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Research article

The relation between host competence and vector-feeding preference in a multi-host model: Chagas and Cutaneous Leishmaniasis

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Abstract: Vector-borne diseases that occur in humans, as well as in domestic and wild reservoir hosts, cause a significant concern in public health, veterinary health, and ecological health in bio-diverse environments. The majority of vector-borne zoonotic diseases are transmitted among diverse host species, but different hosts have their own ability to transmit pathogens and to attract vectors. These combined transmission mechanisms in hosts and vectors are often called "host competencies" and "vector-feeding preferences." The purpose of this research is to assess the relationship between the host's ability to transmit the pathogen to vectors and the different feeding preferences for a specific host using a multi-host mathematical model. Working with zoonotic cutaneous leishmaniasis and Chagas disease, numerical simulations illustrate these vector-host populations' behavior together for the first time. Global sensitivity analyses confirm that the basic reproductive number, R_0, is more sensitive to the the vector-demographic and biting-rate parameters in both diseases. Therefore, in this era of remarkable biodiversity loss and increased vector-borne diseases, it is crucial to understand how vector-host interaction mechanisms affect disease dynamics in humans within wildlife and domestic settings.

Keywords: host competence; reservoirs; feeding preference; zoonotic; vector-borne disease; bio-diverse

1. Introduction

Vector-borne diseases that demonstrate specific feeding preferences and a predilection for competent hosts are a relevant public health issue due to the complexity of these two combined effects, particularly in bio-diverse environments. Existing literature that seeks to understand the

combined effects of host competency and vector-feeding preference is limited, and further research is needed. Existing studies have modeled vector-host transmission using either vector-feeding preference or host competence, albeit separately [1–4]. However, no research has been conducted to analyze the combination of both transmission effects in multiple hosts for cutaneous leishmaniasis and Chagas disease. In this novel study, we build upon the work of [1–7] and analyze how different host competencies and vector-feeding preferences are combined in transmission when the vector's successful biting is fractioned. The vector bites are diverted by the fraction of successful biting from the vector, which potentially amplifies the disease to (humans/domestic host/wild host), and by the fraction of successful biting from vector, which potentially dilutes the disease to (humans/domestic host/ wild host). Although this complex dynamic is exemplified using cutaneous leishmaniasis and Chagas disease, this mathematical model can be applied to other vector-borne diseases. The mathematical model presented in the next section can be used to analyze the combined effects of different host competencies and vector-feeding preferences in leishmaniasis, Chagas disease, dengue fever, west Nile virus, malaria, and other diseases lined to humans and domestic and wild animal hosts [2, 8]. Wild animals commonly serve as a major vector for the transmission of zoonotic agents to hosts such as domestic animals and humans [9]. Managing animal hosts often plays a crucial role in effective disease control [10–13]. Identifying which species are the most common reservoir hosts serving to infect those vectors could help to suggest new host-control strategies.

Host competence is an important component to incorporate in vector-host transmission models and is defined as the ability of a host to effectively transmit infection to another susceptible host or vector [14]. Host competence is determined by several factors, including susceptibility to infection with the pathogen, whether it can sustain infection with the pathogen, and whether it can infect vectors with the pathogen [3]. Host competence is a crucial determinant of epidemiological dynamics, because it considers what happens inside a host to what happens among its hosts communities [3]. A competent host for the agent of a vector-borne disease readily acquires infection from the vector, permits proliferation of the agent, and readily infects another vector [15]. Furthermore, a competent host must be able to sustain the infection agent for an extended period of time [9, 16]. Conversely, the presence of a less-competent host could decrease the risk of disease occurring at the community level [17]. Different host competencies could dilute, maintain, or amplify the presence of a parasite in the environment and facilitate epidemics [3].

Vector-feeding preference is relevant to include in models because vectors with strong host selection contribute to the spread of vector-borne zoonotic diseases. Vector-feeding preference can be defined as the specific trait of vectors' preferentially selecting specific hosts above others [2]. As a rule of thumb, blood is the most important nutritional resource of vectors [18]. Host-selection preference by vectors can be understood as an adaptive factor that leads to optimal reproductive fitness of the vector [2]. Kilpatrick et al. affirmed that *Cx. Pipiens* feeding preference on robins contributes a fitness benefit to the vector that cannot be compared with any other bird [19]. A vector's preference for a specific host is affected by internal and external factors [20]. Internal factors include the genetic and physiological makeup of the host as well as the presence of internal parasites [20]. External factors include odors, color, body heat, body mass, temperature, gender, and parasites [20]. In leishmaniasis, *Lutzomyia longipalpis* reveals specific preference for dogs, chickens, and horses. These animals attract *Lutzomyias* to breeding sites in peri-domestic areas [21]. In Chagas disease, experiments show that the Triatoma infestans bugs prefer to feed on dogs rather than chickens and

cats [22]. In dengue, laboratory studies have reported a very strong preference of *Ae.aegypti* for human odors [20]. In malaria, *Anopheles gambie* shows utmost preference for human blood [23]. Host preference also depends on the time of feeding and the availability of the vector to feed indoors or outdoors. Both human and animal host species are critical for both feeding vectors and serving as reservoirs of zoonotic vector-born pathogens [10]. According to [14], a reservoir is defined as "one or more epidemiologically connected populations or environments in which the pathogen could be permanently maintained and from which infection is transmitted to the defined target host population." Pathogens that can infect more than one host species are commonly found in host populations [11, 17, 24, 25]. As stated in [26], diversity amplification occurs when the vector prefers to feed on the reservoir host with the highest transmission capability, while dilution effect is presented when the vector prefers to bite the host with the least transmission capability or when it does not show any preference. It should be noted that in this work, we derived a general model for the transmission dynamic between vectors and three different hosts. Despite the generality of the mathematical model, we are interested in its application to cutaneous leishmaniasis and Chagas disease, considering the relationship of the most relevant different combinations of vector-feeding preferences with their respective host competencies.

2. Mathematical modeling

The model in Figure 1 describes the dynamic of vectors and humans with two different types of reservoirs. We hypothesized the following:

1. The vector population transmit the pathogen through the amplification and dilution effects to the human population, the domestic and wild reservoir population.
2. Human population (N_h) (indexed by h) is divided in five stages: susceptible (S_h), asymptomatic (E_h), Infectious, clinically ill (I_h), Treated (T_h), Recovered and non-immune (R_h). Domestic reservoir (N_d) (indexed by d) and wild reservoir (N_w) (indexed by w) populations are divided into two stages: susceptible (S_d and S_w), infectious, ill (I_d and I_w), the vector population (indexed by v) is divided into three stages: susceptible (S_v), infected but not infectious (E_v) and infectious (I_v). The biting feeding of the vector population is fractioned of successful biting from vectors that amplify the disease to (human/ domestic reservoir/ wild reservoir) populations and by the fraction of successful biting from vectors that dilute the disease to (human / domestic reservoir/ wild reservoir) populations (See Table 1 for parameter description).
3. The presence of wild and domestic reservoirs for vectors might alter vector's feeding preference away from humans thus reducing or increasing the pathogen transmission [27].
4. The following mathematical model is an extension of the model presented in [1–4], due to the fact that we are comparing both, vector's feeding preferences and host's competencies when bites are fractioned.

We tackle these hypotheses explaining why these effects arise using a compartmental model in Figure 1 that combine the eco-epidemiological interactions between vector, human, domestic and wild reservoir populations. We translate the compartmental model plus the hypotheses formulated above into the following set of differential equations.

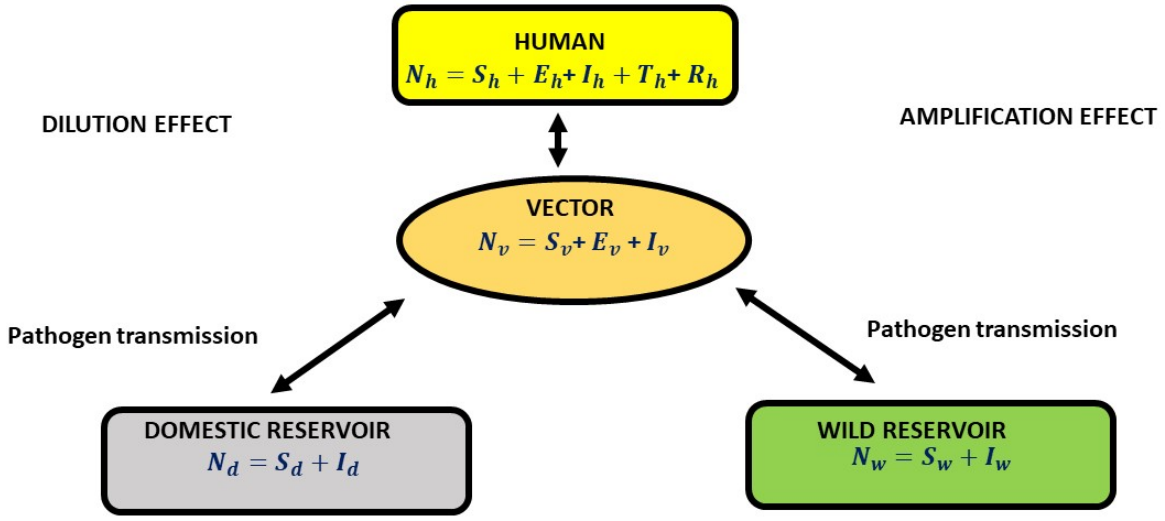

Figure 1. Schematic Diagram of the modeling interaction of pathogen transmission in human, domestic reservoir, wild reservoir, and vector populations.

2.1. Transmission equations

Dynamic of human population:

$$\begin{aligned} S_h^{'} &= \mu_h N_h - \lambda_h S_h + \omega_h I_h - \mu_h S_h \\ E_h^{'} &= \lambda_h S_h - Q_1 E_h \\ I_h^{'} &= f\sigma_h E_h - Q_2 I_h \\ T_h^{'} &= \eta r_h I_h - Q_3 T_h \\ R_h^{'} &= r_h(1-\eta) I_h + (1-f)\sigma_h E_h + \theta_h T_h - (\omega_h + \mu_h) R_h \end{aligned} \tag{2.1}$$

Dynamic of domestic reservoir population:

$$\begin{aligned} S_d^{'} &= \mu_d N_d - \lambda_d S_d + \omega_d I_d - \mu_d S_d \\ I_d^{'} &= \lambda_d S_d - Q_4 I_d \end{aligned} \tag{2.2}$$

Dynamic of wild reservoir population:

$$\begin{aligned} S_w^{'} &= \mu_w N_w - \lambda_w S_w + \omega_w I_w - \mu_w S_w \\ I_w^{'} &= \lambda_w S_w - Q_5 I_w \end{aligned} \tag{2.3}$$

Dynamic of vector population:

$$\begin{aligned} S_v^{'} &= \mu_v N_v - \lambda_v S_v - \mu_v S_v \\ E_v^{'} &= \lambda_v S_v - Q_6 E_v \\ I_v^{'} &= \sigma_v E_v - \mu_v I_v \end{aligned} \tag{2.4}$$

and the forces of infection of the model are:

$$\lambda_h = \frac{b_h \alpha_{avh} \beta_{avh} f_h I_v + \alpha_{dvh} b_h \beta_{dvh} (1 - f_h) I_v}{(\alpha_{avh} + \alpha_{dvh}) N_h + (\alpha_{adr} + \alpha_{dvdr}) N_d + (\alpha_{avwr} + \alpha_{dvwr}) N_w}$$

$$\lambda_d = \frac{b_d \alpha_{avdr} \beta_{avdr} f_d I_v + \alpha_{dvdr} b_d \beta_{dvdr} (1 - f_d) I_v}{(\alpha_{avh} + \alpha_{dvh}) N_h + (\alpha_{avdr} + \alpha_{dvdr}) N_d + (\alpha_{avwr} + \alpha_{dvwr}) N_w}$$

$$\lambda_w = \frac{b_w \alpha_{avwr} \beta_{avwr} f_w I_v + \alpha_{dvwr} b_w \beta_{dvwr} (1 - f_w) I_v}{(\alpha_{avh} + \alpha_{dvh}) N_h + (\alpha_{avdr} + \alpha_{dvdr}) N_d + (\alpha_{avwr} + \alpha_{dvwr}) N_w}$$

$$\lambda_v = \frac{aa(I_h + aE_h) + bbI_d + ccI_w}{(\alpha_{avh} + \alpha_{dvh}) N_h + (\alpha_{avdr} + \alpha_{dvdr}) N_d + (\alpha_{avwr} + \alpha_{dvwr}) N_w}$$

where,

$$Q_1 = (\sigma_h + \mu_h),\ Q_2 = (\omega_h + \mu_h + \delta_h), Q_3 = (\theta_h + \mu_h),\ Q_4 = (\omega_d + \mu_d + \delta_d),$$
$$Q_5 = (\omega_w + \mu_w + \delta_w),\ Q_6 = (\sigma_v + \mu_v),$$

$$aa = b_h c_h (\alpha_{avh} \beta_{avh} f_h + \alpha_{dvh} \beta_{dvh} (1 - f_h))$$

$$bb = b_d c_d (\alpha_{avdr} \beta_{avdr} f_d + \alpha_{dvdr} \beta_{dvdr} (1 - f_d))$$

$$cc = b_w c_w (\alpha_{avwr} \beta_{avwr} f_w + \alpha_{dvwr} \beta_{dvwr} (1 - f_w))$$

Table 1. Description of the parameters for the model in Figure 1.

Parameter	Definition
α_{avh}	feeding preference by vector that amplifies the disease on humans
α_{dvh}	feeding preference by vector that dilutes the disease on humans
α_{avdr}	feeding preference by vector that amplifies the disease on domestic reservoir
α_{dvdr}	feeding preference by vector that dilutes the disease on domestic reservoir
α_{avwr}	feeding preference by vector that amplifies the disease on wild reservoir
α_{dvwr}	feeding preference by vector that dilutes the disease on wild reservoir
β_{avh}	pathogen transmission probability from vector that amplifies the disease to humans
β_{dvh}	pathogen transmission probability from vector that dilutes the disease to humans
β_{avdr}	pathogen transmission probability from vector that amplifies the disease to domestic reservoir
β_{dvdr}	pathogen transmission probability from vector that dilutes the disease to domestic reservoir
β_{avwr}	pathogen transmission probability from vector that amplifies the disease to wild reservoir
β_{dvwr}	pathogen transmission probability from vector that dilutes the disease to wild reservoir
b_h	biting rate from vector to humans
b_d	biting rate from vector to domestic reservoir
b_w	biting rate from vector to wild reservoir
f_h	fraction of successful biting from vector that amplifies the disease to humans
$1 - f_h$	fraction of successful biting from vector that dilutes the disease to humans
f_d	fraction of successful biting from vector that amplifies the disease to domestic reservoir
$1 - f_d$	fraction of successful biting from vector that dilutes the disease to domestic reservoir
f_w	fraction of successful biting from vector that amplifies the disease to domestic reservoir
$1 - f_w$	fraction of successful biting from vector that dilutes the disease to wild reservoir
f	fraction of recovery rate from infectious human
η	fraction of recovery rate by treatment
a	fraction of infected humans transmitting the pathogen
ω_h	loss immunity rate from humans
ω_d	loss immunity rate from domestic reservoir
ω_w	loss immunity rate from wild reservoir
μ_h	human mortality rate
μ_d	domestic reservoir mortality rate
μ_w	wild reservoir mortality rate
μ_v	vector mortality rate
σ_h	intrinsic incubation period in humans
σ_v	extrinsic incubation period in vectors
δ_h	Disease induced death rate in humans
δ_d	Disease induced death rate in domestic reservoirs
δ_w	Disease induced death rate in wild reservoirs
r_h	recovery rate for infectious humans receiving treatment
θ_h	treatment rate
c_h	human ability to transmit the pathogen to vector
c_d	domestic reservoir ability to transmit the pathogen to vector
c_w	wild reservoir ability to transmit the pathogen to vector

2.2. The basic reproduction number (R_0)

According to Anderson and May in [28] the Disease Free equilibrium (DFE) state describes the situation in which there is no disease in the population. The DFE for the mathematical model described before is:

$$E_0 = (N_h^0, 0, 0, 0, 0, N_d^0, 0, N_w^0, 0, N_v^0, 0, 0)$$

The basic reproduction number indicated by R_0, is the expected number of secondary cases produced in a completely susceptible population, by a typical infectious individual. If $R_0 < 1$, then each infectious individual produces on average, less than one new infectious individual during its infectious period, and the infection cannot grow. Contrariwise, if $R_0 > 1$, then each infectious individual produces on average, more than one new infection, and the disease can invade the population [29, 30]. In order to calculate the R_0 of our model, we used the technique presented by Van den Driessche and Watmough in [29]. Essentially, the R_0 analysis is a particular case of stability analysis of the disease free equilibrium state condition. We present the equation of R_0 and its corresponding biological significance as follows:

$$R_0 = \sqrt{\frac{\sigma_v RRWW}{\mu_v Q_5 Q_6} + \frac{\sigma_v MMTT}{\mu_v Q_4 Q_6} + \frac{\sigma_v AA}{\mu_v Q_6}\left(\frac{DDf\sigma_h}{Q_2 Q_1} + \frac{SS}{Q_1}\right)}$$

where

$$\frac{\sigma_v RRWW}{\mu_v Q_5 Q_6}$$

captures the effective transmission of the pathogen from vectors to wild reservoirs plus the dilution and amplification effects. Also, this fraction captures the wild reservoir ability to transmit the pathogen to vectors, plus the dilution and amplification effects.

$$\frac{\sigma_v MMTT}{\mu_v Q_4 Q_6}$$

captures the effective transmission of the pathogen from vectors to domestic reservoirs plus the dilution and amplification effects. Also, this fraction captures the domestic reservoir ability to transmit the pathogen to vectors, plus the dilution and amplification effects.

$$\frac{\sigma_v AA}{\mu_v Q_6}\left(\frac{DDf\sigma_h}{Q_2 Q_1} + \frac{SS}{Q_1}\right)$$

captures the effective transmission of the pathogen from vectors to humans plus the dilution and amplification effects. Also, this fraction captures the humans ability to transmit the pathogen to vectors, plus the dilution and amplification effects.

$$AA = \frac{(b_h\alpha_{dvh}\beta_{dvh}(1-f_h)+\alpha_{avh}\beta_{avh}b_hf_h)N_h^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the successful transmission of the pathogen from vectors to humans plus the dilution and amplification effects.

$$MM = \frac{(b_d\alpha_{dvdr}\beta_{dvdr}(1-f_d)+\alpha_{avdr}\beta_{avdr}b_df_d)N_d^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the successful transmission of the pathogen from vectors to domestic reservoirs plus the dilution and amplification effects.

$$RR = \frac{(b_w\alpha_{dvwr}\beta_{dvwr}(1-f_w)+\alpha_{avwr}\beta_{avwr}b_wf_w)N_w^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the successful transmission of the pathogen from vectors to wild reservoirs plus the dilution and amplification effects.

$$SS = \frac{(ac_h(b_h\alpha_{dvh}\beta_{dvh}(1-f_h)+\alpha_{avh}\beta_{avh}b_hf_h))N_v^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures a portion of humans' ability to transmit the pathogen to vectors plus the dilution and amplification effects.

$$DD = \frac{(c_h(b_h\alpha_{dvh}\beta_{dvh}(1-f_h)+\alpha_{avh}\beta_{avh}b_hf_h))N_v^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the humans' ability to transmit the pathogen to vectors plus the dilution and amplification effects.

$$TT = \frac{(c_d(b_d\alpha_{dvdr}\beta_{dvdr}(1-f_d)+\alpha_{avdr}\beta_{avdr}b_df_d))N_v^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the domestic reservoirs' ability to transmit the pathogen to vectors plus the dilution and amplification effects.

$$WW = \frac{(c_w(b_w\alpha_{dvwr}\beta_{dvwr}(1-f_w)+\alpha_{avwr}\beta_{avwr}b_wf_w))N_w^0}{(\alpha_{avh}+\alpha_{dvh})N_h^0+(\alpha_{avdr}+\alpha_{dvdr})N_d^0+(\alpha_{avwr}+\alpha_{dvwr})N_w^0}$$

is a fraction that captures the wild reservoirs' ability to transmit the pathogen to vectors plus the dilution and amplification effects.

3. Numerical results

3.1. Applications to Cutaneous leishmaniasis and Chagas disease

Cutaneous leishmaniasis is a skin infection that is generated by *Leishmania* protozoa, which is transmitted by the bite of a female sandfly [31–38] to humans and domestic and wild reservoirs. Investigations in [32, 39–41], have determined that sandflies have nocturnal feeding behavior, and

their indoor and outdoor populations are an essential part of the transmission of *Leishmania*. This behavior of sandflies has been reported in approximately 90 countries [39]. The knowledge and the discovery of *Leishmania* species and their natural vectors and reservoirs behavior are helping to determine the nature and amplitude of this disease. Cutaneous leishmaniasis is endemic in most of the places located between latitudes 5S and 13S of the Neotropical ecozone [2, 31].

Chagas disease is caused by *Trypanozoma cruzi* parasite which is transmitted by triatomine bugs to humans and domestic and wild animals [42]. This disease is located only in the Americas, particularly in rural areas of Latin America. The evidence in [22] shows that the domestic reservoirs of Chagas disease, such as dogs, cats, rodents, and guinea pigs, are able to maintain *T. cruzi* in absence of any other reservoirs. According to [43], Chagas disease and its reservoirs and vectors are characterized by enzooty, which means that the disease could be maintained by wild animals and vectors, with reported cases from the southern United States of America to South American countries.

The diseases caused by protozoa of the order Kinetoplastida, collectively known as the Trypanosomiases and leishmaniasis, torture millions of the world's poorest population [44]. Reviews in [24] and [45] described around 87 reservoirs for *Leishmania* and 150 for *T.cruzi* in the Americas. Cutaneous leishmaniasis and Chagas disease are considered to be zoonotic due to the fact that both are naturally transmitted from animals to humans.

In this research we are interested in finding the relationship of cutaneous leishmaniasis and Chagas disease, because they have a domestic and wild route of parasite transmission by vectors to different reservoir hosts, including humans. There are some investigations of mathematical modeling of cutaneous leishmaniasis and Chagas disease in previous literature [1, 2, 6, 22, 39, 46–48], but no other has inserted both characteristics of vector-feeding preference and host competencies.

We use the corresponding parameters of cutaneous leishmaniasis (Table 2, Figure 2, Figure 3) and Chagas disease (Table 3, Figure 4, Figure 5) for illustrating simulations of the relationship between the different feeding preferences by vectors and the host competencies for the mathematical model described in the methods section.

Results from Figure 2(a) and Figure 4(a) contrast the differences in cutaneous leishmaniasis and Chagas disease, respectively, between the relationship of the domestic reservoir competence and the feeding preference by vector that amplifies the disease on domestic reservoir (α_{avdr}). Figure 2(b) and Figure 4(b) contrast the differences in cutaneous leishmaniasis and Chagas disease, respectively, between the relationship of the domestic reservoir competence (c_d) and the feeding preference by vector that dilutes the disease on domestic reservoir (α_{dvdr}).

Figure 2(c) and Figure 4(c) contrast the differences in cutaneous leishmaniasis and Chagas disease, respectively, between the relationship of the human competence (c_h) and the feeding preference by vector that amplifies the disease to humans (α_{avh}). However, Figure 2(d) and Figure 4(d) illustrate a similar pattern for cutaneous leishmaniasis and Chagas disease, respectively, between the wild reservoir competence c_w and the feeding preference by vector that dilutes the disease to wild reservoirs (α_{dvwr}).

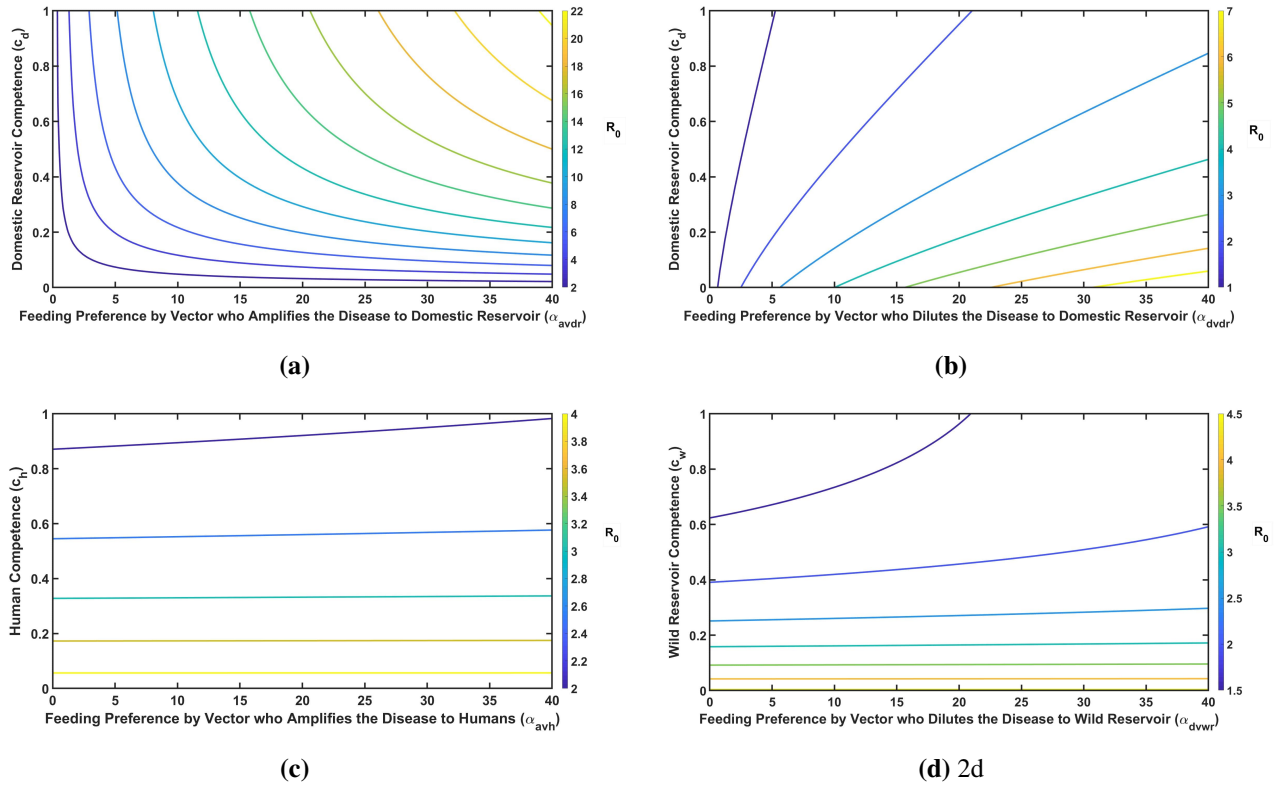

Figure 2. Cutaneous leishmaniasis model simulations loading parameters from Table 2 **(a)** Relationship between the domestic reservoir competence (c_d) and the feeding preference by vector that amplifies the disease on domestic reservoir (α_{avdr}). R_0 and (α_{avdr}) increase while (c_d) decreases.**(b)** Relationship between the domestic reservoir competence (c_d) and the feeding preference by vector that dilutes the disease on domestic reservoir (α_{dvdr}). R_0 and (c_d) decrease while (α_{dvdr}) increases. **(c)** Relationship between the human competence (c_h) and the feeding preference by vector that amplifies on human (α_{avh}). R_0 decreases while the feeding preference by vector that amplifies the disease on human (α_{avh}) and the human competency (c_h) increases.**(d)** Relationship between the wild reservoir competence (c_w) and the feeding preference by vector that dilutes the disease on wild reservoir (α_{dvwr}). R_0 decreases while (c_w) and (α_{dvwr}) increase.

On the other hand, Figure 3(a) illustrates the proportion of infectious vectors (sandflies) and the domestic reservoir competence (c_d) regarding cutaneous leishmaniasis. The proportion of infectious vectors increases, while the domestic reservoir competence increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.26. Figure 5(a) illustrates the proportion of infectious vectors (triatomines) and the domestic reservoir competence (c_d) regarding Chagas disease. The proportion of infectious vectors increases, while the domestic reservoir competence increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.37. Figure 3(b) illustrates the proportion of infectious vectors (sandflies) and the human competence (c_h) regarding cutaneous leishmaniasis. Proportion of infectious vectors increases, while (c_h) increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.22 regarding to cutaneous leishmaniasis.

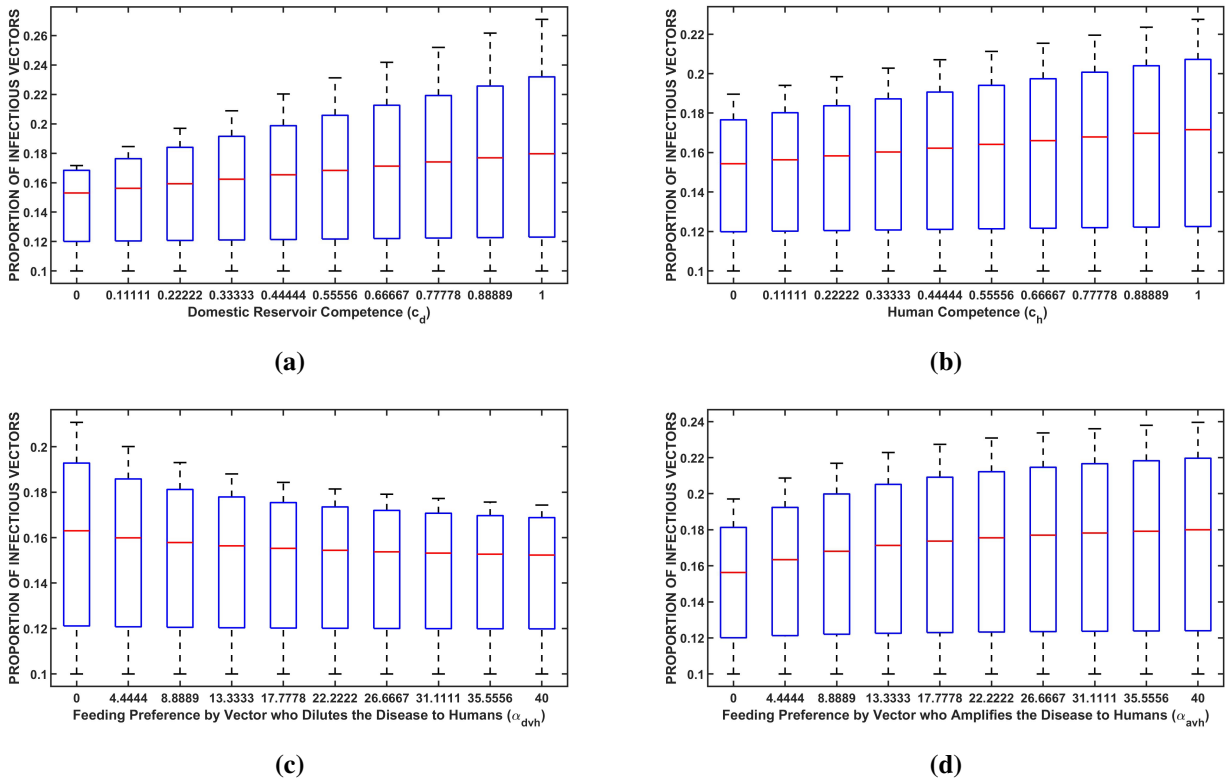

Figure 3. Cutaneous leishmaniasis model simulations loading parameters from Table 2. Box plots are created for the time series obtained by solving the ordinary differential equation system. **(a)** Box plots illustrate the proportion of infectious vectors and the domestic reservoir competence (c_d). Proportion of infectious vectors increases, while (c_d) increases. **(b)** Box plots illustrate the proportion of infectious vectors and the domestic reservoir competence (c_h). Proportion of infectious vectors increases, while (c_h) increases. **(c)** Box plots illustrate the proportion of infectious vectors and the vector feeding preference by vector that dilutes the disease to humans (α_{dvh}). Proportion of infectious vectors decreases, while (α_{dvh}) increases. **(d)** Box plots illustrate the proportion of infectious vectors and the vector that amplifies the disease to humans (α_{avh}). Proportion of infectious vectors increases, while (α_{avh}) increases.

Figure 5(b) illustrates the proportion of infectious vectors (triatomines) and human competence(c_h) regarding Chagas disease. Proportion of infectious vectors increases while the human competence increases. The proportion of infectious vectors varies between the values 0.1 to 0.37. Figure 3(c) illustrates the proportion of infectious vectors (sandflies) and the feeding preference by vector that dilutes the disease to humans (α_{dvh}) regarding cutaneous leishmaniasis. Proportion of infectious vectors decreases, while (α_{dvh}) increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.22.

Figure 5(c) illustrates the proportion of infectious vectors (triatomines) and the feeding preference by vector that dilutes the disease to humans (α_{dvh}) regarding Chagas disease. Proportion of infectious vectors decreases while (α_{dvh}) increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.36. Figure 3(d) illustrates the proportion of infectious vectors (sandflies)

and the feeding preference by vector that amplifies the disease to humans (α_{avh}) regarding cutaneous leishmaniasis. Proportion of infectious vectors increases, while (α_{avh}) increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.23. Figure 5(d) illustrates the proportion of infectious vectors (triatomines) and the feeding preference by vector that amplifies the disease to humans (α_{avh}) regarding Chagas disease. Proportion of infectious vectors increases, while (α_{avh}) increases. The proportion of infectious vectors varies over time between the values 0.1 to 0.46.

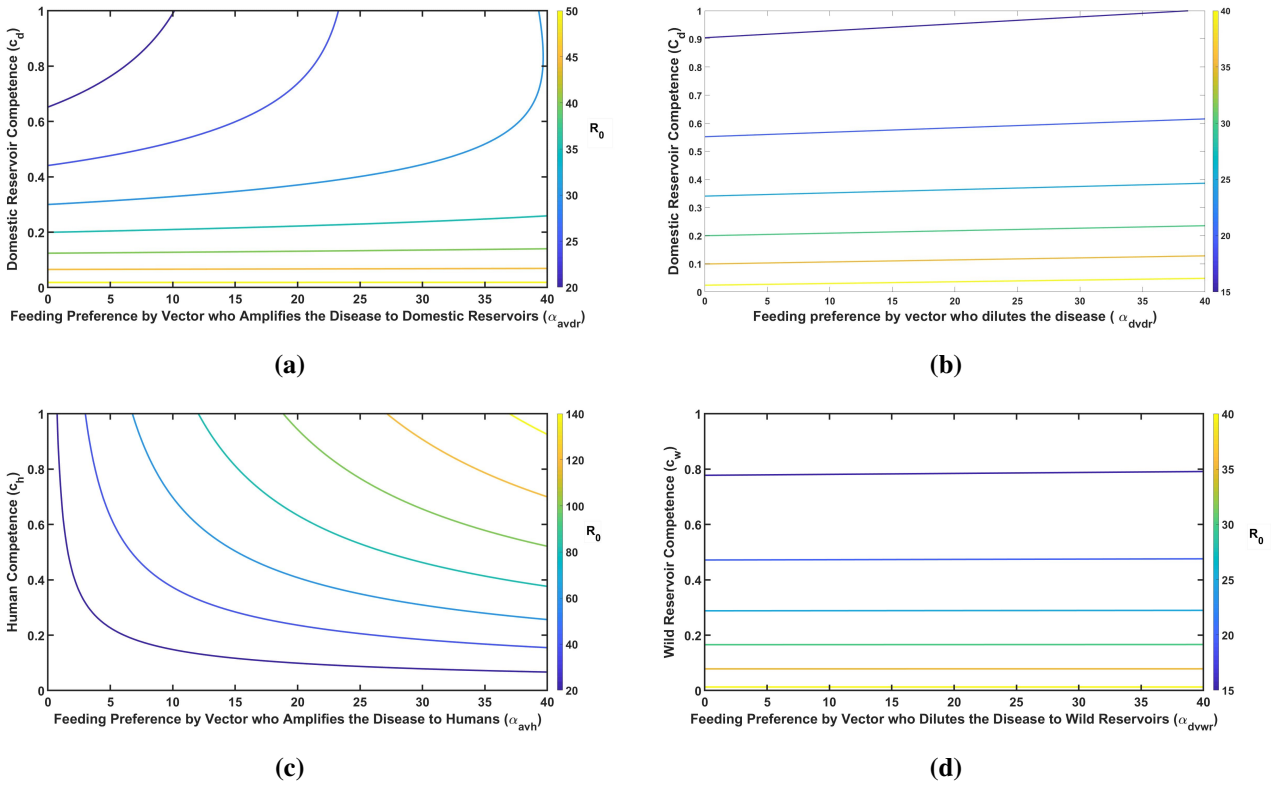

Figure 4. Chagas disease model simulations loading parameters from Table3 **(a)** Relationship between the domestic reservoir competence (c_d) and the feeding preference by vector that amplifies the disease on domestic reservoir (α_{avdr}). R_0 and (α_{avdr}) decrease while (c_d) increases. **(b)** Relationship between the domestic reservoir competence (c_d) and the feeding preference by vector that dilutes the disease on domestic reservoir (α_{dvdr}). (c_d) and (α_{dvdr}) increases while R_0 decreases. **(c)** Relationship between the human competence (c_h) and the feeding preference by vector that amplifies on human (α_{avh}). R_0 and the feeding preference by vector that amplifies the disease on human (α_{avh}) increase while the human competence (c_h) decreases. **(d)** Relationship between the wild reservoir competence (c_w) and the feeding preference by vector that dilutes the disease on wild reservoir (α_{dvwr}). R_0 decreases while (c_w) and (α_{dvwr}) increase slowly.

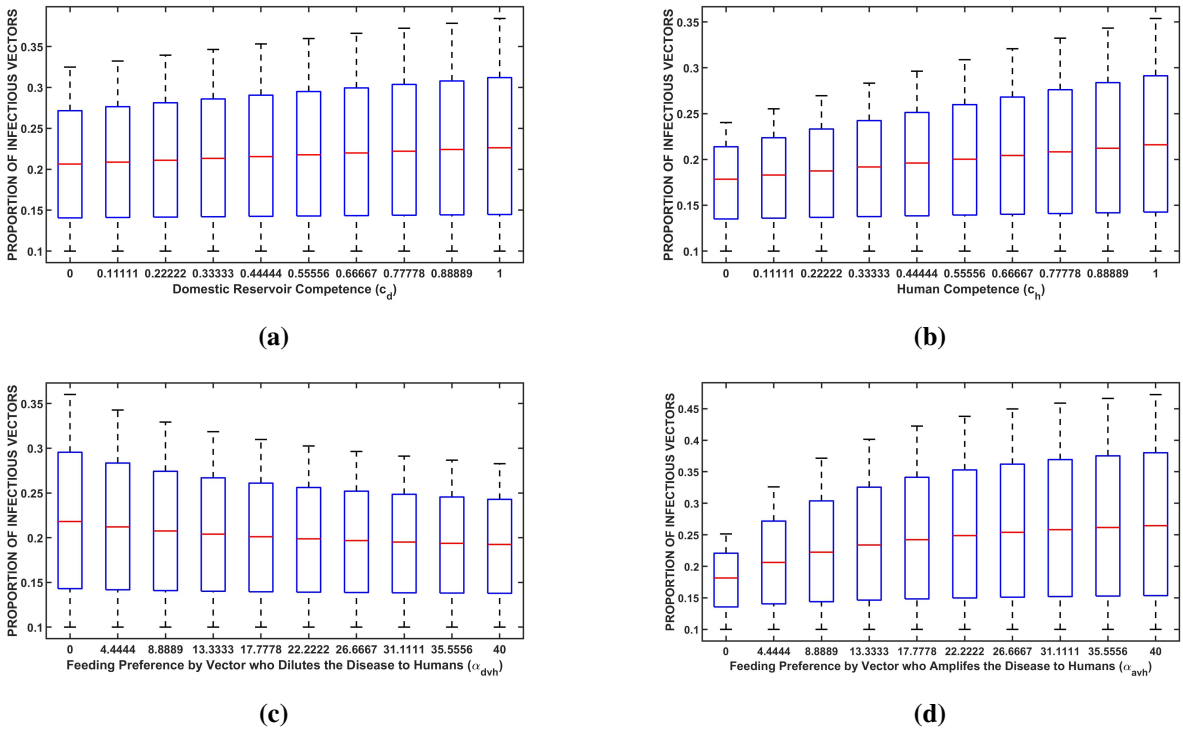

Figure 5. Chagas disease model simulations loading parameters from Table 3. Box plots are created for the time series obtained by solving the ordinary differential equation system. **(a)** Box plots illustrate the proportion of infectious vectors and the domestic reservoir competence (c_d). Proportion of infectious vector increases while (c_d) increases. **(b)** Box plots illustrate the proportion of infectious vectors and the human competence (c_h). Proportion of infectious vectors increases slowly while (c_h) increases. **(c)** Box plots illustrate the proportion of infectious vectors and the feeding preference by vector that dilutes the disease to humans (α_{dvh}). Proportion of infectious vectors decreases while (α_{dvh}) increases. **(d)** Box plots illustrate the proportion of infectious vectors and the feeding preference by vector that amplifies the disease to humans (α_{avh}). Proportion of infectious vectors and (α_{avh}) increases.

Figures 3 and 5 represent the proportion of infectious vectors (y-axes) as a function of parameters (x-axes) and time (box plots) regarding cutaneous leishmaniasis and Chagas disease. The box plots represent the time series data for the proportion of infectious vectors at a given value of parameter on the x-axis: the lower end of the box plot corresponds to time = 0, beginning from a fixed initial condition for solving the ODE. The upper end is at time = 'typical life-span of vectors' (30 days for sand flies in leishmaniasis and 305 days for triatomine bugs in Chagas disease). This is the reason why all box plots indicate the same minimum value while the maximum value and other quantiles (25th, median, 75th percentiles) vary depending on amplification or dilution effects in the system. For amplification the quantiles and maximum value increase monotonically while they decrease monotonically in dilution effect. Therefore, the box plots show a time-series data obtained by solving the ODE system, as opposed to a sample data drawn from any distribution, as is traditionally the case.

In the following Tables 2 and 3, we use some parameters from the literature and we hypothesized some parameter for cutaneous leishmaniasis and Chagas disease in the tropical and subtropical zones.

Table 2. Parameter values from the literature and from the tropical and sub-tropical zones for the cutaneous leishmaniasis.

Parameter	Value	Range	Reference
α_{avh}	3.0	[0–40.0]	hypothetical
α_{dvh}	2.0	[0–40.0]	hypothetical
α_{avdr}	4.0	[0–40.0]	hypothetical
α_{dvdr}	2.0	[0–40.0]	hypothetical
α_{avwr}	5.0	[0–40.0]	hypothetical
α_{dvwr}	2.0	[0–40.0]	hypothetical
β_{avh}	0.7198	[0.01–0.9]	[39] [40]
β_{dvh}	0.0521	[0.01–0.9]	hypothetical
β_{avdr}	0.850	[0.01–0.9]	hypothetical
β_{dvdr}	0.097	[0.01–0.9]	hypothetical
β_{avwr}	0.7	[0.01–0.9]	hypothetical
β_{dvwr}	0.07	[0.01–0.9]	hypothetical
b_h	0.6878	[0.025–2.0]	[39], [40]
b_d	0.3	[0.025–2.0]	[40]
b_w	0.08	[0.025–2.0]	[40]
f_h	0.6	[0.0001–1.0]	hypothetical
f_d	0.8	[0.0001–1.0]	hypothetical
f_w	0.4	[0.0001–1.0]	hypothetical
f	0.005	[0.001–0.9]	hypothetical
η	0.65	[0.07–0.8]	hypothetical
a	0.5	[0.007–0.8]	hypothetical
ω_h	0.0013	[0.000004–0.04]	[41], [49]
ω_d	0.003	[0.00003–0.03]	[50]
ω_w	0.0007	[0.00003–0.002]	[46]
μ_h	0.000000413	[0.0000003,0.0003]	[39]
μ_d	0.0000821	[0.00001,0.009]	[46]
μ_w	0.021	[0.0002–0.09]	[46]
μ_v	0.0135	[0.002–0.9]	[41]
σ_h	0.0158	[0.00013–0.5]	[41], [49]
σ_v	0.035	[0.003–0.7]	[41]
δ_h	0.0000008	[0.0000001–0.009]	[39]
δ_d	0.0008	[0.00005–0.05]	hypothetical
δ_w	0.00008	[0.00005–0.03]	hypothetical
r_h	0.091	[0.00001–0.9]	hypothetical
θ_h	0.035	[0.0002–0.7]	[51]
c_h	0.4	[0.00001–1.0]	hypothetical
c_d	0.3	[0.00001–1.0]	hypothetical
c_w	0.1	[0.00001–1.0]	hypothetical
N_h^0	100,050	[100.0–1000000.0]	hypothetical
N_d^0	100,050	[100.0–200000.0]	hypothetical
N_w^0	50,050	[100.0–100000.0]	hypothetical
N_v^0	5'000,500	[1000.0–10000000.0]	hypothetical

Table 3. Parameter values from the literature and from the tropical and sub-tropical zone for the Chagas disease.

Parameter	Value	Range	Reference
α_{avh}	6.0	[0–40.0]	hypothetical
α_{dvh}	4.0	[0–40.0]	hypothetical
α_{avdr}	7.0	[0–40.0]	hypothetical
α_{dvdr}	3.0	[0–40.0]	hypothetical
α_{avwr}	5.0	[0–40.0]	hypothetical
α_{dvwr}	2.0	[0–40.0]	hypothetical
β_{avh}	0.49	[0.001–0.9]	[14], [52]
β_{dvh}	0.02	[0.001–0.9]	[7]
β_{avdr}	0.5	[0.001–0.9]	hypothetical
β_{dvdr}	0.09	[0.001–0.9]	hypothetical
β_{avwr}	0.4	[0.001–0.9]	[47]
β_{dvwr}	0.05	[0.001–0.9]	[48]
b_h	0.9	[0.0025–3.0]	[6]
b_d	0.3	[0.0025–3.0]	hypothetical
b_w	0.1	[0.0025–3.0]	hypothetical
f_h	0.6	[0.0001–1.0]	hypothetical
f_d	0.8	[0.0001–1.0]	hypothetical
f_w	0.4	[0.0001–1.0]	hypothetical
f	0.7	[0.001–0.9]	hypothetical
η	0.02	[0.007–0.8]	hypothetical
a	0.5	[0.007–0.8]	hypothetical
ω_h	0.0013	[0.000004–0.04]	hypothetical
ω_d	0.003	[0.00003–0.03]	hypothetical
ω_w	0.0007	[0.00003–0.002]	hypothetical
μ_h	0.000000413	[0.0000003,0.0003]	[39]
μ_d	0.001	[0.00001,0.09]	[52]
μ_w	0.00021	[0.0001–0.09]	[46]
μ_v	0.00327	[0.001–0.9]	[53]
σ_h	0.1	[0.00013–0.9]	[54]
σ_v	0.035	[0.003–0.9]	[41]
δ_h	0.000057	[0.0000001–0.0009]	[6]
δ_d	0.0005	[0.00005–0.05]	hypothetical
δ_w	0.0003	[0.00005–0.03]	hypothetical
r_h	0.03	[0.00001–0.9]	hypothetical
θ_h	0.016	[0.0002–0.7]	[44]
c_h	0.9	[0.00001–1.0]	hypothetical
c_d	0.3	[0.00001–1.0]	hypothetical
c_w	0.7	[0.00001–1.0]	hypothetical
N_h^0	500,050	[100.0–1000000.0]	hypothetical
N_d^0	100,050	[100.0–200000.0]	hypothetical
N_w^0	50,050	[100.0–100000.0]	hypothetical
N_v^0	5'000,500	[1000.0–10000000.0]	hypothetical

3.2. *Global sensitivity analysis for R_0*

The precision of the results in mathematical and computational models in eco-epidemiological systems depend on the certainty of the parameters. There are situations where some parameters are subjected to uncertainty due to the absence of a complete information about their source and also due to the lack of laboratory and field experiments. Although, the forty-two parameters in Figure 6 and Figure 7 have biological interpretations for cutaneous leishmaniasis and Chagas disease, they either known imprecisely or vary significantly from region to region. Thus, parameter space sampling is necessary for global sensitivity analysis [2, 39, 55]. Then, it is essential to identify how the parameters of the model may vary over realistic ranges. Therefore, to achieve the global sensitivity analysis for R_0, the Partial Rank Correlation Coefficient (PRCC) is performed, which is a sensitivity analysis method that calculates the partial rank correlation coefficient for the model inputs and outputs. PRCC is performed computationally by sampling parameters from a uniformly distributed range using Latin Hypercube Sampling (LHS), an statistical sampling method that evaluates sensitivity of an outcome variable to all its input variables. PRCC is a robust sensitivity measure for nonlinear but monotonic relationships between the output and input parameters. The calculated PRCC values are between -1 and 1 and they are comparable among different model inputs. Uncertainty and global sensitivity analysis techniques help to determine and control these uncertainties. We use Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) to rank the influence of the 42 input parameters to R_0 in cutaneous leishmaniasis which is linked to the model in Figure 1. The forty-two parameters were computed by sampling them for 100000 times.

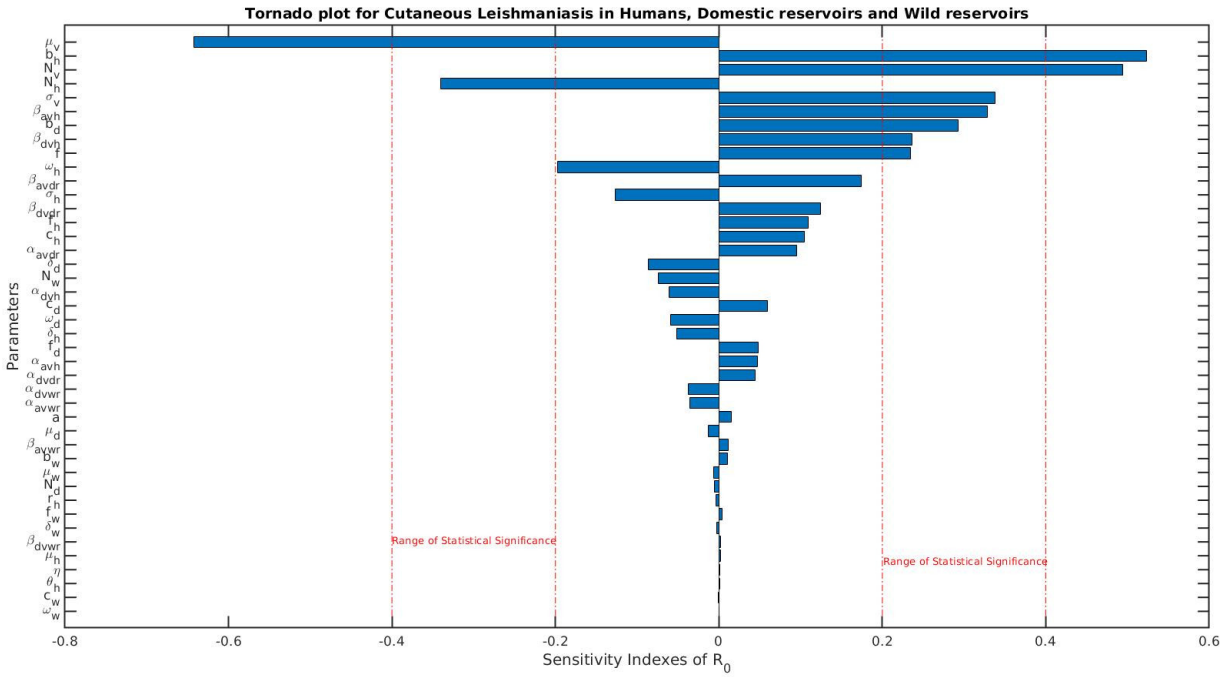

Figure 6. Cutaneous leishmaniasis: Tornado plot of Partial Rank Correlation Coefficient (PRCC). Sensitivity analysis of R_0 with respect to 42 input parameters. Significance test of model parameters and PRCC results for R_0.

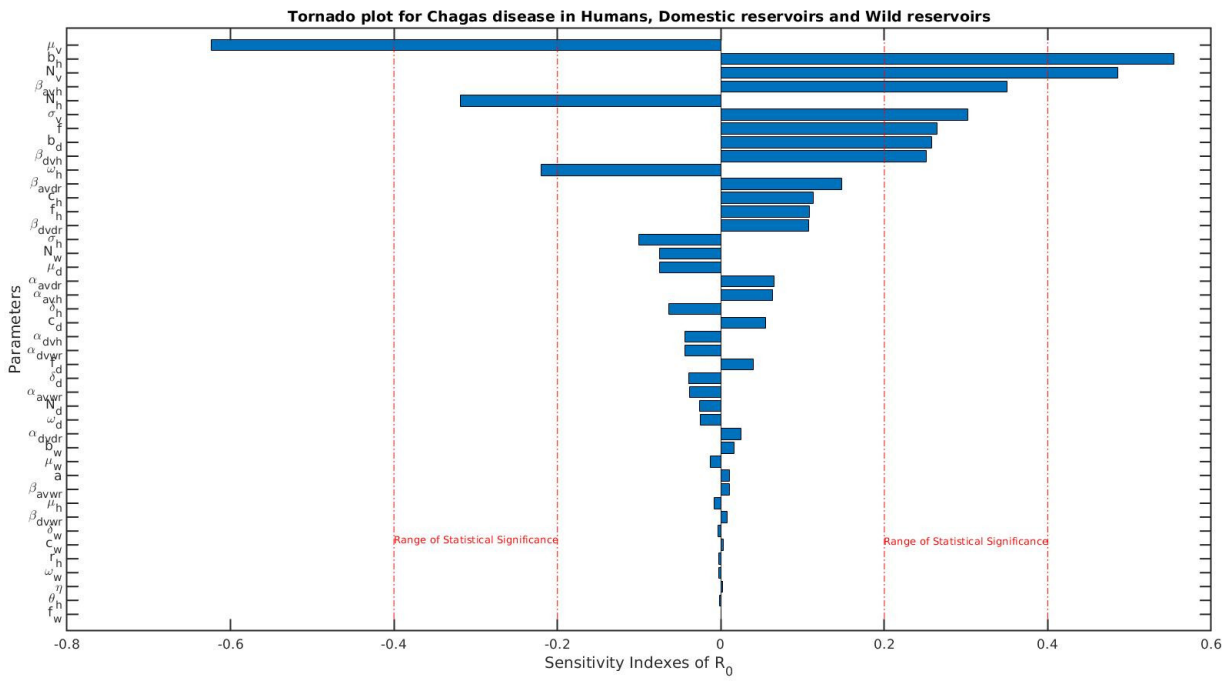

Figure 7. Chagas disease: Tornado plot of Partial Rank Correlation Coefficient (PRCC). Sensitivity analysis of R_0 with respect to 42 input parameters. Significance test of model parameters and PRCC results for R_0.

The most significant PRCC-ranked parameters greater than 0.4 for cutaneous leishmaniasis disease (Figure 6) are the natural mortality rate of sandflies (μ_v), biting rate from vector to humans, and the sandfly population (N_v^0). Then we present the intermediate significant parameters between 0.2 and 0.4, which are the human population (N_h), the extrinsic incubation in sandflies (σ_v), the pathogen transmission probability from sand flies that amplifies the disease to humans (β_{avh}), the biting rate from sand flies to domestic reservoir (b_d), the pathogen transmission probability from sandflies that dilute the disease to humans (β_{dvh}), and the fraction of recovery rate from infectious human (f).

Therefore, this study in cutaneous leishmaniasis suggests the effective disease control based on minimizing the contact that domestic reservoir and human populations have with sandfly vectors by decreasing the total sandfly population (N_v^0), such as spreading insecticide to homes and trees close to homes. Fumigation and spraying repellent are suggested to avoid the sand flies feeding. We use Table 2 for the global sensitivity analysis of R_0. The PRCC results for cutaneous leishmaniasis are shown in Figure 6.

The most significant PRCC-ranked parameters greater than 0.4 for Chagas disease (Figure 7) are the natural mortality rate of triatomine bugs (μ_v), the biting rate from triatomine bugs to humans, and the triatomine bug population (N_v^0). Then we present the intermediate significant parameters between 0.2 and 0.4, which are the extrinsic incubation in triatomine bugs (σ_v), the pathogen transmission probability from triatomine bugs that amplifies the disease to humans(β_{avh}), the human population (N_h), the fraction of recovery rate from infectious human (f), the biting rate from triatomine bugs to domestic reservoir (b_d), the loss immunity rate from humans, and the pathogen transmission probability from triatomine bugs that dilute the disease to humans (β_{dvh}).

Therefore, this study suggests the effective disease control based on minimizing the contact that domestic reservoir and human populations have with triatomine bugs vectors by decreasing the total triatomine bug population (N_v^0) such as spreading insecticide to homes and trees close to homes. Fumigation and spraying repellent are suggested to avoid the bugs biting. Moreover, it will be advisable for veterinarian health to consider control strategies in domestic reservoirs to avoid the higher ability to transmit the pathogen from reservoirs to vectors. We use Table 3 for the global sensitivity analysis of R_0. The PRCC results for Chagas disease are shown in Figure 7.

4. Conclusion

In this work, we build a general mathematical model to help determine the combined effects of host competence and vector feeding preference. We applied this model to cutaneous leishmaniasis and Chagas disease. Based on this general model, we conclude for cutaneous leishmaniasis that when the domestic host competence (c_d) decreases, the feeding preference by the vector that amplifies the disease on the domestic host (α_{avdr}) and the reproduction number R_0 increase. Additionally, the feeding preference by the vector that dilutes the disease on the domestic host (α_{dvdr}) increases while R_0 and the domestic host competency decreases (c_d). R_0 decreases while the feeding preference by vector that amplifies the disease on human (α_{avh}) and the human competency (c_h) increases. The feeding preference by vector that dilutes the disease on wild host (α_{dvwr}) and wild host competency (c_w) increases while R_0 decreases. Moreover, the proportion of infectious vector increases when the domestic host competency (c_d) increases (Figure 3a). According to Figure 3b, the proportion of infectious vector increases when the human competence (c_h) increases. The proportion of infectious vector population decreases when the feeding preference by vectors that dilutes the disease on humans (α_{dvh}) increases (Figure 3c). The proportion of infectious vectors decreases when the feeding preference by vectors that amplify the disease to humans (α_{avh}) increases.

We come up to Chagas disease in Figure 4 and Figure 5 emphasizing that R_0 decreases while the feeding preference by vector that amplifies the disease on domestic reservoir (α_{avdr}) and the domestic host competency increases (c_d). The feeding preference by vector that dilutes the disease on domestic reservoir (α_{dvdr}) and the domestic host competency increases (c_d) while R_0 decreases. The feeding preference by vector that amplifies on human (α_{avh}) and R_0 increases while the human competency (c_h) decreases. R_0 decreases while the wild host competency increases (c_w) as well as the feeding preference by vector that dilutes the disease on wild reservoir (α_{dvwr}). In addition to these, the proportion of infectious vector increases as well as the domestic host competency increases (c_d). The proportion of infectious vector increases as well as the feeding preference by vector that amplifies the disease to humans (α_{avh}). The proportion of infectious vectors increases as well as (c_h). The proportion of infectious vector decreases while the feeding preference by vector that dilutes the disease on human (α_{dvh}) increases.

Due to the lack of data on vector-feeding preferences and host competencies, researchers should focus on laboratory and field experiments to quantify the precise vector-feeding preference value and the host competence value to obtain more specific predictions. Obtaining more specific predictions on multi-host vector systems would contribute to more informed decisions regarding public health policy and intervention. It is important to note that the dynamics of infection can differ between host species. Subsequently, these differing dynamics can affect overall disease prevalence and pose a high risk of

infection to hosts with vector-borne diseases. Due to the scarcity of experimental data, we use the example of cutaneous leishmaniasis and Chagas disease to hypothesize the values for vector feeding preference, human competence, domestic host competence, and wild host competency [16, 56, 57]. Collectively, the establishment of the mathematical model (Section 2), the calculation of R_0 (Section 3) and the numerical simulations (Section 4) help us to understand the relationship between the vector's feeding preference and host competencies in different settings. The global sensitivity analyses show that the best solution and the most effective way to reduce R_0 and avoid an epidemic is to reduce sandfly and triatomine bug populations, and control the biting rates. According to [58], mathematical models are useful tools in understanding eco-epidemiological phenomena and informing strategies to prevent, control or eliminate disease. Understanding the factors that affect the vector-feeding preference for specific host and host competencies are relevant for estimating transmission risks and predicting the effects of control tactics targeting multiple hosts. Key questions related to the identification of infective reservoirs, host competencies, host feeding preference by vectors and ecological mechanisms that affects human health in a domestic and wild environment have been described here in order to bridge knowledge gaps in public health, veterinary, and ecological health.

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Conflicts of interest

The authors declare no conflicts of interest.

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