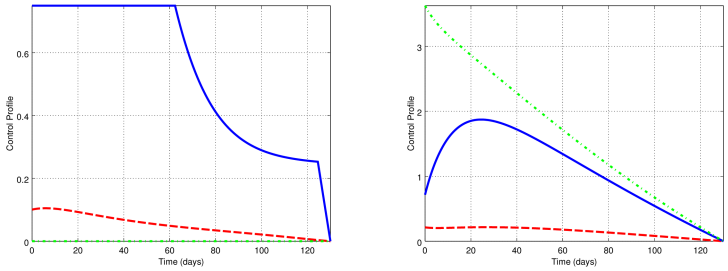

FIGURE 3. (a) Control Profiles when $u_1 \neq 0, u_2 \neq 0$ and $u_3 = 0$. (b) Control profile when $u_1 \neq 0, u_2 \neq 0$, and $u_3 \neq 0$

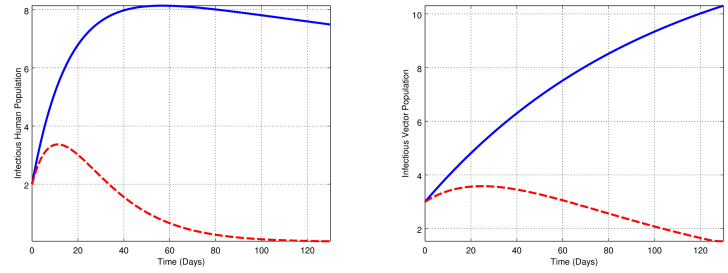

FIGURE 4. The impact of using treatment and insecticides only on reducing the number of infectious individuals.

Strategy II: The use of education and insecticides only to reduce the infected individuals. The results depicted by the figure 5 (b) shows that the use of education and insecticides has a strong impact on reducing the number of infected vectors while figure 5(a) shows that this strategy is not much effective

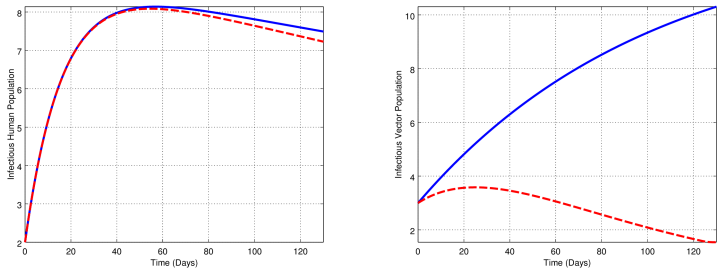

FIGURE 5. The impact of using education and insecticides only to reduce the number of infectious individuals.

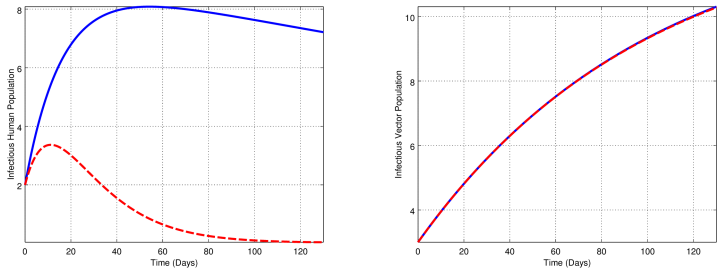

FIGURE 6. The effect of using education and treatment only to reduce the number of infectious individuals.

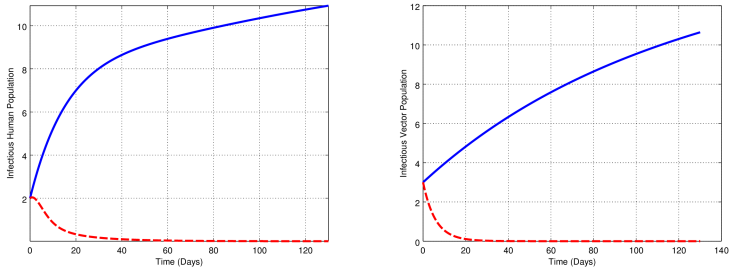

FIGURE 7. The impact of using both education, treatment and insecticides to reduce the number of infectious individuals.

to reduce the infectious human population. Thus, this strategy is effective and efficient to control the infectious tsetse flies.

Strategy III: Combining education and treatment only on infectious vectors and humans. From Figure 6(a),it is observe that the use of education and treatment has a strong effect on reducing the number of infectious individuals however the results depicted by figure 6(b) shows that this strategy is not effective and efficient to control the infectious tsetse flies population.

Strategy IV: Using both education, treatment and insecticides The results depicted from Figure 7 shows that the strategy of using both education, treatment and insecticides has strong impact on reducing the number of both infectious humans and vectors(tsetse flies) implying that this strategy is effective and efficient to control infected cases for both humans and vectors.

5. The Cost-Effectiveness Analysis

In this section, the cost effectiveness of the control measures (education, treatment and insecticides) is analyzed in order to obtain the best cost effective strategy. The Cost-Effectiveness Analysis is very important in decision making especially how to choose the best control strategy with preference to the other. The cost effectiveness analysis has computed by using incremental cost effectiveness ratio (ICER) method at which each control technique is compared with next less effective alternative [36, 37]. From the objective function defined by equation (11) with $b_1u_1^2, b_2u_2^2$ and $b_3u_3^2$ which denote the relative cost weight for education, treatment and insecticides respectively; the total cost is computed by:

$$C(u) = \min \int_0^3 \left(\frac{1}{2} b_1 u_1^2 + \frac{1}{2} b_2 u_2^2 + \frac{1}{2} b_3 u_3^2 \right) dt. \tag{15}$$

The numerical results are arranged according to increasing of infected averted population as shown in Table 3 and the ICER is calculated using the formula defined by equation (16).

$$\text{ICER} = \frac{\text{Difference in costs between strategy m and n}}{\text{Difference in averted individuals between strategy m and n}} \tag{16}$$

In Table 4, strategy I has larger ICER than strategy II implying that is costlier

TABLE 3. The Control strategies arranged in the order of increasing averted

Contol Strategy	**Population**	**Averted**	**Cost**	**Total Cost J**
Strategy I	528.4892	0.6548	29.8285	1.3769×10^5
Strategy II	531.4171	3.5797	25.3342	1.3776×10^5
Strategy IV	531.9653	4.1279	30.3285	1.3643×10^5
Strategy III	531.8374	8.1273	5.4943	1.3646×10^5

strategy on reducing the infected HAT individuals and therefore will be excluded

from the list of control strategies. The new ICER values is recalculated by comparing the strategies II and IV as shown by Table 5

TABLE 4. The Control strategies, cost and ICER for strategy I and II

Contol Strategy	**Population**	**Averted**	**Cost**	**Total Cost J**	**ICER**
Strategy I	528.4892	0.6548	29.8285	1.3769×10^5	45.5536
Strategy II	531.4171	3.5797	25.3342	1.3776×10^5	-1.537

TABLE 5. The Control strategies, cost and ICER after exclusion of most cost strategy I

Contol Strategy	**Population**	**Averted**	**Cost**	**Total Cost J**	**ICER**
Strategy II	531.4171	3.5797	25.3342	1.3776×10^5	7.077
Strategy IV	531.9653	4.1279	30.3285	1.3643×10^5	9.11

The ICER values shown by Table 5 show that strategy IV has larger ICER compared to II, it is dominated by II. The lower ICER value for strategy II indicates that it is a cost effective strategy in reducing the number of infected HAT individuals. The ICER values is recalculated by dropping out strategy IV as shown by Table 6.

TABLE 6. The Control strategies, cost and ICER after exclusion of most cost strategy

Contol Strategy	**Population**	**Averted**	**Cost**	**Total Cost J**	**ICER**
Strategy II	531.4171	3.5797	25.3342	1.3776×10^5	7.077
Strategy III	531.8374	8.1273	5.4943	1.3646×10^5	-4.36

The ICER values from Table 6 depicted that strategy III has negative value implying that, it is the best cost effective strategy compared to other strategies.

6. Discussion

The ICER values in the Table 5 and 6 show that both strategies II, III and IV can be in cost effective quadrant, however the strategy of using education and treatment only is the most cost effective strategy compared to other strategies because it has negative ICER. According to World Bank in 2017 [35], most sub-Saharan countries' where its economy is growing, it is not strong enough compared to Asia and Pacific; more than 40% of sub-Saharan African people remain poor as the daily average income of an individual range from 1.9 to 3 USD, hence these findings are relevant to Africa in terms of the costs required

to eliminate HAT. Again, the results of this paper is more relevant especially when it is compared with other works, for instance, Kanjunguri et el (2013) [18] found that the effective application of insecticides brings about a cost effective method to eliminate HAT in southern Uganda however their results worked only when there are few wild hosts. Moreover, the size of the available budget can be used to decide the best strategy to be used with preference to the other. The strategy IV (using both education, treatment and insecticides) is highly cost method but most effective and efficient compared to other strategies as in Figure 7. Therefore, if the budget is big enough it is advised to apply the strategy IV to eliminate HAT in Africa.

7. Conclusion

This paper intended to analyze the transmission dynamics and optimal control of HAT, furthermore the cost effective analysis of control strategies have been studied by considering the effect of biting rate, contact rate and the contribution of environment on transmission of HAT. The numerical results of optimal control model show that the strategy of using both education, treatment and insecticides is more effective to eliminate both infectious human and tsetse flies. However, the strategy of using education and treatment is the most cost effective in elimination of HAT in Africa, thus we advice the national and international authorities, policy markers, non governmental organizations (NGOs) and other stakeholders to prepare enough budget aimed to combat HAT rather than neglecting the disease.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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Hamenyimana Emanuel Gervas received bachelor degree at University of Dar es Salaam in Tanzania and M.Sc. at African Institute for Mathematical Sciences (AIMS) in Ghana. Since 2018 he has been working as Assistant Lecturer at the University of Dodoma in Tanzania. His research interests include Mathematical Modeling (Epidemiology) and Dynamical Systems.

Department of Mathematics and Statistics, University of Dodoma, P.O. Box 338, Dodoma, Tanzania.
e-mail: hamenyimana@aims.edu.gh

Alfred K. Hugo received M.Sc. and Ph.D. from University of Dar es Salaam in Tanzania. He is currently a Lecturer at the University of Dodoma since 2017. His research interests are Mathematical Modeling (Epidemiology), Ecology and Dynamical Systems.

Department of Mathematics and Statistics, University of Dodoma, P.O. Box 338, Dodoma, Tanzania.
e-mail: alfredkhugo@gmail.com