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Optimal Control Analysis of Fascioliasis Disease Transmission Dynamics

Abstract This paper involves the formulation of a non - linear optimal control model framework depicting fascioliasis disease transmission in the population of domestic ruminants only. The optimal control analysis is studied to investigate the effect of time-dependent preventive controls of treatment of worms in infected animals $c_1(t)$, hygiene compliance of separation/distancing of susceptible animals from infected environment sources $c_2(t)$ and sanitation of the environment $c_3(t)$. The positivity and boundedness of the model solutions are investigated, while the optimal control model solutions are shown to exist. The optimal control model is characterized using the Pontryagins Maximum Principle (PMP), which leads to the derivation of the optimality system. The optimal control model is solved using the forward - backward Runge - Kutta fourth order (RK4) sweep scheme via computational software MATLAB, where simulations reveal that each control is capable of reducing fascioliasis infection, but the combined implementation of the three control strategies are more effective in stemming the high rate of prevalence of the disease in the domestic animal population. Further simulations show that the preventive control profiles of $c_1(t), c_2(t)$ and $c_3(t)$ are sustained for few months before reducing gradually to zero in the final time of 12 months.

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1. Introduction. Fascioliasis is a world global disease caused by *F. hepatica* and *F. gigantica*. It is an acute parasitic infectious disease in humans and domestic ruminants, especially in nations with poor hygiene compliance, treatment against worms in infected animals and the sanitation of environment.The prevalence of the disease is much higher in Africa and Asia where several domestic ruminants are reared and are major host to the disease. The World Health Organization (WHO) estimated that, at least, 24 to 30 million humans and animals are infected from more than 70 countries worldwide [12]. Fascioliasis causes the dilation and thickening of bile duct and liver damage in animals. The symptoms of this disease includes nausea, jaundice, haemorrhage, anaemia and liver failure. Fascioliasis in animals can be treated with drugs like albendazole, netobinim, closatel etc., while ruminants are to be regularly vaccinated [9]. Several models have been formulated to describe fascioliasis disease dynamics. Kostova and Chipev [16] studied the analytical

oscillatory behavior of the model describing the intramolluscan trematode infection, while Goodall *et al.,* [11], formulated a model analysis of the database of fascioliasis infection in animals in Northern Ireland. Smith [8] formulated a model describing the age structure of *F. hepatica* population in sheep and the efficacy of vaccine for controlling liver fluke infection, while Ogunmiloro [22], constructed a mathematical model of fascioliasis epidemic interplay in human and ruminant host population, under the Caputo fractional order sense, where it was shown that the fractional order case of the model converges faster than the integer order case. Some other related works can be seen in [25], [6], [26]. Moreover, optimal control theory is an important area of mathematics which is an extension of calculus of variations and a mathematical optimization method for deriving control policies, due to the work of Pontryagin *et al.,* [24]. Numerical methods for solving optimal control problems can be grouped as direct and indirect methods, where in direct method, optimality criteria are formed through calculus of variation using PMP, which results to a Two Point Boundary Value Problem (TPBVP). In direct methods, the control problem is discretized and changed to a linear programming problem. The indirect numerical method of interest in this work is the forward backward Runge - Kutta fourth order method. This method is an iterative technique for solving (TPBVP) that arises from indirect PMP approach to optimal control, where its advantage includes, straightforward scalability to large systems and moderate computational cost [18]. Several optimal control problems are nonlinear in nature and do not have analytical solutions. Optimal control is an important application in biology and epidemiology. Literature supporting these applications can be seen in [3, 1, 4, 5, 15] [10], [2, 13, 17, 7, 23, 14, 20, 21], , and [19], respectively.

Motivated by the works of the cited authors on modeling of fascioliasis disease in ruminants and the application of optimal control analysis to several models in biology and epidemiology, this work presents an extension of earlier developed models by considering the epidemic interaction of classes of sub-population of susceptible, vaccinated, infected domestic animals and infested environmental sources with the effect of hygiene compliance of distancing, treatment and sanitation as time dependent controls. This has not been considered to the best of the author's understanding. This article is divided into sections. Section 2 involves the optimal control model formulation and basic analysis. Section 3 deals with the optimal assessment and existence of the model solutions, while Section 4 examines the characterization of the model and derivation of the optimality model system. Section 5 discusses the numerical simulations of the optimal control model and Section 6 presents the conclusion of the work.

2. Model Formulation and Basic Analysis Here, the animals in the environment host population are considered. The animal population is partitioned into sub-population of animals who are at risk of acquiring fascioliasis

A_s, animals vaccinated against fascioliasis A_v, animals infected with fascioliasis A_i, and animals who recovered from fascioliasis A_r, so that at time $t > 0$, the total animal host population

$$N_a(t) = A_s(t) + A_v(t) + A_i(t) + A_r(t),$$

while the presence of pathogens (worms) in the environment is denoted $P_e(t)$. The population of susceptible animals is increased by the quantity $(1-\rho)\theta_h$,

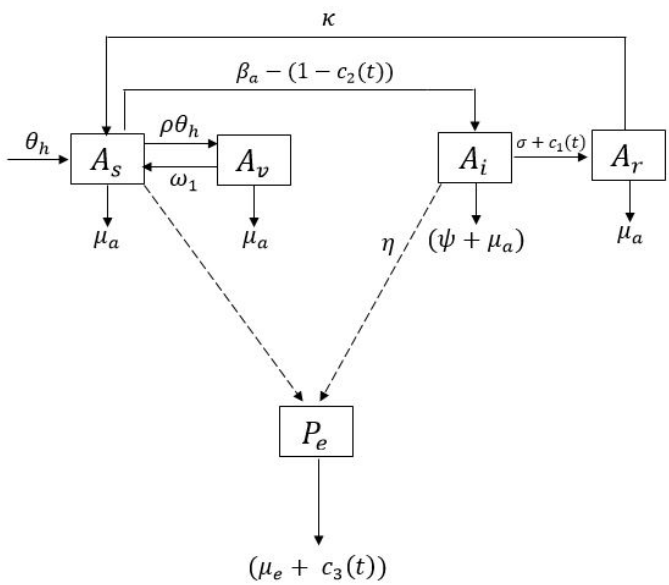


Figure 1: Block diagram of fascioliasis epidemic interactions in animal host population

where θ_h and ρ denotes the recruitment rates of susceptible animals and fraction of susceptible animals with vaccination. The susceptible population is further reduced by the quantities $\beta_a A_s(t) A_i(t)$ and $(1 - c_2(t))\beta_b A_s(t) P_e(t)$, where β_a is the direct transmission rate of fascioliasis infection between susceptible and infected animals and β_b denote the indirect transmission rate of fascioliasis from environment to susceptible animals. Also, time dependent controls are imposed on the system where, $c_1(t)$ denotes the control measure of treatment with drugs administered to fascioliasis infected animals, $c_2(t)$ denotes the control measure of hygiene compliance of separation/distancing of susceptible animals from infected environment sources and $c_3(t)$ denotes the control measure of using disinfectant to sanitize and kill pathogens (worms) present in environment sources. The natural death rate μ_a reduces the animal host population, while the waning rate of vaccination in vaccinated animals

and loss of immunity after recovery are denoted by ω_1 and k respectively. The progression rate of infected animals to recovery state is denoted σ, while death due to fascioliasis infection is denoted by ψ. Finally, the rate of infectious animal contribution to the environment is given by η, and the natural death rate of pathogens (worms) in the environment is denoted by μ_e. The assumptions guiding the model formulation were;

- Both the direct and indirect modes of transmission of fascioliasis disease are considered.
- Proportion of susceptible animals are vaccinated, while vaccination wanes overtime.
- Infectious contribution of infected animals to the environment leads to emergence of pathogens(worms).
- There is natural death and death due to fascioliasis of animals.

These assumptions leads to the deterministic model with controls given by

$$\left.\begin{aligned}
\dot{A}_s &= (1-\rho)\theta_h - \beta_a A_s(t)A_i(t) - (1-c_2(t))\beta_b A_s(t)P_e(t) \\
&\quad - \mu_a A_s(t) + kA_r(t) + \omega_1 A_v(t), \\
\dot{A}_v &= \rho\theta_h - \omega_1 A_v(t) - \mu_a A_v(t), \\
\dot{A}_i &= \beta_a A_s(t)A_i(t) + (1-c_2(t))\beta_b A_s(t)P_e(t) \\
&\quad - (\sigma + \psi + \mu_a + c_1(t))A_i(t), \\
\dot{A}_r &= (\sigma + c_1(t))A_i(t) - (\mu_a + k)A_r(t), \\
\dot{P}_e &= \eta A_i - (\mu_e + c_3(t))P_e.
\end{aligned}\right\} \tag{1}$$

Subject to the initial conditions $A_s \geq 0, A_v \geq 0, A_i \geq 0, A_r \geq 0, P_e \geq 0$.

Table 1: Parameters Descriptions

Parameters	Descriptions	Values	Sources
θ_h	Birth rate of susceptible animals	0.0553	[11]
c_1	Efficacy of treatment control on infected animals	0 - 1	Assumed
c_2	Efficacy of hygiene/separation compliance control in the environment host	0 - 1	Assumed
c_3	Efficacy of sanitation control in the environment host	0 - 1	Assumed
β_a	Rate of fascioliasis disease transmission among animals	0.118	[11]
β_b	Rate of fascioliasis disease transmission from environment to susceptible animals	0.318	[11]
k	Rate of loss of immunity in animals	0.005	[15]
μ_a	Natural mortality of animals	$\frac{1}{1\times365}$	[8]
ρ	Proportion of susceptible vaccinated animals	0.008	[6]
σ	Natural recovery rate of animals	0.008	[6]
ω_1	Waning rate of vaccination	0.001	[6]
ψ	Death rate due to fascioliasis disease in animals	$\frac{1}{1\times365}$	[8]
η	Infectious animal contribution to the environment	0.213	[8]
μ_e	Death rate of worms in the environment	0.134	[8]

2.1. Positivity and Boundedness of the Model Solutions.

THEOREM 2.1 *Given that* $A_s(0) \geq 0, A_v(0) \geq 0, A_i(0) \geq 0, A_r(0) \geq 0$ *and* $P_e(0) \geq 0$, *the solutions* $(A_s(t), A_v(t), A_i(t), A_r(t), P_e(t))$ *of model* (1) *are positive for* $t > 0$.

PROOF Let $t_1 = sup(t > 0 | A_s > 0, A_v > 0, A_v > 0, A_i > 0, P_e > 0)$, from the first equation in (1), that is,

$$\begin{aligned} \dot{A}_s = (1-\rho)\theta_h - \beta_a A_s(t) A_i(t) - (1-c_2(t))\beta_b A_s(t) P_e(t) \\ - \mu_a A_s(t) + k A_r(t) + \omega_1 A_v(t). \end{aligned} \tag{2}$$

The integrating factor of (2) is $\exp(\mu_a t + \int_0^{t_1} \beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)) A_s(s) ds$, which can be re-written as

$$\begin{aligned} &\frac{d}{dt}\left\{ A_s(t) \exp\left(\mu_a t + \int_0^{t_1} \Big(\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)\Big) A_s(s) ds\right)\right\} \\ &\quad = ((1-\rho)\theta + k A_r(\upsilon) + \omega_1 A_v(\upsilon)) \\ &\qquad \times \exp\left(\mu_a t + \int_0^{t_1} \Big(\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)\Big) A_s(s) ds. \end{aligned}$$

Hence,

$$\begin{aligned} &A_s(t_1) \exp\left(\mu_a t_1 + \int_0^{t_1} \Big(\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)\Big) A_s(s) ds\right) - A_s(0) = \\ &\int_0^{t_1} ((1-\rho)\theta_h + k A_r(\upsilon) + \omega_1 A_v(\upsilon)) \\ &\qquad \times \exp\left(\mu_a \upsilon + \int_0^{\upsilon} (\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)) A_s(s) ds\right) d\upsilon. \end{aligned}$$

so that

$$\begin{aligned} A_s(t_1) = \exp\big(- \mu_a t_1 + \int_0^{t_1} \big(\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)\big) A_s(s) ds\big) \\ \times \big(A_s(0) + \int_0^{t_1} ((1-\rho)\theta_h + k A_r(\upsilon) + \omega_1 A_v(\upsilon)) \\ \times \exp\left(\mu_a \upsilon + \int_0^{\upsilon} (\beta_a A_i(s) + (1-c_2(t))\beta_b P_e(s)) A_s(s) ds\right) d\upsilon\big) > 0. \end{aligned} \tag{3}$$

In a similar fashion from (2) to (3), the positivity of the remaining variables $A_v > 0, A_i > 0, A_r > 0$ and $P_e > 0$ in (1) can be proved.

THEOREM 2.2 *The closed set* $\Theta = \Theta_a \cup \Theta_b \subset \Re^4 \cdot \Re^1$, *where*

$$\Theta_a = \left\{ (A_s, A_v, A_i, A_r) \in \Re^4 : N_a(t) \leq \frac{\theta_h}{\mu_a} \right\}$$

and

$$\Theta_b = \left\{ P_e \in \Re^1 : P_e(t) \leq \frac{\eta\theta_h}{\mu_a(\mu_e + c_3(t))} \right\}$$

is positively invariant and bounded for the model (1) *with non-negative initial conditions*

PROOF The model is divided into the animal and pathogen population, so that the addition of the animal host population in the absence of death due to fascioliasis infection yields

$$\frac{dN_a}{dt} = \theta_h - \mu_a N_a(t) - \psi A_i(t) \leq \theta_h - \mu_a N_a(t). \tag{4}$$

Since $\frac{dN_a}{dt} \leq \theta_h - \mu_a N_a(t)$, it follows that $\frac{dN_a}{dt} \leq 0$ if $N_a(t) \geq \frac{\theta_h}{\mu_a}$. Thus, the solution of (4) yields $N_a \leq N_a(0)e^{-\mu_a t} + \frac{\theta_h}{\mu_a}(1 - e^{-\mu_a t})$, where $\lim_{t\to\infty} \sup N_a(t) \leq \frac{\theta_h}{\mu_a}$. Thus $N_a(t) \leq \frac{\theta_h}{\mu_a}$ whenever $N_a(0) \leq \frac{\theta_h}{\mu_a}$. Hence,

$$\Theta_a = \left\{ (A_s, A_v, A_i, A_r) \in \Re^4 : N_a(t) \leq \frac{\theta_h}{\mu_a} \right\}.$$

Similarly, for the pathogen population, $\frac{dP_e}{dt} \leq \eta A_i(t) - (\mu_e + c_3(t))P_e(t)$, where it follows that $\frac{dP_e}{dt} \leq 0$ if $P_e(t) \geq \frac{\eta\theta_h}{\mu_a(\mu_e + c_3(t))}$, so that $P_e(t) \leq P_e(0)e^{-(\mu_e + c_3(t))t} + \frac{\eta\theta_h}{\mu_a(\mu_e + c_3(t))}(1 - e^{-(\mu_e + c_3(t))t})$, and $\lim_{t\to\infty} \sup P_e(t) \leq \frac{\eta\theta_h}{\mu_a(\mu_e + c_3(t))}$. Hence, $\Theta_b = \left\{ P_e(t) \in \Re^1 : P_e(t) \leq \frac{\eta\theta_h}{\mu_a(\mu_e + c_3(t))} \right\}$. Therefore, the closed set $\Theta = \Theta_a \times \Theta_b$ is positively invariant and bounded with respect to model (1). Hence the model (1) is well - posed and realistic in the sense of fascioliasis disease transmission.

3. Optimal Assessment and Existence of the Control Model Here, the time dependent effective controls are achieved in finite time T considering the imposed controls in (1), using the Pontryagins Maximum Principle (PMP). The control variables considered in (1) to assess the optimal control problem in (1) are defined as follows.

- The total cost control $c_1(t) \in [0, 1]$ to implement the treatment of infected animals is given by

$$\int_0^T \left(W_1 c_1^2(t) \right) dt, \tag{5}$$

where W_1 is the weight parameter for the treatment control and T denotes the final time of simulation. Also, the unit of W_1 is $\frac{1}{month^2}$.

- The total cost control $c_2(t) \in [0,1]$ to implement the treatment of hygiene compliance of separation/distancing of animals from infected environment is given by

$$\int_0^T \Big(W_2 c_2^2(t)\Big)dt, \tag{6}$$

where W_2 is the weight parameter for the hygiene compliance of separation/distancing control. The unit of W_2 is $\frac{1}{month^2}$.

- The total cost control $c_3(t) \in [0,1]$ to implement the sanitation of infected environment using chemical disinfectants to kill pathogens is given by

$$\int_0^T \Big(W_3 c_3^2(t)\Big)dt, \tag{7}$$

where W_3 is the weight parameter for the sanitation control. The unit of W_3 is $\frac{1}{month^2}$.

In (5) - (7), the control interventions are considered as nonlinear functions since any public health control measures does not have a linear cost, hence we assume a quadratic cost control as seen in other literature [5], [22], [8]. Considering the cost control assessment in (5) - (7), the objective functional to be minimized is given by

$$\min \; J(c_1(t), c_2(t), c_3(t)) = \int_0^T \Big(A_1 A_i(t) + A_2 P_e(t) + \frac{W_1 c_1^2(t)}{2} + \frac{W_2 c_2^2(t)}{2} + \frac{W_3 c_3^2(t)}{2}\Big)dt. \tag{8}$$

In (8), $A_1 > 0, A_2 > 0, W_1 > 0, W_2 > 0$ and $W_3 > 0$. The aim of the control assessment is to minimize fascioliasis infected animals $A_i(t)$ and worm population in the environment $P_e(t)$, while keeping the cost of treatment, hygiene compliance of separation/distancing and environmental sanitation low. The quantities A_1 and A_2 denotes the weight constant which balance each terms in the integrand, where the goal is to obtain the optimal values $c^*(t) = (c_1^*(t), c_2^*(t), c_3^*(t))$ that minimizes the objective functional in (8) in the time interval [0,T], so that $J(c_1^*(t), c_2^*(t), c_3^*(t)) = \min\{J(c_1(t), c_2(t), c_3(t)) \in C\}$, subject to (1). It is assumed that the control set C is Lebesgue measurable, defined as

$$C = \big\{c(t) = (c_1(t), c_2(t), c_3(t)), \; 0 \le c_1(t) \le 1, 0 \le c_2(t) \le 1, 0 \le c_3(t) \le 1, t \in [0,T]\big\}. \tag{9}$$

In order to show that the control problem exist, we re-write (1) in a vector form as

$$X^{'} = BX + F(X), \tag{10}$$

where

$$X = \begin{pmatrix} A_s(t) \\ A_v(t) \\ A_i(t) \\ A_r(t) \\ P_e(t) \end{pmatrix}, \tag{11}$$

$$B = \begin{pmatrix} -\mu_a & \omega_1 & 0 & k & 0 \\ 0 & -(\omega_1 + \mu_a) & 0 & 0 & 0 \\ 0 & 0 & -(\sigma + \psi + \mu_a + c_1(t)) & 0 & \\ 0 & 0 & (\sigma + c_1(t)) & -(\mu_a + k) & 0 \\ 0 & 0 & \eta & 0 & -(\mu_a + c_3(t)) \end{pmatrix}$$

and

$$F(X) = \begin{pmatrix} (1-\rho)\theta_h - \beta_a A_s(t) A_i(t) - (1 - c_2(t))\beta_b A_s(t) P_e(t) \\ 0 \\ \beta_a A_s(t) A_i(t) + (1 - c_2(t))\beta_b A_s(t) P_e(t) \\ 0 \\ 0 \end{pmatrix}.$$

In (10), $X^{'}$ denotes the derivative with respect to time t. The system (10) is a nonlinear system with bounded coefficients, such that

$$\Xi(X) = BX + F(X)$$

where the term $F(X)$ on the right hand side of (10) satisfies

$$\begin{aligned} &|F(X_1) - F(X)| \leq Q_1(|A_{s_1}(t) - A_{s_2}(t)| + Q_2|A_{v_1}(t) - A_{v_2}(t)| + Q_3|A_{i_1}(t) - A_{i_2}(t)| \\ &+ Q_4|A_{r_1}(t) - A_{r_2}(t)| + Q_5|P_{e_1}(t) - P_{e_2}(t)|) \\ &\leq Q(|A_{s_1}(t) - A_{s_2}(t)| + |A_{v_1}(t) - A_{v_2}(t)| + |A_{i_1}(t) - A_{i_2}(t)| \\ &+ |A_{r_1}(t) - A_{r_2}(t)| + |P_{e_1}(t) - P_{e_2}(t)|), \end{aligned}$$

where Q is a positive constant such that, $Q = \max(Q_1, Q_2, Q_3, Q_4, Q_5)$ is independent of the state variables. Also

$$|\Xi(X_1) - \Xi(X_2)| \leq Q|X_1 - X_2|,$$

where $Q = Q_1 + Q_2 + Q_3 + Q_4 + Q_5 + ||K|| < \infty$. This shows that the function $\Xi(X)$ is uniformly Lipschitz continuous, therefore the solution of (10) exists.

4. Characterization of the Optimal Control Problem The necessary conditions that an optimal control problem must meet are formulated

from the PMP [25]. This technique changes (1) and (8) into a problem of point wise minimization of Hamiltonian H_t with respect to controls $c_1(t), c_2(t)$ and $c_3(t)$. In order to obtain the solution to the optimal control problem, a Lagragian L_g is defined together with (10), so that

$$L_g(A_s(t), A_v(t), A_i(t), A_r(t), P_e(t), c_1(t), c_2(t), c_3(t)) = \Big(A_1A_i(t) + A_2P_e(t) + \frac{W_1c_1^2(t)}{2} + \frac{W_2c_2^2(t)}{2} + \frac{W_3c_3^2(t)}{2}\Big)$$

Also, the H_t is defined for the control model to derive the minimum value of L_g by denoting $A = (A_s(t), A_v(t), A_i(t), A_r(t), P_e(t)), C = (c_1(t), c_2(t), c_3(t))$ and $\Delta = (\delta_1, \delta_2, \delta_3, \delta_4, \delta_5)$. Hence, H_t is defined as

$$\left.\begin{aligned} H_t(A, C, \Delta) &= A_1A_i(t) + A_2P_e(t) + \frac{W_1c_1^2(t)}{2} + \frac{W_2c_2^2(t)}{2} + \frac{W_3c_3^2(t)}{2} \\ &+ \delta_1((1-\rho)\theta_h - \beta_aA_s(t)A_i(t) - (1-c_2(t))\beta_bA_s(t)P_e(t) \\ &- \mu_aA_s(t) + kA_r(t) + \omega_1A_v(t)) + \delta_2(\rho\theta_h - \omega_1A_v(t) - \mu_aA_v(t)) \\ &+ \delta_3(\beta_aA_s(t)A_i(t) + (1-c_2(t))\beta_bA_s(t)P_e(t) \\ &- (\sigma + \psi + \mu_a + c_1(t))A_i(t)) + \delta_4((\sigma + c_1(t))A_i(t) - (\mu_a + k)A_r(t)) \\ &+ \delta_5(\eta A_i(t) - (\mu_e + c_3(t)))P_e(t). \end{aligned}\right\}$$

where $\delta_i (i = 1, .., 5)$ denotes the adjoint or co-state variables for the state equations $A_s(t), A_v(t), A_i(t), A_r(t), P_e(t)$.

THEOREM 4.1 *For the optimal control variables $c_1^*(t), c_2^*(t)$, and $c_3^*(t)$ and the solutions $A_s^*(t), A_v^*(t), A_i^*(t), A_r^*(t)$, and $P_e^*(t)$ of the corresponding state system in (1), there exists adjoint variables $\delta_i (i = 1, .., 5)$ satisfying*

$$\frac{d\delta_i}{dt} = \frac{-\partial H_t}{\partial A} \tag{12}$$

with transversality conditions $\delta_1(T) = \delta_2(T) = \delta_3(T) = \delta_4(T) = \delta_5(T) = 0$ where $A^* = (A_s^*(t), A_v^*(t), A_i^*(t), A_r^*(t), P_e^*(t))$
Further, the optimality conditions

$$\left.\begin{aligned} c_1^*(t) &= \min\left\{1, \max\left\{0, \frac{(\delta_4 - \delta_3)A_i^*(t)}{W_1}\right\}\right\}, \\ c_2^*(t) &= \min\left\{1, \max\left\{0, \frac{(\delta_1 - \delta_3)\beta_bA_s^*(t)P_e^*(t)}{W_2}\right\}\right\}, \\ c_3^*(t) &= \min\left\{1, \max\left\{0, \frac{-\delta_5P_e^*(t)}{W_3}\right\}\right\}. \end{aligned}\right\}$$

PROOF The adjoint or costate variables are derived by differentiating H_t in (12) and evaluating the optimal control variables, which yields

$$\left.\begin{aligned}
\frac{d\delta_1}{dt} &= \frac{-\partial H_t}{\partial A_s^*(t)} = -\delta_1(-\beta_a A_i^*(t) - (1-c_2(t))P_e^*(t) - \mu_a) \\
&\quad + \delta_3(\beta_a A_i^*(t) + (1-c_2(t))\beta_b P_e^*(t)) \\
\frac{d\delta_2}{dt} &= \frac{-\partial H_t}{\partial A_v^*(t)} = -\delta_1\omega_1 - \delta_2(\omega_1 + \mu_a) \\
\frac{d\delta_3}{dt} &= \frac{-\partial H_t}{\partial A_i^*(t)} = A_1 + \delta_1(-\beta_a A_s^*(t)) + \delta_3(\beta_a A_s^*(t) \\
&\quad - (\sigma + \psi + \mu_a + c_1(t))) + \delta_4(\sigma + c_1(t)) + \delta_5\eta \\
\frac{d\delta_4}{dt} &= \frac{-\partial H_t}{\partial A_r^*(t)} = \delta_1 k + \delta_4(-(\mu_a + k)) \\
\frac{d\delta_5}{dt} &= \frac{-\partial H_t}{\partial P_e^*(t)} = A_2 + \delta_1(-(1-c_2(t)))\beta_b A_s^*(t) \\
&\quad + \delta_3((1-c_2(t))\beta_b A_s^*(t)) + \delta_5(-(\mu_e + c_3(t)))
\end{aligned}\right\}$$

with transversality $\delta_1(T) = \delta_2(T) = \delta_3(T) = \delta_4(T) = \delta_5(T) = 0$. Furthermore, differentiating the Hamiltonian function H_t in (10) with respect to the control variables. Then solving for controls $c_1^*(t), c_2^*(t)$ and $c_3^*(t)$ results in the optimality conditions given as

$$\frac{dH_t^*}{dc_1(t)} = W_1 c_1^*(t) + (\delta_4 - \delta_3)A_i^*(t) = 0, \tag{13}$$

$$\frac{dH_t^*}{dc_2(t)} = W_2 c_2^*(t) + (\delta_1 - \delta_3)\beta_b A_s^*(t)P_e^*(t) = 0, \tag{14}$$

and

$$\frac{dH_t^*}{dc_3(t)} = W_3 c_3^*(t) - \delta_5 P_e^*(t) = 0. \tag{15}$$

Solving for $c_1(t) = c_1^*(t)$, $c_2(t) = c_2^*(t)$, and $c_3(t) = c_3^*(t)$ one obtains

$$\left.\begin{aligned}
c_1^*(t) &= \frac{(\delta_4 - \delta_3)A_i^*(t)}{W_1}, \\
c_2^*(t) &= \frac{(\delta_1 - \delta_3)\beta_b A_s^*(t)P_e^*(t)}{W_2}, \\
c_3^*(t) &= \frac{-\delta_5 P_e^*(t)}{W_3},
\end{aligned}\right\} \tag{16}$$

In compact form

$$\left.\begin{aligned} c_1^*(t) &= \min\left\{1, \max\left\{0, \frac{(\delta_4-\delta_3)A_i^*(t)}{W_1}\right\}\right\}, \\ c_2^*(t) &= \min\left\{1, \max\left\{0, \frac{(\delta_1-\delta_3)\beta_b A_s^*(t)P_e^*(t)}{W_2}\right\}\right\}, \\ c_3^*(t) &= \min\left\{1, \max\left\{0, \frac{-\delta_5 P_e^*(t)}{W_3}\right\}\right\}. \end{aligned}\right\} \tag{17}$$

Therefore, the optimality system given by

$$\left.\begin{aligned} \frac{dA_s}{dt} &= (1-\rho)\theta_h - \beta_a A_s(t)A_i(t) - (1-c_2(t))\beta_b A_s(t)P_e(t) \\ &\quad - \mu_a A_s(t) + kA_r(t) + \omega_1 A_v(t), \\ \frac{dA_v}{dt} &= \rho\theta_h - \omega_1 A_v(t) - \mu_a A_v(t), \\ \frac{dA_i}{dt} &= \beta_a A_s(t)A_i(t) + (1-c_2(t))\beta_b A_s(t)P_e(t) \\ &\quad - (\sigma+\psi+\mu_a+c_1(t))A_i(t), \\ \frac{dA_r}{dt} &= (\sigma+c_1(t))A_i(t) - (\mu_a+k)A_r(t), \\ \frac{dP_e}{dt} &= \eta A_i - (\mu_e+c_3(t))P_e(t), \\ \frac{d\delta_1}{dt} &= -\delta_1(-\beta_a A_i^*(t) - (1-c_2(t))P_e^*(t) - \mu_a) + \delta_3(\beta_a A_i^*(t) \\ &\quad + (1-c_2(t))\beta_b P_e^*(t)), \\ \frac{d\delta_2}{dt} &= -\delta_1\omega_1 - \delta_2(\omega_1+\mu_a), \\ \frac{d\delta_3}{dt} &= A_1 + \delta_1(-\beta_a A_s^*(t)) + \delta_3(\beta_a A_s^*(t) - (\sigma+\psi+\mu_a+c_1(t))) \\ &\quad + \delta_4(\sigma+c_1(t)) + \delta_5\eta, \\ \frac{d\delta_4}{dt} &= \delta_1 k + \delta_4(-(\mu_a+k)), \\ \frac{d\delta_5}{dt} &= A_2 + \delta_1(-(1-c_2(t)))\beta_b A_s^*(t) + \delta_3((1-c_2(t))\beta_b A_s^*(t)) \\ &\quad + \delta_5(-(\mu_e+c_3(t))). \end{aligned}\right\} \tag{18}$$

subject to the initial and transversality conditions

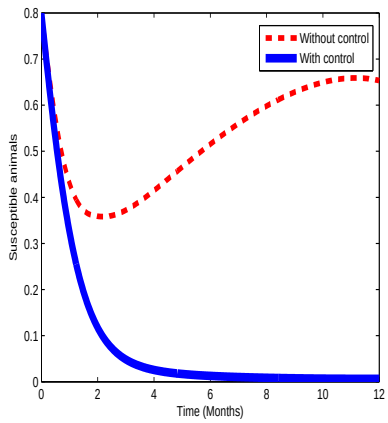
$$A_s(0) \geq 0, A_v(0) \geq 0, A_i(0) \geq 0, A_r(0) \geq 0$$

and

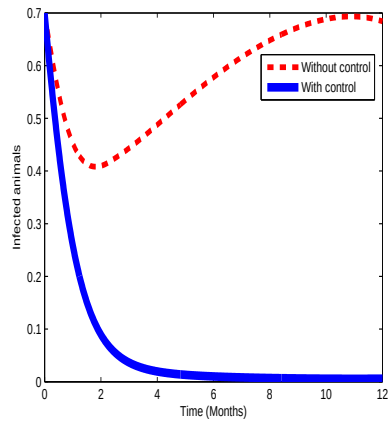
$$P_e(0) \geq 0$$

and

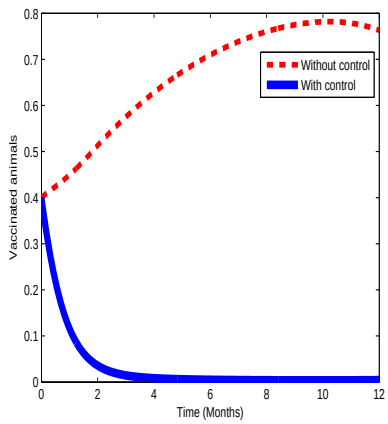
$$\delta_1(T) = \delta_2(T) = \delta_3(T) = \delta_4(T) = \delta_5(T) = 0.$$



(a)



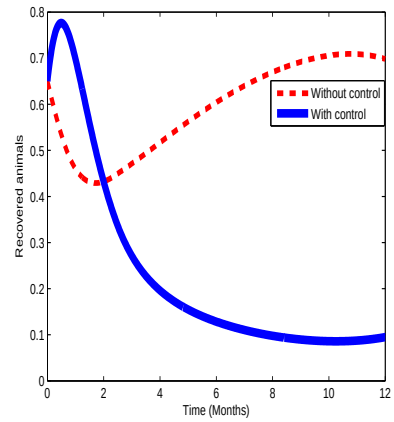
(b)



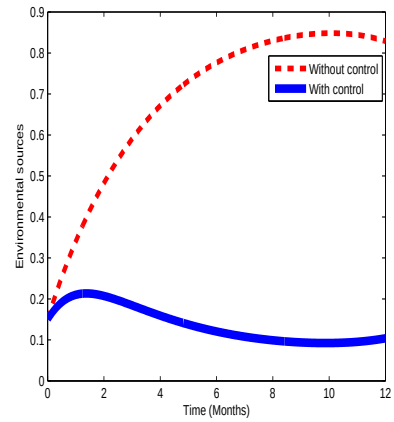
(c)

Figure 2: Simulations of the model state variables with and without controls

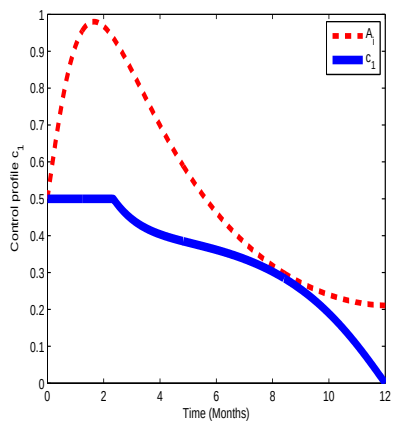
5. Numerical Simulations and Discussion of Results The model describing the fascioliasis epidemic interplay in the animal host population according to their disease status is constructed in (1) and described by Figure 1. The positivity and boundedness of (1) are established in Theorems 1 and 2 and objective of the optimal control model to be minimized is given by (8). The existence of the optimal control model is established and with the aid of PMP, the Hamiltonian is formed in (12) and the optimal control variables are characterized and the adjoint equations are derived in (13)-(18).



(a)



(b)



(c)

Figure 3: Simulations of the model state variables with and without controls and the effect of control profile $c_1(t)$ in infected animals

In order to solve the optimal control model, the forward - backward Runge - Kutta fourth order numerical approximation technique is employed via MATLAB program [18]. Firstly, the state equation in (18) with an initial guess for the controls is solved forward in time and the adjoint system in (18) is solved backward in time subject to initial and transversality conditions. The controls are then updated by employing the convex combination of the former controls and the values from (18). This process continues until the state equations solutions are very near the former iteration values [20], [18], and [19].

The values of parameters in Table 1 and the state variables which are assumed to be $A_s = 0.85, A_v = 0.40, A_i = 0.70, A_r = 0.63$ and $P_e = 0.18$

are used for the simulations. Also, the weight factors are as $A_1 = 700, A_2 = 400, W_1 = 90, W_2 = 75$ and $W_3 = 77$. These weight factors were adopted on the efforts required to provide the control measures under consideration. The weight factors $A_i (i = 1, 2)$ are much higher that $W_i (i = 1, 2, 3)$ because minimization of fascioliasis is of utmost importance, while the final time T for the control implementation is taken to be 12 months. Figures 2a-2c and 3a-3b

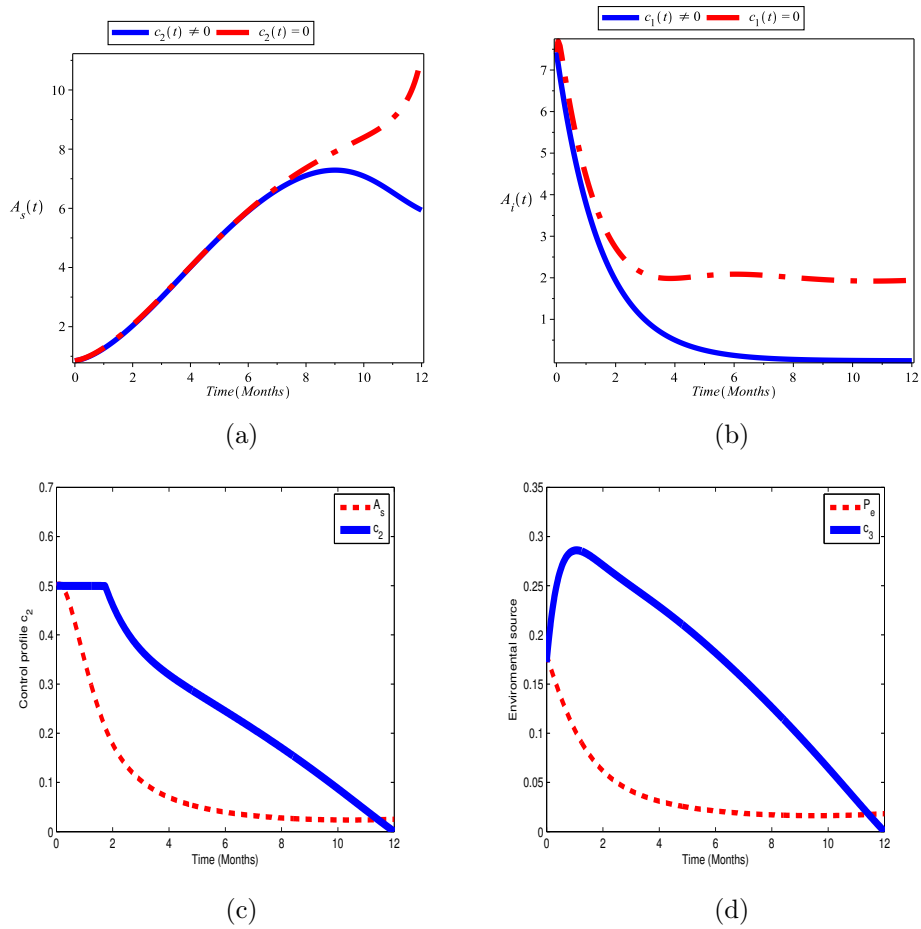


Figure 4: Simulations of the model state variables with and without controls

shows the combined effect of the three controls on the susceptible, infected and vaccinated groups of animals. In the absence of the three combined controls $c_1(t), c_2(t)$ and $c_3(t)$, there is an increase in the number of infected animals but in the presence of controls, a sharp decline which flattens out within 5-12 months is observed to reduce infection in the animals. Also in Figure 3c, the control profile of treatment $c_1(t)$ effective in treating the animal is sustained at maximum in 2.3 months before declining to zero in 12 months. The control of hygiene compliance of separation/distancing $c_2(t)$ of susceptible animals

from the environment infected with pathogens is observed to reduce infection slightly, while the absence of control leads to steady increase of the animals with infection in Figure 4a, but the control treatment proves more effective in Figure 4b. The control profiles of hygiene compliance of distancing of animals and sanitation in 4c and 4d increases and sustains within 2-3 months, but becomes effective after the decline to zero in 12 months.

6. Conclusion A model system based on ordinary differential equations with time - dependent controls describing the dynamics of the spread of fascioliasis disease in domestic animals and the environment is formulated. The hygiene compliance of distancing/separation, treatment and sanitation controls are incorporated into the model to minimize the numbers of infected animals and environment sources. The cost of quadratic objective functional is chosen, since the cost of intervention is nonlinear. Also the existence analysis of the optimal control model and the optimality system are established, while the derived optimality system is solved using the Runge - Kutta fourth order algorithm via MATLAB. It is observed from the numerical simulations that, each of the controls posses its own importance in reducing the disease but the combined effort of the controls proved to be more potent in minimizing fascioliasis disease in animal and environment host population. The simulations of the control profiles show that consistent and timely application of the controls in the first two months leads to the gradual reduction of fascioliasis disease to zero in final time of 12 months. In view of these results, it is suggested to veterinary health policy makers that intense application of hygiene compliance, treatment and sanitation are capable of eliminating fascioliasis in domestic ruminants annually. This work is open to further research by considering the cost effective analysis of the controls.

References

[1] H. Berhe, O. Makinde, and D. Theuri. Optimal control and cost-effectiveness analysis for dysentery epidemic model. *Applied Mathematics & Information Sciences*, 12:1183–1195, 11 2018. doi: 10.18576/amis/120613. Cited on p. 268.

[2] H. W. Berhe. Optimal control strategies and cost-effectiveness analysis applied to real data of cholera outbreak in Ethiopia's Oromia region. *Chaos Solitons Fractals*, 138:109933, 14, 2020. ISSN 0960-0779. doi: 10.1016/j.chaos.2020.109933. MR 4104873. Cited on p. 268.

[3] H. W. Berhe and O. D. Makinde. Computational modelling and optimal control of measles epidemic in human population. *Biosystems*, 190:104102, 2020. ISSN 0303-2647. doi: https://doi.org/10.1016/j.biosystems.2020.104102. URL https://www.sciencedirect.com/science/article/pii/S0303264720300101. Cited on p. 268.

[4] M. H. A. Biswas, M. M. Haque, and U. K. Mallick. Optimal control strategy for the immunotherapeutic treatment of hiv infection with state constraint. *Optimal Control Applications and Methods*, 40(4):807–818, 2019. doi: https://doi.org/10.1002/oca.2516. Cited on p. 268.

[5] E. Bonyah, M. Khan, K. Okosun, and J. Gómez-Aguilar. Modelling the effects of heavy alcohol consumption on the transmission dynamics of gonorrhea with optimal control. *Mathematical Biosciences*, 309:1–11, 2019. ISSN 0025-5564. doi: 10.1016/j.mbs.2018.12.015. Cited on pp. 268 and 273.

[6] C. Bürli, H. Harbrecht, P. Odermatt, S. Sayasone, and N. Chitnis. Mathematical analysis of the transmission dynamics of the liver fluke, Opisthorchis viverrini. *Journal of Theoretical Biology*, 439:181–194, 2018. ISSN 0022-5193. doi: https://doi.org/10.1016/j.jtbi.2017.11.020. PMID: 29197514 [PubMed]. Cited on pp. 268 and 270.

[7] K. R. Fister and J. Hughes Donnelly. Immunotherapy: an optimal control theory approach. *Math. Biosci. Eng.*, 2(3):499–510, 2005. ISSN 1547-1063. doi: 10.3934/mbe.2005.2.499. Cited on p. 268.

[8] S. G. An analysis of variations in the age structure of Fasciola hepatica populations in sheep. *Parasitology*, 84(1):49–61, 1982. ISSN 0031-1820 (Print), 1469-8161 (Online). doi: 10.1017/s0031182000051659. PMID: 7063254 [PubMed]. Cited on pp. 268, 270, and 273.

[9] P. Gandhi, E. K. Schmitt, C.-W. Chen, S. Samantray, V. K. Venishetty, and D. Hughes. Triclabendazole in the treatment of human fascioliasis: a review. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 113(12):797–804, 10 2019. ISSN 0035-9203. doi: 10.1093/trstmh/trz093. Cited on p. 267.

[10] J. K. Ghosh, U. Ghosh, M. H. A. Biswas, and S. Sarkar. Qualitative analysis and optimal control strategy of an sir model with saturated incidence and treatment. *Differential Equations and Dynamical Systems*, 27:15pp., 2019. ISSN 0974-6870. doi: 10.1007/s12591-019-00486-8. Cited on p. 268.

[11] E. Goodall, S. McIlroy, R. McCracken, E. McLoughlin, and S. Taylor. A mathematical forecasting model for the annual prevalence of fasciolosis. *Agricultural Systems*, 36(2):231–240, 1991. ISSN 0308-521X. doi: 10.1016/0308-521X(91)90026-7. Cited on pp. 268 and 270.

[12] World Health Organization (WHO). Foodborne parasitic infections: Fascioliasis (Liver fluke). World Health Organization, World Organisation

for Animal Health and Food Agriculture Organization of the United Nations, June 2021. Fact Sheet of Neglected Infectious Diseases–Fascioliasis on PAHO. Cited on p. 267.

[13] H. R. Joshi. *Optimal Control Problems in PDE and ODE Systems*. PhD thesis, The University of Tennessee, Knoxville, 2002. URL http://etd.utk.edu/2002/JoshiHem.pdf. Cited on p. 268.

[14] M. Khatun and M. Biswas. Optimal control strategies for preventing hepatitis b infection and reducing chronic liver cirrhosis incidence. *Infect. Dis. Model.*, 5:91–110, 2019. ISSN 2468-0427. doi: 10.1016/j.idm.2019.12.006. PMID: 31930183 [PubMed]; PMC6948267. Cited on p. 268.

[15] D. Kirschner, S. Lenhart, and S. Serbin. Optimal control of the chemotherapy of hiv. 35, (1997). *J Math Biol*, 35:775–792, 1997. doi: 10.1007/s002850050076. Cited on pp. 268 and 270.

[16] T. Kostova and N. Chipev. A model of the dynamics of intramolluscan trematode populations: Some problems concerning oscillatory behavior. *Computers & Mathematics with Applications*, 21(5):1–15, 1991. ISSN 0898-1221. doi: 10.1016/0898-1221(91)90212-M. Cited on p. 267.

[17] J. Kutch and P. Gurfil. Optimal control of hiv infection with a continuously-mutating viral population. In *Proceedings of the 2002 American Control Conference (IEEE Cat. No.CH37301)*, volume 5, pages 4033–4038 vol.5, 2002. doi: 10.1109/ACC.2002.1024560. Cited on p. 268.

[18] S. Lenhart and J. T. Workman. *Optimal control applied to biological models*. Chapman & Hall/CRC Mathematical and Computational Biology Series. Chapman & Hall/CRC, Boca Raton, FL, 2007. ISBN 978-1-58488-640-2; 1-58488-640-4. MR 2316829. Cited on pp. 268 and 279.

[19] R. M. Neilan and S. Lenhart. An introduction to optimal control with an application in disease modeling. In A. B. Gumel and S. Lenhart, editors, *Modeling paradigms and analysis of disease transmission models. Selected papers based on the presentations at the U.S.-African advanced study institute on mathematical modeling of infectious desease in Africa, Muizenberg, South Africa, June 11–22, 2007 and the DIMACS workshop, Stellenbosch, South Africa, June 25–27, 2007*, pages 67–81. Providence, RI: American Mathematical Society (AMS), 2010. ISBN 978-0-8218-4384-0. Zbl 1352.92164. Cited on pp. 268 and 279.

[20] E. Numfor, S. Bhattacharya, S. Lenhart, and M. Martcheva. Optimal control in coupled within-host and between-host models. *Math.*

Model. Nat. Phenom., 9(4):171–203, 2014. ISSN 0973-5348. doi: 10.1051/mmnp/20149411. MR 3264301. Cited on pp. 268 and 279.

[21] O. M. Ogunmiloro. Stability analysis and optimal control strategies of direct and indirect transmission dynamics of conjunctivitis. *Math. Methods Appl. Sci.*, 43(18):10619–10636, 2020. ISSN 0170-4214. doi: 10.1002/mma.6756. MR 4177214. Cited on p. 268.

[22] O. M. Ogunmiloro. Mathematical analysis and approximate solution of a fractional order caputo fascioliasis disease model. *Chaos Solitons Fractals*, 146:Paper No. 110851, 10, 2021. ISSN 0960-0779. doi: 10.1016/j.chaos.2021.110851. MR 4234768. Cited on pp. 268 and 273.

[23] K. O. Okosun and O. D. Makinde. Optimal control analysis of hepatitis C virus with acute and chronic stages in the presence of treatment and infected immigrants. *Int. J. Biomath.*, 7(2):1450019, 23, 2014. ISSN 1793-5245. doi: 10.1142/S1793524514500193. Cited on p. 268.

[24] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, and E. F. Mishchenko. *The mathematical theory of optimal processes*. Interscience Publishers John Wiley & Sons, Inc., New York-London, 1962. Translated from the Russian by K. N. Trirogoff; edited by L.W. Neustadt. MR 0166037. Cited on p. 268.

[25] J. Turner, A. Howell, C. McCann, C. Caminade, R. G. Bowers, D. Williams, and M. Baylis. A model to assess the efficacy of vaccines for control of liver fluke infection. *Scientific Reports*, 6(1):2045–2322, 2016. doi: 10.1038/srep23345. Article number: 23345. Cited on p. 268.

[26] M. Wilhamson and R. Wilson. The use of mathematical models for predicting the incidence of fascioliasis [sheep]. Technical report, World Meterological Organization, 1978. Cited on p. 268.

Optymalne sterowanie dynamiki przenoszenia fascjolozy.

Oluwatayo Michael Ogunmiloro

Streszczenie Fascjoloza jest ostrą pasożytniczą chorobą zakaźną u ludzi i domowych przeżuwaczy, zwłaszcza w krajach o słabym przestrzeganiu higieny, braku leczenia z robaczycy u zakażonych zwierząt i utrzymywaniu warunków sanitarnych środowiska. Niniejsza praca dotyczy sformułowania nieliniowego modelu optymalnego sterowania, ilustrująca przenoszenie fascjolozy przy założeniu ograniczenia do populacji domowych przeżuwaczy. Optymalne sterowanie jest badane w celu ustalenia wpływu zależnych od czasu prewencyjnych kontroli leczenia robaków u zakażonych zwierząt $c_1(t)$, przestrzegania higieny oddzielania/oddalania podatnych na zakażenie zwierząt od istniejących źródeł środowiskowych $c_2(t)$ i sanitacja środowiska $c_3(t)$. Zbadano dodatniość i ograniczoność rozwiązań modelowych oraz wykazano istnienie optymalnych sterowań w modelu kontrolnym. Optymalne sterowanie scharakteryzowano za

pomocą zasady maksimum Pontryagina, która prowadzi do wyprowadzenia systemu warunków optymalności. Sterowania optymalne są uzyskane przy użyciu schematu czwartego rzędu Runge - Kutta. Obliczenia wykonano za pomocą oprogramowania **MATLAB**. Symulacje pokazują, że każde sterowanie jest w stanie zmniejszyć infekcję fascjolozą, ale połączone użycie trzech strategii sterowania jest bardziej skuteczne gdy mamy do czynienia z wysokim wskaźnikiem występowania choroby w populacji zwierząt domowych. Dalsze symulacje pokazują, że profile sterowań prewencyjnej $c_1(t)$, $c_2(t)$ i $c_3(t)$ utrzymują się przez kilka miesięcy, po czym stopniowo zmniejszają się do zera w końcowym okresie 12 miesięcy.

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Słowa kluczowe: Fascjoloza, system optymalny, zasad maksimum Pontryagina (ZMP), metoda Runge'go-Kutta czwartego rzędu.

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