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Research Article

Analysis of the dynamics and optimal control of cutaneous Leishmania during human immigration

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Abstract

Leishmania is an infectious disease that is difficult to control and has an impact on morbidity and mortality around the world. This study investigates the dynamics of cutaneous Leishmania and optimal control measures, particularly in regards to human immigration. Applying a mathematical model to evaluate the dynamics of human immigration and sand flies population. The human population is classified into four compartments: susceptible, exposed, infectious, and recovered. The sand fly population is divided into three categories: susceptible, exposed, and infectious. The

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mathematical analysis involves positivity, existence and the uniqueness of the solution. We analyzed the global stability of the system around the endemic equilibrium point by contracting the Lyapunov function. Optimal control measures are used to reduce the number of infected and exposed individuals among humans, sand flies, and migrants. These techniques are described using Pontryagin's Maximum Principle to derive necessary conditions for optimal control. The numerical simulations confirm the theoretical results by showing that following these controls effectively reduces the spread of the disease, and immigration has a major impact on the spread of human-borne Leishmania.

AMS subject classifications (2020): Primary 93A30, Secondary 03C45, 49J15.

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1 Introduction

Humans have suffered from skin diseases since antiquity, that is around the tenth century. Al-Bukhari, an Iranian physician of that era, reported this skin disease, and Ibn Sina identified it as a sand flies bite[10, 7]. In 1882, McNaught made the first modern clinical description; three years later, Kouzem discovered parasites in a sample of the eastern button; in 1898, the military doctor mentioned Borowski protozoa ulcer samples without specifying their taxonomic status; and in 1900, Sir William Aleishman discovered parasites in the swabs of the spleen of a soldier who died in Dum Dum, a municipality in close proximity to the city of Calcutta [19]. In 1903, Charles Donoval identified the same parasite in a spleen biopsy and named it Leishemania dovani, which has since been known as Leishmania [7, 31]. Leishmania is a vector-borne infection carried by phlebotomine sand flies (Dipetra: Psychodidae) and transmitted by members of the Leishmania genus (Kinetoplashida: Trypanosomatidae) [12]. The disease is common in tropical and subtropical regions of 98 countries in America, Europe, Africa, and Asia [2].

Leishmania has three major forms: Visceral, cutaneous, and mucocutaneous.

Moreover, 1.5 to 2.5 million fresh clinical cases are recorded annually [33]. Today, living in Leishmania-endemic areas puts over 1 billion individuals at risk of contracting the disease. Yearly, there are reportedly over a million new cases of Leishmania of the skin, along with approximately 30,000 new cases of Leishmania of the viscera [35].

The predominant type of Leishmania, cutaneous Leishmania (CL), leads to the formation of skin lesions on parts of the body, often in the form of ulcers, that are exposed. It may result in serious limitations or stigma plus lifelong scars [36]. During 2001 and 2021, according to WHO-collected accounts of 105545 cases of the two types of CL and mucosal Leishmania (ML), an average of $52,645$ cases per year [25]. A lot of factors contribute to the rise in Leishmania cases, including lack of housing, sanitary conditions, and clean drinking water in populated regions, among other things that make the environment conducive to the growth of Leishmania. In addition, the main contributing variables are population shifts climate and environmental changes [36].

This research highlights the main risk factors for Leishmania incidence and prevalence, including environment, socioeconomic level, demographics, and human behaviors [34, 28]. The global incidence of Leishmania has increased due to man-made risks such as growing immigration, urbanization, forest clearing, and immunosuppression. Changes in the environment and population immigration can increase human exposure to infected sand flies [3].

Leishmania mostly affects rural impoverished communities, and outbreaks typically happen during harvest times [4]. Due to agricultural improvements in the region in the late 1970s, a significant number of migrant workers from the lowlands were sent to the endemic regions in order to harvest crops. The aforementioned demographic shifts subsequently facilitated the dissemination of visceral Leishmania, thereby giving rise to elevated rates of morbidity and mortality [11].

CL, considered a parasitic disease, can pose a significant concern for travelers and tourists, particularly those engaging in outdoor activities in regions where the disease is prevalent. This condition is commonly diagnosed among a diverse range of individuals, including tourists, workers in the con-

struction industry, immigrants, researchers, military men, and expatriates. Those involved in high-risk activities such as ecotourism, adventure travel, forestry work, and nighttime research are particularly vulnerable. A study conducted over a period of 5.3 years, focusing on American CL among US travelers, revealed that 39% of cases happened among travelers and 46% of scientists traversing South and Central America. Even short-term travel exposes individuals to the risk of contracting the disease, with male travelers accounting for $64 - 71\%$ of reported cases due to their higher participation in dangerous outside pursuits. Around 80% of traveler cases of imported Leishmania contain CL, often acquired in rural or forested regions, particularly the Amazon basin in Bolivia. Although mucocutaneous Leishmania (ML) is less frequently reported; there is a growing trend of its identification among travelers to South America, primarily in the Amazon basin. The delayed diagnosis of ML and CL in homecoming voyagers, frequently after the beginning of symptoms, even years or months, highlights the absence of knowledge among international travelers regarding the disease and appropriate protective measures. Inadequate management of Leishmania cases is also prevalent, resulting in unnecessary medical procedures and expenses. Travel and immigration can introduce new Leishmania species to areas where the disease is not endemic, potentially leading to public health consequences such as the importation of canine visceral Leishmania to new regions. Promoting awareness, educating travelers, and implementing preventive measures are critical to reducing the risk of CL transmission during travel and avoiding its introduction into non-endemic regions [27].

To date, research on Leishmania has primarily focused on a singular or limited set of parameters, predominantly carried out in regions where Leishmania is prevalent. Consequently, there exists an imperative need to undertake more comprehensive investigations into environmental conditions, including clinical, resistance predictors, and co-infection of Leishmania in endemic areas. Presently, Leishmania exhibits a broader geographical distribution than in previous times, continuing to be one of the most ignored illnesses in the world that disproportionately impacts impoverished and developing nations [24].

The transfer or displacement of people or groups from one geographic location to another, either from one with good health conditions to one with a high frequency of illnesses, or vice versa, is known as human immigration [14]. As a result, population growth or immigration becomes the main driving force behind the fast spread of numerous diseases [16]. Several research papers have since looked at the various ways that immigration affects the transmission of infectious illnesses. The one of concrete example is the work of Fared Braurer [8] employed the popular SI and SIS models, which are frequently used in analyzing infectious illnesses, to analyze the likelihood of infected people relocating. He made the erroneous assumption that immigration was steady. His study's findings clearly imply that it is essential to keep infected migrants isolated. Li, Zhang, and Ma [22] studied the SIR and SIRS epidemic models, especially looking at general contact rates and ongoing immigration for each class. The study investigates endemic and disease-free equilibriums and provides requirements for global asymptotic stability. Article [21] centers its research on an SEIR epidemic model that takes into account the infectious force in multiple stages. Additionally, it considers constant immigration rates for exposed and susceptible individuals. The primary objective is to investigate the conditions that lead to make the endemic equilibrium and their global stability. Article [17] examines the influence of immigration on dynamics of tuberculosis transmission, as a case study, using theoretical frameworks and numerical simulations to underscore its significant influence on disease persistence. Additionally, a myriad of other scholarly articles delve into the intricacies of mathematical modeling of diseases and their correlation with immigration [30, 32]. Similarly, more articles study the mathematical modeling regarding Leishmania [13, 9].

To study the presence of potential strategies and the impact of these strategies on the any model had population, a mere examination and analysis of epidemic models' dynamics is inadequate. Hence, the original model incorporates control variables that encompass possible intervention methods, like vaccination,treatment, and also confinement. Consequently, the task of determining the appropriate assigned values for these introduced variables, with the aim of minimizing the densities of all the compartments of populations exactly the exposed and infected individuals while maximizing the

person population take immunity agianst the disease, is handled by finding the required optimality criteria and solving an infinite-dimensional optimization problem. There has been a great deal of research done on finding the best control measures for time-dependent epidemic models, and many writers have emphasized the benefits of treatment and vaccine, for example, the results presented in [29, 5, 20]. As more researchers studied the optimal control for Leishmania disease [1, 37]

The remainder of the paper is organized as follows: The formulation and description of the model are in Section 2. Section 3 contains the basic properties of the model. Analyzing the model to show the equilibrium points describes in Section 4. The global stability at the endemic equilibrium point of the system is in Section 5. In Section 6, we apply Pontryagin's maximum principle to analysis and determine the optimal control strategy for the Leishmania disease. In Section 7, numerical simulations are reported to verify the analysis results. Finally, the paper ends with a conclusion in Section 8.

2 The mathematical model description

The analysis will use the Leishmania model by Zamir, Zaman, and Alshomrani [37], focusing on the dynamics of Zoonotic CL, a disease affecting humans and sand flies, using a formal mathematical model with an invariant region. The study categorizes the human population into four compartments: susceptible (S_h), exposed (E_h), infectious (I_h), and recovered (R_h). The total human population can be represented as the sum of these compartments during a specific time frame: $N_h = S_h + E_h + I_h + R_h$. Sand flies are divided into three compartments: Susceptible (S_s), exposed (E_s), and infectious (I_s), which account for variations in their role in the disease transmission cycle, and the total sand flies population at any given time is defined as $N_s = S_s + E_s + I_s$. A mathematical model will be developed to describe the dynamics of Zoonotic CL by completely dividing the populations involved, accounting for interactions and transitions within and between these compartments. The goal of this model is to get a knowledge of the disease and the interactions among all of these groups. The rate Γ_h represents the addition of new members to the human population, interpreted as recruitment.

Among these new individuals, it is assumed that a fraction P_S is susceptible, P_E is exposed, and P_I is infected. Susceptible hosts become exposed through being bitten by infectious sand flies, which is modeled by the incidence function $S_h f(I_s) = \frac{ab_1 I_s S_h}{N_h}$. Therefore, those who have been exposed to radiation heal naturally at a rate of θ, whereas those who have not are infectious at a rate of k_1, where Γ_s is the sand fly recruitment rate. Disease transmission from sick individuals to sand flies occurs at a rate of ??.

The rate at which sand flies get infected following contact with human carriers is $S_s g(I_h) = \frac{ac_1 I_h S_s}{N_h}$, where c_1 is the chance of sand flies receiving CL from people. When the incubation period ends, the parameter k_2 indicates that the sand flies got infected. The system can be represented as follows:

$$\begin{aligned}
\dot{S_h} &= P_S\Lambda_I + \Gamma_h - S_h f(I_s) - \mu_h S_h,\\
\dot{E_h} &= P_E\Lambda_I + S_h f(I_s) - (k_1 + \theta + \mu_h)E_h,\\
\dot{I_h} &= P_I\Lambda_I + k_1 E_h - (\mu_h)I_h,\\
\dot{R_h} &= \theta E_h - \mu_h R_h,\\
\dot{S_s} &= \Gamma_s - S_s g(I_h) - \mu_s S_s,\\
\dot{E_s} &= S_s g(I_h) - (\mu_s + k_2)E_s,\\
\dot{I_s} &= k_2 E_s - \mu_s I_s,
\end{aligned} \tag{1}$$

where

$$P_h + P_I + P_E = 1, \quad P_h\Lambda_I + P_I\Lambda_I + P_E\Lambda_I = \Lambda_I,$$

$$N_h = S_h + E_h + I_h + R_h, \quad N_s = S_s + E_s + I_s.$$

$$\begin{aligned}
f(I_s) &= \tfrac{ab_1 I_s}{N_h},\\
g(I_h) &= \tfrac{ac_1 I_h}{N_h},
\end{aligned}$$

with

$$S_h(0) = S_{h0}, \quad E_h(0) = E_{h0}, \quad I_h(0) = I_{h0}, \quad R_h(0) = R_{h0},$$
$$S_s(0) = S_{s0}, \quad E_s(0) = E_{s0}, \quad I_s(0) = I_{s0}.$$

It is assumed that all parameters have positive values, whereas the values of P_S, P_E, and P_I are constrained to a range of 0 to 1. Table 1 presents the model's parameter definitions based on their biological meaning.

3 Basic proprieties of the model

3.1 Positivity of solutions

Theorem 1. On the conditions that $S_h(0)$, $E_h(0)$, $I_h(0)$, $R_h(0)$, $S_s(0)$, $E_s(0)$, and $I_s(0)$, the solutions of every compartment of the system (1) are positive for all $t \geq 0$.

Proof. Based on the initial equation of the system (1), we have

$$\dot{S}_h = P_S\Lambda_I + \Gamma_h - \tfrac{ab_1 I_s S_h}{N_h} - \mu_h S_h,$$

$$\dot{S}_h \geq -\tfrac{ab_1 I_s S_h}{N_h} - \mu_h S_h.$$

Then

$$\dot{S}_h + (\tfrac{ab_1 I_s S_h}{N_h} + \mu_h S_h) \geq 0.$$

Therefore

$$\dot{S}_h + (\tfrac{ab_1 I_s}{N_h} + \mu_h) S_h \geq 0.$$

Noted that $F(t) = \frac{ab_1 I_s(t)}{N_h} + \mu_h$.

By multiplying the two sides of the above inequality by $\int_0^t F(s)ds$, we obtain

$$\exp^{(\int_0^t F(s)ds)}\, \dot{S}_h + F(t) \exp^{(\int_0^t F(s)ds)}\, S_h(t) \geq 0.$$

Then

$$\exp\left(\int_0^t F(s)ds\right)\dot{S}_h + F(t)\exp\left(\int_0^t F(s)ds\right)S_h(t) = \frac{d}{dt}\left(S_h(t)\exp\left(\int_0^t F(s)ds\right)\right).$$

Integrating the inequality from 0 to t yields

$$\int_0^t \frac{d}{ds}\left(S_h(s)\exp\left(\int_0^t\left(\frac{ab_1I_s}{N_h}+\mu_h\right)ds\right)\right) \geq 0,$$

$$S_h(t)\exp\left(\int_0^t\left(\frac{ab_1I_s}{N_h}+\mu_h\right)ds\right) - S_h(0) \geq 0,$$

$$S_h(t) \geq S_h(0)\exp\left(-\int_0^t\left(\frac{ab_1I_s}{N_h}+\mu_h\right)ds\right),$$

$$S_h(t) \geq S_h(0)\exp\left(-\int_0^t F(s)ds\right),$$

$$S_h(t) \geq 0.$$

Similarly, it can be proven that $E_h(t)$, $I_h(t)$, $R_h(t)$, $S_s(t)$, $E_s(t)$, and $I_s(t)$ of system (1) are positive for all $t \geq 0$.

□

3.2 Invariant region

Theorem 2. The set

$\mathscr{E} = \{(S_h, E_h, I_h, R_h, S_s, E_s, I_s) \in {\mathbb{R}_+}^7 : N_h \leq \frac{\Lambda_I+\Gamma_h}{\mu_h}, N_s \leq \frac{\Gamma_s}{\mu_s}\}$ is positively invariant under system (1) with initial condition $S_h(0)$, $E_h(0)$, $I_h(0)$, $R_h(0)$, $S_s(0)$, $E_s(0)$, and $I_s(0)$.

Proof. Adding the first four equations of system (1) yields

$$\dot{N_h}(t) = \dot{S_h}(t) + \dot{E_h}(t) + \dot{I_h}(t) + \dot{R_h}(t),$$

$$\dot{N_h}(t) = \Lambda_I + \Gamma_h - \mu_h N_h,$$

Thus, that implies

$$N_h(t) = N_h(0)\exp^{-\mu_h(t)} + (\tfrac{\Lambda_I+\Gamma_h}{\mu_h})(1-\exp^{-\mu_h(t)}).$$

As $t \longrightarrow +\infty$, then $N_h(t) \longrightarrow \frac{\Lambda_I+\Gamma_h}{\mu_h}$. Similarly, $N_s(t) \longrightarrow \frac{\Gamma_s}{\mu_s}$ as $t \longrightarrow +\infty$.

□

3.3 Existence and uniqueness of the solution

Theorem 3. There is only one solution for the system (1) that meets the initial condition $(S_h(0), E_h(0), I_h(0), R_h(0), S_s(0), E_s(0), I_s(0))$.

Proof.

$$Let \quad X = \begin{bmatrix} S_h(t) \\ E_h(t) \\ I_h(t) \\ R_h(t) \\ S_s(t) \\ E_s(t) \\ I_s(t) \end{bmatrix} \qquad and \qquad \rho(X) = \begin{bmatrix} \dot{S_h}(t) \\ \dot{E_h}(t) \\ \dot{I_h}(t) \\ \dot{R_h}(t) \\ \dot{S_s}(t) \\ \dot{E_s}(t) \\ \dot{I_s}(t) \end{bmatrix}.$$

Thus, the system (1) may be reformulated as follows:

$$\rho(X) = AX + B(X), \tag{2}$$

where

$$A = \begin{bmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -(k_1+\theta+\mu_h) & 0 & 0 & 0 & 0 & 0 \\ 0 & k_1 & -(\mu_h) & 0 & 0 & 0 & 0 \\ 0 & \theta & 0 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_s & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu_s+k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & k_2 & -\mu_s \end{bmatrix}$$

and

$$B(X) = \begin{bmatrix} P_S\Lambda_I + \Gamma_h - \frac{ab_1 I_s S_h}{N_h} \\ P_E\Lambda_I + \frac{ab_1 I_s S_h}{N_h} \\ P_I\Lambda_I \\ 0 \\ -\frac{ac_1 I_h S_s}{N_h} \\ \frac{ac_1 I_h S_s}{N_h} \\ 0 \end{bmatrix},$$

$$\begin{aligned} |B(X_1) - B(X_2)| &= 2(|\tfrac{ab_1 I_{v_2} S_{h_2}}{N_h} - \tfrac{ab_1 I_{v_1} S_{h_1}}{N_h} + \tfrac{ac_1 I_{h_2} S_{v_2}}{N_h} - \tfrac{ac_1 I_{h_1} S_{v_1}}{N_h}|) \\ &\leq 2\tfrac{Z}{\mu_h}(||\tfrac{b_1}{N_h}|S_{h_2} - S_{h_1}| + |\tfrac{b_1}{N_h}||I_{v_2} - I_{v_1}| \\ &\quad +|\tfrac{c_1}{N_h}||S_{v_2} - S_{v_1}| + |\tfrac{c_1}{N_h}||I_{h_2} - I_{h_1}|) \\ &\leq M||X_2 - X_1||, \end{aligned}$$

where $M = 2\frac{Z}{\mu_h}(|\frac{b_1}{N_h}| + |\frac{c_1}{N_h}|; |\frac{b_1}{N_h}| + |\frac{c_1}{N_h}|)$.

Therefore

$$|\rho(X_1) - \rho(X_2)| \leq \Omega||X_1 - X_2||, \tag{3}$$

where $\Omega = \max\{M, ||A||\} < \infty$. The constraint is $S_h(t) \geq 0$, $E_h(t) \geq 0$, $I_h(t) \geq 0$, $R_h(t) \geq 0$, $S_s(t) \geq 0$, $E_s(t) \geq 0$, and $I_s(t) \geq 0$. Moreover, ρ is uniformly Lipschitz continuous. Thus, a solution exists for the system (1) [6]. □

4 Analysis of the model

To investigate disease transmission, the model (1) is constructed, considering the flow of immigrants. The model does not have a disease-free equilibrium, resulting in the following theorem.

Theorem 4. The system (1) shows only endemic equilibrium points without a disease-free equilibrium.

Proof. Let each equation in (1) equal 0. Then we get

$$\begin{aligned}
P_S\Lambda_I + \Gamma_h - \tfrac{ab_1 I_s S_h}{N_h} - \mu_h S_h &= 0,\\
P_E\Lambda_I + \tfrac{ab_1 I_s S_h}{N_h} - (k_1+\theta+\mu_h)E_h &= 0,\\
P_I\Lambda_I + k_1 E_h - (\mu_h)E_h &= 0,\\
\theta E_h - \mu_h R_h &= 0,\\
\Gamma_s - \tfrac{ac_1 I_h S_s}{N_h} - \mu_s S_s &= 0,\\
\tfrac{ac_1 I_h S_s}{N_h} - (\mu_s+k_2)E_s &= 0,\\
k_2 E_s - \mu_s I_s &= 0.
\end{aligned} \tag{4}$$

Let the endemic equilibrium of the system (4) be $E = (S_h^*, E_h^*, I_h^*, R_h^*, S_s^*, E_s^*, I_s^*)$,

$$\begin{aligned}
S_h^* &= \frac{P_s\Lambda_I}{T_1 I_s^* + \mu_h},\\
E_h^* &= \frac{P_E\Lambda_I}{k_1+\theta+\mu_h} + \frac{T_1 I_s^* S_h^*}{k_1+\theta+\mu_h},\\
I_h^* &= \frac{P_I\Lambda_I}{\mu_h} + \frac{k_1 P_E\Lambda_I}{(\mu_h)(k_1+\theta+\mu_h)} + \frac{k_1 T_1 I_s^* S_h^*}{(\mu_h)(k_1+\theta+\mu_h)},\\
R_h^* &= \frac{\theta E_h^*}{\mu_h},
\end{aligned}$$

$$S_s^* = \frac{\Gamma_s}{T_2 I_h^* + \mu_s},$$
$$E_s^* = \frac{T_2 I_h^* S_s^*}{k_2 + \mu_s},$$
$$I_s^* = \frac{k_2 E_s^*}{\mu_s},$$

where $T_1 = \frac{ab_1}{N_h}$, $T_2 = \frac{ac_1}{N_h}$.

By substituting I_h^* and S_s^* in E_s^* and also by substituting E_s^* in I_s^*, we found the cubic equation

$$F_1(I_s^*)^3 + F_2(I_s^*)^2 + F_3 I_s^* + F_4 = 0, \tag{5}$$

where

$$F_1 = T_1^2 T_2 \frac{P_I \Lambda_I}{\mu_h} + T_1^2 T_2 \frac{k_1}{(\mu_h)(k_1 + \theta + \mu_h)}(P_E \Lambda_I + P_S \Lambda_I + \Gamma_h), \tag{6}$$

$$\begin{aligned} F_2 = {} & T_1 T_2 \frac{P_I \Lambda_I}{\mu_h} \left(2\mu_h - \frac{k_2}{\mu_s(\mu_s + k_2)}\right) \\ & + \frac{T_1 T_2 k_1}{\mu_h(k_1 + \theta + \mu_h)} (P_E \Lambda_I + P_S \Lambda_I + \Gamma_h) \left(\mu_h - \frac{k_2}{\mu_s(\mu_s + k_2)}\right), \end{aligned} \tag{7}$$

$$F_3 = \frac{T_2 P_I \Lambda_I}{\mu_h}(\mu_h^2 - \frac{2\Gamma_s k_2}{\mu_s(\mu_s + k_2)}) + \frac{T_2 \mu_h k_1 P_E \Lambda_I}{(\mu_h)(k_1 + \theta + \mu_h)}(\mu_h - \frac{2\Gamma_s k_2 T_1}{\mu_s(\mu_s + k_2)}), \tag{8}$$

$$F_4 = -\frac{\Gamma_s \mu_h^2 k_2 T_2}{\mu_s(\mu_s + k_2)(\mu_h)}(P_I \Lambda_I + \frac{k_1 P_E \Lambda_I}{k_1 + \theta + \mu_h}). \tag{9}$$

Moreover, F_1 is positive, while F_4 is negative. To determine the signs of F_2 and F_3, use Descartes' rules of signs to determine all scenarios as shown in the following theorem.

Theorem 5. The polynomial equation (5) with odd degree, has at least one real root with sign opposite to the sign of the last term.

- **Case I:** If $F_2 > 0$ and $F_3 > 0$, then there is one root with positive sign.
- **Case II:** If $F_2 < 0$ and $F_3 < 0$, then there is exactly one root with positive sign.

- **Case III:** If $F_2 > 0$ and $F_3 < 0$, then there is exactly one root with positive sign.
- **Case IV:** If $F_2 < 0$ and $F_3 > 0$, then there is more than one root with positive sign (exactly three roots).

□

5 Global stability analysis

In this section, the global stability of the disease-free equilibrium point was determined by constructing the Lyapunov function V in the following approach:

Theorem 6. For the mathematical model (1), the endemic equilibrium E is globally asymptotically stable.

Proof. Consider the following function:

$$\Psi(x) = x - 1 - \ln(x).$$

For the endemic equilibrium E, the Lyapunov function V is provided by

$$\begin{aligned} V =& n_1 S_h^* \Psi(\frac{S_h}{S_h^*}) + n_2 E_h^* \Psi(\frac{E_h}{E_h^*}) + n_3 I_h^* \Psi(\frac{I_h}{I_h^*}) + n_4 S_s^* \Psi(\frac{S_s}{S_s^*}) + n_5 E_s^* \Psi(\frac{E_s}{E_s^*}) \\ &+ n_6 I_s^* \Psi(\frac{I_s}{I_s^*}), \end{aligned}$$

with $n_1 = n_2 = 1$, $n_3 = \frac{T_1 I_s^* S_h^*}{k_1 E_h^*}$, $n_4 = \frac{T_1 I_s^* S_h^*}{T_2 I_h^* S_s^*}$, $n_5 = \frac{T_1 I_s^* S_h^*}{T_2 I_h^* S_s^*}$, and $n_6 = \frac{T_1 I_s^* S_h^*}{k_2 E_s^*}$,

$$\begin{aligned} (1 - \tfrac{S_h^*}{S_h})\dot{S_h} &= (1 - \tfrac{S_h^*}{S_h})(P_S \Lambda_I + \Gamma_h - T_1 I_s S_h - \mu_h S_h) \\ &= (1 - \tfrac{S_h^*}{S_h})(T_1 I_s^* S_h^* + \mu_h S_h^* - T_1 I_s S_h - \mu_h S_h) \\ &= (1 - \tfrac{S_h^*}{S_h}) T_1 I_s^* S_h^* (1 - \tfrac{I_s S_h}{I_s^* S_h^*}) + \mu_h S_h^* (1 - \tfrac{S_h^*}{S_h})(1 - \tfrac{S_h}{S_h^*}) \\ &= T_1 I_s^* S_h^* \left(1 - \tfrac{I_s S_h}{I_s^* S_h^*} - \tfrac{S_h^*}{S_h} + \tfrac{I_s}{I_s^*}\right) - \mu_h \tfrac{(S_h - S_h^*)^2}{S_h S_h^*}, \end{aligned}$$

$$
\begin{aligned}
(1-\tfrac{E_h^*}{E_h})\dot{E}_h &= (1-\tfrac{E_h^*}{E_h})(P_E\Lambda_I + T_1 I_s S_h - (k_1+\theta+\mu_h)E_h)\\
&= (1-\tfrac{S_h^*}{S_h})(P_E\Lambda_I + T_1 I_s S_h - (\tfrac{P_E\Lambda_I + T_1 I_s^* S_h^*}{E_h^*})E_h)\\
&= T_1 I_s^* S_h^*\left(1-\tfrac{E_h}{E_h^*}+\tfrac{I_s S_h}{I_s^* S_h^*}-\tfrac{E_h^* I_s S_h}{E_h I_s^* S_h^*}\right) - P_E\Lambda_I\tfrac{(E_h-E_h^*)^2}{E_h E_h^*},\\
(1-\tfrac{I_h^*}{I_h})\dot{I}_h &= (1-\tfrac{I_h^*}{I_h})(P_I\Lambda_I + k_1 E_h - (\mu_h)E_h)\\
&= (1-\tfrac{I_h^*}{I_h})(P_I\Lambda_I + k_1 E_h - \tfrac{P_I\Lambda_I + k_1 E_h^*}{I_h^*}I_h)\\
&= k_1 E_h^*\left(1+\tfrac{E_h}{E_h^*}-\tfrac{E_h I_h^*}{E_h^* I_h}-\tfrac{I_h}{I_h^*}\right) - P_I\Lambda_I\tfrac{(I_h-I_h^*)^2}{I_h I_h^*},\\
(1-\tfrac{S_s^*}{S_s})\dot{S}_s &= (1-\tfrac{S_s^*}{S_s})(\Gamma_s - T_2 I_h S_s - \mu_s S_s)\\
&= (1-\tfrac{S_h^*}{S_h})(T_2 I_h^* S_s^* + \mu_s S_s^* - T_2 I_h S_s - \mu_s S_s)\\
&= T_2 I_h^* S_s^*\left(1-\tfrac{I_h S_s}{I_h^* S_s^*}+\tfrac{I_h}{I_h^*}-\tfrac{S_s^*}{S_s^*}\right) - \mu_s\tfrac{(S_s^*-S_s)^2}{S_s},\\
(1-\tfrac{E_s^*}{E_s})\dot{E}_s &= (1-\tfrac{E_s^*}{E_s})(T_2 I_h S_s - (\mu_s+k_2)E_s)\\
&= (1-\tfrac{E_s^*}{E_s})(T_2 I_h^* S_s^* - (\tfrac{T_2 I_h^* S_s^*}{E_s^*})E_s)\\
&= T_2 I_h^* S_s^*\left(\tfrac{I_h S_s}{I_h^* S_s^*}-\tfrac{E_s}{E_s^*}-\tfrac{E_s^* I_h S_s}{E_s I_h^* S_s^*}+1\right),\\
(1-\tfrac{I_s^*}{I_s})\dot{I}_s &= (1-\tfrac{I_s^*}{I_s})(k_2 E_s - \mu_s I_s)\\
&= (1-\tfrac{I_s^*}{I_s})(k_2 E_s - (\tfrac{k_2 E_s^*}{I_s^*})I_s)\\
&= k_2 E_s^*(\tfrac{E_s}{E_s^*}-\tfrac{I_s}{I_s^*}-\tfrac{I_s^* E_s}{I_s E_s^*}+1).
\end{aligned}
$$

Therefore,

$$
1-\frac{I_s S_h}{I_s^* S_h^*}-\frac{S_h^*}{S_h}+\frac{I_s}{I_s^*} = -\Psi(\frac{S_h^*}{S_h})-\Psi(\frac{I_s S_h}{I_s^* S_h^*})+\Psi(\frac{I_s}{I_s^*}), \tag{10}
$$

$$1-\frac{I_h}{I_h^*}-\frac{E_hI_h^*}{E_h^*I_h}+\frac{E_h}{E_h^*}=-\Psi(\frac{I_h}{I_h^*})-\Psi(\frac{E_hI_h^*}{E_h^*I_h})+\Psi(\frac{E_h}{E_h^*}), \tag{11}$$

$$1-\frac{E_h}{E_h^*}-\frac{E_h^*I_sS_h}{E_hI_s^*S_h^*}+\frac{I_sS_h}{I_s^*S_h^*}=-\Psi(\frac{E_h}{E_h^*})-\Psi(\frac{E_h^*I_sS_h}{E_hI_s^*S_h^*})+\Psi(\frac{I_sS_h}{I_s^*S_h^*}), \tag{12}$$

$$1-\frac{S_s^*}{S_s}-\frac{I_hS_s}{I_h^*S_s^*}+\frac{I_h}{I_h^*}=-\Psi(\frac{S_s^*}{S_s})-\Psi(\frac{I_hS_s}{I_h^*S_s^*})+\Psi(\frac{I_h}{I_h^*}), \tag{13}$$

$$1-\frac{E_s}{E_s^*}-\frac{E_s^*I_hS_s}{E_sI_h^*S_s^*}+\frac{I_hS_s}{I_h^*S_s^*}=-\Psi(\frac{E_s}{E_s^*})-\Psi(\frac{E_s^*I_hS_s}{E_sI_h^*S_s^*})+\Psi(\frac{I_hS_s}{I_h^*S_s^*}), \tag{14}$$

$$1-\frac{I_s}{I_s^*}+\frac{E_s}{E_s^*}-\frac{I_s^*E_s}{I_sE_s^*}=-\Psi(\frac{I_s}{I_s^*})+\Psi(\frac{E_s}{E_s^*})-\Psi(\frac{I_s^*E_s}{I_sE_s^*}). \tag{15}$$

By substitution, we obtained

$$\begin{aligned}\dot{V}=T_1I_s^*S_h^*\Bigg[&-\Psi\left(\frac{S_h^*}{S_h}\right)-\Psi\left(\frac{I_sS_h}{I_s^*S_h^*}\right)+\Psi\left(\frac{I_s}{I_s^*}\right)-\Psi\left(\frac{I_h}{I_h^*}\right)\\&-\Psi\left(\frac{E_hI_h^*}{E_h^*I_h}\right)+\Psi\left(\frac{E_h}{E_h^*}\right)-\Psi\left(\frac{E_h}{E_h^*}\right)-\Psi\left(\frac{E_h^*I_sS_h}{E_hI_s^*S_h^*}\right)\\&+\Psi\left(\frac{I_sS_h}{I_s^*S_h^*}\right)-\Psi\left(\frac{S_s^*}{S_s}\right)-\Psi\left(\frac{I_hS_s}{I_h^*S_s^*}\right)+\Psi\left(\frac{I_h}{I_h^*}\right)\\&-\Psi\left(\frac{E_s}{E_s^*}\right)-\Psi\left(\frac{E_s^*I_hS_s}{E_sI_h^*S_s^*}\right)+\Psi\left(\frac{I_hS_s}{I_h^*S_s^*}\right)-\Psi\left(\frac{I_s}{I_s^*}\right)\\&+\Psi\left(\frac{E_s}{E_s^*}\right)-\Psi\left(\frac{I_s^*E_s}{I_sE_s^*}\right)\Bigg]\\&-\mu_h\frac{(S_h-S_h^*)^2}{S_h}-n_2P_E\Lambda_I\frac{(E_h-E_h^*)^2}{E_hE_h^*}\\&-n_3P_I\Lambda_I\frac{(I_h-I_h^*)^2}{I_hI_h^*}-n_4\mu_s\frac{(S_s-S_s^*)^2}{S_s},\end{aligned} \tag{16}$$

$$\begin{aligned}\dot{V} = T_1 I_s^* S_h^* \Bigg[& -\Psi\left(\frac{S_h^*}{S_h}\right) - \Psi\left(\frac{E_h I_h^*}{E_h^* I_h}\right) - \Psi\left(\frac{E_h^* I_s S_h}{E_h I_s^* S_h^*}\right) \\ & - \Psi\left(\frac{S_s^*}{S_s}\right) - \Psi\left(\frac{E_s^* I_h S_s}{E_s I_h^* S_s^*}\right) - \Psi\left(\frac{I_s^* E_s}{I_s E_s^*}\right)\Bigg] \\ & - \mu_h \frac{(S_h - S_h^*)^2}{S_h} - n_2 P_E \Lambda_I \frac{(E_h - E_h^*)^2}{E_h E_h^*} \\ & - n_3 P_I \Lambda_I \frac{(I_h - I_h^*)^2}{I_h I_h^*} - n_4 \mu_s \frac{(S_s - S_s^*)^2}{S_s}.\end{aligned} \tag{17}$$

□

We have the function Ψ, which is positive, and it can be observed that Ψ attains a strict global minimum at $\Psi(1)$ with a value of 0. Finally, we get $\dot{V} < 0$, which implies that the system (1) is globally stable.

6 Optimal control

6.1 Formulation of the optimal control problem

Four control variables are proposed to minimize exposure and infection risks in human populations and sand flies, as well as Leishmania transmission and dissemination. u_1; awareness and promoting safety measures, u_2; pharmaceutical interventions; u_3; various interventions targeting sand flies throughout their life cycle to reduce their population and reduce Leishmania transmission in residential areas and animal shelters. Lastly, u_4; Leishmania screening. To manage those variables, the optimal control system, illustrating the impact of various interventions on our basic model (1), is provided as follows:

$$
\begin{aligned}
\dot{S}_h &= (1-u_4)P_S\Lambda_I + \Gamma_h - S_h(1-u_1)f(I_s) - \mu_h S_h,\\
\dot{E}_h &= (1-u_4)P_E\Lambda_I + S_h(1-u_1)f(I_s) - (k_1+\theta+\mu_h)E_h,\\
\dot{I}_h &= (1-u_4)P_I\Lambda_I + k_1E_h - (u_2+\mu_h)I_h,\\
\dot{R}_h &= \theta E_h + (u_2)I_h - \mu_h R_h,\\
\dot{S}_s &= \Gamma_s - S_s(1-u_1)g(I_h) - (\mu_s+u_3)S_s,\\
\dot{E}_s &= S_s(1-u_1)g(I_h) - (\mu_s+k_2+u_3)E_s,\\
\dot{I}_s &= k_2E_s - (\mu_s+u_3)I_s,
\end{aligned}
\tag{18}
$$

with $S_h(0) \geq 0, E_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0, S_s(0) \geq 0, E_s(0) \geq 0, I_s(0) \geq 0$.

6.2 Existence and characterization of optimal control

To reduce the number of individuals exposed and infected by Leishmania in both populations, we define the objective function to be minimized as:

$$
\begin{aligned}
J(u_1,u_2,u_3,u_4) = \int_0^T \big[g_1E_h + g_2I_h + g_3E_s + g_4I_s + \frac{1}{2}(\tau_1u_1^2 + \tau_2u_2^2\\
+ \tau_3u_3^2 + \tau_4u_4^2)\big]dt,
\end{aligned}
$$

where $g_1 \geq 0$, $g_2 \geq 0$, $g_3 \geq 0$, and $g_4 \geq 0$ are the cost coefficients. They are chosen in order to determine $u_1, u_2, u_3,$ and u_4 relative value at time t, where T is the end time.

We aim an optimal controls $u_1^*, u_2^*, u_3^*,$ and u_4^* such that the objective function to minimize

$$
J(u_1^*,u_2^*,u_3^*,u_4^*) = \min_{(u_1,u_2,u_3,u_4)\in U_{ad}^T} J(u_1,u_2,u_3,u_4), \tag{19}
$$

where U_{ad}^T is the set of admissible controls defined by

$$U_{ad}^T = \{(u_1, u_2, u_3, u_4)/0 \leq u_{\min} \leq u_1(t), u_2(t), u_3(t), u_4(t) \leq u_{max} \leq 1, \text{ with } t \in [0, T]\}.$$

6.2.1 Existence of an optimal control

Theorem 7. Consider the control system (18). There exist an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*) \in U_{ad}^T$
such that $J(u_1^*, u_2^*, u_3^*, u_4^*) = \min_{(u_1,u_2,u_3,u_4)\in U_{ad}^T} J(u_1, u_2, u_3, u_4)$.

Proof. We proceed to the conclusion stated in [15] to show that an optimal control exists. The state and control variables are nonnegative values. This minimization issue satisfies the convexity condition of the objective functional. The aforementioned control space is closed and convex by definition. For optimal control to exist, it is crucial that the ideal system be compact. The optimal system's boundedness and the necessary compactness dictate this. Furthermore, the objective function J is a convex integrated on U_{ad}^T. □

6.2.2 Characterization of the optimal control

To study the necessary conditions for the optimal control, the Pontryagin's maximum principle is applied to the Hamiltonian $H(t)$ at time t defined by

$$H(t) = g_1 E_h + g_2 I_h + g_3 E_s + g_4 I_s + \frac{1}{2}(\tau_1 u_1^2 + \tau_2 u_2^2 + \tau_3 u_3^2 + \tau_4 u_4^2) + \lambda_1 \dot{S}_h + \lambda_2 \dot{E}_h + \lambda_3 \dot{I}_h + \lambda_4 \dot{R}_h + \lambda_5 \dot{S}_s + \lambda_6 \dot{E}_s + \lambda_7 \dot{I}_s. \quad (20)$$

Theorem 8. Given the optimal controls $(u_1^*, u_2^*, u_3^*, u_4^*)$ and the solution $S_h^*(t), E_h^*(t), I_h^*(t), R_h^*(t), S_s^*(t), E_s^*(t), I_s^*(t)$ of the corresponding state system, the exists adjoint variables $\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t), \lambda_6(t), \lambda_7(t)$ satisfying

$$\dot{\lambda_1}(t) = -\frac{\partial H(t)}{\partial S_h(t)} = \frac{a(1-u_1)b_1 I_s^*(R_h^* + E_h^* + I_h^*)}{N_h^{*2}}(\lambda_1 - \lambda_2)$$

$$
\begin{aligned}
&+\frac{a(1-u_1)c_1I_h^*S_s^*}{N_h^{*2}}(\lambda_6-\lambda_5)+\mu_h\lambda_1,\\
\dot{\lambda_2}(t)=&-\frac{\partial H(t)}{\partial E_h(t)}=-g_1+\lambda_2(k_1+\theta+\mu_h)-\lambda_3k_1-\lambda_4\theta\\
&+\frac{a(1-u_1)b_1I_s^*S_h^*}{N_h^{*2}}(\lambda_2-\lambda_1)+\frac{a(1-u_1)c_1I_h^*S_s^*}{N_h^{*2}}(\lambda_6-\lambda_5),\\
\dot{\lambda_3}(t)=&-\frac{\partial H(t)}{\partial I_h(t)}=-g_2+\lambda_3(u_2+\mu_h)-\lambda_4(u_2)\\
&+\frac{a(1-u_1)c_1S_s^*(S_h^*+E_h^*+R_h^*)}{N_h^{*2}}(\lambda_5-\lambda_6)+\frac{a(1-u_1)b_1I_s^*S_h^*}{N_h^{*2}}(\lambda_2-\lambda_1),\\
\dot{\lambda_4}(t)=&-\frac{\partial H(t)}{\partial R_h(t)}=\frac{a(1-u_1)b_1I_s^*S_h^*}{N_h^{*2}}(\lambda_2-\lambda_1)+\mu_h\lambda_4\\
&+\frac{a(1-u_1)c_1S_s^*I_h^*}{N_h^{*2}}(\lambda_6-\lambda_5),\\
\dot{\lambda_5}(t)=&-\frac{\partial H(t)}{\partial S_s(t)}=\frac{a(1-u_1)c_1I_h^*}{N_h^*}(\lambda_5-\lambda_6)+\lambda_5(u_3+\mu_v),\\
\dot{\lambda_6}(t)=&-\frac{\partial H(t)}{\partial E_s(t)}=-g_3+(u_3+\mu_v+k_2)\lambda_6-k_2\lambda_7,\\
\dot{\lambda_7}(t)=&-\frac{\partial H(t)}{\partial I_s(t)}=-g_4+\frac{a(1-u_1)b_1S_h^*}{N_h^*}(\lambda_1-\lambda_2)+(u_3+\mu_v)\lambda_7,
\end{aligned}
$$

with the transversality conditions at time T

$$\lambda_1(T)=\lambda_4(T)=\lambda_5(T)=0,$$

$$\lambda_2(T)=g_1,\ \lambda_3(T)=g_2,\ \lambda_6(T)=g_3 \text{ and } \lambda_7(T)=g_4.$$

Furthermore, for $t\in[0,T]$, the optimal controls u_1^*, u_2^*, u_3^*, and u_4^* are given by

$$
\begin{aligned}
u_1^*&=\frac{1}{\tau_1}(\frac{ab_1I_s^*S_h^*}{N_h^*}(\lambda_2-\lambda_1)+\frac{ac_1I_h^*S_s^*}{N_h^*}(\lambda_6-\lambda_5)),\\
u_2^*&=\frac{1}{\tau_2}(I_s^*(\lambda_3-\lambda_4)),\\
u_3^*&=\frac{1}{\tau_3}(S_s^*\lambda_5+E_s^*\lambda_6+I_s^*\lambda_7),\\
u_4^*&=\frac{\Lambda_I}{\tau_4}(\lambda_1P_S+\lambda_2P_E+\lambda_3P_I).
\end{aligned}
$$

Proof. To determine the adjoint equations and transversality conditions, we use Hamiltonian and Pontryagin's maximum principle. Let $S_h(t)=$

$S_h^*(t)$, $E_h(t) = E_h^*(t)$, $I_h(t) = I_h^*(t)$, $R_h(t) = R_h^*(t)$, $S_s(t) = S_s^*(t)$, $E_s(t) = E_s^*(t)$, and $I_s(t) = I_s^*(t)$, to get

$$
\begin{aligned}
\dot{\lambda_1} &= \frac{\partial H(t)}{\partial S_h(t)} \\
&= \lambda_1 \left[\frac{a(1-u_1)b_1 I_s^*(R_h^* + E_h^* + I_h^*)}{N_h^{*2}}\right] - \lambda_2 \left[\frac{a(1-u_1)b_1 I_s^*(R_h^* + E_h^* + I_h^*)}{N_h^{*2}}\right] \\
&+ \lambda_5 \left[-\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right] + \lambda_6 \left[\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right] + \mu_h \lambda_1, \\
&= \frac{a(1-u_1)b_1 I_s^*(R_h^* + E_h^* + I_h^*)}{N_h^{*2}}(\lambda_1 - \lambda_2) + \frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}(\lambda_6 - \lambda_5) + \mu_h \lambda_1, \\
\dot{\lambda_2} &= \frac{\partial H(t)}{\partial E_h(t)} \\
&= -\Bigg[(g_1 + \lambda_1(\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}) + \lambda_2(-\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}} - (k_1 + \theta + \mu_h)) \\
&+ k_1\lambda_3 + \theta\lambda_4) + \lambda_5 \left[\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right] - \lambda_6 \left[\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right]\Bigg] \\
&= -g_1 + \lambda_2(k_1 + \theta + \mu_h) - \lambda_3 k_1 - \lambda_4 \theta + \frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}(\lambda_2 - \lambda_1) \\
&+ \frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}(\lambda_6 - \lambda_5), \\
\dot{\lambda_3} &= \frac{\partial H(t)}{\partial I_h(t)} \\
&- \Bigg[(g_2 + \lambda_1(\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}) + \lambda_2(-\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}) - (u_2 + \mu_h)\lambda_3 + (u_2)\lambda_4) \\
&+ \lambda_5 \left[-\frac{a(1-u_1)c_1 I_h^*(S_h^* + E_h^* + R_h^*)}{N_h^{*2}}\right] + \lambda_6 \left[\frac{a(1-u_1)c_1 I_h^*(S_h^* + E_h^* + R_h^*)}{N_h^{*2}}\right]\Bigg] \\
&= -g_2 + \lambda_3(u_2 + \mu_h) - \lambda_4(u_2) + \frac{a(1-u_1)c_1 S_s^*(S_h^* + E_h^* + R_h^*)}{N_h^{*2}}(\lambda_5 - \lambda_6) \\
&+ \frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}(\lambda_2 - \lambda_1), \\
\dot{\lambda_4} &= \frac{\partial H(t)}{\partial R_h(t)} \\
&= -\Bigg[\lambda_1(\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}) + \lambda_2(-\frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}) + (-\mu_h)\lambda_4 \\
&+ \lambda_5 \left[\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right] + \lambda_6 \left[-\frac{a(1-u_1)c_1 I_h^* S_s^*}{N_h^{*2}}\right]\Bigg]
\end{aligned}
$$

$$= \frac{a(1-u_1)b_1 I_s^* S_h^*}{N_h^{*2}}(\lambda_2 - \lambda_1) + \mu_h \lambda_4 + \frac{a(1-u_1)c_1 S_s^* I_h^*}{N_h^{*2}}(\lambda_6 - \lambda_5),$$

$$\dot{\lambda_5} = \frac{\partial H(t)}{\partial S_s(t)}$$

$$= -\left[\lambda_5(-\frac{a(1-u_1)c_1 I_h^*}{N_h^*} - (u_3 + \mu_v)) - \lambda_6(\frac{a(1-u_1)c_1 I_h^*}{N_h^*})\right]$$

$$= \frac{a(1-u_1)c_1 I_h^*}{N_h^*}(\lambda_5 - \lambda_6) + \lambda_5(u_3 + \mu_v),$$

$$\dot{\lambda_6} = \frac{\partial H(t)}{\partial E_s(t)}$$

$$= -\left[g_3 + \lambda_6(-(u_3 + \mu_v + k_2)) + \lambda_7(k_2)\right]$$

$$= -g_3 + (u_3 + \mu_v + k_2)\lambda_6 - k_2\lambda_7$$

$$\dot{\lambda_7} = \frac{\partial H(t)}{\partial I_s(t)}$$

$$= -\left[g_4 + \lambda_1(-\frac{a(a-u_1)b_1 S_h^*}{N_h^*}) + \lambda_2(\frac{a(a-u_1)b_1 S_h^*}{N_h^*}) + \lambda_7(-(u_3 + \mu_v))\right]$$

$$= -g_4 + \frac{a(1-u_1)b_1 S_h^*}{N_h^*}(\lambda_1 - \lambda_2) + (u_3 + \mu_v)\lambda_7.$$

Using the optimality conditions, we conclude

$$u_1 = \frac{\partial H(t)}{\partial u_1(t)}$$

$$= \tau_1 u_1 + \lambda_1(S_h^* f(I_h^*)) + \lambda_2(-S_h^* f(I_h^*)) + \lambda_5(S_s g(I_h^*)) + \lambda_6(-S_s^* g(I_h^*))$$

$$= \tau_1 u_1 + S_h^* f(I_h^*)(\lambda_1 - \lambda_2) + S_s^* g(I_h^*)(\lambda_5 - \lambda_6),$$

$$u_2 = \frac{\partial H(t)}{\partial u_2(t)}$$

$$= \tau_2 u_2 + \lambda_3(-I_h^*) + \lambda_4(I_h^*)$$

$$= \tau_2 u_2 + I_h^*(\lambda_4 - \lambda_3),$$

$$u_3 = \frac{\partial H(t)}{\partial u_3(t)}$$

$$= \tau_3 u_3 + \lambda_5(-S_s^*) + \lambda_6(-E_s^*) + \lambda_7(-I_s^*)$$

$$= \tau_3 u_3 - S_s^*\lambda_5 - E_s^*\lambda_6 - I_s^*\lambda_7,$$

$$u_4 = \frac{\partial H(t)}{\partial u_4(t)}$$

$$= \tau_4 u_4 + \lambda_1(-P_S\Lambda_I) + \lambda_2(-P_E\Lambda_I) + \lambda_3(-P_I\Lambda_I)$$

$$= \tau_4 u_4 - \Lambda_I(\lambda_1 P_S + \lambda_2 P_E + \lambda_3 P_I).$$

Hence

$$\begin{aligned}
&\frac{\partial H}{u_1} = 0 \Rightarrow \ u_1^* = \tfrac{1}{\tau_1}(\tfrac{ab_1 I_s^* S_h^*}{N_h^*}(\lambda_2 - \lambda_1) + \tfrac{ac_1 I_h^* S_s^*}{N_h^*}(\lambda_6 - \lambda_5)),\\
&\frac{\partial H}{u_2} = 0 \Rightarrow \ u_2^* = \tfrac{1}{\tau_2}(I_s^*(\lambda_3 - \lambda_4)),\\
&\frac{\partial H}{u_3} = 0 \Rightarrow \ u_3^* = \tfrac{1}{\tau_3}(S_s^*\lambda_5 + E_s^*\lambda_6 + I_s^*\lambda_7),\\
&\frac{\partial H}{u_4} = 0 \Rightarrow \ u_4^* = \tfrac{\Lambda_I}{\tau_4}(\lambda_1 P_S + \lambda_2 P_E + \lambda_3 P_I).
\end{aligned}$$

Applying the propriety of control space yields the following results:

$$u_1^* = \begin{cases} 0 & \text{if } \frac{1}{\tau_1}(\frac{ab_1 I_s S_h}{N_h}(\lambda_2 - \lambda_1) + \frac{ac_1 I_h S_s}{N_h}(\lambda_6 - \lambda_5)) \le 0, \\ \frac{1}{\tau_1}(\frac{ab_1 I_s S_h}{N_h}(\lambda_2 - \lambda_1) + \frac{ac_1 I_h S_s}{N_h}(\lambda_6 - \lambda_5)) & \\ \qquad \text{if } 0 < \frac{1}{\tau_1}(\frac{ab_1 I_s S_h}{N_h}(\lambda_2 - \lambda_1) + \frac{ac_1 I_h S_s}{N_h}(\lambda_6 - \lambda_5)) < 1, \\ 1 & \text{if } \frac{1}{\tau_1}(\frac{ab_1 I_s S_h}{N_h}(\lambda_2 - \lambda_1) + \frac{ac_1 I_h S_s}{N_h}(\lambda_6 - \lambda_5)) \ge 1. \end{cases}$$

$$u_2^* = \begin{cases} 0 & \text{if } \frac{1}{\tau_2}(I_s(\lambda_3 - \lambda_4)) \le 0, \\ \frac{1}{\tau_2}(I_s(\lambda_3 - \lambda_4)) & \text{if } 0 < \frac{1}{\tau_2}(I_s(\lambda_3 - \lambda_4)) < 1, \\ 1 & \text{if } \frac{1}{\tau_2}(I_s(\lambda_3 - \lambda_4)) \ge 1, \end{cases}$$

$$u_3^* = \begin{cases} 0 & \text{if } \frac{1}{\tau_3}(S_s\lambda_5 + E_s\lambda_6 + I_s\lambda_7) \le 0, \\ \frac{1}{\tau_3}(S_s\lambda_5 + E_s\lambda_6 + I_s\lambda_7) & \text{if } 0 < \frac{1}{\tau_3}(S_s\lambda_5 + E_s\lambda_6 + I_s\lambda_7) < 1, \\ 1 & \text{if } \frac{1}{\tau_3}(S_s\lambda_5 + E_s\lambda_6 + I_s\lambda_7) \ge 1, \end{cases}$$

$$u_4^* = \begin{cases} 0 & \text{if } \frac{1}{\tau_4}(P_E\Lambda_I(\lambda_2 - \lambda_1) + P_I\Lambda_I(\lambda_3 - \lambda_1)) \le 0, \\ \frac{\Lambda_I}{\tau_4}(\lambda_1 P_S + \lambda_2 P_E + \lambda_3 P_I) & \text{if } 0 < \frac{1}{\tau_4}(P_E\Lambda_I(\lambda_2 - \lambda_1) + P_I\Lambda_I(\lambda_3 - \lambda_1)) < 1, \\ 1 & \text{if } \frac{1}{\tau_4}(P_E\Lambda_I(\lambda_2 - \lambda_1) + P_I\Lambda_I(\lambda_3 - \lambda_1)) \ge 1. \end{cases}$$

Thus, the optimal control can be defined based on the control space property. Therefore,

$$
\begin{aligned}
u_1^* &= \max\{\min\{\tfrac{1}{\tau_1}(\tfrac{ab_1 I_s S_h}{N_h}(\lambda_2-\lambda_1)+\tfrac{ac_1 I_h S_s}{N_h}(\lambda_6-\lambda_5)),1\},0\},\\
u_2^* &= \max\{\min\{\tfrac{1}{\tau_2}(I_s(\lambda_3-\lambda_4)),1\},0\},\\
u_3^* &= \max\{\min\{\tfrac{1}{\tau_3}(S_s\lambda_5+E_s\lambda_6+I_s\lambda_7),1\},0\},\\
u_4^* &= \max\{\min\{\tfrac{\Lambda_I}{\tau_4}(\lambda_1 P_S+\lambda_2 P_E+\lambda_3 P_I),1\},0\}.
\end{aligned}
$$

□

7 Numerical simulations

The model is analyzed numerically to study the behavior of the disease transmission. The parameter values per day with descriptions are derived from previous research, and others are estimated as shown in Table 1. The 4th-order Runge–Kutta method is implemented to perform the numerical simulations using the MATLAB program. The initial values of the state variables are determined as $S_h(0) = 100$, $E_h(0) = 20$, $I_h(0) = 20$, $R_h(0) = 10$, $S_s(0) = 1000$, $E_s(0) = 20$, and $I_s(0) = 30$ [37]. The values of weight constants utilized in the objective functional are $g_1 = 70$, $g_2 = 10$, $g_3 = 2$, $g_4 = 5$, $\tau_1 = 2$, $\tau_2 = 2$, $\tau_1 = 15$, and $\tau_1 = 10$. The graphs below demonstrate the impact of optimal strategies applied with and without controls.

Figures 1–4 illustrate the dynamics of CL and the impact of control measures on human populations during a 50-day period, comparing scenarios with and without control strategies.

Figure 1 shows the dynamics of susceptible human individuals. In the absence of control measures, the results indicate a steady decline in the number of susceptible individuals, decreasing from an initial value of 100 to approximately 46 individuals during 50 days. Conversely, when control strategies are implemented, the number of susceptible individuals stabilizes over all period.

Figure 2 focuses on the evolution of exposed human individuals. The results show that, in the absence of control measures, the number of exposed initially displays a slow increase in the first three days, reaching a peak. Subsequently, the number steadily decreases, reaching approximately two

Table 1: Parameter values with description

Parameter	Description	Value per day	Source
Λ_I	The growth rate of immigration	0.2016	Assumed
P_S	The proportion of susceptible immigration	0.40	Assumed
P_E	The proportion of exposed immigration	0.25	Assumed
P_I	The proportion of infected immigration	0.15	Assumed
Γ_h	The recruitment of humans	0.0000416	[26]
Γ_s	The recruitment of sand flies	0.124	[26]
μ_h	Natural rate of mortality for humans	0.00004	[23]
μ_s	Natural rate of mortality for sand flies	0.189	[23]
a	Sand flies biting rate	0.4856	Assumed
b_1	Transmission rate of CL from sand flies to humans	0.2856	Assumed
c_1	Transmission rate of CL in sand flies from humans	0.28	[23]
θ	CL recovery rate from exposed class	0.002	Assumed
k_1	Period of CL incubation for humans	0.23	[18]
k_2	Period of CL incubation for sand flies	0.2	[23]

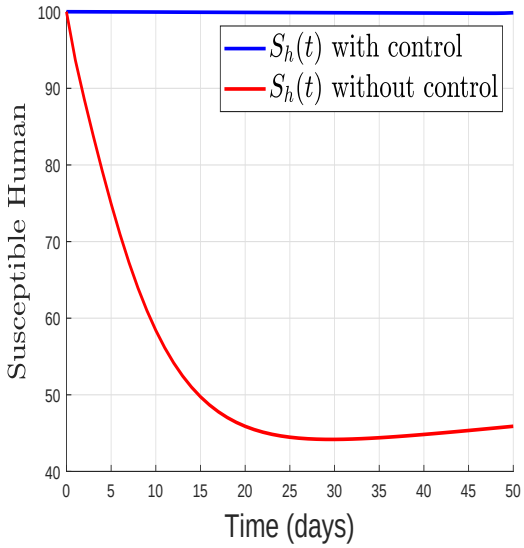

Figure 1: Susceptible human behavior with and without controls with immigration

individuals after 50 days, highlighting a dynamic pattern. However, when control measures are implemented, the number of exposed individuals slowly declines, eventually reaching zero on day 23.

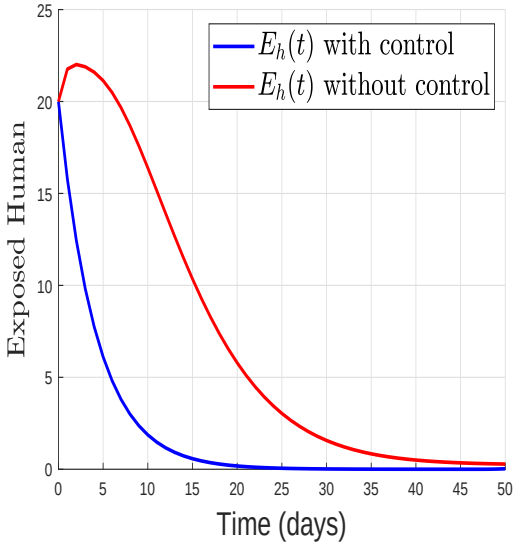

Figure 2: Exposed human behavior with and without controls with immigration

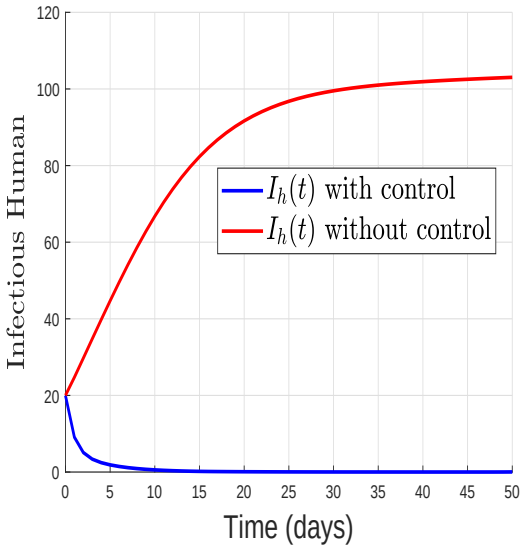

Figure 3: Infected human behavior with and without controls with immigration

Figure 3 represents the dynamics of infected humans. Without control measures, the number of infected people increased significantly, from 20 to

more than 100 for the whole time period. Conversely, the application of control measures leads to a rapid decrease in the infected individuals, reaching zero after 10 days.

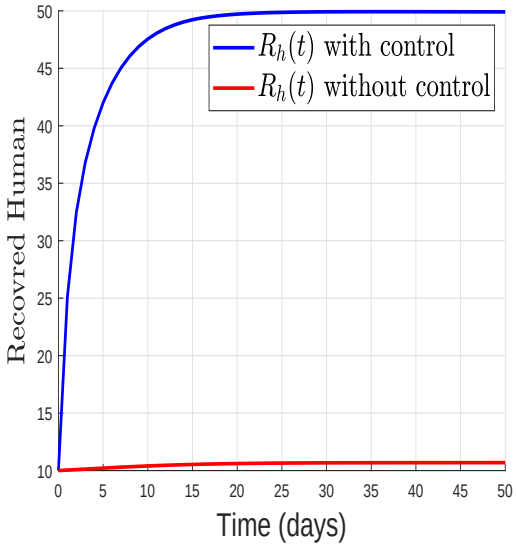

Figure 4: Recovered human behavior with and without controls with immigration

Figure 4 shows the trajectory of recovered individuals. In the absence of control measures, the number of recovered individuals rose from 10 to only about 11 after 50 days. This gradual increment signifies a natural progression of recovery. Conversely, when control measures were implemented, the number of recovered people climbed dramatically, reaching 50 within 50 days.

As a result, there is a need for effective control strategies to control CL, focusing on reducing infected individuals and improving recovery rates.

Figure 5 shows a significant decrease in susceptible sand fly populations without control strategies, but when control techniques are used, the decline is more rapid, surpassing the initial decline.

Figure 6 illustrates the progression of the number of exposed sand flies individuals. Control measures led to an increase in exposed sand flies, reaching 63 individuals after 4 days, causing a gradual decrease in their population. This has rapidly decreased after the implementation of control measures.

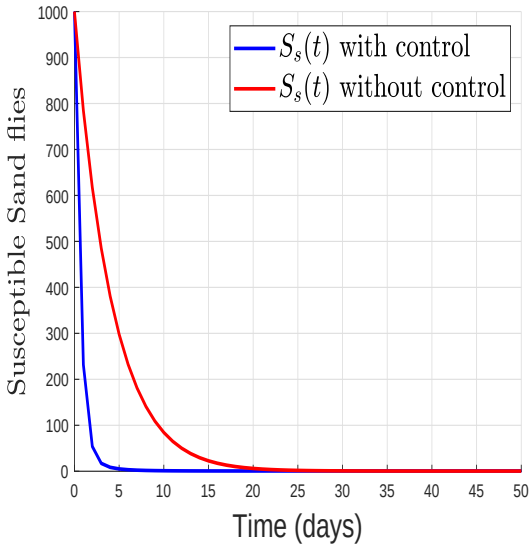

Figure 5: Susceptible sand flies behavior with and without controls with immigration

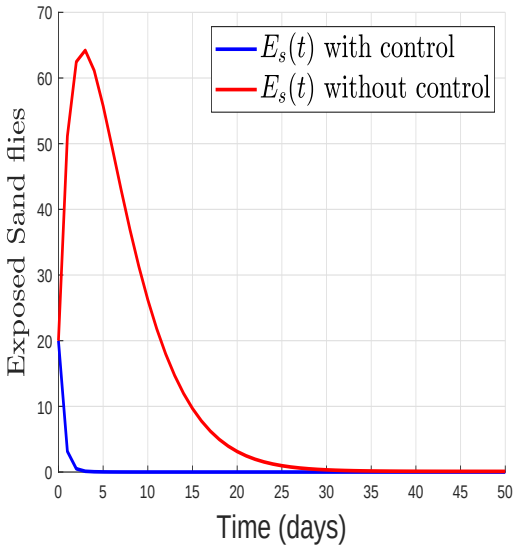

Figure 6: Exposed sand flies behavior with and without controls with immigration

Figure 7 shows the temporal evolution of infected sand flies populations. After control measures, the population increases, reaching a peak of 58 indi-

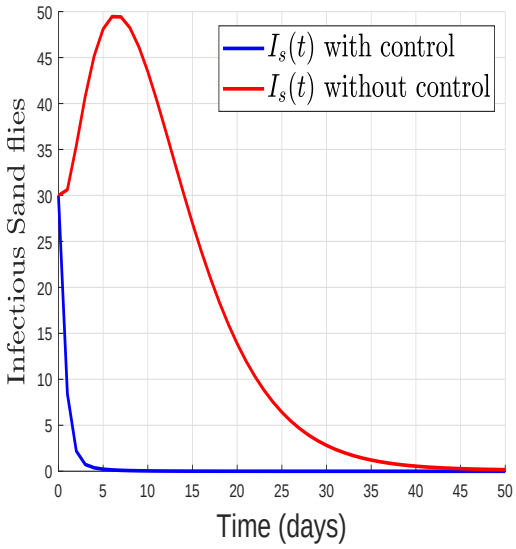

Figure 7: Infected sand flies behavior with and without controls with immigration

viduals after 7 days. Clearly, control strategies result in a rapid decrease in the total number of sand flies. In summary, as shown in Figures 5, 6, and 7 the control strategy applied to the model led to a decrease in susceptible, exposed, and infected sand flies.

In Figure 8, the optimal control u_1 is at the upper bound of 100% in the first week and gradually declines to the lower bound, whereas the control u_2 is at the upper bound of 100% in the first 15 days and gradually drops to a minimum of roughly 10% by the end of the period.

In Figure 9, the control u_3 is at the upper bound of 100% in the first two days and gradually drops to the lower bound in the 30^{th} day, whereas the control u_4 is at the upper bound of 100% in all 47 days and gradually declines to less than 40% by the end of the period.

To minimize the number of exposed in both population and the number of infected individuals in humans, the awareness program u_1 should remain with maximum intensity for at least 8 days before steadily decreasing to a lower bound in the last 40 days. While the pharmaceutical interventions should be implemented with maximum intensity for the first two weeks and relaxing gradually to a minimum of 10% by the end of 50 days. This recommend

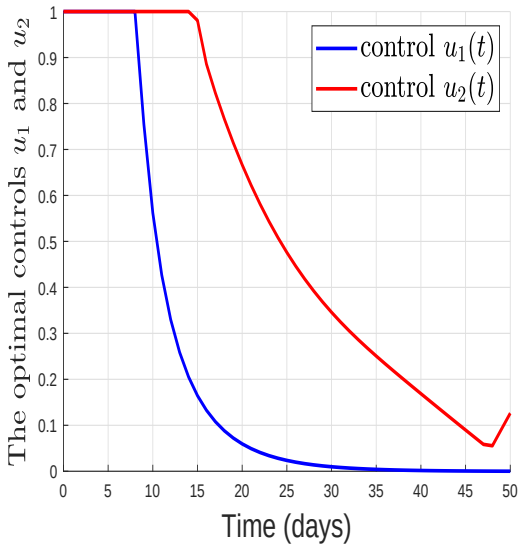

Figure 8: The controls u_1 and u_2

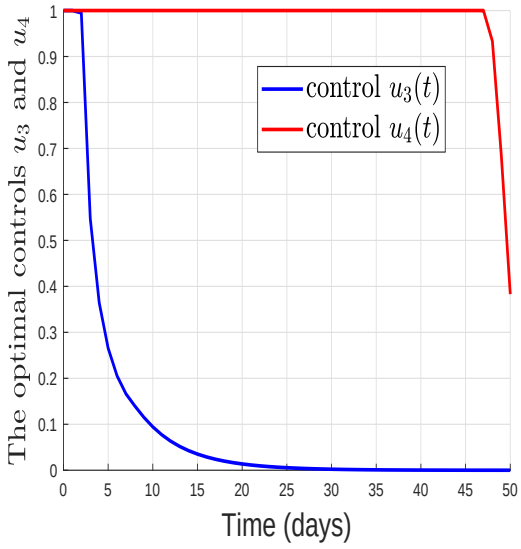

Figure 9: The controls u_3 and u_4

that there is a high effort in Leishmania screening control u_4, which can

be implemented for at least 47 days. On the other hand a low effort for pharmaceutical interventions u_3.

8 Conclusion

In this study, a model of human and sand fly populations was considered for Leishmania disease in the absence of a disease-free equilibrium. The endemic equilibrium of the model was investigated, and the Lyapunov function was applied to determine the global stability. Minimizing the objective function was the main goal. To reduce the spread of Leishmania disease in the human population and sand flies, four controls were implemented in the system. The existence and characterization of optimal control were verified, and Pontryagin's Maximum Principle was applied to find the necessary conditions of the optimality system. The optimal problem was simulated using the Forward-Backward Sweep approach. Therefore, the analysis and numerical results indicated that all of the control measures had a significant impact on decreasing the variation of exposed and infected individuals within both the human and sand fly populations. Leishmania screening control u_4 was the most effective control and should be applied to combat the infection of Leishmania disease in humans and sand flies. Implementing high levels of screening for an extended time frame (up to 47 days) significantly reduced the number of infected individuals in both populations. This highlighted the need for early detection and surveillance in preventing disease transmission. Overall, a combination of these control measures, particularly focusing on awareness, timely pharmaceutical interventions, various controls, and screening, had the potential to drastically reduce CL transmission.

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Data availability statements All data generated or analysed during this study are included in this published article.

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