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# Control measures for Chagas disease

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ABSTRACT

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi*. The main mode of transmission of this disease in endemic areas is through an insect vector called triatomine bug. Triatomines become infected with *T. cruzi* by feeding blood of an infected person or animal. Chagas disease is considered the most important vector borne infection in Latin America. It is estimated that between 16 and 18 millions of persons are infected with *T. cruzi*, and at least 20,000 deaths each year.

In this work we formulate a model for the transmission of this infection among humans, vectors and domestic mammals. Our main objective is to assess the effectiveness of Chagas disease control measures. For this, we do sensitivity analysis of the basic reproductive number $R_0$ and the endemic proportions with respect to epidemiological and demographic parameters.



## 1. Introduction

Chagas disease, also known as American trypanosomiasis, is a life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi*. The main mode of transmission of Chagas disease in endemic areas is through an insect vector called a triatomine bug. During the day, most domestic triatomines hide in crevices in walls and rustic roofs. The bugs emerge at night, when the inhabitants are sleeping, altough in Mexico there is at least is one that is diurnal. Because they tend to feed on peoples' faces, triatomine bugs are also known as *kissing bugs*. Triatomines pass *T. cruzi* parasites (called trypomastigotes) in feces left near the site of the bite wound. Scratching the site of the bite causes the trypomastigotes to enter the host through the wound, or through intact mucous membranes, such as the conjunctiva. Once inside the host, the trypomastigotes invade cells, where they differentiate into intracellular amastigotes. The amastigotes multiply by binary fission and differentiate into trypomastigotes, which are then released into the bloodstream. The triatomine bug becomes infected by feeding on human or animal blood that contains circulating parasites [1]. All the species of Triatominae are capable of transmitting Chagas disease, but the most important from an epidemiological point of view are *Triatoma infestans*, *Rhodnius prolixus*, *Triatoma dimidiate*, *T. brasiliensis*, *Triatoma barberi*, and *Panstrongylus megistus*. Given its wide distribution and ability to domestic and peridomestic invation, *T. infestants*, is the major cause of infection of *T. cruzi* in South America, meanwhile, *T. barberi*, and *T. dimidiate* are the most important transmitters in Mexico [2,3].

Chagas disease may also be spread through blood transfusion, organ transplantation, ingestion of food contaminated with parasites, and from mother to fetus. The proportion of trans–placental transmission from mothers with chronic *T. cruzi* infection to their newborns is 2–10% [4]. Risk factors for vertical transmission are not fully understood, but effectiveness of the adaptive immune response and the genetic susceptibility of both the mother and the child are suspected. Neonatal infection by *T. cruzi* causes an acute form of Chagas disease, which may be accompanied by a severe infectious syndrome that can causes death if not treated early. This form of the disease is frequent, severe, identifiable and curable. Indeed, almost all newborns diagnosed and treated before the end of their first year of life can be definitely cured [5].

In the early acute stage of the disease, the symptoms are mild and usually produce no more than local swelling at the site of infection, in general around the eyes in children. Current treatment consist of benznidazol and nifurtimox that in the acute phase may result in cure rates between 60% and 90%, but have limited efficacy in the chronic phase, toxic side effects, and are not readily accessible to patients due to difficulty for the supply [6].

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There is an asymptomatic middle stage in which the infection can not be detected at all, even blood test results are negative, and the length of this period is not well determined. After around 4–8 weeks, individuals with active infections enter the chronic phase of Chagas disease which has a variable duration that goes from 10 to 20 years, and around 60–80% of chronically infected individuals remain asymptomatic through their lifetime. The antiparasitic treatment also appears to delay or prevent the development of disease symptoms during the chronic phase of the disease, but 20–40% of chronically infected individuals will still eventually develop life-threatening heart and digestive system disorders [7].

*T. cruzi* infection has been found in more than 150 mammalian species throughout Latin America, and south of the United States. Mammals typically involved in wild cycles of transmission include opossums, armadillos, raccoons, monkeys, wood rats, and coyotes, among many others [2,8]. In some situations, dogs have been shown to be an important link in the maintenance of the domestic cycle and consequently in the transmission to humans [9]. Livestock have occasionally been found to be infected with *T. cruzi*, but the parasite is not known to affect the health of livestock. Birds, amphibians, and reptiles are naturally resistant to *T. cruzi* infection; however, in some situations, birds may be important sources of blood meals for triatomines [9].

Chagas disease is endemic in the Americas, particularly in poor, rural areas of Mexico, Central America, and South America. In 1991, the Health Authorities of Argentina, Brazil, Chile, Paraguay and Uruguay signed the 'Cono Sur Iniciative' to conduct a simultaneous campaign to stop the transmission of Chagas disease eliminating domestic *T. infestant,* and other important local species, together with screening of blood donors, and other control measures. This campaign opened the way to other similar initiatives against Chagas disease in Central America, Mexico, and countries in the Amazon region [10,11]. It has been documented that *T. infestans* has been eliminated from most of Chile, Brazil and Uruguay, and some regions of Argentina and Paraguay. However, there are still domestic populations of *T. infestans* in several provinces of Argentina, Paraguay, Bolivia, Peru, and north of Brazil [12]. Without a sustained surveillance and selective intervention against the last remaining of *T. domestic* and peridomestic infestans, this will always be a risk of renewed spread of this specie, and therefore of Chagas disease.

Despite campaigns as 'Cono Sur Iniciative', Chagas disease is still considered the most important vector borne infection in Latin America. It is estimated that between 16 and 18 millions of persons are infected with *T. cruzi*, with at least 20,000 deaths each year, and 100 millions considered at risk [13].

The nature of Chagas disease limits control measures. No vaccines to prevent the infection are available, and drugs are effective only in the acute and early chronic phase of infection, but have adverse effects. Control measures include elimination of the vector, screening blood donors, and treatment to patients in the acute phase. Since 1982, the World Health Organization has recommended the use of animals for zooprophylaxis, as a protective measure against vector borne diseases, for instance, the use of cattle in control of malaria [14]. This controversial technique consists of attracting vectors to domestic animals in which the pathogen cannot amplify (a dead-end host). However, there are two positions concerning this practice: the first one proposes that reduced feeding on people by vectors due to availability of alternative blood sources could lead to reduce the transmission of the infection. The second one claims that transmission could be increased due to an expanded vector population resulting from unlimited access to blood meals. Particular field studies on malaria support both theories [15–17].

Chagas disease is most common among people who live in substandard housing in rural and semi rural areas. Most cases are acquired by exposure to insects in domestic or peridomestic cycles, or by congenital transmission. For this reason, we focus on the study of the transmission of Chagas infection taking into account the domestic structure in rural villages, where animals and humans are in continuous contact.

In this work we present a mathematical model for the dynamics of Chagas disease in the presence of humans, transmitter and non-transmitter domestic animals. We will not include blood transmission and organ donation, since this kind of transmissions are not so important in the rural environment as vector bites and congenital transmission. The main objective is to assess the epidemiological impact of elimination of vectors, early treatment, and zooprophylaxis as a mean of control, and how this impact is influenced by changes of such measures. To this end, we will carry out sensitive analysis of the basic reproductive number of the disease with respect to the control parameters. Furthermore, the study will present a rigorous analysis of the resulting model.

Previous mathematical modeling studies have been done to understand different aspects on the transmission and spread of Chagas disease. For instance, in [18] the authors study the effect of demographic factors on the endemicity of Chagas disease. Vector dynamics and blood transfusion are considered in the transmission of the disease in [19]. A model with infection-age-dependent infectivity was developed in [20]. In [9] the authors used a model and data from villages in Argentina to demonstrate that the infection risk was reduced if domestic animals are excluded from the dormitories. The effects of insecticide spraying and of the recovery of vector population with cessation of spraying was analyzed in [21] for a model of the dynamics of transmission among humans, vectors, and domestic animals in a dwelling. The model predicts that if insecticide is discontinued, the vector population and the disease can return to the pre-spraying levels in approximately 5–8 years. The same authors presented in [22] a modified model with a delayed logistic growth term to simulate the vector carrying capacity when the blood meal supply is large.

The paper is organized as follows. The model is formulated in Section 2. Existence and stability of the equilibria of the model are investigated in Section 3. Sensitivity analysis and numerical simulations are presented in Section 4, and conclusions are given in the final section.

## 2. Formulation of the model

As was mentioned in the Introduction, the common transmission of the protozoan *T. cruzi* to mammals is by the bite of triatomine bugs. The disease may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from mother to fetus. In the model we only consider the transmission by triatomine bites and vertical transmission since these are the most common routes of infection.

We assume that the following populations coexist in the same environment:

- Humans.
- *Transmitters*: mammals that can be infected by the Triatomines, and can transmit the infection (dogs, cats).
- *Non-transmitters*: animals that can be bitten by the Triatomines, but can not be infected, and in consequence do not transmit the infection (chickens, birds).
- *Vectors*: Triatomines.

We denote by $N_h, N_t, N_{nt}$, and $N_v$, the population sizes of humans, transmitters, non-transmitters, and vectors, respectively. Since the non-transmitters population do not enter in the infection process, we consider $N_{nt}$ as a parameter rather than a dynamical variable,

with value $N_{nt} = \bar{N}_{nt}$. We assume that human and transmitter populations have constant recruitment rates $\Lambda_h$, and $\Lambda_t$, respectively, and mortality rates given by $\mu_h$, and $\mu_t$, respectively.

Triatomines feed on mammals and birds for nutrition and reproduction. In a study about the influence of blood meal and mating on reproduction patterns of *T. brasiliensis* females (Hemiptera: *Reduviidae*) under laboratory conditions, the authors found that feeding was a powerful stimulus for egg production since fed females produced approximately 15 fold the number of eggs compared to their unfed counterparts [23]. Further, the source of food may be a factor on fecundity since as a result of obtaining their nutrition from a single food source, the triatome diet may lack certain nutrients that can influence their fecundity [24]. From these findings, it is reasonable to assume that growth of triatomine population depends upon the number of blood meals they take, their species preference, and the number of individuals of each species. For instance, it has been shown that triatomines are several times more likely to take blood meals from dogs and chickens than from humans. Therefore, if we denote by $b_h, b_t$, and $b_{nt}$ the number of triatomine bites per day in humans, transmitters, and non-transmitters, respectively, we let the triatomines daily recruitment rate equal

$$\phi_h b_h N_h + \phi_t b_t N_t + \phi_{nt} b_{nt} \bar{N}_{nt}, \tag{2.1}$$

where $\phi_h, \phi_t$, and $\phi_{nt}$ are the egg-production rates due to blood meals taken from human, transmitter, and non-transmitters, respectively. The mortality rate of triatomines is denoted by $\mu_v$.

The human population $N_h$ is divided into susceptible, $S_h$; infected in the acute phase, $I_a$; and infected in the chronic phase, $I_c$. The transmitters and vector populations are divided in susceptibles, $S_t, S_v$; and infectious, $I_t, I_v$, respectively.

The infection rate for each species depends on the number of bites per unit of time, the transmission probability per bite, and the proportion of infected mosquitoes in the population.

An individual from the human, transmitter, and non-transmitter populations receives on average $b_h \times N_v/N, b_t \times N_v/N$, and $b_{nt} \times N_v/N$ bites per unit of time, respectively, where $N = N_h + N_t + \bar{N}_{nt}$. Hence, the infection rates per susceptible human and susceptible transmitter are given by

$$b_h \beta_h \frac{N_v}{N} \frac{I_v}{N_v} = \frac{b_h \beta_h}{N} I_v,$$

and

$$b_t \beta_t \frac{N_v}{N} \frac{I_v}{N_v} = \frac{b_t \beta_t}{N} I_v,$$

respectively, where $\beta_h$, and $\beta_t$ are the transmission probabilities from vector to susceptible humans and susceptible transmitters.

The vectors get infected when they bite an infectious human or transmitter. A triatomine bug takes $b_h N_h/N$ blood meals per unit of time from humans, and $b_t N_t/N$ from transmitters. Then, the infection rate per susceptible vector is

$$\frac{b_h N_h}{N}\left(\frac{\alpha_a I_a}{N_h} + \frac{\alpha_c I_c}{N_h}\right) + \frac{b_t \alpha_t N_t}{N} \frac{I_t}{N_t} = \frac{b_h \alpha_a I_a + b_h \alpha_c I_c + b_t \alpha_t I_t}{N},$$

where $\alpha_a, \alpha_c, \alpha_t$ are the transmission probabilities from infective humans and transmitters to susceptible vectors.

For the vertical transmission in humans we consider that a proportion $p$ of newborns from chronical infected humans are acutely infected. Let $\gamma I_a$ denote the proportion of individuals that are acutely infectious that become chronically infectious $I_c$, where $1/\gamma$ is the acute period. Due to treatment, a proportion $q\gamma I_a$ returns to the susceptible class. The chronic individuals do not recover from the disease, i.e., their infectious period ends in death, and they have a disease-induced death rate $\sigma$.

According to assumptions above, the model is given by the following system of ODEs.

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - p\frac{\Lambda_h}{N_h} I_c - \frac{b_h \beta_h}{N} I_v S_h - \mu_h S_h + q\gamma I_a,\\
\frac{dI_a}{dt} &= p\frac{\Lambda_h}{N_h} I_c + \frac{b_h \beta_h}{N} I_v S_h - \gamma I_a - \mu_h I_a,\\
\frac{dI_c}{dt} &= (1-q)\gamma I_a - (\mu_h + \sigma) I_c,\\
\frac{dS_t}{dt} &= \Lambda_t - \frac{b_t \beta_t}{N} I_v S_t - \mu_t S_t\\
\frac{dI_t}{dt} &= \frac{b_t \beta_t}{N} I_v S_t - \mu_t I_t,\\
\frac{dS_v}{dt} &= \phi_h b_h N_h + \phi_t b_t N_t + \phi_{nt} b_{nt} \bar{N}_{nt} - \frac{b_h \alpha_a I_a + b_h \alpha_c I_c + b_t \alpha_t I_t}{N} S_v - \mu_v S_v,\\
\frac{dI_v}{dt} &= \frac{b_h \alpha_a I_a + b_h \alpha_c I_c + b_t \alpha_t I_t}{N} S_v - \mu_v I_v,
\end{aligned} \tag{2.2}$$

with the conditions $S_h + I_a + I_c = N_h$, $S_t + I_t = N_t$, $S_v + I_v = N_v$.

The population size of the three species satisfy the equations:

$$\begin{aligned}
\frac{dN_h}{dt} &= \Lambda_h - \sigma I_c - \mu_h N_h,\\
\frac{dN_t}{dt} &= \Lambda_t - \mu_t N_t,\\
\frac{dN_v}{dt} &= \phi_h b_h N_h + \phi_t b_t N_t + \phi_{nt} b_{nt} \bar{N}_{nt} - \mu_v N_v.
\end{aligned} \tag{2.3}$$

Since $S_h = N_h - I_a - I_c, S_t = N_t - I_t$, and $S_v = N_v - I_v$, system (2.2) becomes

$$\begin{aligned}
\frac{dI_a}{dt} &= p\frac{\Lambda_h}{N_h} I_c + \frac{b_h \beta_h}{N}(N_h - I_a - I_c) I_v - (\gamma + \mu_h) I_a,\\
\frac{dI_c}{dt} &= (1-q)\gamma I_a - (\mu_h + \sigma) I_c,\\
\frac{dI_t}{dt} &= \frac{b_t \beta_t}{N}(N_t - I_t) I_v - \mu_t I_t,\\
\frac{dI_v}{dt} &= \frac{b_h \alpha_a I_a + b_h \alpha_c I_c + b_t \alpha_t I_t}{N}(N_v - I_v) - \mu_v I_v
\end{aligned} \tag{2.4}$$

in the invariant region

$$\Omega = \{0 \leqslant I_a + I_c \leqslant N_h, 0 \leqslant I_t \leqslant N_t, 0 \leqslant I_v \leqslant N_v\} \subset R^4.$$

## 3. Mathematical analysis of the model

In the absence of the disease, $I_c = 0$, and the solutions $N_h, N_t$, and $N_v$ of system (2.3) approach the equilibrium values given by

$$\bar{N}_h = \frac{\Lambda_h}{\mu_h}, \quad \bar{N}_t = \frac{\Lambda_t}{\mu_t}, \quad \bar{N}_v = \frac{\Lambda_v}{\mu_v}, \tag{3.5}$$

where $\Lambda_v = \phi_h b_h \bar{N}_h + \phi_t b_t \bar{N}_t + \phi_{nt} b_{nt} \bar{N}_{nt}$.

### 3.1. Disease-free equilibrium

We denote the disease-free equilibrium by $E_0 = (0, 0, 0, 0)$. Using the next generation operator approach [25,26], we compute the *basic reproduction number* $R_0$ associated with the disease free equilibrium. The non-negative matrix, $F$, of the infection terms, and the non-singular $M$-matrix, $T$, of the transition terms are given by

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{b_h \beta_h \bar{N}_h}{\bar{N}} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{b_t \beta_t \bar{N}_t}{\bar{N}} \\ \frac{b_h \alpha_a \bar{N}_v}{\bar{N}} & \frac{b_h \alpha_c \bar{N}_v}{\bar{N}} & \frac{b_t \alpha_t \bar{N}_v}{\bar{N}} & 0 \end{pmatrix}, \quad T = \begin{pmatrix} \gamma + \mu_h & -p\mu_h & 0 & 0 \\ -(1-q)\gamma & \mu_h + \sigma & 0 & 0 \\ 0 & 0 & \mu_t & 0 \\ 0 & 0 & 0 & \mu_v \end{pmatrix},$$

where $\bar{N} = \bar{N}_h + \bar{N}_t + \bar{N}_{nt}$.

According to [25], $R_0$ is equal to the spectral radius, $\rho$, of the *next generation matrix*, $FT^{-1}$ given by

$$\begin{pmatrix} 0 & 0 & 0 & \frac{b_h\beta_h\bar{N}_h}{\bar{N}\mu_v} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{b_t\beta_t\bar{N}_t}{\bar{N}\mu_v} \\ \frac{b_h\alpha_a\bar{N}_v(\sigma+\mu_h)}{\bar{N}K}+\frac{b_h\alpha_c\bar{N}_v(1-q)\gamma}{\bar{N}K} & \frac{b_h\alpha_a\bar{N}_vp\mu_h}{\bar{N}K}+\frac{b_h\alpha_c\bar{N}_v(\gamma+\mu_h)}{\bar{N}K} & \frac{b_t\alpha_t\bar{N}_v}{\bar{N}\mu_t} & 0 \end{pmatrix},$$

where $K=(\gamma+\mu_h)(\sigma+\mu_h)-p(1-q)\gamma\mu_h$.

Calculating the eigenvalues of $FT^{-1}$ we obtain that the basic reproductive number is equal to

$$R_0=\sqrt{\frac{b_h^2\beta_h\bar{N}_h\bar{N}_v}{\mu_vK\bar{N}^2}\left[(\mu_h+\sigma)\alpha_a+(1-q)\gamma\alpha_c\right]+\frac{b_t^2\beta_t\alpha_t\bar{N}_t\bar{N}_v}{\mu_v\mu_t\bar{N}^2}}. \tag{3.6}$$

Hence, using Theorem 2 of [26], the following result is established.

**Proposition 1.** *The disease-free equilibrium, $E_0$, of model (2.4) is locally-asymptotically stable (LAS) if $R_0<1$, and unstable if $R_0>1$.*

The above theorem shows that Chagas disease disappears if the initial conditions of model (2.4) are sufficiently close to the disease-free equilibrium. To ensure the elimination of the disease, regardless of the initial population sizes, a global stability result is needed. When the disease related mortality $\sigma$ is zero we prove this result using a Lyapunov function. Numerical simulations further suggest that this result also holds for $\sigma\neq 0$.

**Proposition 2.** *Assume $\sigma=0$. The disease-free-equilibrium, $E_0$, of model (2.4) is globally asymptotically stable in the region $\Omega$, whenever $R_0\leqslant 1$.*

**Proof.** Appendix A. □

Note that $R_0$ can be written as

$$R_0=\sqrt{R_h^2\left(\frac{\bar{N}_h+\bar{N}_{nt}}{\bar{N}}\right)^2+R_t^2\left(\frac{\bar{N}_t+\bar{N}_{nt}}{\bar{N}}\right)^2}, \tag{3.7}$$

where

$$R_h=\sqrt{\frac{b_h^2\beta_h\bar{N}_v\bar{N}_h}{\mu_vK\left(\bar{N}_h+\bar{N}_{nt}\right)^2}\left((\sigma+\mu_h)\alpha_a+(1-q)\gamma\alpha_c\right)} \tag{3.8}$$

is the number of secondary infections derived from an infected individual in the absence of transmitters, i.e., only the human–vector cycle. And

$$R_t=\sqrt{\frac{b_t^2\beta_t\alpha_t\bar{N}_v\bar{N}_t}{\mu_v\mu_t\left(\bar{N}_t+\bar{N}_{nt}\right)^2}} \tag{3.9}$$

is the number of secondary infections derived from an infected individual in the absence of humans, i.e., only the transmitter–vector cycle.

It is interesting to observe that $R_0$ given in (3.7) is the average of the basic reproductive numbers of the humans and transmitters, weighted by the corresponding number of hosts in absence of the other population over the total number of hosts, $\bar{N}$. Then, the balance between the competence of humans and transmitters, and their corresponding population density will determine the evolution of the disease.

### 3.2. Endemic equilibria

The endemic equilibria are given by the solution of the algebraic system obtained from (2.4) setting the left-hand side equal to zero. The reported life expectancy of an individual with chronic Chagas disease is between 15 and 20 years, which means that the daily disease-induced mortality rate $\sigma$ is between 0.00013 and 0.00018 [19]. Numerical simulations show small differences between the basic reproduction numbers, and endemic equilibrium obtained with $\sigma=0.00018$, and $\sigma=0$. For these reasons, it is reasonable to neglect this parameter to obtain closed analytical expressions which will be used in the next section for the analysis of the control techniques of the vector.

When $\sigma=0$, the endemic equilibria satisfy the following algebraic system

$$\begin{aligned} 0&=p\mu_hI_c+\frac{b_h\beta_h}{\bar{N}}(\bar{N}_h-I_a-I_c)I_v-(\gamma+\mu_h)I_a,\\ 0&=(1-q)\gamma I_a-\mu_hI_c,\\ 0&=\frac{b_t\beta_t}{\bar{N}}(\bar{N}_t-I_t)I_v-\mu_tI_t,\\ 0&=\frac{b_h\alpha_aI_a+b_h\alpha_cI_c+b_t\alpha_tI_t}{\bar{N}}(\bar{N}_v-I_v)-\mu_vI_v. \end{aligned} \tag{3.10}$$

Solving $I_a, I_c$, and $I_t$ in terms of $I_v$ from system (3.10) we obtain

$$\begin{aligned} I_a&=\frac{\mu_hb_h\beta_h\bar{N}_hI_v}{\bar{N}K+b_h\beta_h(\mu_h+(1-q)\gamma)I_v},\\ I_c&=\frac{(1-q)\gamma}{\mu_h}I_a,\\ I_t&=\frac{b_t\beta_t\bar{N}_tI_v}{b_t\beta_tI_v+\mu_t\bar{N}}. \end{aligned} \tag{3.11}$$

Substituting the expressions for $I_a, I_c$ and $I_t$ of (3.11) in the fourth equation of (3.10), and eliminating the zero solution, we obtain that $I_v$ must be a root contained in the interval $(0,\bar{N}_v)$, of the quadratic equation

$$p(I_v)=a_1I_v^2+a_2I_v+a_3, \tag{3.12}$$

where

$$\begin{aligned} a_1&=-(AE+BC+\mu_vCE),\\ a_2&=-AF-BD-\mu_v(CF+ED)+(AE+BC)\bar{N}_v,\\ a_3&=(AF+BD)\bar{N}_v-\mu_vDF, \end{aligned} \tag{3.13}$$

and

$$\begin{aligned} A&=\frac{b_h^2\beta_h\bar{N}_h}{\bar{N}}\left(\alpha_a\mu_h+\alpha_c(1-q)\gamma\right),\\ B&=\frac{b_t^2\beta_t\alpha_t\bar{N}_t}{\bar{N}},\\ C&=b_h\beta_h\left(\mu_h+(1-q)\gamma\right),\\ D&=K\bar{N},\\ E&=b_t\beta_t,\\ F&=\mu_t\bar{N}. \end{aligned} \tag{3.14}$$

We observe that $p(I_v)$ is a parabola that opens downward with

$$p(\bar{N}_v)=-\mu_v(CE\bar{N}_v^2+(CF+ED)\bar{N}_v+DF)<0.$$

Substituting $A, B, D$, and $F$ in the expression for $a_3$, it can be seen that

$$a_3=\mu_v\mu_tK\bar{N}^2(R_0^2-1).$$

Then, if $R_0>1, p(0)=a_3>0$, which implies that there exists a unique positive root $\bar{I}_v\in(0,\bar{N}_v)$.

If $R_0 = 1$, one of the roots of $p(I_v)$ is zero, and the other is negative.

If $R_0 < 1$ then $a_3 < 0$, and in this case there are zero or two positive roots in the interval $(0, \bar{N}_v)$. The last case is possible only if $a_2 > 0$. But $a_3 < 0$ is equivalent to

$$F(A\bar{N}_v - \mu_v D) + BD\bar{N}_v = D(B\bar{N}_v - \mu_v F) + AF\bar{N}_v < 0,$$

which implies that $A\bar{N}_v - \mu_v D < 0$, and $B\bar{N}_v - \mu_v F < 0$. These inequalities lead to

$$a_2 = -AF - BD + E(A\bar{N}_v - \mu_v D) + C(B\bar{N}_v - \mu_v F) < 0,$$

implying no existence of positive roots when $R_0 < 1$. Therefore we have proved the following result

**Proposition 3.** *System (2.4) has a unique endemic equilibrium* $E_1 = (\bar{I}_a, \bar{I}_c, \bar{I}_t, \bar{I}_v)$ *in* $\Omega$ *if and only if* $R_0 > 1$.

In the following we shall prove the local asymptotic stability of the endemic equilibrium when $R_0 > 1$. For this, we shall follow the method given in [27,28] which is based on [29]. The method essentially consists in proving that the linearization of system (2.4) around the endemic equilibrium $E_1$ has no solutions of the form

$$\bar{Z}(t) = \bar{Z}_0 e^{\omega t}, \tag{3.15}$$

with $\bar{Z}_0 = (Z_1, Z_2, Z_3, Z_4), Z_i \in \mathbb{C}, \omega \in \mathbb{C}$, with $\Re(\omega) \geqslant 0$. The consequence of this is that the eigenvalues of the characteristic polynomial associated with the linearized model will have negative real part; in which case, the equilibrium $E_1$ is locally asymptotically stable.

Recalling that $\bar{I}_a, \bar{I}_c, \bar{I}_t, \bar{I}_v$ are the coordinates of $E_1$, and substituting a solution of the form (3.15) in the linearization of system (2.4) around $E_1$, we obtain the following linear system in the variables $Z_i$

$$\begin{aligned}
\omega Z_1 &= -\left(\gamma + \mu_h + \frac{b_h\beta_h}{\bar{N}}\bar{I}_v\right)Z_1 + \left(p\mu_h - \frac{b_h\beta_h}{\bar{N}}\bar{I}_v\right)Z_2 \\
&\quad + \left(\frac{b_h\beta_h}{\bar{N}}(\bar{N}_h - \bar{I}_a - \bar{I}_c)\right)Z_4, \\
\omega Z_2 &= (1-q)\gamma Z_1 - \mu_h Z_2, \\
\omega Z_3 &= -\left(\mu_t + \frac{b_t\beta_t}{\bar{N}}\bar{I}_v\right)Z_3 + \left(\frac{b_t\beta_t}{\bar{N}}(\bar{N}_t - \bar{I}_t)\right)Z_4, \\
\omega Z_4 &= \left(\frac{b_h\alpha_a}{\bar{N}}(\bar{N}_v - \bar{I}_v)\right)Z_1 + \left(\frac{b_h\alpha_c}{\bar{N}}(\bar{N}_v - \bar{I}_v)\right)Z_2 + \left(\frac{b_t\alpha_t}{\bar{N}}(\bar{N}_v - \bar{I}_v)\right)Z_3 \\
&\quad - \left(\mu_v + \frac{b_h\alpha_a\bar{I}_a + b_h\alpha_c\bar{I}_c + b_t\alpha_t\bar{I}_t}{\bar{N}}\right)Z_4.
\end{aligned} \tag{3.16}$$

Substituting $Z_2 = (1-q)\gamma\omega + \mu_h Z_1$ in the term $\frac{b_h\beta_h}{\bar{N}}\bar{I}_v Z_2$ of the first equation of (3.16), and after some manipulations we obtain the equivalent system

$$(1 + F_i(\omega))Z_i = (H\bar{Z})_i, \quad i = 1, \ldots, 4, \tag{3.17}$$

where

$$\begin{aligned}
F_1(\omega) &= \frac{1}{\gamma + \mu_h}\left[\omega + \frac{b_h\beta_h\bar{I}_v}{\bar{N}}\left(1 + \frac{(1-q)\gamma}{\omega + \mu_h}\right)\right], \\
F_2(\omega) &= \frac{\omega}{\mu_h}, \\
F_3(\omega) &= \frac{1}{\mu_t}\left[\omega + \frac{b_t\beta_t\bar{I}_v}{\bar{N}}\right], \\
F_4(\omega) &= \frac{1}{\mu_v}\left[\omega + \frac{b_h\alpha_a\bar{I}_a + b_h\alpha_c\bar{I}_c + b_t\alpha_t\bar{I}_t}{\bar{N}}\right],
\end{aligned} \tag{3.18}$$

and $H$ is a $4 \times 4$ matrix given by

$$H = \begin{pmatrix}
0 & \frac{p\mu_h}{\gamma+\mu_h} & 0 & \frac{b_h\beta_h(\bar{N}_h - \bar{I}_a - \bar{I}_c)}{(\gamma+\mu_h)\bar{N}} \\
\frac{(1-q)\gamma}{\mu_h} & 0 & 0 & 0 \\
0 & 0 & 0 & \frac{b_t\beta_t(\bar{N}_t - \bar{I}_t)}{\mu_t\bar{N}} \\
\frac{(b_h\alpha_a(\bar{N}_v - \bar{I}_v))}{\mu_v\bar{N}} & \frac{(b_h\alpha_c(\bar{N}_v - \bar{I}_v))}{\mu_v\bar{N}} & \frac{b_t\alpha_t(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}} & 0
\end{pmatrix}.$$

We observe that $H$ has non-negative entries, and $E_1$ satisfies

$$HE_1 = E_1. \tag{3.19}$$

Further, since the coordinates of $E_1$ are positive, and $Z_i$ are bounded, there exists a minimum $s$ such that

$$|\bar{Z}| \leqslant s|E_1|, \tag{3.20}$$

where $|\bar{Z}| = (|Z_1|, |Z_2|, |Z_3|, |Z_4|)$, and $|\cdot|$ denotes the norm in $\mathbb{C}$.

Now, we want to prove that $\Re(\omega) < 0$. Assume the contrary, i.e., $\Re(\omega) \geqslant 0$. We distinguish two cases: $\omega = 0$, and $\omega \neq 0$. In the first case, (3.17) is an homogeneous system in the variables $Z_i, i = 1, \ldots, 4$ with determinant given by

$$\Delta = \begin{vmatrix}
1 + F_1(0) & -\frac{p\mu_h}{\gamma+\mu_h} & 0 & -\frac{b_h\beta_h(\bar{N}_h - \bar{I}_a - \bar{I}_c)}{(\gamma+\mu_h)\bar{N}} \\
-\frac{(1-q)\gamma}{\mu_h} & 1 & 0 & 0 \\
0 & 0 & 1 + F_3(0) & -\frac{b_t\beta_t(\bar{N}_t - \bar{I}_t)}{\mu_t\bar{N}} \\
-\frac{b_h\alpha_a(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}} & -\frac{b_h\alpha_c(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}} & -\frac{b_t\alpha_t(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}} & 1 + F_4(0)
\end{vmatrix}.$$

From Eqs. (3.10) we obtain the equivalent expressions

$$\begin{aligned}
1 + F_1(0) &= 1 + \frac{1}{\gamma + \mu_h}\left[\frac{b_h\beta_h\bar{N}_h\bar{I}_v}{\bar{N}\bar{I}_a} - (\gamma(1 - p(1-q)) + \mu_h)\right], \\
1 + F_3(0) &= 1 + \frac{\bar{I}_t}{\bar{N}_t - \bar{I}_t}, \\
1 + F_4(0) &= 1 + \frac{\bar{I}_v}{\bar{N}_v - \bar{I}_v}.
\end{aligned}$$

Developing $\Delta$ with respect to the first row, and substituting the expressions for $1 + F_i(0)$ we obtain

$$\begin{aligned}
\Delta &= \frac{b_h\beta_h\bar{N}_h\bar{I}_v}{(\gamma+\mu_h)\bar{N}\bar{I}_a}\left[1 + \frac{\bar{I}_t}{\bar{N}_t - \bar{I}_t} + \frac{\bar{I}_v}{\bar{N}_v - \bar{I}_v} + \frac{\bar{I}_t\bar{I}_v}{(\bar{N}_t - \bar{I}_t)(\bar{N}_v - \bar{I}_v)} + \frac{b_t^2\beta_t\alpha_t(\bar{N}_t - \bar{I}_t)(\bar{N}_v - \bar{I}_v)}{\mu_t\mu_v\bar{N}^2}\right] \\
&\quad + \left(1 + \frac{\bar{I}_t}{\bar{N}_t - \bar{I}_t}\right)\frac{b_h^2\beta_h(\alpha_a + \alpha_c(1-q)\gamma\mu_h)(\bar{N}_h - \bar{I}_a - \bar{I}_c)(\bar{N}_v - \bar{I}_v)}{(\gamma + \mu_h)\mu_v\bar{N}^2}.
\end{aligned} \tag{3.21}$$

From the second, third and fourth equations of (3.10) we obtain respectively

$$\begin{aligned}
\bar{I}_c &= \frac{(1-q)\gamma\bar{I}_a}{\mu_h}, \quad \frac{b_t\beta_t(\bar{N}_t - \bar{I}_t)}{\mu_t\bar{N}} = \frac{\bar{I}_t}{\bar{I}_v}, \\
\frac{b_t\alpha_t(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}} &= \frac{\bar{I}_v}{\bar{I}_t} - \frac{b_h(\alpha_a\bar{I}_a + \alpha_c\bar{I}_c)(\bar{N}_v - \bar{I}_v)}{\mu_v\bar{N}\bar{I}_t}.
\end{aligned}$$

Substituting the expressions above in (3.21) and simplifying

$$\begin{aligned}
\Delta &= \frac{b_h\beta_h\bar{N}_h\bar{I}_v}{(\gamma+\mu_h)\bar{N}\bar{I}_a}\left[\frac{\bar{I}_v}{\bar{N}_v - \bar{I}_v} + \frac{\bar{I}_t\bar{I}_v}{(\bar{N}_t - \bar{I}_t)(\bar{N}_v - \bar{I}_v)}\right] \\
&\quad + \frac{b_h^2\beta_h\left(\alpha_a + \alpha_c\frac{(1-q)\gamma}{\mu_h}\right)(\bar{I}_a + \bar{I}_c)(\bar{N}_v - \bar{I}_v)}{(\gamma+\mu_h)\mu_v\bar{N}^2} \\
&\quad + \frac{\bar{I}_t}{\bar{N}_t - \bar{I}_t}\left[\frac{b_h\beta_h\bar{N}_h\bar{I}_v}{(\gamma+\mu_h)\bar{N}\bar{I}_a} - \frac{b_h^2\beta_h(\alpha_a + \alpha_c(1-q)\gamma\mu_h)(\bar{N}_h - \bar{I}_a - \bar{I}_c)(\bar{N}_v - \bar{I}_v)}{(\gamma+\mu_h)\mu_v\bar{N}^2}\right].
\end{aligned}$$

From the last equation of (3.10)

$$\frac{b_h\left(\alpha_a+\alpha_c\frac{(1-q)\gamma}{\mu_h}\right)(\bar{N}_v-\bar{I}_v)}{\mu_v\bar{N}}=\frac{\bar{I}_v}{\bar{I}_a}-\frac{b_t\alpha_t I_t(\bar{N}_v-\bar{I}_v)}{\mu_v\bar{N}\bar{I}_a}.$$

Substituting this expression in the last summand of $\Delta$ and simplfying we finally obtain

$$\begin{aligned}\Delta=&\frac{b_h\beta_h\bar{N}_h\bar{I}_v}{(\gamma+\mu_h)\bar{N}\bar{I}_a}\left[\frac{\bar{I}_v}{\bar{N}_v-\bar{I}_v}+\frac{\bar{I}_t\bar{I}_v}{(\bar{N}_t-\bar{I}_t)(\bar{N}_v-\bar{I}_v)}\right]\\&+\frac{b_h^2\beta_h\left(\alpha_a+\alpha_c\frac{(1-q)\gamma}{\mu_h}\right)(\bar{I}_a+\bar{I}_c)(\bar{N}_v-\bar{I}_v)}{(\gamma+\mu_h)\mu_v\bar{N}^2}\\&+\frac{\bar{I}_t}{\bar{N}_t-\bar{I}_t}\left[\frac{b_h\beta_h\bar{N}_h\bar{I}_v}{(\gamma+\mu_h)\bar{N}\bar{I}_a}(\bar{I}_a+\bar{I}_c)+\frac{b_h\beta_h\beta_t\alpha_t\bar{I}_t(\bar{N}_v-\bar{I}_v)(\bar{N}_h-\bar{I}_a-\bar{I}_c)}{(\gamma+\mu_h)\mu_v\bar{N}^2\bar{I}_a}\right]\\>&0.\end{aligned}$$

Therefore, for $\omega=0$, the only solution of system (3.17) is the trivial one which implies $\omega\neq 0$.

Assume now $\omega\neq 0$, and $\Re(\omega)>0$. In this case it is easy to see that $|1+F_i(\omega)|>1$ for $i=1,\dots 4$, and therefore $F(\omega)=\min|1+F_i(\omega)|>1$. Taking norms on both sides of the equations in system (3.17), and using the fact that the entries of $H$ are non-negative we obtain the inequality

$$F(\omega)|\bar{Z}|\leqslant H|\bar{Z}|, \tag{3.22}$$

which implies by (3.20), and then by (3.19)

$$F(\omega)|\bar{Z}|\leqslant sH|E_1|=s|E_1|. \tag{3.23}$$

From this inequality it follows $|\bar{Z}|\leqslant s|E_1|F(\omega)<s|E_1|$, which contradicts the minimality of $s$. Therefore $\Re(\omega)<0$. we have proved the following proposition

**Proposition 4.** *The endemic equilibrium is locally asymptotically stable when $R_0>1$.*

Global stability of the endemic equilibrium is established for the case $\sigma=p=q=0$ in the next proposition. Numerical simulations suggest that this result also holds for $\sigma, p$, and $q$ different from zero.

**Proposition 5.** *Assume $\sigma=p=q=0$. The endemic equilibrium $E_1$ is globally asymptotically stable in the interior of $\Omega$.*

**Proof.** Appendix A. □

## 4. Sensitivity analysis and simulations

As mentioned in the Introduction, measures to control Chagas disease are limited. Among them are reduction of vector population, early identification treatment of the acute cases, and reduction of infected bites in humans by the use of no transmitters and mosquito nets.

In this section we analyze the effect of the control measures mentioned above on the spread of Chagas disease. The parameter values used in the simulations and their references are given in Table 1. In the following we discuss the values of some of the parameters used in this work.

In a field study conducted in Argentina to determine host preference of *T. infestants*, it was found that the number of dog blood meals per dog was 2.3–2.6 times the number of human blood meals per human. Similarly, in the same study, it was found that triatomines selected chickens for blood meals can go from 3 to 8 times as often as the number of chickens relative to humans [30]. In our study we follow [9], and we approximate the ratio of feeding on transmitters and non-transmitters relative to humans as 2.5 and 3, respectively, which gives $b_t=2.5b_h$, and $b_{nt}=3b_h$.

**Table 1**
Parameters in numerical simulations of Chagas model (2.2). Time units are in days.

| Parameter | Meaning | Value | Sources |
|---|---|---|---|
| $p$ | Vertical transmission | 2–10% | [4] |
| $b_f$ | Feeding rate per triatomine | 0.26 day$^{-1}$ | [2] |
| $b_h$ | Triatomine bites in humans | 0.04 day$^{-1}$ | [9] |
| $b_t$ | Triatomine bites in transmitters | 0.1 day$^{-1}$ | [9] |
| $b_{nt}$ | Triatomine bites in non-transmitters | 0.12 day$^{-1}$ | [9] |
| $\beta_h$ | Transmission vector–human | 0.0009 | [9] |
| $\beta_t$ | Transmission vector–transmitter | 0.0009 | [33] |
| $\alpha_a$ | Transmission acute human–vector | 0.03 | [9] |
| $\alpha_c$ | Transmission chronic human–vector | 0.03 | [9] |
| $\alpha_t$ | Transmision transmitter–vector | 0.49 | [34] |
| $1/\gamma$ | Acute period | 28–56 days | [7] |
| $q$ | Treated and cured humans | 0.04% | |
| $\mu_h$ | Human mortality | 0.000042 day$^{-1}$ | |
| $\mu_t$ | Transmitter mortality | 0.00027 day$^{-1}$ | |
| $\mu_{nt}$ | Non-transmiter mortality | 0.00039 day$^{-1}$ | |
| $\mu_v$ | Triatomine mortality | 0.005 day$^{-1}$ | [32] |
| $\sigma$ | Disease-induced mortality | 0.00013–0.00018 day$^{-1}$ | [19] |
| $\bar{N}_h$ | Human population | 5000 | |
| $\bar{N}_t$ | Transmitter population | $2/5\times N_h$ | |
| $\bar{N}_{nt}$ | Non-transmitter population | $3/5\times N_h$ | |
| $\bar{N}_v$ | Vector population | $100\times N_h$ | |

The feeding frequency of triatomines depends on the species; when hosts are available, bugs commonly feed every four to nine days, [2]. We assume the value of four days, giving an approximated daily blood feeding rate of $b_f=1/4=0.25$ days$^{-1}$. Since $b_f=b_h+b_t+b_{nt}=6.5b_h$ then $b_h=0.25/6.5\approx 0.04$ days$^{-1}$.

Adult triatomines life span, greatly depends on species, and ranges from 50 to more than 300 days. For instance, life span of females of *T. brasiliensis* is about 90–120 days [23], whereas life span of females of *T. flavida* ranges from 285 up to 486 days [31]. We assume a mean adult longevity of approximately six months for *T. infestants* as was obtained in [32] based on cohort experiments conducted under controlled laboratory conditions, thus the daily mortality rate is $\mu_v=1/6$ months$^{-1}$=0.005 days$^{-1}$. For humans, transmitters and non-transmitters, we assume a life span of 65, 10, and 7 years, respectively.

Once infected, the host remains infectious the rest of his life if not treated, and we assume for humans, a daily disease related death rate $\sigma=0.00014$ days$^{-1}$ [19].

### 4.1. Sensitivity analysis of the basic reproductive numbers

Periodic use of insecticides is the usual way to reduce the vector population [9], and this control means increasing vector mortality. If the vector mortality increases by a factor $\theta>1, R_0$ decreases by a factor $1/\theta$. As an example, if insecticide application is every three months, and assuming almost all bugs disappear, then the life span $1/\mu_v$, in the best of the cases, decreases from six months to three months. This would imply that $\mu_v$ increases twice, and consequently $R_0$ would decrease by 1/2. Being optimistic, the disease could be controlled by the mere application of insecticide every three months, if $\frac{R_0}{2}<1$.

In the numerical simulations illustrated in Figs. 1–3, we assume two dogs, three chickens and five humans per household, then $\bar{N}_t=2\bar{N}_h/5, \bar{N}_{nt}=3\bar{N}_h/5$, and $\bar{N}=2\bar{N}_h$. Taking $\bar{N}_v=100\bar{N}_h, \bar{N}_h=5000, p=0.06, q=0.04, \gamma=0.02675$, and the other parameters as in Table 1, we obtain $R_0=5.8, R_h=1.3$, and $R_t=11.4$. In this example, disease can be eradicated if $\frac{1}{\theta}\times 5.8<1$, or $5.8<\theta$, which means

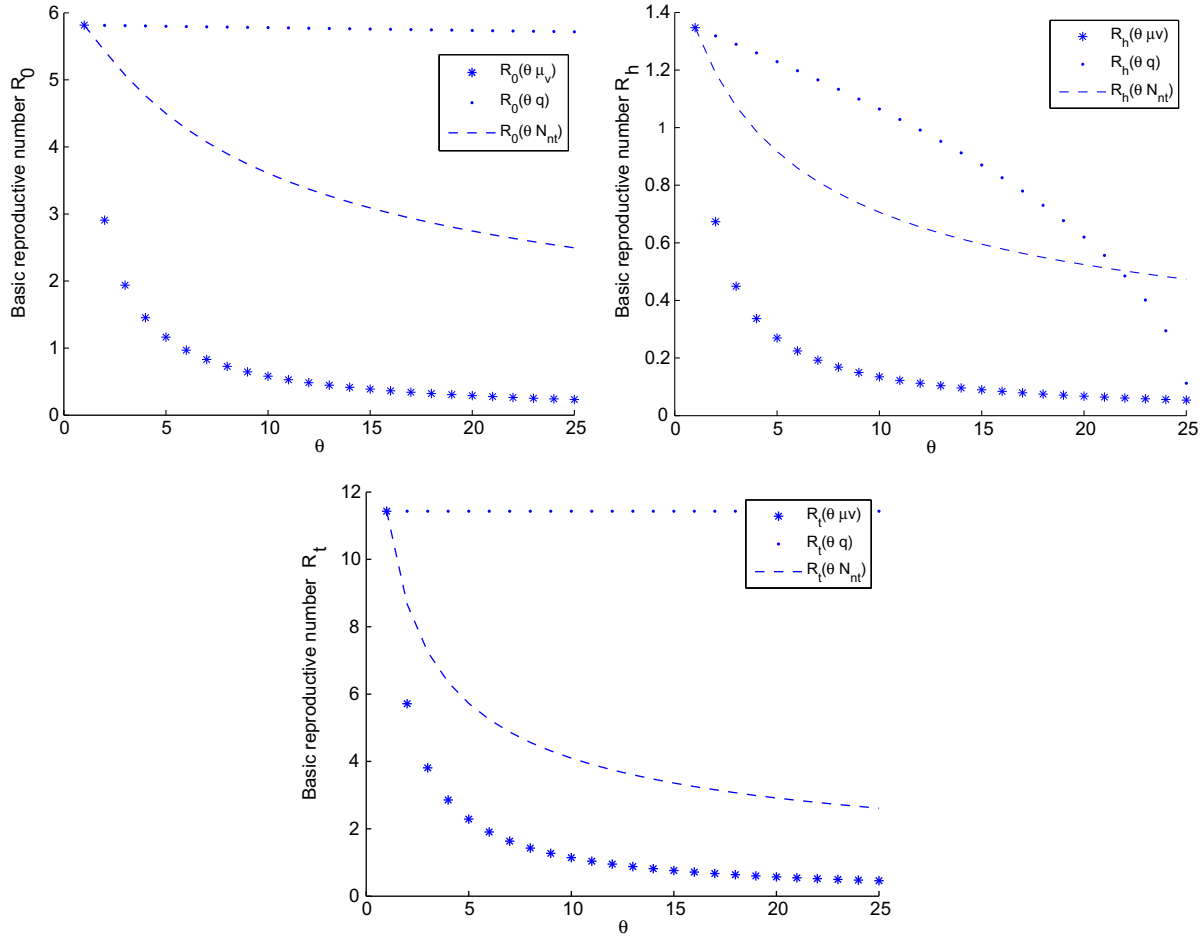


**Fig. 1.** Evolution of the basic reproductive numbers as a function of the control variables represented by $\theta\mu_v, \theta q$, and $\theta N_{nt}$ when $\theta$ increments from 1 to 25. Although to increase the controls twenty five times is probably unrealistic, we decide to keep this number in order to appreciate the long-term trend of the basic reproduction numbers for each control. In the simulations $\mu_v = 0.005, q = 0.04$, and $N_{nt} = 5 \times 10^5$, and the rest of the parameters are as in Table 1: (a) $R_0$, (b) $R_h$, (c) $R_t$.

that vector mortality should be increased more than 6 times. Assuming again the extreme case, i.e., almost all bugs disappear after each application, $R_0$ would be less than one if insecticide is sprayed at least once every month.

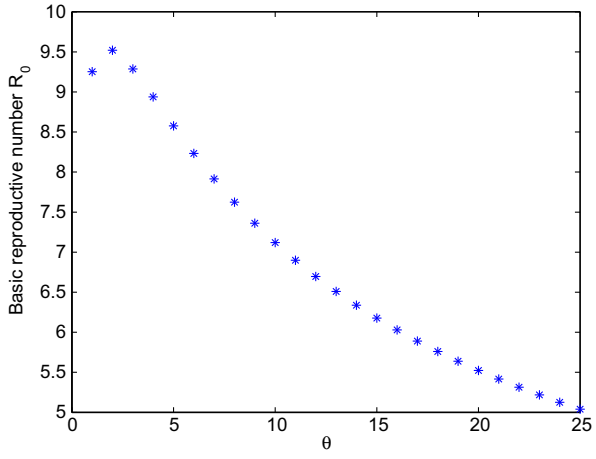


**Fig. 2.** Evolution of the basic reproductive number $R_0$ as a function of $\theta Nnt$ when $\theta$ increases from one to twenty five, and $b_{nt} = 0.5$. The rest of the parameters are as in Table 1.

Starred lines in Figs. 1(a)–(c) show the behavior of $R_0, R_h$, and $R_t$ when $\mu_v$ is incremented by the factor $\theta$. Since the curves are hyperbolas, the basic reproductive numbers decrease sharply for moderate values of theta, for example between one to five, but for bigger values of $\theta$ the decreasing is slower, indicating that after a certain number, for example five, the reduction of vector population has not an important impact on the basic reproductive numbers.

Early treatment of the disease is simulated in our model incrementing the proportion $q$ of acute infectious that are treated and cured. To assess the effect of this parameter on $R_0$, we assume as in the previous case, that it increases by a factor $\theta > 1$, with $\theta q \leqslant 1$ since $\theta q$ is a proportion. Then, denoting $\bar{q} = \theta q$, and expanding $R_0$ in terms of $q$ we obtain

$$\begin{aligned} R_0(\bar{q}) &\approx R_0(q) + \frac{\partial R_0}{\partial q}(\theta - 1)q \\ &= R_0(q) + \frac{\partial}{\partial q}\left[R_h^2\left(\frac{\bar{N}_h + \bar{N}_{nt}}{\bar{N}}\right)^2 + R_t^2\left(\frac{\bar{N}_t + \bar{N}_{nt}}{\bar{N}}\right)^2\right]^{1/2}(\theta - 1)q \\ &= R_0(q) + \frac{Q}{2R_0(q)}(\theta - 1)q \\ &= R_0(q)\left[1 + \frac{Q}{2R_0^2(q)}\right](\theta - 1)q, \end{aligned} \tag{4.24}$$

where $R_h, R_t$ are defined by (3.8), (3.9), respectively, and

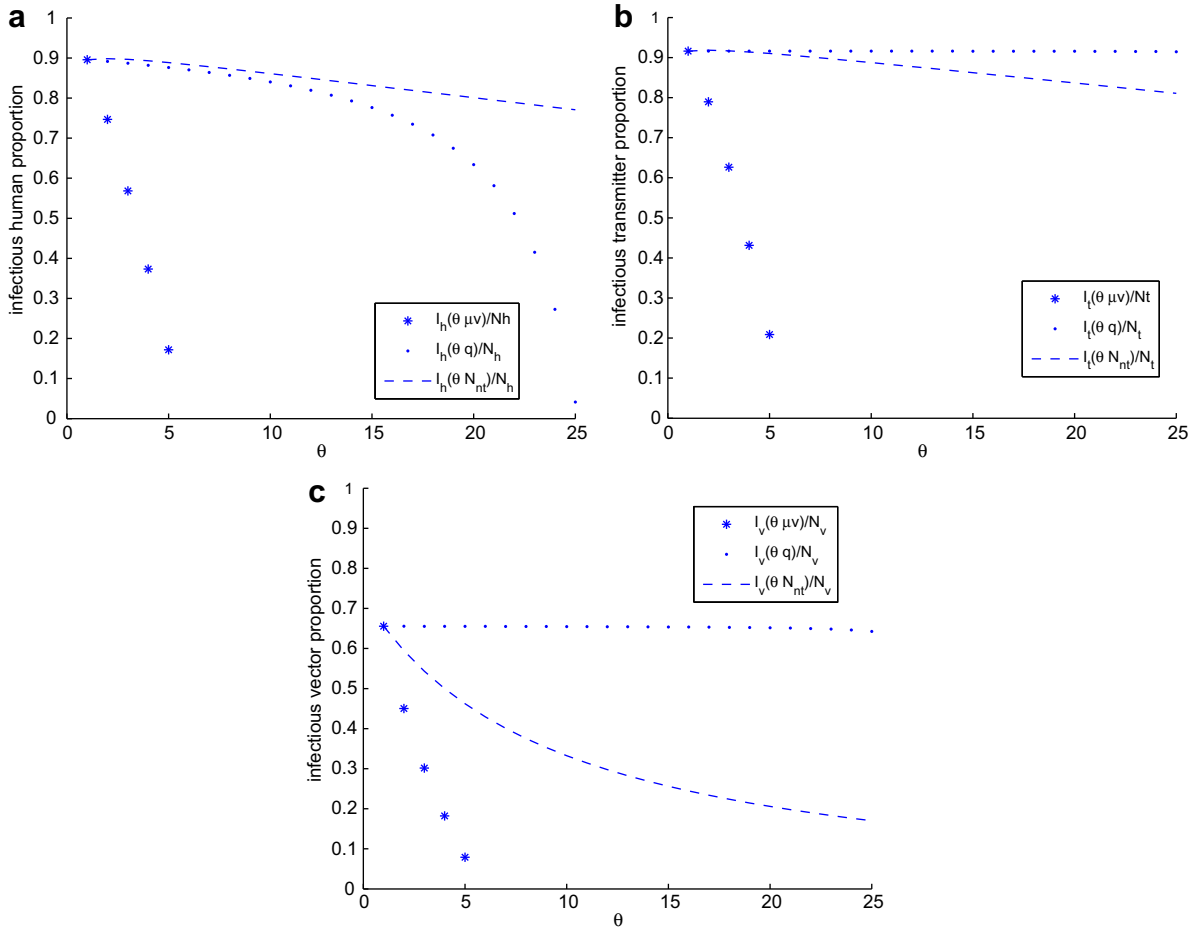


**Fig. 3.** The endemic proportions as a function of the control variables $\theta\mu_v, \theta q$, and $\theta N_{nt}$ when $\theta$ increments from 1 to 25. In the simulations $\mu_v = 0.005, q = 0.04$, and $N_{nt} = 5 \times 10^5$: (a) infected humans proportion $I_h/N_h$, with $I_h = I_a + I_c$, (b) infected transmitters proportion $I_t/N_t$, (c) infected vectors proportion $I_v/N_v$.

$$
\begin{aligned}
Q &= \frac{\partial R_h^2}{\partial q}\left(\frac{\bar{N}_h + \bar{N}_{nt}}{\bar{N}}\right)^2 \\
&= \frac{b_h^2 \beta_h N_v N_h}{\mu_v (N_h + N_{nt})^2} \\
&\quad \cdot \frac{\partial}{\partial q}\left(\frac{(\sigma+\mu_h)\alpha_a + (1-q)\gamma\alpha_c}{(\gamma+\mu_h)(\sigma+\mu_h) - p(1-q)\gamma\mu_h}\right)\left(\frac{\bar{N}_h + \bar{N}_{nt}}{\bar{N}}\right)^2 \\
&= \frac{b_h^2 \beta_h N_v N_h}{\mu_v (N_h + N_{nt})^2}\left(-\frac{\gamma(\sigma+\mu_h)\left(p\alpha_a\mu_h + \alpha_c(\mu_h+\gamma)\right)}{\left((\gamma+\mu_h)(\sigma+\mu_h) - p(1-q)\gamma\mu_h\right)^2}\right)\left(\frac{\bar{N}_h + \bar{N}_{nt}}{\bar{N}}\right)^2.
\end{aligned}
$$

Multiplying and dividing Q by $(\sigma+\mu_h)\alpha_a + (1-q)\gamma\alpha_c$, and using the definition of $K$, and $R_h$ we finally obtain

$$
Q = -R_h^2 \frac{\gamma(\sigma+\mu_h)(p\alpha_a\mu_h + \alpha_c(\mu_h+\gamma))}{K((\sigma+\mu_h)\alpha_a + (1-q)\gamma\alpha_c)}\left(\frac{\bar{N}_h + \bar{N}_{nt}}{\bar{N}}\right)^2 < 0. \tag{4.25}
$$

Since the proportion of treated infectious can not go beyond the total population, the minimum value that $R_0$ can achieve by this control is approximately $R_0\left[1 + \frac{Q}{2R_0^2(q)}\right](1-q)$ when $\theta = 1/q$. In the example illustrated by dotted lines in Figs. 1(a) and (c), we see that $R_0$ decreases only from 5.88 to 5.71, and $R_t$ keeps constant when $q$ goes from 0.04 to 1 and the other parameters remain as in Table 1. This behavior is explained in the following way. $R_0$ is a weighted average of $R_h$, and $R_t$, and with the values taken from the literature for the field study given by Cohen and Gürtler [9], $R_h$ is of the order of ten times smaller than $R_t$, and since this last parameter does not depend of $q, R_h$ remains almost unchanged. On the other hand, dotted line in Fig. 1(b) shows that $R_h$ decreases from its initial value of around 1.3–0.5, which indicates that human treatment is a very effective control when the transmission is mainly between humans and vectors, i.e., in the absence of transmitters.

In the following we will test the effectiveness of zooprophylaxis for control of Chagas disease. For this end, we assume that the population of non- transmitters, $\bar{N}_{nt}$, increases to $\tilde{N}_{nt} = \theta\bar{N}_{nt}$, with $\theta > 1$, and we expand $R_0$ given by (3.6) in Taylor series in terms of $\bar{N}_{nt}$ to get

$$
R_0\left(\tilde{N}_{nt}\right) \approx R_0\left(\bar{N}_{nt}\right) + \frac{\partial R_0\left(\bar{N}_{nt}\right)}{\partial \bar{N}_{nt}}(\theta - 1)\bar{N}_{nt}, \tag{4.26}
$$

where

$$
\begin{aligned}
\frac{\partial R_0(\bar{N}_{nt})}{\partial \bar{N}_{nt}} &= \frac{1}{2R_0}\left(\frac{b_h^2\beta_h\bar{N}_h}{\mu_v K}\left[(\mu_h+\sigma)\alpha_a + (1-q)\gamma\alpha_c\right] + \frac{b_t^2\beta_t\alpha_t\bar{N}_t}{\mu_v\mu_t}\right)\frac{\partial}{\partial\bar{N}_{nt}}\left(\frac{\bar{N}_v}{\bar{N}^2}\right) \\
&= \frac{1}{2R_0}R_0^2\frac{\bar{N}^2}{\bar{N}_v}\frac{\partial}{\partial\bar{N}_{nt}}\left(\frac{\bar{N}_v}{\bar{N}^2}\right).
\end{aligned}
$$

Recalling that $\bar{N}_v = \frac{\phi_h b_h \bar{N}_h + \phi_t b_t \bar{N}_t + \phi_{nt} b_{nt} \bar{N}_{nt}}{\mu_v}$, and $\bar{N} = \bar{N}_h + \bar{N}_t + \bar{N}_{nt}$, we obtain after some simplifications

$$
\frac{\partial R_0(\bar{N}_{nt})}{\partial \bar{N}_{nt}} = R_0\left(\bar{N}_{nt}\right)\frac{\left[(\phi_{nt}b_{nt} - 2\phi_h b_h)\bar{N}_h + (\phi_{nt}b_{nt} - 2\phi_t b_t)\bar{N}_t - \phi_{nt}b_{nt}\bar{N}_{nt}\right]}{2\mu_v N\bar{N}_v}. \tag{4.27}
$$

We see that $R_0$ has a unique local maximum when

$$\bar{N}_{nt} = \frac{(\phi_{nt} b_{nt} - 2\phi_h b_h)\bar{N}_h + (\phi_{nt} b_{nt} - 2\phi_t b_t)\bar{N}_t}{\phi_{nt} b_{nt}}, \tag{4.28}$$

which is positive if $(\phi_{nt} b_{nt} - 2\phi_h b_h)\bar{N}_h + (\phi_{nt} b_{nt} - 2\phi_t b_t)\bar{N}_t > 0$. It follows that depending on the density, biting rate, and egg-production rate from blood meals of the populations involved, $R_0$ increases or decreases. For instance, if $\frac{\phi_{nt} b_{nt}}{2} \leqslant \min\{\phi_h b_h, \phi_t b_t\}$, there is a negative local maximum, and $R_0$ always decreases monotonically to zero, as it is shown by the dashed line in Fig. 1(a), where $b_{nt} = 0.12$, $\phi_h = \phi_t = \phi_{nt} = 3.28$, and the other parameters are as in Table 1. This decreasing is very slow since it is necessary to increase the initial value of $\bar{N}_{nt} = (3/5)\bar{N}_h$ more than 160 times to get $R_0 < 1$. The basic reproductive numbers $R_h$, and $R_t$ show similar behavior with respect to $\bar{N}_{nt}$, as it is illustrated by the dashed lines in Figs. 1(b) and (c). Now, if $\frac{\phi_{nt} b_{nt}}{2} > \max\{\phi_h b_h, \phi_t b_t\}$, $R_0$ increases to a maximum value and then decreases asymptotically to zero as it is shown in Fig. 2, where $b_{nt} = 0.5$.

### 4.2. Analysis of the endemic proportions

So far we have investigated the behavior of the basic reproductive number with respect to vector controls. This number measures the intensity of an outbreak, but for diseases with a long infectious period such as Chagas disease, it is also important to study the effect of the control measures on the endemic levels. For this end, we carry out numerical simulations to obtain the values of the endemic proportions subject to different intensities of the control measures. These simulations are illustrated in Figs. 3(a)–(c).

Starred lines in Figs. 3(a)–(c) represent the infectious proportions of humans, transmitters, and vectors when $\mu_v$ is decreasing by a factor $\theta$, with initial $\mu_v = 0.005$. For the three populations, the proportions decline rapidly, being virtually zero when the vector mortality increases six times, according to the results illustrated in Fig. 1 for the basic reproduction numbers.

On the other side, increasing the treatment parameter $q$ has effect only in the proportion of infected humans, being this effect very small for $\theta$ less than ten, as it is shown by the dotted curve in Fig. 3(a). The same curve also shows that efficacy of the treatment should be close to 100% in order to have an important decrement of the endemic proportion, a goal which is not realistic in most of the cases. These results again are in agreement with the behavior of the basic reproductive numbers with respect to $q$.

Dashed lines in Figs. 3(a)–(c) illustrate the endemic proportions when the non-transmitters population $\bar{N}_{nt}$ increases. Here, we observe an interesting behavior different from the one observed for the basic reproductive numbers. The calculations show for small increments of $\bar{N}_{nt}$ a slight increase (between 0.02 and 0.03) in the human and non-transmitter proportions, which is hard to observe in the graphs. This is followed by a very slow decrease (around 0.1 for $\theta = 25$), showing that this parameter does not have a major impact on those proportions. On the other hand, the dashed curve in Fig. 3(c) shows that infected vector proportion has a considerable decrease. This is because the total population of vectors increases at a faster rate than the population of infected ones when they feed on animals that do not transmit the disease (see Fig. 4). However, although the proportion of infectious triatomines decreases, their number increases, and this leads to only an small decrease in the infected humans and transmitters, and in some cases even to an increase.

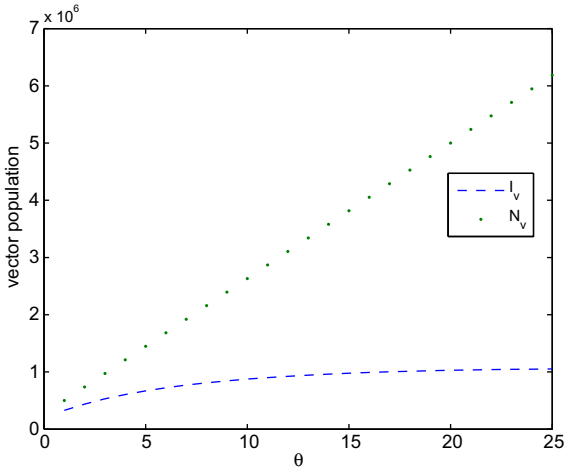


**Fig. 4.** Population size of triatomines and infected triatomines as a function of the number of non-transmitters $N_{nt}$.

**Table 2**
Relative rate of decrease of the infected humans proportion when the corresponding control is incremented by the factor shown in the first line.

| $\theta$ | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Increment of mortality $\mu_v$ | 0.16 | 0.37 | 0.58 | 0.80 |
| Increment of treatment $q$ | 0.005 | 0.009 | 0.01 | 0.02 |
| Increment of non-transmitters $N_{nt}$ | −0.003 | −0.0008 | 0.003 | 0.008 |

To have a quantity that allow us to evaluate the impact of a control measure in the human population, we define the relative rate of decrease as

$$\eta = \frac{p_i - p_f}{p_i},$$

where $p_i$, and $p_f$ denote the proportions of infectious at the start and at the end of the control, respectively.

In Table 2, we show the relative rate of decrease of the human infected proportion when mortality $\mu_v$, treatment $q$, and zooprophylaxis $\bar{N}_{nt}$ are incremented up to five times. As evidenced by the results, elimination of vectors is by far the best way to control the disease, followed by early detection and treatment of acute cases. Zooprophylaxis seems to have no major impact in reducing this disease.

## 5. Conclusions

In this work we modeled Chagas disease dynamics considering humans, animals, and triatomines in order to reproduce the domestic structure of a rural village where the disease prevalence is high. Our main objective was to explore the effectiveness of different control measures, namely, reduction of the vector population in the houses, screening and treatment of the early cases in humans, and zooprophylaxis technique.

We found an expression for the basic reproductive number of the disease, $R_0$, which corresponds to the average of the basic reproductive numbers of the humans and transmitters, $R_h, R_t$, weighted by a factor which is a measure of the density of the corresponding hosts in absence of the other population. Calculation of the basic reproductive number using the values reported in the literature indicates that domestic transmitters, i.e., cats and dogs, constitute a major risk factor for the spread of the disease. Studies performed in rural towns corroborates this fact [9].

We performed a sensitivity analysis with respect to key parameters for the control of the disease, to determine their impact on reducing the basic reproduction number, and the endemic proportions. Our study corroborates that reduction of vectors is the most effective measure to control the disease. However, this obvious conclusion is difficult to implement since in some regions people do not associate triatomines with the disease. Also, spraying

houses with insecticides monthly is both costly and triatomines could potentially become resistant to the insecticide treatment, besides the potential thread to people's health. We believe that the best way to control Chagas disease is alerting the population that kissing bugs are related to the illness, as well as improving the households conditions in order to eliminate vector breeding sites.

Early detection and treatment of disease is very important, however, the model shows that close proximity to domestic animals may prevent this treatment as a good control measure. Also, our results show that for this measure to be efficient, treatment levels must be close to 100% (Fig. 1(b)), but difficulty of acquiring the required drugs, as well as the adverse reaction they produce in some patients may affect the treatment, and in consequence may prevent this measure to reach the levels for an efficient disease control.

As was mention in the Introduction, the efficacy of zooprophylaxis is under discussion. In the case of malaria, there have been reports where the introduction of livestock has reduced the prevalence of the disease. In fact, the reduction of malaria that occurred in Europe and United States early last century have been attributed to the increase of livestock in these regions [35]. Zooprophylaxis studies applied to malaria, carried out in several areas of sub-Saharan Africa, have shown that this control may have an effect on certain species of Anopheles mosquitoes, particularly in *An. arabiensis*, suggesting the potential of this intervention in areas where *An. arabiensis* dominates [15,35–37]. However, in a study of cattle and *An. arabiensis* in northern Ethiopia, it was noted that cases of malaria infection nearly doubled in situations in which cattle were kept in houses where families slept [38]. Also, in rural Gambia, where *Anopheles gambiae* mosquitoes are the main vectors of malaria, passive zooprophylaxis with cattle was found to have little or no effect on *P. falciparum* parasite prevalence and intensity in children [16]. The main conclusion derived from these reports is that efficacy depends primarily on the biology and behavior of local mosquito species, social behavior, and relationship with cattle, and pets [15,17]. It is also worth to mention that determining the efficiency of zooprophylaxis also comes with methodological obstacles. Primary among them are the difficulties posed by the interplay of the large numbers of variables in experimental studies of this sort; the multiple and sometimes contradictory methods for determining mosquito behavior and feeding preferences.

In our theoretical study of Chagas disease, we found different sets of parameters where the situations mentioned above where observed. Feeding preferences of the vector as well as the population sizes of the transmitters and not transmitters determines the efficacy of the zooprophylaxis as a control measure of the illness. In particular, the right hand side of expression (4.28) is a threshold that indicates the efficiency of this measure, namely, if the value of the threshold is negative, the number of new infections decreases in the presence of non-transmitters population, the contrary occurs when the threshold is positive. Further, in this work we show values of the parameters where zooprophylaxis helps but the effect on the prevalence of the disease is very small, and in fact it could be overlooked in practice (Fig. 2).

To conclude, we can say that reducing the population of triatomines, and keeping domestic animals out of the dormitories is the best way to decrease the risk of human infections as mentioned in [9,30].

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## Appendix A. Global stability of the equilibria

### A.1. Proof of Proposition 2

Condition $\sigma = 0$ implies $N_h \to \bar{N}_h, N_t \to \bar{N}_t$, and $N_v \to \bar{N}_v$ as $t \to \infty$. We define in $\Omega$ the Lyapunov function

$$\mathcal{V} = b_1 I_a + b_2 I_c + b_3 I_t + I_v, \tag{A.29}$$

with

$$\begin{aligned} b_1 &= \frac{\mu_h b_h \alpha_a \bar{N}_v}{K\bar{N}} + \frac{b_h \alpha_c (1-q)\gamma \bar{N}_v}{K\bar{N}}, \\ b_2 &= \frac{\mu_h p b_h \alpha_a \bar{N}_v}{K\bar{N}} + \frac{(\gamma+\mu_h) b_h \alpha_c \bar{N}_v}{K\bar{N}}, \\ b_3 &= \frac{b_t \alpha_t \bar{N}_v}{\mu_t \bar{N}}. \end{aligned} \tag{A.30}$$

The orbital derivative of $\mathcal{V}$ is given by

$$\begin{aligned} \dot{\mathcal{V}} = {} & b_1 \left[ p\mu_h I_c + \frac{b_h \beta_h}{\bar{N}} (\bar{N}_h - I_a - I_c) I_v - (\gamma + \mu_h) I_a \right] \\ & + b_2 \left[ (1-q)\gamma I_a - \mu_h I_c \right] + b_3 \left[ \frac{b_t \beta_t}{\bar{N}} (\bar{N}_t - I_t) I_v - \mu_t I_t \right] \\ & + \frac{b_h \alpha_a I_a + b_h \alpha_c I_c + b_t \alpha_t I_t}{\bar{N}} (\bar{N}_v - I_v) - \mu_v I_v. \end{aligned} \tag{A.31}$$

Substituting $b_1, b_2, b_3$, and using the expression for $R_0$ given in (3.6), we obtain after some simplifications that

$$\begin{aligned} \dot{\mathcal{V}} = {} & -\mu_v \left(1 - R_0^2\right) I_v - b_1 \frac{b_h \beta_h}{\bar{N}} (I_a + I_c) I_v - b_3 \frac{b_t \beta_t}{\bar{N}} I_t I_v \\ & - \frac{b_h (\alpha_a I_a + \alpha_c I_c) + b_t \alpha_t I_t}{\bar{N}} I_v, \end{aligned}$$

which implies that $\dot{\mathcal{V}} \leqslant 0$ for $R_0 \leqslant 1$. From inspection of system (2.4) it can be seen that $E_0$ is the only invariant set in $\Omega$ contained in $\dot{\mathcal{V}} = 0$, therefore, from the La Salle–Lyapunov theorem, it follows that for $R_0 \leqslant 1, E_0$ is globally asymptotically stable, and all trajectories starting in $\Omega$ approach $E_0$ when $t \to \infty$.

### A.2. Proof of Proposition 5

We propose the following Lyapunov function

$$\begin{aligned} \mathcal{U}(S_h, I_a, I_c, S_t, I_t, S_v, I_v) = {} & c_1 \left( S_h - \bar{S}_h - \bar{S}_h \ln \frac{S_h}{\bar{S}_h} \right) \\ & + c_2 \left( I_a - \bar{I}_a - \bar{I}_a \ln \frac{I_a}{\bar{I}_a} \right) \\ & + c_3 \left( I_c - \bar{I}_c - \bar{I}_c \ln \frac{I_c}{\bar{I}_c} \right) \\ & + c_4 \left( S_t - \bar{S}_t - \bar{S}_t \ln \frac{S_t}{\bar{S}_t} \right) \\ & + c_5 \left( I_t - \bar{I}_t - \bar{I}_t \ln \frac{I_t}{\bar{I}_t} \right) \\ & + c_6 \left( S_v - \bar{S}_v - \bar{S}_v \ln \frac{S_v}{\bar{S}_v} \right) \\ & + c_7 \left( I_v - \bar{I}_v - \bar{I}_v \ln \frac{I_v}{\bar{I}_v} \right), \end{aligned} \tag{A.32}$$

where $\bar{S}_h = N_h - \bar{I}_a - \bar{I}_c$, $\bar{S}_t = N_t - \bar{I}_t$, $\bar{S}_v = N_v - \bar{I}_v$, and

$$
\begin{aligned}
c_1 &= c_2 = \frac{b_h(\alpha_a \bar{I}_a + \alpha_c \bar{I}_c)\bar{S}_v}{N},\\
c_3 &= \frac{b_h^2 \beta_h \alpha_c \bar{S}_h \bar{S}_v \bar{I}_c \bar{I}_v}{N^2 \gamma \bar{I}_a},\\
c_4 &= c_5 = \frac{b_h \beta_h \alpha_t \bar{S}_h \bar{S}_v \bar{I}_t}{N \beta_t \bar{S}_t},\\
c_6 &= c_7 = \frac{\beta_h b_h \bar{S}_h \bar{I}_v}{N}.
\end{aligned}
\tag{A.33}
$$

The orbital derivative of $\mathcal{U}$ is given by

$$
\begin{aligned}
\dot{\mathcal{U}} = {} & c_1\left(1-\frac{\bar{S}_h}{S_h}\right)\left(\mu_h N_h - p\mu_h I_c - \frac{b_h\beta_h}{N} I_v S_h - \mu_h S_h + q\gamma I_a\right)\\
& - c_2\left(1-\frac{\bar{I}_a}{I_a}\right)\left(p\mu_h I_c + \frac{b_h\beta_h}{N} I_v S_h - \gamma I_a - \mu_h I_a\right)\\
& + c_3\left(1-\frac{\bar{I}_c}{I_c}\right)((1-q)\gamma I_a - \mu_h I_c)\\
& + c_4\left(1-\frac{\bar{S}_t}{S_t}\right)\left(\mu_t N_t - \frac{b_t\beta_t}{N} I_v S_t - \mu_t S_t\right)\\
& + c_5\left(1-\frac{\bar{I}_t}{I_t}\right)\left(\frac{b_t\beta_t}{N} I_v S_t - \mu_t I_t\right)\\
& + c_6\left(1-\frac{\bar{S}_v}{S_v}\right)\left(\mu_v N_v - \frac{b_h\alpha_a I_a + b_h\alpha_c I_c + b_t\alpha_t I_t}{N} S_v - \mu_v S_v,\right)\\
& + c_7\left(1-\frac{\bar{I}_v}{I_v}\right)\left(\frac{b_h\alpha_a I_a + b_h\alpha_c I_c + b_t\alpha_t I_t}{N} S_v - \mu_v I_v\right).
\end{aligned}
\tag{A.34}
$$

From system (2.2) at equilibrium with $p = q = \sigma = 0$, we obtain the following relations

$$
\begin{aligned}
\mu_h N_h &= \mu_h \bar{S}_h + p\mu_h \bar{I}_c + \frac{b_h\beta_h}{N}\bar{I}_v\bar{S}_h - q\gamma\bar{I}_a,\\
\gamma + \mu_h &= \frac{p\mu_h\bar{I}_c}{\bar{I}_a} + \frac{b_h\beta_h}{N}\frac{\bar{I}_v\bar{S}_h}{\bar{I}_a},\\
\mu_h &= \frac{\gamma\bar{I}_a}{\bar{I}_c},\\
\mu_t N_t &= \mu_t\bar{S}_t + \frac{b_t\beta_t}{N}\bar{I}_v\bar{S}_t,\\
\mu_t &= \frac{b_t\beta_t}{N}\bar{I}_v\bar{S}_t\bar{I}_t,\\
\mu_v N_v &= \mu_v\bar{S}_v + \frac{b_h\alpha_a\bar{I}_a + b_h\alpha_c\bar{I}_c + b_t\alpha_t I_t}{N}\bar{S}_v,\\
\mu_v &= \frac{b_h\alpha_a\bar{I}_a + b_h\alpha_c\bar{I}_c + b_t\alpha_t I_t}{N}\frac{\bar{S}_v}{\bar{I}_v}.
\end{aligned}
\tag{A.35}
$$

Substituting the constants $c_i$, and the parameters $\mu_h$ up to $\mu_v$ in the Lyapunov derivative (A.34), we obtain after several calculations and simplifications

$$
\begin{aligned}
\dot{\mathcal{U}} = {} & -c_1\mu_h\frac{(S_h-\bar{S}_h)^2}{S_h} - c_4\mu_t\frac{(S_t-\bar{S}_t)^2}{S_t} - c_6\mu_v\frac{(S_v-\bar{S}_v)^2}{S_v}\\
& - \frac{b_h^2}{N^2}\beta_h\alpha_a\bar{S}_h\bar{S}_v\bar{I}_a\bar{I}_v\left[\frac{\bar{S}_h}{S_h}+\frac{\bar{S}_v}{S_v}+\frac{\bar{I}_a I_v S_h}{I_a\bar{I}_v\bar{S}_h}+\frac{I_a\bar{I}_v S_v}{\bar{I}_a I_v\bar{S}_v}-4\right]\\
& - \frac{b_h^2\beta_h\alpha_c\bar{S}_h\bar{S}_v\bar{I}_c\bar{I}_v}{N^2}\left[\frac{\bar{S}_h}{S_h}+\frac{\bar{S}_v}{S_v}+\frac{I_a\bar{I}_c}{\bar{I}_a I_c}+\frac{I_c\bar{I}_v S_v}{\bar{I}_c I_v\bar{S}_v}+\frac{\bar{I}_a I_v S_h}{I_a\bar{I}_v\bar{S}_h}-5\right]\\
& - \frac{b_h\beta_h b_t\alpha_t\bar{S}_h\bar{S}_v\bar{I}_t\bar{I}_v}{N^2}\left[\frac{\bar{S}_t}{S_t}+\frac{\bar{S}_v}{S_v}+\frac{\bar{I}_t I_v S_t}{I_t\bar{I}_v\bar{S}_t}+\frac{I_t\bar{I}_v S_v}{\bar{I}_t I_v\bar{S}_v}-4\right].
\end{aligned}
\tag{A.36}
$$

Let

$$
x_1 = \frac{\bar{S}_h}{S_h},\quad x_2 = \frac{S_v}{\bar{S}_v},\quad x_3 = \frac{\bar{I}_a I_v}{I_a\bar{I}_v},\quad x_4 = \frac{\bar{I}_c I_v}{I_c\bar{I}_v},\quad x_5 = \frac{\bar{I}_t I_v}{I_t\bar{I}_v}.
$$

It follows that the expressions in the square parenthesis of the last three terms of (A.36) can be written as

$$
\begin{aligned}
f_1(x_1,x_2,x_3) &= x_1 + \frac{1}{x_2} + \frac{x_3}{x_1} + \frac{x_2}{x_3} - 4,\\
f_2(x_1,x_2,x_3,x_4) &= x_1 + \frac{1}{x_2} + \frac{x_4}{x_3} + \frac{x_2}{x_4} + \frac{x_3}{x_1} - 5,\\
f_1(x_1,x_2,x_5) &= x_1 + \frac{1}{x_2} + \frac{x_5}{x_1} + \frac{x_2}{x_5} - 4.
\end{aligned}
$$

Using the fact that the geometric mean is less or equal than the arithmetic mean, it is straightforward to see that the functions $f_i \geqslant 0$, for $x_j$ in $\mathbb{R}, i = 1,\ldots 3, j = 1,\ldots,5$, and they are zero only when $x_j = 1$ Hence, it follows that $\dot{\mathcal{U}} \leqslant 0$ and $\dot{\mathcal{U}} = 0$ if and only if $S_H = \bar{S}_H$, $I_a = \bar{I}_a, I_c = \bar{I}_c, I_t = \bar{I}_t$, and $I_v = \bar{I}_v$. This implies that all trajectories in the interior of $\Omega$ approach $E_1$ as $t \to \infty$, completing the proof.

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