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AN OPTIMAL CONTROL MODEL FOR RABIES TRANSMISSION WITH PRE-EXPOSURE VACCINATION AND POST-EXPOSURE TREATMENT OF DOMESTIC AND STRAY DOGS

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Abstract: In this paper, we formulate and analyze a mathematical model to study the effect of pre-exposure vaccination and post-exposure treatment on the spread of rabies in domestic and stray dogs. The effective reproduction number ($\mathcal{R}_e$) was calculated using the next-generation matrix approach. Using the Castillo-Chavez method, the disease-free equilibrium (DFE) point is proven to be locally asymptotically stable if $\mathcal{R}_e < 1$. Using the quadratic Lyapunov function, the endemic equilibrium (EE) point is determined to be globally asymptotically stable if $\mathcal{R}_e > 1$. In addition, sensitivity analysis of model parameters on $\mathcal{R}_e$ was carried out using the normalized forward sensitivity index method. Optimal control analysis using Pontryagin's minimal principle was carried out to minimize the number of exposed and infected individuals as well as the control costs of vaccinating susceptible individuals and treating exposed individuals. Numerical simulations were carried out to verify the analytical results using MATLAB software. The results of the sensitivity analysis show that the transmission rate in stray dogs and the vaccination rate of stray dogs are the most sensitive parameters and are key factors in reducing the prevalence of rabies. The implementation of a combination of two optimal controls (pre-exposure vaccination and post-exposure treatment)

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results in a significant reduction in the number of cases in infected individuals, as demonstrated numerically by optimal control analysis.

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1. INTRODUCTION

Rabies is a zoonotic viral disease that causes progressive and fatal inflammation of the brain and spinal cord. Clinically, it has two forms, namely malignant rabies (characterized by hyperactivity and hallucinations) and paralytic rabies (characterized by paralysis and coma). Although fatal when clinical signs appear, rabies is completely avoidable. To prevent death from rabies, vaccines, medicines and technology have been used. Despite this, rabies still kills tens of thousands of people every year. Of these cases, approximately 99% are from infected dog bites. Rabies is estimated to cause 59,000 human deaths annually in more than 150 countries, with 95% of cases occurring in Africa and Asia. Due to unreported and uncertain estimates, this figure is likely an underestimate. The burden of the disease is largely borne by poor rural communities, with about half of cases caused by children under 15 years of age [1]. Rabies is estimated to cause 59,000 human deaths annually and WHO recommends intradermal administration of rabies vaccines, as this reduces the number of vaccines required and costs by 60–80% without compromising safety or efficacy. To control tropical diseases, rabies is included in the WHO Roadmap 2021–2030, which sets regional and progressive targets for targeted disease eradication. As a zoonotic disease, rabies requires close cross-sectoral coordination at the national, regional and global levels [2].

The transmission of rabies to humans can occur either in stray animals such as stray cats, wolves, coyotes, foxes, raccoons, skunks, bats, and rodents, or domestic animals like dogs and cats, depending on the environmental context. Therefore, it is crucial to prevent its spread among both humans and animals. There are very effective vaccines available to immunize individuals either before or after exposure to rabies, such as Post-exposure prophylaxis (PEP). Pre-exposure prophylaxis (PrEP), is advised for individuals in high-risk occupations (e.g., laboratory workers

handling live rabies virus and viruses associated with rabies) and for those whose work or personal activities may put them close to bats or other potential mammals [2]. Today, vaccination has been carried out throughout the world to prevent the spread of the infectious disease rabies. In the field of public health, especially in the prevention and treatment of infectious diseases, significant progress occurred in the 20th century. To achieve these results, vaccination is necessary [3]. However, early studies only assumed that mandatory and/or voluntary vaccination should be carried out due to a lack of vaccination and knowledge. To date, network vaccination programs have proven more successful when random vaccinations are administered in pairs, combining targeted vaccination with regular immunization [4].

Until now, the mechanism of rabies spread is still being studied for prevention and mitigation purposes. One approach to understanding the dynamics of the spread of infectious diseases is through mathematical modelling. Many epidemic models are based on the classic SEIR (Susceptible-Exposed-Infectious-Recovered) model. Several rabies epidemic models based on the classical SEIR compartment model used to simulate rabies disease dynamics can be found in [5-10] and the references therein. A deterministic model was created to examine the dynamics of dog-to-human and dog-to-dog rabies transmission in China [5]. This model is a SEIR model, which looks at four groups in dog and human populations. The results of this study indicate that an efficient way to reduce human rabies in China is to reduce the fertility rate of dogs and increase dog vaccination coverage. Ruan et al. [10] built a SEIR basic type model for the spread of rabies virus between dogs and from dogs to humans and used the model to simulate human rabies data in China from 1996 to 2010. Subsequently, this basic model was modified to include pet dogs and stray dogs and applied the model to simulate human rabies data from Guangdong Province, China. Asamoah et al. [11] investigated the best strategy to stop the spread of rabies from dogs to humans, namely by using pre-exposure prophylaxis (vaccine) and post-exposure prophylaxis (treatment) as a result of public awareness. Furthermore, Taib et al. [12] proposed a deterministic compartmental model with the SEIRS framework to fit actual data regarding the number of rabies cases infected in humans in Sarawak from June 2017 to January 2019. The study results show that controlling

dog births can prevent the spread of rabies in the state and increasing dog vaccination coverage and reducing the number of newborn dogs would be a more effective strategy to deal with the current rabies outbreak in Sarawak. Hailemhicael et al. [14] constructed a mathematical model by dividing the dog population into two categories, namely: stray dogs and domestic dogs. On the other hand, the rabies virus tends to spread in both populations. In this model, disease control strategies use vaccination and culling of infected dogs, and the impact is studied.

Optimal control theory is an effective mathematical technique for analyzing a variety of epidemiological models to determine the optimal control strategy to minimize the number of infected individuals [15]. More studies on the applications of optimal control to infectious diseases can be found in [16-21] and the references therein. Additional research on the use of optimum control for infectious diseases, including rabies, may be found in [22–25] and the reference therein.

This research will expand the model [14] by adding treatment control for infected dogs and the method will be expanded by analyzing optimal control in a model of rabies transmission from a stray dog population to domestic dogs. The research aims to examine the optimal control of vaccination interventions for susceptible individuals (pre-exposure vaccination) and treatment of exposed individuals (post-exposure vaccination) in a model of rabies transmission from stray dogs to domestic dogs. The urgency of this research is because currently, the rate of rabies infection is still high, a significant number of deaths have occurred, and the administration of vaccines and treatment has not been optimal. The problem studied is still a real problem faced by people in the world. The facts on the ground also show that transmission of dogs from stray dogs to domestic dogs, a dog care system that is late in providing vaccinations and treatment after dogs are exposed, has an impact on increasing cases of rabies. Based on this, mathematical modelling of rabies transmission from stray dogs to domestic dogs is needed using optimal control, vaccination for susceptible dogs and treatment for exposed dogs to reduce rabies cases.

Our paper is arranged as follows. In section 2, we formulate the rabies transmission model with pre-exposure vaccination and post-exposure vaccination. In section 3, the positivity and boundedness of the solutions, the equilibrium point, the fundamental reproduction number, and a

study of the equilibrium point's global stability are all covered in model analysis. Section 4 presents the sensitivity analysis of the effective reproduction number. In Section 5, the optimal control problem is defined, the existence of an optimal control is demonstrated and characterized, and numerical simulations are shown. Several conclusions are presented in Section 6.

2. MODEL FORMULATION

A SEIR model with pre-exposure vaccination and post-exposure treatment are formulated to study and analyze the dynamics of rabies infection. The total population of domestic dogs is denoted by N_d which consists of susceptible domestic dogs (S_d), exposed domestic dogs (E_d), infected domestic dogs (I_d), and partially immune domestic dogs (R_d). Meanwhile, the total stray dog population is denoted by N_s which consists of susceptible stray dogs (S_s), exposed stray dogs (E_s), infected stray dogs (I_s), and partially immune stray dogs (R_s). The graphical representation of the proposed model is shown in Figure 1.

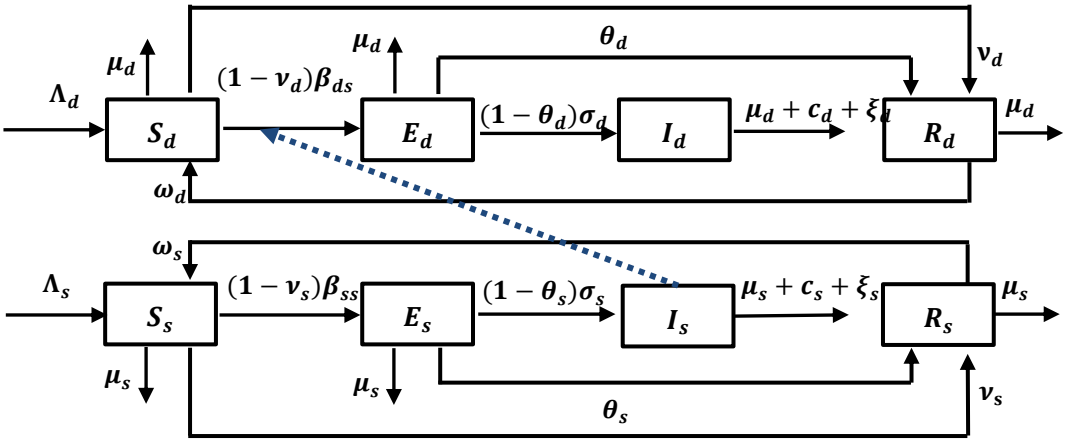


Figure 1: Flow diagram for rabies transmission among domestic and stray dog subgroups.

The detailed descriptions of all the parameters of the model are given in Table 1. Several assumptions used in constructing this model are as follows.

1. Susceptible individuals (S_d and S_s) are vaccinated to become recovered subpopulations (R_d and R_s) and can return to susceptible subpopulations if vaccination rates fall.

2. The spread of the disease is assumed to mean that stray dogs can transmit rabies to domestic dogs but not vice versa.
3. The exposed individuals (E_d and E_s) received treatment.
4. Infected individuals with reported symptoms will be hospitalized.
5. Natural death occurs in every subpopulation.
6. Deaths due to rabies occur in subpopulations infected with I_d and I_s. In this subpopulation there is also culling of infected dogs.
7. All parameters are assumed to be nonnegative.

Table 1: The description and numerical values for the model parameters.

Parameter	Description	Values	Source
Λ_d	The recruitment rate of domestic dogs	120	[7]
β_{ds}	Transmission rate (stray dogs to domestic dogs)	4.1e-6	[14]
σ_d	Latency rate of domestic dogs	0.37	[6]
μ_d	The natural death rate of domestic dogs	0.11	[10]
ξ_d	Domestic dog mortality due to disease	1	[10]
ν_d	Rate of vaccination (domestic dogs)	0.54	[7]
ω_d	Loss of immunity (domestic dog)	1	[10]
θ_d	Treatment rate for exposed domestic dogs	0.25	[7]
c_d	Death rate of domestic dogs due to culling	0.5	[7]
Λ_s	The recruitment rate of domestic dogs	250	[12]
β_{ss}	Transmission rate in stray dogs	0.0087	Assumed
σ_s	Latency rate of stray dogs	0.84	[9]
μ_s	Natural death rate of stray dogs	0.32	[8]
ξ_s	Stray dogs' mortality due to disease	1	[10]
ν_s	Rate of vaccination (stray dogs)	0.25	[13]
ω_s	Loss of immunity (stray dogs)	0.5	[10]
θ_s	Treatment rate for exposed stray dogs	0.25	Assumed
c_s	Death rate of stray dogs due to culling	0.1	[13]

Based on the assumptions and Figure 1, we get the rabies model as follows:

$$\begin{cases} \frac{dS_d}{dt} = \Lambda_d + \omega_d R_d - (1-\nu_d)\beta_{ds} S_d I_s - (\nu_d + \mu_d)\mathrm{S}_d, \\ \frac{dE_d}{dt} = (1-\nu_d)\beta_{ds} S_d I_s - \big((1-\theta_d)\sigma_d + \theta_d + \mu_d\big)E_d, \\ \frac{dI_d}{dt} = (1-\theta_d)\sigma_d E_d - (\mu_d + c_d + \xi_d)I_d, \\ \frac{dR_d}{dt} = \nu_d S_d + \theta_d E_d - (\omega_d + \mu_d)R_d, \\ \frac{dS_s}{dt} = \Lambda_s + \omega_s R_s - (1-\nu_s)\beta_{ss} S_s I_s - (\nu_s + \mu_s)\mathrm{S}_s, \\ \frac{dE_s}{dt} = (1-\nu_s)\beta_{ss}\beta_{ss} S_s I_s - \big((1-\theta_s)\sigma_{\_s} + \theta_s + \mu_s\big)E_s, \\ \frac{dI_s}{dt} = (1-\theta_s)\sigma_s E_s - (\mu_s + c_s + \xi_s)I_s, \\ \frac{dR_s}{dt} = \nu_s S_s + \theta_s E_s - (\omega_s + \mu_s)R_s. \end{cases} \quad (1)$$

with initial conditions

$$S_d(0) > 0,\ E_d(0) \geq 0,\ I_d(0) \geq 0, R_d(0) \geq 0, S_s(0) > 0, E_s(0) \geq 0, I_s(0) \geq 0, R_s(0) \geq 0. \quad (2)$$

3. MODEL ANALYSIS

3.1. Positivity of the solutions

Model system (1) describes the human population, it is very important to prove that all the solution of the system (1) is positive. We stated and proved the following lemma.

Lemma 1. *The solution* $(S_d(t), E_d(t), I_d(t), R_d(t), S_s(t), E_s(t), I_s(t), R_s(t))$ *of the model (1) are nonnegative for all* $t \geq 0$ *with initial conditions nonnegative (2) in* $\mathbb{R}^8_{+0}$.

Proof. We apply the technique [26] to demonstrate this lemma. From model (1), we have

$$\left.\frac{dS_d}{dt}\right|_{S_d=0} = \Lambda_d + \omega_d R_d > 0, \qquad \left.\frac{dS_s}{dt}\right|_{S_s=0} = \Lambda_s + \omega_s R_s > 0$$

$$\left.\frac{dE_d}{dt}\right|_{E_d=0} = (1-\nu_d)\beta_{ds} S_d I_s > 0, \quad \left.\frac{dE_d}{dt}\right|_{E_{d=0}} = (1-\nu_d)\beta_{ds} S_d I_s > 0,$$

$$\left.\frac{dI_d}{dt}\right|_{I_d=0} = (1-\theta_d)\sigma_d E_d > 0, \qquad \left.\frac{dI_s}{dt}\right|_{I_s=0} = (1-\theta_s)\sigma_s E_s > 0,$$

$$\left.\frac{dR_d}{dt}\right|_{R_d=0} = \nu_d S_d + \theta_d E_d > 0, \qquad \left.\frac{dR_s}{dt}\right|_{R_s=0} = \nu_s S_s + \theta_s E_s > 0.$$

Based on Lemma 2 in [27], the invariant region of the model (1) is $\mathbb{R}^8_{+0}$. As a result, the solution of the model (1) with initial conditions nonnegative is nonnegative. The proof of Lemma 1 is complete ■

3.2. Invariant region

Lemma 2. *The solution* $(S_d, E_d, I_d, R_d, S_s, E_s, I_s, R_s)$ *of the model (1) with initial conditions* $S_d(0), E_d(0), I_d(0), R_d(0), S_s(0), E_s(0), I_s(0), R_s(0)$ *nonnegative defined in the region* Ω *in* $\mathbb{R}^8_{+0}$ *where* $\Omega = \left\{(S_d, E_d, I_d, R_d, S_s, E_s, I_s, R_s) \in \mathbb{R}^8_{+0} : N_d \leq \frac{\Lambda_d}{\mu_d}, N_s \leq \frac{\Lambda_s}{\mu_s}\right\}$ *is positively invariant.*

Proof. The total population is the population of domestic dogs and the population of stray dogs is $N_d = S_d + E_d + I_d + R_d$ and $N_s = S_s + E_s + I_s + R_s$, respectively. By adding differential equations for the total population of the domestic dog and the stray dog, the model (1) produces the rate of change

$$\begin{aligned} \frac{dN_d}{dt} &= \Lambda_d - \mu_d N_d - \left(c_d + \xi_d\right) I_d, \\ \frac{dN_s}{dt} &= \Lambda_s - \mu_s N_s - \left(c_s + \xi_s\right) I_s. \end{aligned} \tag{3}$$

Since $c_d + \xi_d \geq 0$ and $c_s + \xi_s \geq 0$, then we have

$$\begin{cases} \frac{dN_d}{dt} \leq \Lambda_d - \mu_d N_d, \\ \frac{dN_s}{dt} \leq \Lambda_s - \mu_s N_s. \end{cases} \tag{4}$$

By integrating the first equation of (4) using the integral factor method and applying initial condition, we get

$$N_d(t) \leq \frac{\Lambda_d}{\mu_d} + \left(N_d(0) - \frac{\Lambda_d}{\mu_d}\right) e^{-\mu_d t}. \tag{5}$$

It is clear that, $0 \leq N_d(t) \leq \frac{\Lambda_d}{\mu_d}$ for all $t \geq 0$ whenever $0 \leq N_d(0) \leq \frac{\Lambda_d}{\mu_d}$ for all $t \geq 0$. Thus,

N_d is nonnegative and bounded. Hence, the set $\Omega_1 = \left\{(S_d, E_d, I_d, R_d) \in \mathbb{R}^4_{+0} : N_d \leq \frac{\Lambda_d}{\mu_d}\right\}$ are the feasible solutions of the domestic dogs.

In the same way, by integrating the second equation of (4) using the integral factor method and applying initial condition, we get

$$N_s(t) \leq \frac{\Lambda_s}{\mu_s} + \left(N_s(0) - \frac{\Lambda_s}{\mu_s}\right) e^{-\mu_s t}. \quad (6)$$

It is clear that, $0 \leq N_s(t) \leq \frac{\Lambda_s}{\mu_s}$ for all $t \geq 0$ whenever $0 \leq N_s(0) \leq \frac{\Lambda_s}{\mu_s}$ for all $t \geq 0$. Thus, N_s is bounded. Hence, the set $\Omega_2 = \left\{(S_s, E_s, I_s, R_s) \in \mathbb{R}^4_{+0} : N_s \leq \frac{\Lambda_s}{\mu_s}\right\}$ are the feasible solutions of the stray dogs. Therefore, the region $\Omega = \Omega_1 \times \Omega_2$ is positively invariant and the model (1) is well-posed or biologically and epidemiologically. The proof of Lemma 2 is complete. ■

Next, for convenience in the discussion, we make the following substitutions
$\mathcal{P}_d = (1-\theta_d)\sigma_d + \theta_d + \mu_d,\ \mathcal{P}_s = (1-\theta_s)\sigma_s + \theta_s + \mu_s,\ Q_d = \mu_d + c_d + \xi_d,$
$Q_s = \mu_s + c_s + \xi_s,\ A_s = \nu_s + \mu_s,\ A_d = \nu_d + \mu_d,\ B_s = \omega_s + \mu_s,$ and $B_d = \omega_d + \mu_d.$

3.3. Disease-free Equilibrium point

The model exhibits a disease-free equilibrium (DFE) point when we set the right-hand sides of the equations of the model (1) to zero. The DFE for the rabies model is a steady-state solution of disease without infection or disease (rabies). In the absence of rabies, model (1) has a disease-free equilibrium point, $E_0 = (S_d^0, E_d^0, I_d^0, R_d^0, S_s^0, E_s^0, I_s^0, R_s^0)$,

$$E_0 = \left(\frac{B_d\Lambda_d}{\mu_d(\omega_d + \nu_d + \mu_d)}, 0, 0, \frac{\nu_d\Lambda_d}{\mu_d(\omega_d + \nu_d + \mu_d)}, \frac{B_s\Lambda_s}{\mu_s(\omega_s + \nu_s + \mu_s)}, 0, 0, \frac{\nu_s\Lambda_s}{\mu_s(\omega_s + \nu_s + \mu_s)}\right). \quad (7)$$

3.4. The effective reproduction number

Using the next-generation matrix method described by [28], we can calculate the effective reproduction number of the model (1). By using the notation as in [28], $\mathcal{F}_i$ is the rate at which new infections appear in compartment i and V_i is the rate of transfer of individuals into and out of compartment i. Let $X = (E_d, I_d, E_s, I_s)^T$. The right-hand side of the model (1) is written as $\dot{x} = \mathcal{F}_i(X) - V_i(X)$, where

$$\mathcal{F}_i(X) = \begin{bmatrix} (1-\nu_d)\beta_{ds}S_dI_s \\ 0 \\ (1-\nu_s)\beta_{ss}S_sI_s \\ 0 \end{bmatrix} \text{ and } V_i(X) = \begin{bmatrix} \mathcal{P}_dE_d \\ \mathcal{Q}_dI_d - (1-\theta_d)\sigma_dE_d \\ \mathcal{P}_sE_s \\ \mathcal{Q}_sI_s - (1-\theta_s)\sigma_sE_s \end{bmatrix}.$$

Evaluating the Jacobian matrix of $\mathcal{F}_i(X)$ and $V_i(X)$ at the disease-free equilibrium point E_0, we get, respectively,

$$F = \begin{bmatrix} 0 & 0 & 0 & \frac{(1-\nu_d)\beta_{ds}B_d\Lambda_d}{\mu_d(\omega_d+\nu_d+\mu_d)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{(1-\nu_s)\beta_{ss}B_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)} \\ 0 & 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \mathcal{P}_d & 0 & 0 & 0 \\ -(1-\theta_d)\sigma_d & \mathcal{Q}_d & 0 & 0 \\ 0 & 0 & \mathcal{P}_s & 0 \\ 0 & 0 & -(1-\theta_s)\sigma_s & \mathcal{Q}_s \end{bmatrix}.$$

The next-generation matrix is

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{(1-\nu_d)\beta_{ds}\Lambda_dB_d(1-\theta_s)\sigma_s}{\mu_d(\omega_d+\nu_d+\mu_d)\mathcal{P}_s\mathcal{Q}_s} & \frac{(1-\nu_d)\beta_{ds}\Lambda_dB_d}{\mu_d(\omega_d+\nu_d+\mu_d)\mathcal{Q}_s} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{(1-\nu_s)\beta_{ss}\Lambda_sB_s(1-\theta_s)\sigma_s}{\mu_s(\omega_s+\nu_s+\mu_s)\mathcal{P}_s\mathcal{Q}_s} & \frac{(1-\nu_s)\beta_{ss}B_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)\mathcal{Q}_s} \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

Hence, the effective reproduction number of the model (1) is the spectral radius of matrix FV^{-1}, that is,

$$\mathcal{R}_e = \frac{(1-\nu_s)(1-\theta_s)\beta_{ss}\Lambda_s\sigma_sB_s}{\mathcal{P}_s\mathcal{Q}_s\mu_s(\omega_s+\nu_s+\mu_s)} \tag{8}$$

The effective reproduction number, $\mathcal{R}_e$, shows the average number of new infections that are caused by a single rabies-infected individual in a population during its infectious period with pre-exposure vaccination and post-exposure treatment of domestic and stray dogs used to control strategies.

3.5. Endemic equilibrium point

When rabies is present in a population, model (1) has a steady-state E_1 which is called the endemic equilibrium (EE) point. By solving the equilibrium conditions of the model (1) are obtained an endemic equilibrium point $E_1 = (S_d^*, E_d^*, I_d^*, R_d^*, S_s^*, E_s^*, I_s^*, R_s^*)$, where

$$S_s^* = \frac{\mathcal{P}_s\mathcal{Q}_s}{(1-\nu_s)(1-\theta_s)\beta_{ss}\sigma_s},$$

$$E_s^* = \frac{(1-\nu_s)(1-\theta_s)B_s\Lambda_s\beta_{ss}\sigma_s - \mathcal{P}_s Q_s(A_s B_s - \nu_s\omega_s)}{(1-\nu_s)(1-\theta_s)\beta_{ss}\sigma_s(B_s\mathcal{P}_s - \theta_s\omega_s)},$$

$$I_s^* = \frac{(1-\theta_s)\sigma_s E_s^*}{Q_s},\ R_s^* = \frac{\nu_s S_s^* + \theta_s E_s^*}{B_s},$$

$$S_d^* = \frac{B_d\Lambda_d\mathcal{P}_d}{(1-\nu_d)\beta_{ds}I_s^*(\theta_d\omega_d - B_d\mathcal{P}_d) + \mathcal{P}_d(\nu_d\omega_d - A_d B_d)},$$

$$E_d^* = \frac{(1-\nu_d)\beta_{ds}I_s^* S_d^*}{\mathcal{P}_d},\ I_d^* = \frac{(1-\theta_d)\sigma_d E_d^*}{Q_d},\ R_d^* = \frac{\nu_d S_d^* + \theta_d E_d^*}{B_d}.$$

The effective reproduction number, $\mathcal{R}_e$, shows the average number of new infections that are caused by a single rabies-infected individual in a population during its infectious period with pre-

3.6. Global stability of DFE

The method of Castillo-Chavez et al. [29] is used to examine the global stability of DFE. Next, the model system (1) can be expressed as follows:

Let Y stands for the number of the uninfected compartment, Z stand for the number of uninfected compartments, and $E_0 = (Y^0, 0)$ stands for the disease-free equilibrium point. Then, the model (1) can be expressed as follows:

$$\begin{cases} \dfrac{dY}{dt} = F(Y,Z), \\ \dfrac{dZ}{dt} = G(Y,Z), G(Y,0) = 0. \end{cases} \tag{9}$$

To ensure the global asymptotic stability of DFE, the following conditions ($H1$) and (H_2) must be satisfied.

(H_1) For $\frac{dY}{dt} = F(Y,0)$, Y^0 is globally asymptotically stable

(H_2) $G(Y,Z) = AZ - \hat{G}(Y,Z)$, $\hat{G}(Y,Z) \geq 0$ for $(Y,Z) \in \Omega$ and $A = D_Z G(Y^0, 0)$ is a

Metzler-matrix because the off-diagonal elements of A are nonnegative.

Consequently, the following theorem is true if the system satisfies the above conditions (H_1) and (H_2).

Theorem 1. *The disease-free equilibrium $E_0 = (Y^0, 0)$ of the model (1) is globally asymptotically stable in Ω if $\mathcal{R}_e < 1$.*

Proof. The model (1) can be written as $Y = (S_d, R_d, S_s, R_s)$, $Z = (E_d, I_d, E_s, I_s)$, and

$E_0 = \left(\frac{B_d\Lambda_d}{\mu_d(\omega_d+\nu_d+\mu_d)}, 0,0, \frac{\nu_d\Lambda_d}{\mu_d(\omega_d+\nu_d+\mu_d)}, \frac{B_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)}, 0,0, \frac{\nu_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)}\right)$.

From the first equation of system (8), we have

$$\frac{dY}{dt} = F(Y,Z) = \begin{bmatrix} \Lambda_d + \omega_d R_d - (1-\nu_d)\beta_{ds} S_d I_s - A_d S_d \\ \nu_d S_d + \theta_d E_d - B_d R_d \\ \Lambda_s + \omega_s R_s - (1-\nu_s)\beta_{ss} S_s I_s - A_s)S_s \\ \nu_s S_s + \theta_s E_s - B_s R_s \end{bmatrix}.$$

At the disease-free equilibrium point E_0, we get

$$\frac{dY}{dt} = F(Y^0,0) = \begin{bmatrix} \Lambda_d + \omega_d R_d^0 - A_d S_d^0 \\ \nu_d S_d^0 - B_d R_d^0 \\ \Lambda_s + \omega_s R_s^0 - A_s S_s^0 \\ \nu_s S_s^0 - B_s R_s^0 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

$F(Y^0,0)$ has a unique point of equilibrium

$Y^0 = \left(\frac{B_d\Lambda_d}{\mu_d(\omega_d+\nu_d+\mu_d)}, \frac{\nu_d\Lambda_d}{\mu_d(\omega_d+\nu_d+\mu_d)}, \frac{B_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)}, \frac{\nu_s\Lambda_s}{\mu_s(\omega_s+\nu_s+\mu_s)}\right)$

which is globally asymptotically stable. Thus, condition (H_1) is satisfied.

Next, from the second equation of system (9), we have

$$G(Y,Z) = \begin{bmatrix} (1-\nu_d)\beta_{ds} S_d I_s - \mathcal{P}_d E_d \\ (1-\theta_d)\sigma_d E_d - Q_d I_d \\ (1-\nu_s)\beta_{ss} S_s I_s - \mathcal{P}_s E_s \\ (1-\theta_s)\sigma_s E_s - Q_s I_s \end{bmatrix}.$$

It is clear that, $G(Y,0) = 0$. Then, we get

$$A = D_Z G(Y^0,0) = \begin{bmatrix} -\mathcal{P}_d & 0 & 0 & (1-\nu_d)\beta_{ds} S_d^0 \\ (1-\theta_d)\sigma_d & -Q_d & 0 & 0 \\ 0 & 0 & -\mathcal{P}_s & (1-\nu_s)\beta_{ss} S_s^0 \\ 0 & 0 & (1-\theta_s)\sigma_s & -Q_s \end{bmatrix}.$$

Here, A is a Metzler-matrix since all off-diagonal entries of the matrix A are non-negative. Then, we calculated $\hat{G}(Y,Z) = AZ - G(Y,Z)$,

$$\hat{G}(Y,Z) == \begin{bmatrix} (1-\nu_d)\beta_{ds} I_s (S_d^0 - S_d) \\ 0 \\ (1-\nu_s)\beta_{ss} I_s (S_s^0 - S_s) \\ 0 \end{bmatrix}.$$

Since $S_d^0 \geq S_d$ and $S_s^0 \geq S_s$, then $\hat{G}(Y,Z) \geq 0$. As a result, condition (H_2) is satisfied. Here, condition (H_1) and (H_2) is satisfied. Thus, E_0 is globally asymptotically stable when $\mathcal{R}_e < 1$. The proof of Theorem 1 is complete. ■

It can be observed from Theorem 1 that the globally asymptotically stable disease-free equilibrium point E_0 is if $\mathcal{R}_e < 1$. Thus, the infected individuals eventually vanish and the disease dies out.

3.7. Global stability of EE

Using the Lyapunov function, the global asymptotic stability of the endemic equilibrium is explored. We will create a Lyapunov function by referring to [30, 31].

$$\mathcal{L} = \frac{1}{2}[(S_d - S_d^*) + (E_d - E_d^*) + (I_d - I_d^*) + (R_d - R_d^*) + (S_s - S_s^*) + (E_s - E_s^*) + (I_s - I_s^*) + (R_s - R_s^*)]^2 \quad (10)$$

Clearly that $\mathcal{L} : \mathbb{R}^8_{+0} \to \mathbb{R}$ is a continuous and differentiable function. Then, the derivative of $\mathcal{L}$ along the solutions of the model (1) is given by

$$\frac{d\mathcal{L}}{dt} = [(S_d - S_d^*) + (E_d - E_d^*) + (I_d - I_d^*) + (R_d - R_d^*) + (S_s - S_s^*) + (E_s - E_s^*) + (I_s - I_s^*) + (R_s - R_s^*)]\frac{d}{dt}[S_d + E_d + I_d + R_d + S_s + E_s + I_s + R_s].$$

$$= [(N_d - N_d^*) + (N_s - N_s^*)]\ \frac{d}{dt}(N_d + N_s).$$

From (3),

$$\frac{dN_d}{dt} = \Lambda_d - \mu_d N_d - (c_d + \xi_d)I_d^*,\ \ \frac{dN_s}{dt} = \Lambda_s - \mu_s N_s - (c_s + \xi_s)I_s^* \quad (11)$$

and all the solutions of the model (1) satisfy

$$S_d^* + E_d^* + I_d^* + R_d^* = \frac{\Lambda_d - (c_d+\xi_d)I_d^*}{\mu_d},\ \ S_s^* + E_s^* + I_s^* + R_s^* = \frac{\Lambda_s - (c_s + \xi_s)I_s^*}{\mu_s}. \quad (12)$$

Substitute (11) and (12) into $\frac{d\mathcal{L}}{dt}$ gives

$$\frac{d\mathcal{L}}{dt} = \left[\left(N_d - \frac{\Lambda_d-(c_d+\xi_d)I_d^*}{\mu_d}\right) + \left(N_s - \frac{\Lambda_s-(c_s+\xi_s)I_s^*}{\mu_s}\right)\right][(\Lambda_d - \mu_d N_d - (c_d + \xi_d)I_d^*) + (\Lambda_s - \mu_s N_s - (c_s + \xi_s)I_s^*)]$$

$$= \left[\left(N_d - \frac{\Lambda_d-(c_d+\xi_d)I_d^*}{\mu_d}\right) + \left(N_s - \frac{\Lambda_s-(c_s+\xi_s)I_s^*}{\mu_s}\right)\right]\left[-\mu_d\left(N_d - \frac{\Lambda_d-(c_d+\xi_d)I_d^*}{\mu_d}\right) - \mu_s\left(N_s - \frac{\Lambda_s-(c_s+\xi_s)I_s^*}{\mu_s}\right)\right]$$

$$= -\mu\left[\left(N_d - \frac{\Lambda_d}{\mu_d} + \frac{(c_d+\xi_d)I_d^*}{\mu_d}\right) + \left(N_s - \frac{\Lambda_s}{\mu_s} + \frac{(c_s+\xi_s)I_s^*}{\mu_s}\right)\right]\left[\left(N_d - \frac{\Lambda_d}{\mu_d} + \frac{(c_d+\xi_d)I_d^*}{\mu_d}\right)\right.$$

$$+\left(N_s-\frac{\Lambda_s}{\mu_s}+\frac{(c_s+\xi_s)I_s^*}{\mu_s}\right)\Bigg]$$

$$\leq -\mu\left[\left(N_d-\frac{\Lambda_d}{\mu_d}\right)+\left(N_s-\frac{\Lambda_s}{\mu_s}\right)\right]\left[\left(N_d-\frac{\Lambda_d}{\mu_d}\right)+\left(N_s-\frac{\Lambda_s}{\mu_s}\right)\right]=-\mu\left[\left(N_d-\frac{\Lambda_d}{\mu_d}\right)+\left(N_s-\frac{\Lambda_s}{\mu_s}\right)\right]^2$$

< 0, where $\mu = min\{\mu_d, \mu_s\}$.

Consequently, $\frac{d\mathcal{L}}{dt} < 0$ for $\mathcal{R}_e > 1$ indicates that the endemic equilibrium point E_1 is asymptotically stable globally. The proof of Theorem 2 is complete. ■

4. OPTIMAL CONTROL PROBLEM

In this section, we formulate the optimal control problem for rabies by including four time-dependent controls in the model (1). The control variables ν_d and ν_s are the control efforts aimed at improving the immunity of susceptible domestic and stray dogs (pre-exposed prophylaxis), respectively. The control variables θ_d and θ_s are the control efforts aimed at treating the exposed domestic and stray dogs (post-exposed prophylaxis), respectively. The controls are bounded between 0 and 1 in the intervention time interval $[0, T_f]$, where T_f stands for the last time the controls were utilized. Thus, the model (1) became

$$\begin{cases} \frac{dS_d}{dt} = \Lambda_d + \omega_d R_d - (1-\nu_d)\beta_{ds} S_d I_s - A_d S_d, \\ \frac{dE_d}{dt} = (1-\nu_d)\beta_{ds} S_d I_s - \mathcal{P}_d E_d, \\ \frac{dI_d}{dt} = (1-\theta_d)\sigma_d E_d - Q_d I_d, \\ \frac{dR_d}{dt} = \nu_d S_d + \theta_d E_d - B_d R_d, \\ \frac{dS_s}{dt} = \Lambda_s + \omega_s R_s - (1-\nu_s)\beta_{ss} S_s I_s - A_s S_s, \\ \frac{dE_s}{dt} = (1-\nu_s)\beta_{ss}\beta_{ss} S_s I_s - \mathcal{P}_s E_s, \\ \frac{dI_s}{dt} = (1-\theta_s)\sigma_s E_s - Q_s I_s, \\ \frac{dR_s}{dt} = \nu_s S_s + \theta_s E_s - B_s R_s. \end{cases} \tag{13}$$

with the initial conditions (2).

Our goal is to find optimal controls such as v_d^*, θ_d^*, v_s^*, and θ_s^* that minimize the objective functional

$$J(\theta_d, v_d, \theta_s, v_s) = \int_0^{T_f} (A_1 E_d + A_2 I_d + A_3 E_s + A_4 I_s + \frac{1}{2} B_1 \theta_d^2 + \frac{1}{2} B_2 v_d^2 + \frac{1}{2} B_3 \theta_s^2 + \frac{1}{2} B_4 v_s^2) dt \tag{14}$$

The constants A_1 and A_3 denote the weight of the exposed classes and A_2 and A_4 denote the weight of the infectious classes, respectively. The constants $B_i \geq 0$ $(i = 1, 2, 3, 4)$ are weights of the domestic dog and the stray dog controls, and $B_1\theta_d^2, B_2 v_d^2, B_3\theta_s^2, B_4 v_s^2$ describe the costs of rabies vaccination and treatment. In other words, we seek an optimal control triple $(\theta_d^*, v_d^*, \theta_s^*, v_s^*)$ such that

$$J(\theta_d^*, v_d^*, \theta_s^*, v_s^*) = \min_{\theta_d, v_d, \theta_s, v_s} \{J(\theta_d, v_d, \theta_s, v_s) : \theta_d, v_d, \theta_s, v_s \in U\}. \tag{15}$$

where $U = \{(\theta_d, v_d, \theta_s, v_s) : 0 \leq \theta_d(t) \leq 1, 0 \leq v_d(t) \leq 1, 0 \leq \theta_s(t) \leq 1, 0 \leq v_s(t) \leq 1, t \in [0, 1]\}$ is the control set.

4.1. Existence of the Optimal Controls

In relation to the conclusion of Fleming and Rishel described in [32], the existence of an optimal control four that minimizes (14) subject to (13) is demonstrated.

Theorem 3. *For the rabies model (13) with control measures and initial conditions at* $t = 0$, *exists an optimal control* $(\theta_d^*, v_d^*, \theta_s^*, v_s^*) \in \Omega$ *with a corresponding solution* $(S_d^*, E_d^*, I_d^*, R_d^*, S_s^*, E_s^*, I_s^*, R_s^*)$, *that minimizes the objective functional (14) over* U.

The existence of optimal can be proved by showing that, the following conditions hold.

(1) The set of controls U and the corresponding state variables is nonempty.

(2) The set of controls U is closed and convex.

(3) The right-hand side of the state systems (17) is bounded by a linear function in both the state and control variables.

(4) The integrand L in the objective functional (18) is convex to control.

(5) There exist constants $k_1 \geq 0, k_2 \geq 0,$ and $k_3 > 1$ that make the integrand L in the objective functional (18) bounded by

$$k_1(|\theta_d|^2 + |\nu_d|^2 + |\theta_s|^2 + |\nu_s|^2)^{k_3/2} - k_2.$$

Proof. We create the proof in the following steps:

(1) Using the fact that all model states $(S_d, E_d, I_d, R_d, S_s, E_s, I_s, R_s) \in \Omega$ are bounded below and above, any solutions to the state equations are also bounded. Because the state solutions are bounded, the Lipschitz property of the state system with respect to the state variables is satisfied. Hence, condition (1) is met.

(2) By the definition, the control set $U = [0,1]^4$ is closed. Again, we let $y, z \in U$, so that $y = (\theta_{d1}, \nu_{d1}, \theta_{s1}, \upsilon_{s1})$ and $z = (\theta_{d2}, \nu_{d2}, \theta_{s2}, \upsilon_{s2})$. Then, for every $\pi \in [0,1]$, we have $0 \leq \pi y + (1-\pi)z$. Additionally, we observe $\pi y \leq \pi$ and $(1-\pi)z \leq (1-\pi)$. Then $\pi y + (1-\pi)z \leq \pi + (1-\pi) = 1$. Hence, $0 \leq \pi y + (1-\pi)z \leq 1$, for all $y, z \in U$ and $\pi \in [0,1]$.

(3) From the system of differential equation (13),

$$\begin{aligned}\frac{dN}{dt} &= \frac{dN_d}{dt} + \frac{dN_s}{dt} \\ &= \Lambda_d - \mu_d N_d - (c_d + \xi_d) I_d + \Lambda_s - \mu_s N_s - (c_s + \xi_s) I_s \\ &\leq \Lambda_d + \Lambda_s - \mu_d N_d - \mu_s N_s \\ &\leq \Lambda_d + \Lambda_s - \mu N,\end{aligned}$$

where $\mu = \min(\mu_d, \mu_s)$.

Hence, $\limsup_{t\to\infty} N(t) \leq \frac{\Lambda_d + \Lambda_s}{\mu}$. Therefore, all solutions of the model (13) are bounded.

From the state equation system (13), the state equations are linearly dependent on the controls $\theta_d, \nu_d, \theta_s,$ and υ_s. Hence, the right-hand sides of the state systems (13) can be

written as a linear function of $\theta_d, \nu_d, \theta_s,$ and υ_s with coefficients depending on time and state [33]. Thus, condition (3) holds.

(4) The integrand L in the objective functional expressed by (14)

$$L = A_1E_d + A_2I_d + A_3E_s + A_4I_s + \frac{1}{2}B_1\theta_d^2 + \frac{1}{2}B_2\nu_d^2 + \frac{1}{2}B_3\theta_s^2 + \frac{1}{2}B_4\nu_s^2$$

is clearly convex since it is a quadratic function of $(\theta_d, \nu_d, \theta_s, \upsilon_s)$ on the control set *U*.

It is left to demonstrate the existence of constants $k_1 \geq 0, k_2 \geq 0,$ and $k_3 > 1$ such that L satisfies

$$\begin{aligned} L &= A_1E_d + A_2I_d + A_3E_s + A_4I_s + \frac{1}{2}B_1\theta_d^2 + \frac{1}{2}B_2\nu_d^2 + \frac{1}{2}B_3\theta_s^2 + \frac{1}{2}B_4\nu_s^2 \\ &\geq \tfrac{1}{2}(B_1\theta_d^2 + B_2\nu_d^2 + B_3\theta_s^2 + B_4\nu_s^2) \\ &\geq \tfrac{1}{2}(B_1\theta_d^2 + B_2\nu_d^2 + B_3\theta_s^2 + B_4\nu_s^2) - B_1 \quad \text{since } B_1\theta_d^2 - B_1 \leq 0 \\ &\geq \mathbf{\tfrac{1}{2}}\min\{B_1, B_2, B_3, B_4\}(|\theta_d|^2 + |\nu_d|^2 + |\theta_s|^2 + |\nu_s|^2) - B_1 \\ &= k_1(|\theta_d|^2 + |\nu_d|^2 + |\theta_s|^2 + |\nu_s|^2)^{k_3/2} - k_2, \end{aligned}$$

with $k_1 = \mathbf{\tfrac{1}{2}}\min\{B_1, B_2, B_3, B_4\}$, $k_2 = B_1$, and $k_2 = 2$. Thus, condition (4) also holds.

The proof of Theorem 3 is complete. ■

4.2. Characterization of the Optimal Controls

To obtain the necessary conditions for optimal control, we use Pontryagin's maximum [34] principle to the Hamiltonian function H is defined for all $t \in [0, T_f]$ by

$$H = L + \sum_{i=1}^{8} \lambda_i f_i(S_d, E_d, I_d, R_d, S_s, E_s, I_s, R_s), \tag{16}$$

where f_i is the right side of the differential equations of the *i*th state variable and λ_i are the respective adjoint variables for the state $S_d, E_d, I_d, R_d, S_s, E_s, I_s,$ and R_s.

Theorem 4. *Given the optimal controls* $(\theta_d^*, \nu_d^*, \theta_s^*, \nu_s^*)$ *and the solutions* $S_d^*, E_d^*, I_d^*, R_d^*, S_s^*, E_s^*, I_s^*,$ *and* R_s^* *of the corresponding state system (13), there exist the adjoint variables* $\lambda_j, j = 1, 2, 3, 4, 5, 6, 7, 8$ *satisfying*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= (\lambda_1-\lambda_2)(1-\nu_d)\beta_{ds}I_s + (\lambda_1-\lambda_4)\nu_d + \lambda_1\mu_d\\
\frac{d\lambda_2}{dt} &= -A_1 + (\lambda_2-\lambda_3)(1-\theta_d)\sigma_d + (\lambda_2-\lambda_4)\theta_d + \lambda_2\mu_d\\
\frac{d\lambda_3}{dt} &= -A_2 + \lambda_3(\mu_d + c_d + \xi_d)\\
\frac{d\lambda_4}{dt} &= (\lambda_4-\lambda_1)\omega_d R_d + \lambda_4\mu_d\\
\frac{d\lambda_5}{dt} &= (\lambda_5-\lambda_6)(1-\nu_s)\beta_{ss}I_s + (\lambda_5-\lambda_8)\nu_s + \lambda_5\mu_s\\
\frac{d\lambda_6}{dt} &= -A_3 + (\lambda_6-\lambda_7)(1-\theta_s)\sigma_s + (\lambda_6-\lambda_8)\theta_s + \lambda_6\mu_s\\
\frac{d\lambda_7}{dt} &= -A_4 + (\lambda_1-\lambda_2)(1-\nu_d)\beta_{ds}S_d + (\lambda_5-\lambda_6)(1-\nu_s)\beta_{ss}S_s\\
&\quad +\lambda_7(\mu_s + c_s + \xi_s)\\
\frac{d\lambda_8}{dt} &= (\lambda_8-\lambda_5)\omega_s + \lambda_8\mu_s,
\end{aligned} \tag{17}$$

with the transversality conditions at time T_f,

$$\lambda_j\left(T_f\right) = 0, j = 1,2,3,4,5,6,7,8. \tag{18}$$

Furthermore, for $t \in [0, T_f]$, *the optimal controls* $\theta_d^*, \nu_d^*, \theta_s^*$, *and* ν_s^* *are given by*

$$\begin{aligned}
\theta_d^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_3-\lambda_2)\sigma_d E_d + (\lambda_2-\lambda_4)E_d}{B_1}\right\}\right\}.\\
\nu_d^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_2-\lambda_1)\beta_{ds}S_d I_s + (\lambda_1-\lambda_4)S_d}{B_2}\right\}\right\}.\\
\theta_s^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_7-\lambda_6)\sigma_s E_s + (\lambda_6-\lambda_8)E_s}{B_3}\right\}\right\}.\\
\nu_s^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_6-\lambda_5)\beta_{ss}S_s I_s + (\lambda_5-\lambda_8)S_s}{B_4}\right\}\right\}.
\end{aligned} \tag{19}$$

Proof. Referring to the Hamiltonian function (16), given by

$$\begin{aligned}
H &= A_1E_d + A_2I_d + A_3E_s + A_4I_s + \tfrac{1}{2}B_1\theta_d^2 + \tfrac{1}{2}B_2\nu_d^2 + \tfrac{1}{2}B_3\theta_s^2 + \tfrac{1}{2}B_4\nu_s^2\\
&\quad +\lambda_1\left(\Lambda_d + \omega_d R_d - (1-\nu_d)\beta_{ds}S_d I_s - (\nu_d + \mu_d)S_d\right)\\
&\quad +\lambda_2\left((1-\nu_d)\beta_{ds}S_d I_s - \left((1-\theta_d)\sigma_d + \theta_d + \mu_d\right)E_d\right)
\end{aligned} \tag{20}$$

$$+\lambda_3\big((1-\theta_d)\sigma_d E_d-(\mu_d+c_d+\xi_d)I_d\big)$$

$$+\lambda_4\big(\nu_d S_d+\theta_d E_d-\big(\omega_d+\mu_d\big)R_d\big)$$

$$+\lambda_5\big(\Lambda_s+\omega_s R_s-(1-\nu_s)\beta_{ss}S_s I_s-(\nu_s+\mu_s)\mathrm{S}_s\big)$$

$$+\lambda_6\big((1-\nu_s)\beta_{ss}S_s I_s-\big((1-\theta_s)\sigma_s+\theta_s+\mu_s\big)E_s\big)$$

$$+\lambda_7\big((1-\theta_s)\sigma_s E_s-\big(\mu_s+c_s+\xi_s\big)I_s\big)$$

$$+\lambda_8\big(\nu_s S_s+\theta_s E_s-\big(\omega_s+\mu_s\big)R_s\big).$$

The adjoint system (13) is generated by partially differentiating the Hamiltonian function (20) to the corresponding state variables $S_d, E_d, I_d, R_d, S_s, E_s, I_s,$ and R_s as

$$\begin{aligned}&\frac{d\lambda_1}{dt}=-\frac{\partial H}{\partial S_d},\ \frac{d\lambda_2}{dt}=-\frac{\partial H}{\partial E_d},\ \frac{d\lambda_3}{dt}=-\frac{\partial H}{\partial I_d},\ \frac{d\lambda_4}{dt}=-\frac{\partial H}{\partial R_d},\ \frac{d\lambda_5}{dt}=-\frac{\partial H}{\partial S_s},\\&\frac{d\lambda_6}{dt}=-\frac{\partial H}{\partial E_s},\frac{d\lambda_7}{dt}=-\frac{\partial H}{\partial I_s},\ \text{and}\ \frac{d\lambda_8}{dt}=-\frac{\partial H}{\partial R_s}.\end{aligned}\tag{21}$$

For $t\in[0,T_f]$, the optimal control $\theta_d^*,\nu_d^*,\theta_s^*,$ and ν_s^* can be solved from the optimality condition,

$$\begin{aligned}\frac{\partial H}{\partial\theta_d}&=B_1\theta_d-\lambda_2(1-\sigma_d)E_d-\lambda_3\sigma_d E_d+\lambda_4E_d=0,\\\frac{\partial H}{\partial\nu_d}&=B_2\nu_d+\lambda_1(\beta_{ds}I_sS_d-S_d)-\lambda_2\beta_{ds}I_sS_d+\lambda_4S_d=0,\\\frac{\partial H}{\partial\theta_s}&=B_3\theta_s-\lambda_6(1-\sigma_s)E_s-\lambda_7\sigma_sE_s+\lambda_8E_s=0,\\\frac{\partial H}{\partial\nu_s}&=B_4\nu_s+\lambda_5\big(\beta_{ss}I_sS_s-S_s\big)-\lambda_6\beta_{ss}I_sS_d+\lambda_8S_s=0.\end{aligned}\tag{22}$$

Solving (30) for $\theta_d,\nu_d,\theta_s,$ and υ_s yields

$$\begin{aligned}&\theta_d^*=\frac{(\lambda_3-\lambda_2)\sigma_dE_d+(\lambda_2-\lambda_4)E_d}{B_1},\ \nu_d^*=\frac{(\lambda_2-\lambda_1)\beta_{ds}S_dI_s+(\lambda_1-\lambda_4)S_d}{B_2},\\&\theta_s^*=\frac{(\lambda_7-\lambda_6)\sigma_sE_s+(\lambda_6-\lambda_8)E_s}{B_3},\nu_s^*=\frac{(\lambda_6-\lambda_5)\beta_{ss}S_sI_s+(\lambda_5-\lambda_8)S_s}{B_4}.\end{aligned}\tag{23}$$

By using the bounds on the control $\theta_d,\nu_d,\theta_s,$ and υ_s, we get the following solutions

$$\begin{aligned}
\theta_d^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_3-\lambda_2)\sigma_d E_d+(\lambda_2-\lambda_4)E_d}{B_1}\right\}\right\}.\\
\nu_d^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_2-\lambda_1)\beta_{ds} S_d I_s+(\lambda_1-\lambda_4)S_d}{B_2}\right\}\right\}.\\
\theta_s^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_7-\lambda_6)\sigma_s E_s+(\lambda_6-\lambda_8)E_s}{B_3}\right\}\right\}.\\
\nu_s^* &= \min\left\{1, \max\left\{0, \frac{(\lambda_6-\lambda_5)\beta_{ss} S_s I_s+(\lambda_5-\lambda_8)S_s}{B_4}\right\}\right\}.
\end{aligned} \tag{24}$$

The proof of Theorem 4 is complete. ■

5. NUMERICAL SIMULATIONS

5.1 Sensitivity analysis of the effective reproduction number

The sensitivity analysis discusses how the model parameters affect the effective reproduction number $\mathcal{R}_e$ as well as the transmission of the disease. The purpose of the sensitivity index is to quantify the initial disease's spread as well as the relative change in $\mathcal{R}_e$ when one parameter changes while the others stay the same. The applications of a sensitivity index on parameters that have a high influence can help target interventions to control the spread of disease.

We perform the analysis by applying the method of [35] to determine the sensitivity index of the model parameters. The normalized forward sensitivity index of the variable $\mathcal{R}_e$, that depends on the differentiability of a parameter k, is defined as,

$$\Upsilon_k^{\mathcal{R}_e} = \frac{\partial \mathcal{R}_e}{k} \times \frac{k}{\mathcal{R}_e}, \tag{25}$$

where $\Upsilon_k^{\mathcal{R}_e}$ represent the sensitivity index and k is the parameter in the effective reproduction number.

Using parameter values in Table 1, we have the sensitivity indices $of\ \mathcal{R}_e$ (Table 2). The sensitivity index is from the most sensitive to the least sensitive.

TABLE 2. The sensitivity indices of $\mathcal{R}_e$

Parameter	Value
μ_s	-1.4161
Λ_s	1
β_{ss}	1
ξ_s	-0.7519
ν_s	-0.5669
σ_s	0.4750
θ_s	-0.3667
ω_s	0.1425
c_s	-0.0075

The effective reproduction number of the model (1), $\mathcal{R}_e$, is determined by the nine parameters and the sensitivity indices of $\mathcal{R}_e$ are presented in Table 2 (arrange from the most sensitive to the least) and graph of sensitivity indices of $\mathcal{R}_e$ with respect to the model parameters can be seen in Figure 2 below.

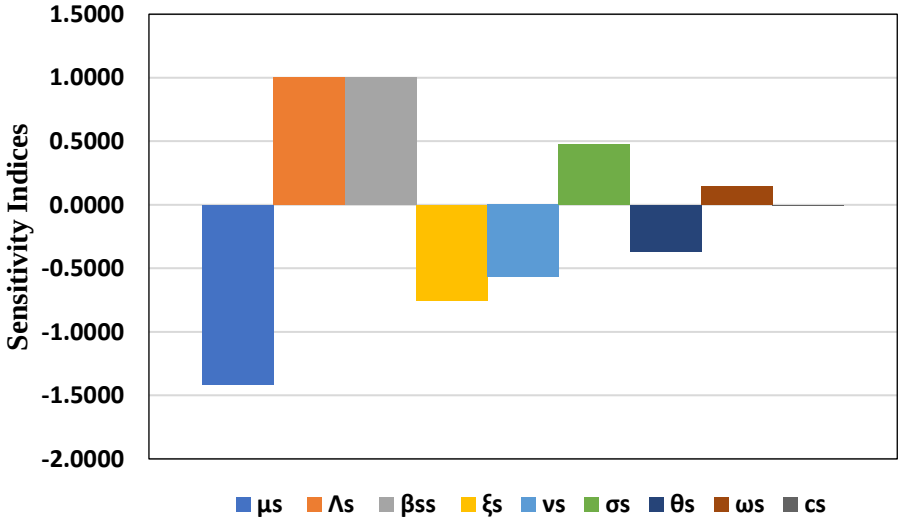


Figure 2. Graph of sensitivity indices of $\mathcal{R}_e$ with respect to the model parameters.

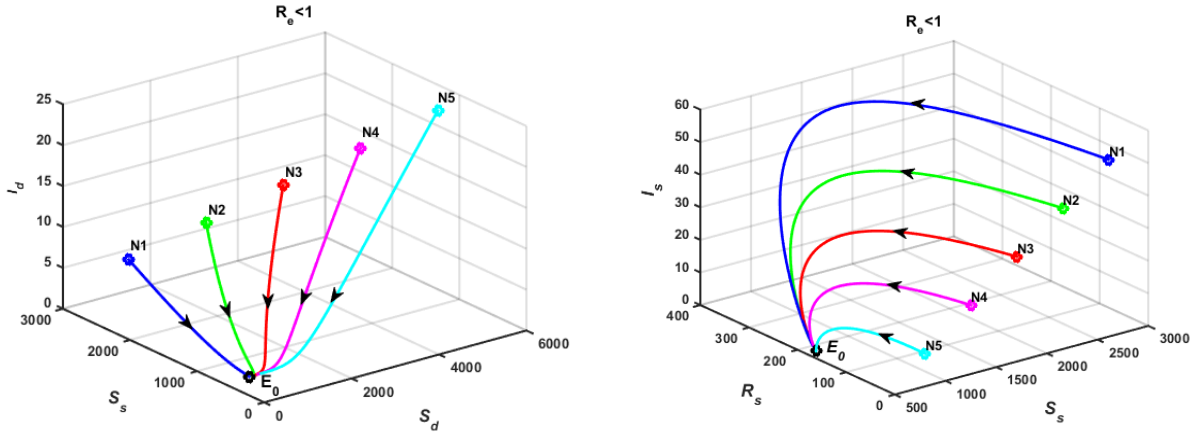
It can see that $\beta_{ss}, \xi_s,$ and ν_s have a high impact on $\mathcal{R}_e$. On the other hand, parameters that have a high sensitivity index but cannot be controlled are μ_s and Λ_s. The parameter has negative impacts and positive impacts on $\mathcal{R}_e$. The positive sign of sensitivity indices of $\mathcal{R}_e$ to the model parameters indicates that a decrease (or increase) in the value of each of the parameters in this case, leads to a decrease (or increase) in $\mathcal{R}_e$. On the contrary, the negative sign of the sensitivity indices of $\mathcal{R}_e$ to the model parameters indicates that an increase (or decrease) in the value of each of the parameters, in this case, leads to a decrease (or increase) in $\mathcal{R}_e$. To illustrate, the index of treatment rate for exposed stray dogs (θ_s) is $\Upsilon_{\theta_s}^{\mathcal{R}_e} = +0.1242$. This implies that an increase (or decrease) by 10% in θ_s while other parameters remain constant, will be followed by an increase (or decrease) in the effective reproduction number ($\mathcal{R}_e$) by 12.42 %. On the other hand, the index of vaccination rate for exposed stray dogs (ν_s) has a negative sensitivity index (-0.8650). This implies that the effective reproduction number ($\mathcal{R}_e$) will immediately decrease (or increase) by 86.5% upon a 10% increase (or decrease) in ν_s while all other parameters stay constant. Consequently, the indices for the remaining parameters are shown in Table 2.

5.2 Numerical Simulations

In this section, we performed numerical simulations to study the impact of various parameters on the spread of rabies infection. To perform this study, we used the following initial values $S_d(0) = 3200$, $E_d(0) = 60$, $I_d(0) = 15$, $R_d(0) = 25$, $S_s(0) = 2800$, $E_s(0) = 80$, $I_s(0) = 20$, $R_s(0) = 0$ and the set of parameter values given in Table 1.

First, we choose $\beta_{ss} = 0.0017$. The numerical simulation of the model (1) shows that the disease-free equilibrium (DFE) point is globally stable for some other parameter values in Table 1. The corresponding effective reproduction number is equal to $\mathcal{R}_e = 0.301326$. Figure 3 illustrates the global stability of the disease-free equilibrium point proved in Theorem 1. Figure 3(a) shows the dynamics of the population of susceptible domestic (S_d), susceptible stray (S_s), and infected domestic (I_d). Figure 3(b) shows the dynamics of the population of susceptible stray (S_s), recovered stray (R_s), and infected stray (I_s). In these figures, all solution trajectories converge to

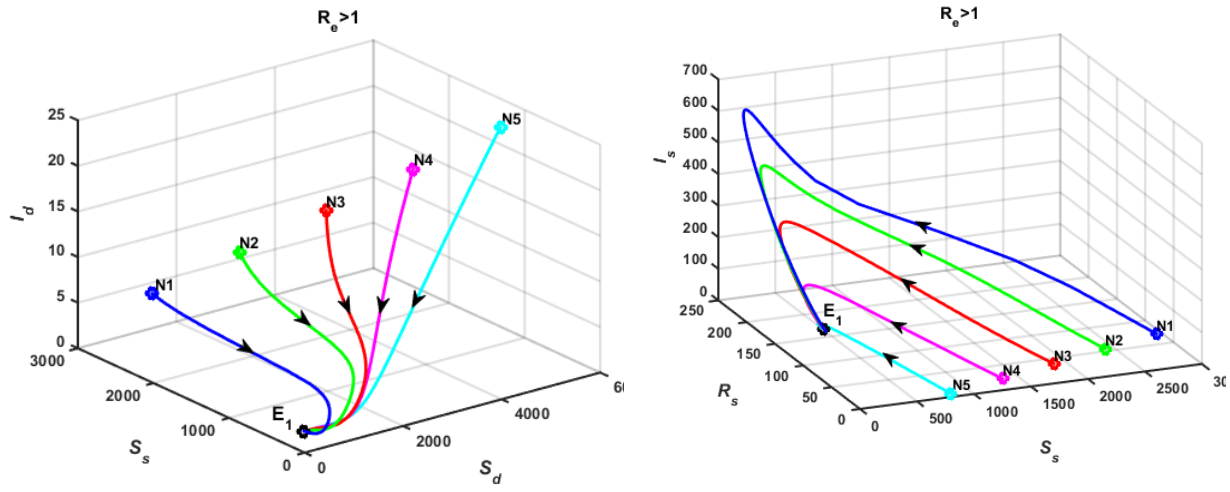
the disease-free equilibrium point $E_0 = (578.7, 0, 0, 512.3, 598.7, 0, 0, 182.5)$ for five different initial conditions.



(a) (b)

Figure 3. Simulation of the model (1) showing the global asymptotic stable of the E_0. (a) the dynamics of S_d, S_s, and I_d (b) the dynamics of S_s, R_s, and I_s.

Second, the numerical simulation of the model (1) shows that the endemic equilibrium point is globally stable for $\beta_{ss} = 0.0087$ and some other parameter values in Table 1. The corresponding effective reproduction number is equal to $\mathcal{R}_e = 1.54289 > 1$. This implies that the rabies infection will persist in the population. Theorem 2 is numerically illustrated in Figure 4. Figure 4(a) shows the dynamics of the population of susceptible domestic (S_d), susceptible stray (S_s), and infected domestic (I_d) and Figure 4(b) shows the dynamics of the population of susceptible stray (S_s), recovered stray (R_s), and infected stray (I_s). In these figures, all solution trajectories converge to the endemic equilibrium point $E_1 = (578.5, 0.07, 0.01, 512.2, 388.3, 83.9, 39.7, 143.9)$ for five different initial conditions.



(a) (b)

Figure 4. Simulation of the model (1) showing the global asymptotic stable of the E_1.
(a) the dynamics of f S_d, S_s, and I_d (b) the dynamics of S_d, R_s, and I_s.

The numerical result illustrated in Figure 3 confirms that model (1) has only one unique positive endemic equilibrium point when $\mathcal{R}_e > 1$. This implies that the rabies infection will persist in the population. Theorem 2 is numerically illustrated in Figure 3.

5.3 Numerical simulations of the optimal control

In this section, we discuss the numerical results of the system (17) to investigate the effect of the following itemized optimal control strategies on the spread of the disease in a population. With the help of the software Matlab. This section focuses on demonstrating some numerical results of qualitative analysis and optimal control problem (17)-(19) through the forward-backwards Sweep method [10]. Using a forward fourth-order Runge-Kutta scheme and the conditions (20) and (21), we start with an initial guess for the controls over the time interval $[0, T_f]$ and solve the state system (1). Using the new state values, the adjoint system (21) is solved by a backward fourth-order Runge-Kutta scheme. The controls are updated using a convex combination of the previous control values and the new control values from (28). The iterative method is repeated until convergence. Furthermore, in describing the control strategy the parameter values are used in [8,

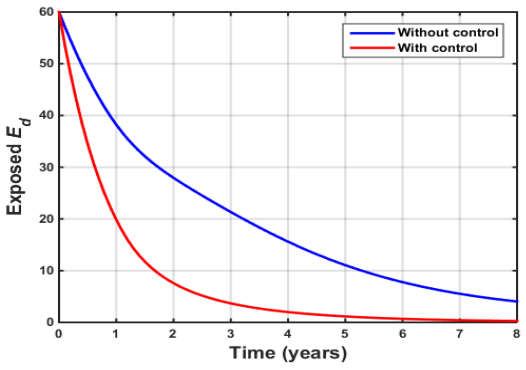
9] and weights at the end of the period ($T_f = 8$),

$$A_1 = A_2 = A_3 = A_4 = 1, B_1 = 20, B_2 = 10, B_3 = 40, B_4 = 20. \quad (26)$$

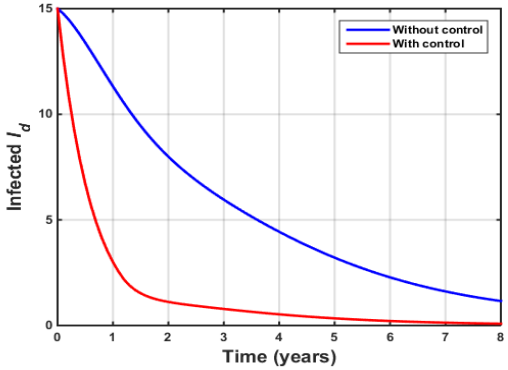
We examine and compare two different combinations of control intervention strategies for both domestic and stray dogs. The simulations of the optimal control are divided into three strategies: implementation of post-exposure treatment (θ_d,θ_s), implementation of pre-exposure vaccination (ν_d,ν_s), and implementation of the combination of pre-exposure vaccination (ν_d, ν_s) and post-exposure treatment (θ_d, θ_s).

- **Strategy 1** (implementation of post-exposure treatment)

The combination of control of post-exposure treatment for domestic dogs (θ_d) and stray dogs (θ_s) is used to optimize the objective function J, whereas we set both domestic and stray dogs' pre-exposure vaccinations to zero ($\nu_d = \nu_s = 0$). For both domestic and stray dogs, there is a significant reduction in the number of exposed individuals (E_d,E_s) and infected individuals (I_d, I_s) when compared to cases without controls (Figure 5(a-d)). The control profile is shown in Fig. 5(e), and control θ_d is at the upper bound for about 1.1 years and the control of θ_s is at the upper bound for about 6.1 years. Then it gradually decreased to zero (the lower limit) at the end of the control period. The objective function value of Strategy 1 at the end of the control period is close to $J = 512.79$.



(a)



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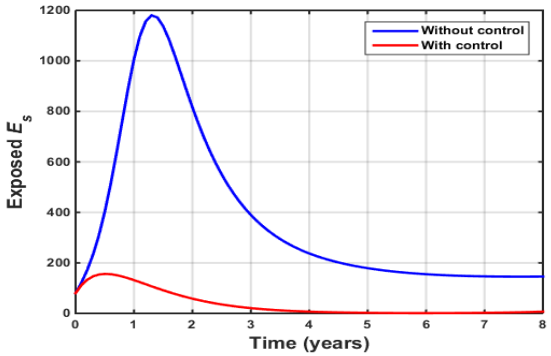

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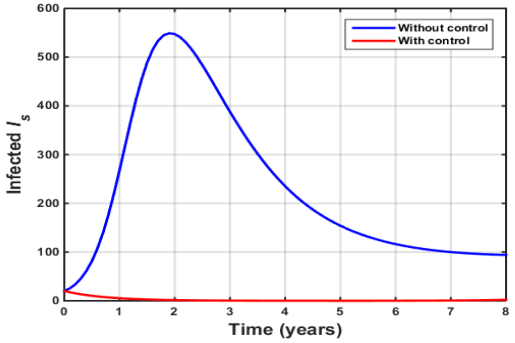
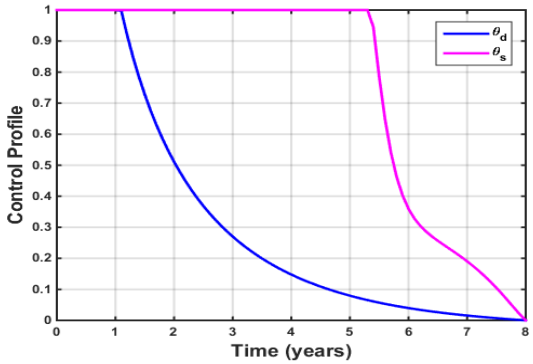


(d)



(e)

Figure 5. The simulation results of the model (1) show the effect of post-exposure treatment for domestic dogs (θ_d) and stray dogs (θ_s) on the spread of rabies.

- **Strategy 2** (implementation of pre-exposure vaccination)

The combination of control of pre-exposure vaccination for domestic dogs (ν_d) and stray dogs (ν_s) is used to optimize the objective function J, whereas we set both domestic and stray dogs' post-exposure treatment to zero ($\theta_d = \theta_s = 0$). For both domestic and stray dogs, there is a significant reduction in the number of infected individuals (I_d,I_s) when compared to cases without controls (Fig. 6(c-d). The control profile is shown in Fig. 6(e), and control ν_s is at the upper bound for about 4.7 years and the control of ν_d at the beginning of the period is around 0.14 and then drops to zero at the end of the control period ($T_f = 8$). Then it gradually decreased to zero (the lower limit) at the end of the control period. The objective function value of Strategy 2 at the end of the control period is close to $J = 347.19$.

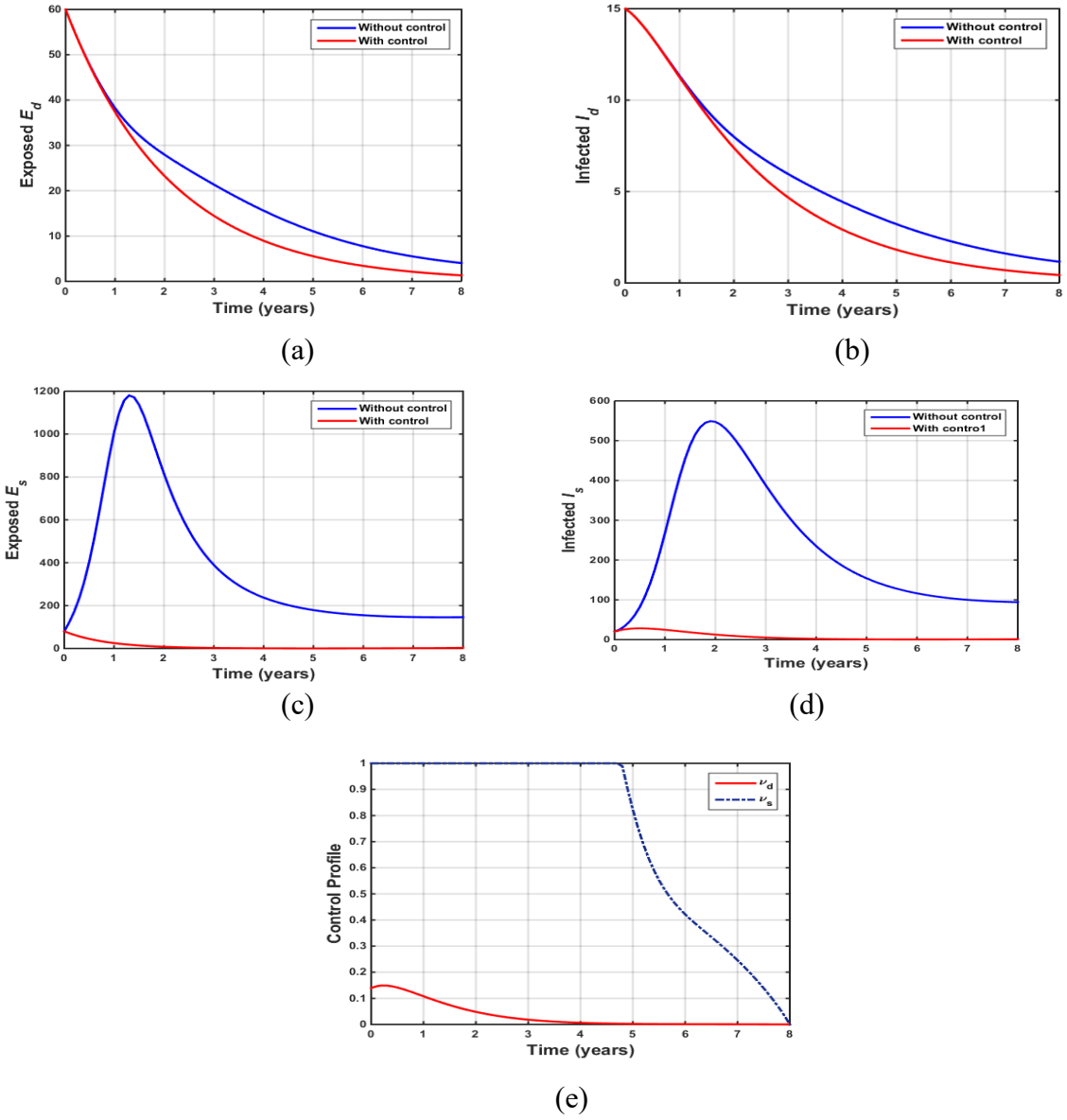


Figure 6. The simulation results of the model show the effect of post-exposure vaccination for domestic dogs (ν_d) and stray dogs (ν_s) on the spread of rabies.

- **Strategy 3** (implementation of pre-exposure vaccination and post-exposure treatment)

The combination of control of pre-exposure vaccination and post-exposure treatment for domestic dogs (ν_d, θ_d) and stray dogs (ν_s, θ_s) is used to optimize the objective function J. Strategy 3 produces a pattern similar to Strategy 1. For both domestic and stray dogs, there is a significant reduction in the number of exposed individuals (E_d,E_s) and infected individuals (I_d,I_s) when

compared to cases without controls (Fig. 7(a-d)). The control profile is shown in Fig. 7(e), and control θ_d and θ_s are at the upper bound for about 0.4 and 1 years, respectively. Then it gradually decreased to zero at the end of the control period ($T_f = 8$). The objective function value of Strategy 3 at the end of the control period is close to $J = 251.85$.

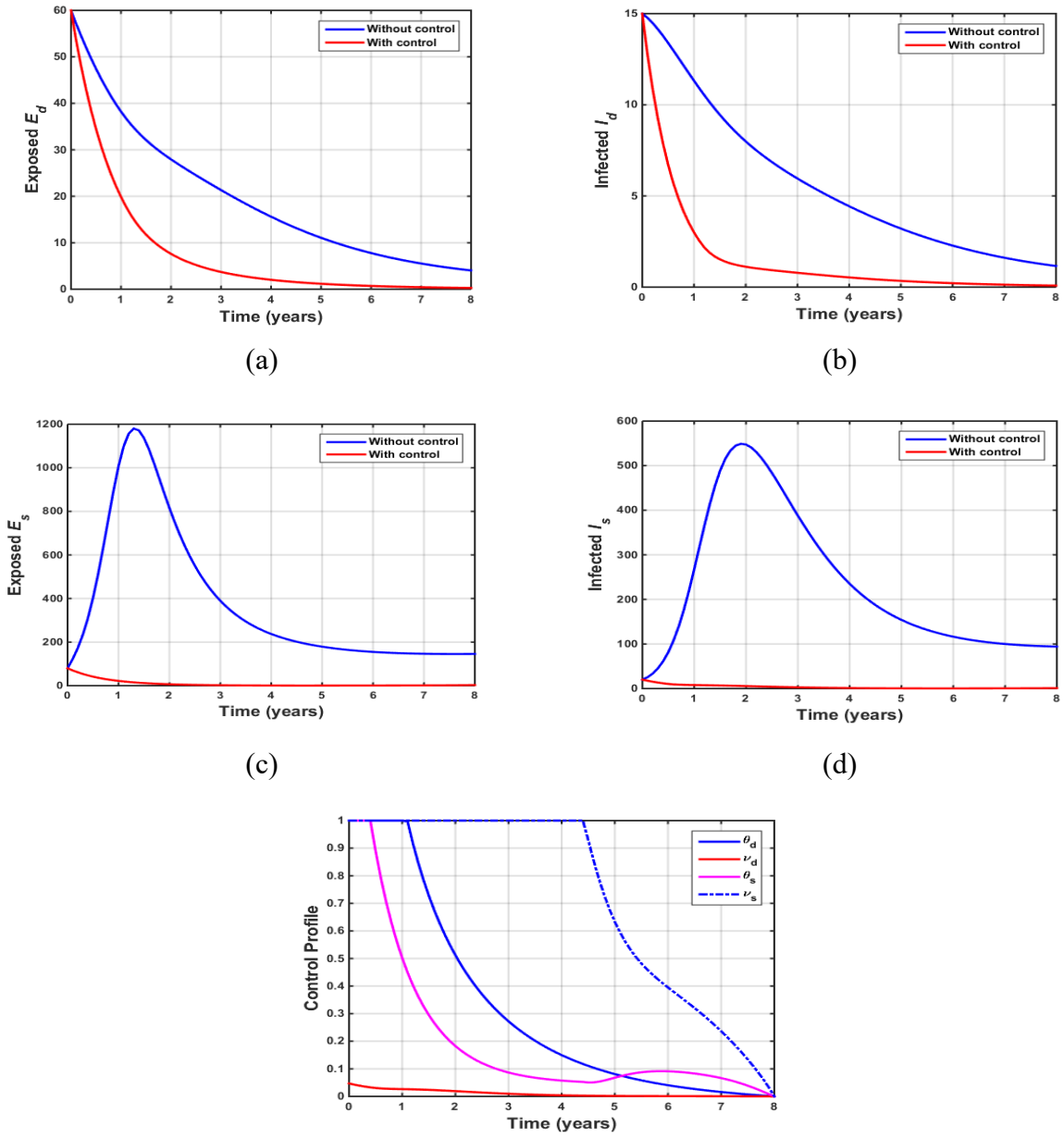


Figure 7. The simulation results of the model show the effect of the combination of pre-exposure vaccination and post-exposure treatment for domestic dogs (ν_d, θ_d) and stray dogs (ν_s, θ_s) on the spread of rabies.

The calculations above, it shows that by using parameter values as in Table 1 and using the objective function as in equation (18) with weights at the end of the control period $(T_f = 8)$, the results obtained are that Strategy 3 (combination of pre-exposure vaccination and post-exposure treatment on domestic dogs and stray dogs) is a strategy with minimum objective function value over the 8 year intervention period.

6. CONCLUSION

In this study, rabies transmission in pet and stray dog populations with pre-exposure vaccination and post-exposure treatment was studied using a nonlinear mathematical model. The model has a disease-free equilibrium point and an endemic equilibrium point. The global dynamics of the model are determined by the effective reproduction number, which is obtained from the next generation matrix method. Using the next-generation matrix approach, the effective reproduction number $\mathcal{R}_{\mathrm{e}}$ can be determined. It has been demonstrated that, assuming $\mathcal{R}_{\mathrm{e}} < 1$, the disease-free equilibrium point is globally asymptotically stable using the Castillo-Chavez method. However, if $\mathcal{R}_{\mathrm{e}} > 1$, the endemic equilibrium will be globally asymptotically stable, which is proven using the nonlinear Lyapunov function.

Sensitivity analysis and numerical simulations were carried out on model parameters that influence the spread of rabies in domestic and wild dog populations. The results of the sensitivity analysis shows that the transmission rate in wild dogs (β_{ss}) and the death rate for wild dogs due to a disease ξ_s are the most sensitive (positive) parameters. This means that it plays an important role in influencing the spread of rabies in a population. On the other hand, the vaccination rate of stray dogs (ν_s) is the most sensitive (negative) parameter, which means that the vaccine is a key factor in reducing the prevalence of rabies. Next, the model was developed by considering pre-exposure vaccination and post-exposure treatment in pet dogs and stray dogs as control variables. In addition, the existence of optimal control has been proven and Pontryagin's minimum principle is used to determine the analytical characterization of optimal control. Numerically, optimal control analysis shows that the application of a combination of two optimal controls (pre-exposure

vaccination and post-exposure treatment) results in a significant reduction in the number of cases in infected individuals.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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