A voluntary use of insecticide treated nets can stop the vector transmission of Chagas disease

Cheol Yong Han1*, Habeeb Issa2*, Jan Rychtář3†, Dewey Taylor3‡, Nancy Umana2,4‡

1 Department of Mechanical and Nuclear Engineering, Virginia Commonwealth University, Richmond, Virginia, USA, 2 Department of Biology, Virginia Commonwealth University, Richmond, Virginia, USA, 3 Department of Mathematics and Applied Mathematics, Virginia Commonwealth University, Richmond, Virginia, USA, 4 Department of Psychology, Virginia Commonwealth University, Richmond, Virginia, USA

* These authors contributed equally to this work.
† These authors also contributed equally to this work.
‡ rychtarj@vcu.edu

Abstract

One of the stated goals of the London Declaration on Neglected Tropical Diseases is the interruption of domiciliary transmissions of Chagas disease in the region of the Americas. We used a game-theoretic approach to assess the voluntary use of insecticide treated nets (ITNs) in the prevention of the spread of infection through vector bites. Our results show that individuals behave rationally and weigh the risks of insect bites against the cost of the ITNs. The optimal voluntary use of ITNs results in predicted incidence rates that closely track the real incidence rates in Latin America. This means that ITNs are effective and could be used to control the spread of the disease by relying on individual decisions rather than centralized policies. Our model shows that to completely eradicate the vector transmission through the voluntary individual use of ITNs, the cost of ITNs should be as low as possible.

Authors summary

We construct a game-theoretic model of individual use of insecticide treated nets (ITNs) to prevent the vector transmission of Chagas disease within the household.

Our results show that individuals behave rationally and weigh the risks of insect bites against the cost of the ITNs. The optimal voluntary use of ITNs results in predicted incidence rates that closely track the incidence rates in Latin America.

This means that ITNs are effective and could be used to control the spread of the disease by relying on individual decisions rather than centralized policies.

Introduction

American trypanosomiasis, in humans known as Chagas disease, is one of the world’s most important neglected tropical diseases [1] and is most prevalent in Latin America where it is...
endemic in all 33 countries [2]. One of the stated goals of the London Declaration on Neglected Tropical Diseases is the interruption of domiciliary transmissions in the region of the Americas [3]. Worldwide 6–7 million people had been diagnosed with Chagas disease [4], and the actual numbers may be even higher [5]. There is a lack of research on Chagas disease despite the fact that (1) there are 50,000 to 200,000 new infections per year [6], (2) the disease results in an estimated $627.46 million in healthcare costs and $7.19 billion in societal costs annually [7], and (3) Chagas disease is still the largest parasitic disease burden on the American continent [8].

Chagas disease is a parasitic infection caused by the protozoan *Trypanosoma cruzi* [9]. There are two main forms of transmission: blood transfusion, most common in urban areas, and vector biting, most common in rural areas [10]. Chagas disease can also be contracted through organ transplantation, ingestion of parasite-contaminated food, and from mother to fetus [11, 12]. Three species of *Triatominae* insects, nicknamed kissing bugs, are the most common vectors. *T. infestans* is the primary vector in sub-Amazonian endemic regions (southern South America), *Rhodnius prolixus* is typically reported in northern South America and Central America, and *T. dimidiata* occupies a similar area, but also extends further north into Mexico [13].

Historically, the control of Chagas disease has focused on vector reduction using insecticides or indirect vector control through housing modifications [1, 14]. Still, preventive measures for vector transmission have remained a challenge due to the disease being closely linked to poverty and poor housing infrastructure such as mud and thatched houses that lack sanitary supervision [6]. Currently, no vaccine has been created in order to help stop the spread of Chagas disease [15]. Preventative measures in high risk areas include (1) avoiding sleeping in mud and thatched housing, (2) using insecticide treated netting (ITN) over one’s bed, and (3) using insect repellent on exposed skin [11, 16, 17]. Even in relatively poor areas, the use of ITNs was already demonstrated to be very cost-effective [18]. However, human behavior such as inconsistent use due to hot weather or inadequate education diminishes the effectiveness of ITNs [19].

From the behavioral perspective, disease prevention, such as ITNs use, produces public goods (herd immunity) that is non-rivalrous and non-exclusive [20]. Individuals often act in a way that maximizes their self-interests rather than the interests of the entire group [21, 22]. Disease prevention is thus prone to free-riding. The “free-riders” avoid the costs associated with the use of ITNs while they benefit from the preventive actions of others. This social dilemma is captured by the game theory framework [23]. The framework has now been applied to help model the prevention of many diseases such as African trypanosomiases [24], chikungunya [25], cholera [26], dengue [27], ebola [28], hepatitis B [29], hepatitis C [30], meningitis [31], monkeypox [32], polio [33], toxoplasmosis [34], typhoid [35] and many others, see for example [36] and [22] for recent reviews.

There are many mathematical models of Chagas disease [37], including [1, 10, 11, 38–43]. In this paper, we consider a recent, yet relatively simple model of Chagas disease dynamics developed in [44]. This model includes vector transmission by *Rhodnius prolixus* as well as the interplay of palm plantations and human settlements (domestic) habitats for the vectors. We consider the use of ITNs as a mode of voluntary protection from vector bites, similarly to what was done in [45] for malaria. We apply a game-theoretic approach to evaluate individual and population-wide use of ITNs. We also perform the sensitivity analysis and validate the model on Chagas disease incidence data.

**Mathematical model of Chagas disease dynamics**

We extend the compartmental epidemiological model of Chagas disease introduced in [44] by incorporating the use of ITNs. The model, shown in Fig 1, describes the interactions between
the vectors, *Rhodnius prolixus*, and the host (human) populations denoted by $r$ and $h$ subscripts, respectively. The model involves two separate areas: the palm plantation and human settlement. The palm plantation acts as a potential reservoir of vectors. Since *R. prolixus* usually bites humans at night [46], the transmission is modelled only through contact between vectors and humans in the settlement. For simplicity, we do not consider any infected vectors in the plantation area, although infected *R. prolixus* can be found in the palm trees as well [47]. We also do not consider any human dynamics in the plantation area.

There is no recovery from Chagas disease [16] so the total human population is divided into (1) susceptible ($S_h$), i.e. not infected with *T. cruzi*, (2) exposed ($E_h$), i.e. infected with *T. cruzi* but not yet infectious, and (3) infectious ($I_h$). The population size is normalized so that $N_h = S_h + E_h + I_h = 1$. The vector population is divided into vectors living in the plantation ($M_r$) and the settlement ($N_r$). The population in the plantation is always susceptible. The vector population in the settlement is divided into susceptible ($S_r$), exposed ($E_r$) and infectious ($I_r$).

Humans are born as susceptible at the per capita rate $\alpha$. While there is a disease induced mortality [48], we follow [44] in omitting this for the sake of simplicity of the model. To keep the human population constant, the human natural death rate is considered the same as the birth rate and the same across all classes. The vectors are born as susceptible at per capita rate $\beta$; the birth rate is considered the same in the plantation and the settlement. The vectors follow a logistic growth with carrying capacity $K_p$ in the plantation and $K_s$ in the settlement. The vectors migrate from the plantation to the settlement at rate $\omega$. The natural death rate of vectors, $\mu$, is considered the same across all classes. We assume $\mu < \beta$.

The disease is transmitted from an infectious vector to susceptible humans at rate $(1 - p)a_0$ and from an infectious human to susceptible vectors at rate $(1 - p)b_0$. Here, $p$ is the frequency of ITN use while $a_0$ and $b_0$ are the transmission rates without ITN use. After the incubation period, the exposed individuals become infectious at rate $\delta$ for humans and $\sigma$ for vectors.

The values and ranges of model parameters are summarized in Table 1, details are presented below.

**Parameter estimation**

The vector-to-human transmission rate, $a_0$, is estimated as $5.8 \times 10^{-4}$, i.e. $1.74 \times 10^{-4}$ per day with range $[5.2, 44] \times 10^{-5}$ by the following reasoning. Using various datasets from
literature, \[49\] estimated the probability of vector-to-human transmission (per contact) as \(5.8 \times 10^{-4}\) (with 95% CI: \([2.6, 11.0] \times 10^{-4}\)). This estimate is consistent across triatomine species, robust to variations in other parameters, and corresponds to 900–4,000 contacts per case. Moreover, \[59\] estimates the biting rate to be between 0.2–0.4 and \[60\] and \[49\] further confirm this by stating that the biting rate on average is 0.3 per day. We note that \[61\] found feeding rate of \textit{T. infestans} to be between 0.3 and 0.6 per day.

Similarly, from the data presented in \[50, Table 4\], we estimate the host-to-vector transmission rate, \(b_0\), as 0.0062 \(\times 10^{-4}\) per day with the range \([3.8, 32] \times 10^{-4}\) per day.

The average life expectancy age in Latin America is 75 years, ranging from 63 in Haiti to 80 in Chile and Costa Rica \[51\]. This gives the average rate \((75 \times 365)^{-1}\) = 3.65 \(\times 10^{-5}\) per day with the range \([3.42, 4.35] \times 10^{-5}\) per day.

The average instantaneous birth rate, \(\beta\), is given as 0.158 per week with a range \([0.120, 0.208]\) per week in \[52, Table 7\]. This yields the average 0.022 per day with the range \([0.017, 0.30]\) per day.

The life expectancy of various \textit{Triatoma} species ranges from 73 days to 268 days \[62\]. This gives the range for the vector death rate as \([0.0037, 0.0136]\) per day. Further estimates for instantaneous death rate of \textit{T. infestans} ranging from 0.023–0.109 per week are given in \[52, Table 7\]. This yields an average \(\frac{\mu_s}{\delta}\) = 0.008 per day and the range \([0.0033, 0.016]\) per day. We note that \[63\] assume the death rate (for \textit{T. infestans}) to be 0.0046 per day with a reference to \[52\]; however we believe that this discrepancy is likely caused by \[63\] considering the standard deviation 0.034 instead of the average rate 0.056 per week in \[52\]. Also, \[1\] uses the death rate 1.73 per year (i.e. 0.0047 per day) with a reference to \[62\]. For the purpose of our study we will use 0.008 per day as the average death rate with the range \([0.0033, 0.016]\) per day.

The incubation period for humans after exposure to a triatomine bite is 5–14 days \[13\]. As noted by \[12\], definitive data is not available because persons who live in areas of active transmission are generally continually at risk for exposure to the vectors. We assume that the
incubation is 10 days on average. Therefore, the incubation rate in humans, \( \delta \), was estimated as 0.1 per day on average with a range can be represented by \([0.071, 0.2]\) per day.

The average incubation rate in vectors, \( \sigma \), is estimated as \(\frac{1}{7}\) per day with the range \([\frac{1}{8}, \frac{1}{6}]\) per day. This is based on [53] who found that 3–4 days post-infection, the \( T. cruzi \) parasite population begins to colonize the triatomine hosts to reach a climax at day 7 post-infection, which is maintained during the next two weeks.

Our model is normalized with a total human population equal to 1, and we use \( K_s = 10 \), i.e. 10 bugs per person as used in [1]. We note that [54] use 10, 50, 100 and cite variable bug numbers in studies [64–67]. Other study, [43], uses 158 bugs per household [68].

The carrying capacity of vectors in the field is 31, 900 per \( \text{km}^2 \) [55]. The small plantation size is about 5ha [69], yielding 1600 bugs, i.e. after renormalization for a 8 person household, we get \( K_p = 200 \).

The migration rate, \( \omega \), was set to 0.01 per day on average with the range \([0, 0.02]\) [56]. We note that [56] cites [70] as the source for that number, but we were not able to locate the information in [70]. Also, [44] and [2] use \( \omega = 0.05 \). However, for the other values of the parameters, most notably the vector birth rate \( \beta \) and death rate \( \mu \) such a high value of \( \omega \) would result in no bugs in the plantation area. Consequently, we adapted the value 0.01 from [56]. Moreover, as seen from the sensitivity analysis, the results are not overly sensitive to values of \( \omega \).

**Analysis**

The model of the transmission dynamics shown in Fig 1 yields the following system of differential equations.

\[
\frac{dS_h}{dt} = \alpha - \alpha S_h - (1 - p)\alpha I_h S_h \quad (1)
\]

\[
\frac{dE_h}{dt} = (1 - p)\alpha I_h S_h - (\alpha + \delta)E_h \quad (2)
\]

\[
\frac{dI_h}{dt} = \delta E_h - \alpha I_h \quad (3)
\]

\[
\frac{dM_r}{dt} = (\beta - \mu)M_r \left( 1 - \frac{M_r}{K_p} \right) - \omega M_r \quad (4)
\]

\[
\frac{dS_r}{dt} = \omega M_r + \beta N_r - ((1 - p)b_0 I_h + \mu + \mu,N_r)S_r \quad (5)
\]

\[
\frac{dE_r}{dt} = (1 - p)b_0 I_h S_r - (\mu + \sigma + \mu,N_r)E_r \quad (6)
\]

\[
\frac{dI_r}{dt} = \sigma E_r - (\mu + \mu,N_r)I_r \quad (7)
\]

**Equilibria of the ODE system (1)–(7)**

There are four possible equilibria of the dynamics (1)–(7): (i) an unstable disease-free equilibrium \( E^o_1 = (1, 0, 0, 0, 0, 0, 0) \), (ii) a disease-free equilibrium \( E^o_2 = (1, 0, 0, 0, K_s, 0, 0) \), (iii) a
disease-free equilibrium $E^*_0 = (1, 0, 0, M^*_r, N^*_r; 0, 0)$ where

$$M^*_r = K_p \frac{\beta - \mu - \omega}{\beta - \mu},$$

$$N^*_r = \frac{1 + \sqrt{1 + 4 \frac{\omega M^*_r}{K_r(\beta - \mu)}}}{2},$$

and finally (iv) the endemic equilibrium $E^* = (S^*_r, E^*_r, I^*_r, M^*_r, E^*_r, I^*_r)$ where

$$N^*_r (1 - p)a_h - \frac{\mu^* + \mu^* + \sigma}{\sigma} \left( \delta + \frac{\delta}{\alpha} \right)$$

$$E^*_h = \frac{(\alpha + \delta) \left( 1 + \frac{\mu^* + \omega M^*_r}{\alpha} \right)}{(\alpha + \delta) \left( 1 + \frac{\mu^* + \omega M^*_r}{\alpha} \right)}$$

$$I^*_h = \delta \frac{\alpha}{\alpha} E^*_h$$

$$S^*_h = 1 - E^*_h - \frac{\delta}{\alpha} E^*_h$$

$$I^*_r = \frac{E^*_h (\alpha + \delta)}{(1 - p)a_h \left( 1 - E^*_r \left( 1 + \frac{\delta}{\alpha} \right) \right)}$$

$$E^*_r = \frac{\mu^*}{\sigma} I^*_r$$

$$S^*_r = \frac{\sigma + \mu^*}{(1 - p)b_k I^*_h} \left( I^*_h \frac{\mu^*}{\sigma} \right)$$

and $\mu^* = \mu + \mu N^*_r$ denotes the vector mortality rate in the settlement when the population levels reach the equilibrium. See the section below for detailed calculations.

**Step-by-step calculations for equilibria**

Let us set $N_r = S_r + E_r + I_r$ and investigate the system

$$\frac{dM_r}{dt} = (\beta - \mu)M_r \left( 1 - \frac{M_r}{K_r} \right) - \omega M_r,$$

$$\frac{dN_r}{dt} = (\beta - \mu)N_r \left( 1 - \frac{N_r}{K_r} \right) + \omega M_r,$$

that results from (4) and from the sum of eqs (5) and (6), and (7).
The system (16) and (17) has three equilibria: (a) (0, 0) which is always unstable (if $\beta > \mu$),
(b) $(0, K_s)$ which is locally stable if $\beta - \mu < \omega$, and finally (c) $(M^*_r, N^*_r)$ where

$$
M^*_r = K_p \frac{\beta - \mu - \omega}{\beta - \mu},
$$

$$
N^*_r = K_s \frac{1 + \sqrt{1 + 4 \frac{\omega M^*_r}{K_s(\beta - \mu)}}}{2},
$$

which is defined and locally stable if $\omega < \beta - \mu$.

Now, let us proceed to solve for the equilibria of the system (1)–(7). Based on above calculations, we have to solve the following system of algebraic equations

$$
0 = x(1 - S_h) - (1 - p)a_0 S_h I_r
$$

(20)

$$
0 = (1 - p)a_0 S_h I_r - E_h (x + \delta)
$$

(21)

$$
0 = \delta E_h - x I_h
$$

(22)

$$
0 = \omega M^*_r + \beta N^*_r - S_r ((1 - p)b_0 I_h + \mu + \mu^* N^*_r)
$$

(23)

$$
0 = (1 - p)b_0 S_r I_h - E_r (\mu + \sigma + \mu^* N^*_r)
$$

(24)

$$
0 = \sigma E_r - I_r (\mu + \mu^* N^*_r)
$$

(25)

where $M^*_r$ is given by (18) and $N^*_r$ is given by (19). Let us set $\mu^* = \mu + \mu^* N^*_r$.

By adding (20), (21), and (22), we get

$$
N_h = S_h + I_h + E_h = 1.
$$

(26)

We have the disease-free equilibrium with $S_h = 1$, $E_h = 0$, $I_h = 0$, $S_r = N_r$, $E_r = 0$, $I_r = 0$ whenever any of the following happens: (1) $I_r = 0$ (in particular when $N_r^* = 0$), or (2) $I_h = 0$, or (3) $p = 1$.

For the rest of the section, we will assume that $p < 1$, $I_h > 0$ and $I_r > 0$. By (22),

$$
I_h = \frac{\delta E_h}{x}
$$

(27)

and so by (26) and (27),

$$
S_h = 1 - E_h - \frac{\delta}{x} E_h.
$$

(28)

By (25),

$$
E_r = I_r \frac{\mu^*}{\sigma}
$$

(29)

Using Eq (24)

$$
S_r = \frac{E_r (\sigma + \mu^*)}{(1 - p)b_0 I_h} = \left(\frac{\sigma + \mu^*}{(1 - p)b_0 I_h}\right) \left(\frac{I_r \mu^*}{\sigma}\right)
$$

(30)
By (20),

\[ I_r = \frac{z(1 - S_h)}{(1 - p)a_0S_h} = \frac{z(I_h + E_h)}{(1 - p)a_0S_h} \]  
\[ = \frac{E_h(\alpha + \delta)}{(1 - p)a_0(1 - E_h(1 + \frac{\delta}{\alpha}))} \]  

Finally,

\[ N_r = S_r + I_r + E_r \]  
\[ = \frac{\mu^r + \sigma}{(1 - p)b_0I_h} \frac{\mu^r + \sigma}{\sigma} I_r + \frac{\mu^r}{\sigma}I_r \]  
\[ = I_r \left( 1 + \frac{\mu^r}{\sigma} + \frac{\mu^r + \sigma}{(1 - p)b_0I_h} \frac{\mu^r}{\sigma} \right) \]  
\[ = E_h \frac{\alpha + \delta}{(1 - p)a_0(1 - E_h(1 + \frac{\delta}{\alpha}))} \left( 1 + \frac{\mu^r}{\sigma} + \frac{\mu^r + \sigma}{(1 - p)b_0E_h} \frac{\mu^r}{\sigma} \right) \]  

and thus

\[ N_r(1 - p)a_0 - \frac{\mu^r}{\sigma} \frac{\mu^r + \sigma}{(1 - p)b_0} \frac{\delta}{\alpha}(\alpha + \delta) \]  
\[ E_h^* = \frac{E_h(\alpha + \delta)}{(\alpha + \delta)(1 + \frac{\mu^r}{\sigma} + N_r(1 - p)a_0)} \]  

and the remaining values are given by

\[ I_h^* = \frac{\delta}{\alpha} E_h^* \]  
\[ S_h^* = 1 - E_h^* - \frac{\delta}{\alpha} E_h^* \]  
\[ I_r^* = \frac{E_h^*(\alpha + \delta)}{(1 - p)a_0(1 - E_h^*(1 + \frac{\delta}{\alpha}))} \]  
\[ E_r^* = I_r^* \frac{\mu^r}{\sigma} \]  
\[ S_r^* = \frac{\sigma + \mu^r}{(1 - p)b_0I_h^*} \left( I_r^* \frac{\mu^r}{\sigma} \right). \]
The basic reproduction number

The basic reproduction number, i.e. the number of secondary infections caused by a single infectious individual in an otherwise disease-free population is given by

$$R_0 = (1 - p)^2 R_0^{\text{noITN}}$$  \hspace{1cm} (43)$$

where

$$R_0^{\text{noITN}} = \left( \frac{1}{\alpha} \right) \left( b_0 N_s \right) \left( \frac{\sigma}{\sigma + \mu_s} \right) \left( \frac{1}{\mu_s} \right) \left( \frac{\delta}{\delta + \alpha} \right)$$  \hspace{1cm} (44)$$
is the number of secondary infections caused by a single infectious individual if nobody uses ITN. The formula can be derived as follows. An infectious individual lives on average for a time $\alpha^{-1}$. During that time, they expose susceptible vectors at the rate $(1 - p) b_0 N_s$. Each of the exposed vectors become infectious with probability $\frac{\sigma}{\sigma + \mu_s}$. Each of the infectious vectors then lives for the time $\mu_s^{-1}$ during which it exposes susceptible individuals at the rate $(1 - p) a_0 N_h = (1 - p) a_0$. Each of those exposed individuals will become infectious with probability $\frac{\delta}{\delta + \alpha}$.

The equilibrium $E^*_0$ is always unstable. The disease-free equilibrium $E^0$ exists if $\omega > \beta - \mu$ and is stable if $R_0 < 1$. The endemic equilibrium $E^*$ is defined and locally stable if $\omega < \beta - \mu$ and $R_0 > 1$.

Herd immunity

It follows from (43) that $\frac{dR_0}{dp} < 0$, i.e. $R_0$ is decreasing in $p$. Consequently, the population will reach herd immunity at the smallest value of $p \in [0, 1]$ for which $R_0 \leq 1$, i.e.

$$p_{\text{HI}} = \max \left( 0, 1 - \left( R_0^{\text{noITN}} \right)^{-1/2} \right).$$  \hspace{1cm} (45)$$

Game-theoretic model of ITN use

Model setup

In this section, we set up and solve a game-theoretic model of individual ITN use decisions. We will assume that the system (1)–(7) is in an equilibrium. Individuals can either use or not use an ITN. We assume that all individuals are rational and act in their own self-interest [21]. As usual in vaccination games, see for example [35], individuals weigh the perceived cost of ITN use against the risks of infection. The risk of infection depends on the population-wide ITN use rate. This results in a public goods game in which individuals base their ITN use decision on the decisions of others.

For simplicity, we will consider only the actual monetary costs of ITN use, but we note that perceived costs could involve other factors such as possible discomfort associated with limited air circulation, and possible side effects of the insecticide [45]. The cost varies, it can be about $5 in Mexico and $9 in Columbia [58]. An ITN lasts about 2 years [57], so the annual cost is $C_{\text{ITN}} = $2.50 in Mexico and $C_{\text{ITN}} = $4.5 in Columbia. The annual cost of a T. cruzi infection, $C_{\text{Chagas}}$, in Latin America is estimated as $383 with a range $207–$636 [7]. From the perspective of an individual, the expected cost of not using ITNs when the probability of ITN use in the overall population is $p$, denoted by $C_{\text{noITN}}(p)$, is given as a product of $C_{\text{Chagas}}$ and the probability of getting infected (the probability of moving from the $S_h$ compartment to the
When the ITN use is at Nash equilibrium, see Fig 4. This agrees with the annual incidence rate due to vector transmission, which is in close agreement with the predicted incidence rate around 8.37 person per year per 100,000 individuals, again in close agreement with the published values of 4.5 to 6.1 person per year per 100,000 individuals 

\[ \frac{\partial C_{\text{ITN}}}{\partial p} < 0 \]

where the herd immunity level of ITN use, \( p_{\text{HI}} \), is given in (45).

**Dependence of \( C_{\text{noITN}} \) on \( p \)**

Here we show that \( C_{\text{noITN}}(p) \) is decreasing in \( p \); this is illustrated in Fig 2.

By (46), \( \frac{\partial C_{\text{noITN}}}{\partial p} \neq \frac{\partial C_{\text{noITN}}}{\partial p} \). Since \( \frac{\partial C_{\text{noITN}}}{\partial p} > 0 \) and, as seen below, \( \frac{\partial C_{\text{noITN}}}{\partial p} < 0 \), we will get that \( \frac{\partial C_{\text{noITN}}}{\partial p} < 0 \). By (37),

\[
E^*_T = \frac{a_0}{\delta} \left( \frac{N_r(1-p)}{1 + \frac{\mu^*}{\sigma} + N_r (1-p) a_0} \right) - \frac{\mu^* (\mu^* + \sigma) \delta}{\sigma(1-p) b_0 \delta} \left( 1 + \frac{\mu^*}{\sigma} + N_r (1-p) a_0 \right)
\]

and the first term is increasing in \( 1-p \) and thus decreasing in \( p \) while the second term is decreasing in \( 1-p \) and thus increasing in \( p \). Thus, \( \frac{\partial C_{\text{noITN}}}{\partial p} < 0 \).

Consequently, by (38), \( \frac{\partial C_{\text{ITN}}}{\partial p} < 0 \). Now, for the contradiction, assume that \( \frac{\partial C_{\text{noITN}}}{\partial p} > 0 \). By (41), \( \frac{\partial C_{\text{noITN}}}{\partial p} > 0 \). Since \( S_r^* = N_r^* - E^*_r - I_r^* \) and \( \frac{\partial C_{\text{ITN}}}{\partial p} = 0 \), we get \( \frac{\partial C_{\text{noITN}}}{\partial p} < 0 \). By (24), \( E^*_r = \frac{(1-p) b_0 S_r^*}{\mu^* + \sigma + N_r \mu^*} \) and thus, as \( S_r^* \) and \( I_r^* \) are decreasing in \( p \), \( E^*_r \) should be decreasing in \( p \), contradiction with an already established fact that \( \frac{\partial C_{\text{noITN}}}{\partial p} > 0 \).

**Nash equilibria**

When the ITN use \( p \) is such that \( C_{\text{noITN}}(p) = C_{\text{ITN}} \), the ITN use is at Nash equilibrium, \( p_{\text{NE}} \). This means that no individual has an incentive to deviate from their current ITN usage.

Because \( C_{\text{noITN}}(p) \) is decreasing in \( p \), \( p_{\text{NE}} \) is in fact a convergently stable Nash equilibrium which indicates that the population will evolve toward it, see [71]. When \( p < p_{\text{NE}} \), it is beneficial for the individual to use the ITN (the cost of using the ITN is smaller than the expected cost of infection); when \( p > p_{\text{NE}} \), it is beneficial for the individual not to use the ITN (the cost of the net is larger than the expected cost of infection).

**Results, sensitivity analysis and model validation**

The values of \( p_{\text{HI}} \) and \( p_{\text{NE}} \) are close together, see Figs 2 and 3. For the parameters as in Table 1, the model predicts \( p_{\text{HI}} = 0.5026 \) and \( p_{\text{NE}} = 0.5017 \).

More than 50% of the households in endemic areas of Colombia use bednets (although some were not insecticide treated) [73]. In Nicaragua, 34.2% households had bednets [19]; the use of bednets is highest for the infants (45.8%) and decreases to 31.8% for children aged 1–4 years [19].

Our model predicts the annual incidence rate, the number of new infections per year, \( i = (1-p)a_J S_n \left( \frac{\delta}{\delta + \alpha} \right) \), to be about 4.72 person per year per 100,000 individuals when ITN use is at Nash equilibrium, see Fig 4. This agrees with the annual incidence rate due to vector transmission in Latin America and Mexico, both at 5 person per year per 100,000 individuals [74]. When we assume \( C_{\text{ITN}} = 4.5 \), to more closely match the price in Colombia, our model predicts incidence rate around 8.37 person per year per 100,000 individuals, again in close agreement with the published values of 4.5 to 6.1 person per year per 100,000 individuals.\]
agreement with the real incidence rate of 11 person per year per 100,000 individuals [74]. This all indicates that individuals behave rationally as predicted in general by [21]. Our findings also agree with [75] whose results showed that peoples’ acceptance of ITN use is related to the perception of an immediate protective effect against vectors.

Our crucial result is that the incidence rate is essentially linear and increasing with the cost of the ITNs, see Fig 4A. It follows that \( p_{\text{NE}} < p_{\text{HI}} \), but also \( p_{\text{NE}} \approx p_{\text{HI}} \).

Fig 4B shows how the incidence rates depend on the number of triatomines at home \( (K_s) \). When \( K_s \) is small, the incidence rate is 0. Once \( K_s \) increases above a certain threshold, the incidence rate increases rapidly, but then it decreases in \( K_s \). This agrees with [39]; they showed that it is best to have no dogs in the household (low \( K_s \)) but that once there are dogs in the

https://doi.org/10.1371/journal.pntd.0008833.g002
house, human infection declines with the number of dogs (i.e. with increasing $K_s$), allowing the dogs to sufficiently divert vectors away from the humans. In [11] they also conclude that reducing the population of triatomines and keeping domestic animals out of the households is the best way to decrease the risk of human infections.

Table 2 shows the sensitivity indices of $p_{HI}$, $p_{NE}$, the difference $p_{HI} - p_{NE}$ and the incidence $i$ on model parameters. Since $p_{NE}$ and $p_{HI}$ are very close to each other, their sensitivity indices are almost identical. We note that, if we disregard human birth rate, $\alpha$, that cannot be easily individually adjusted, the herd immunity level $p_{HI}$ is most sensitive to the vector birth rate $\beta$.

Fig 3. Dependence of $p_{HI}$ (solid) and $p_{NE}$ (dotted) on different parameter values. Unless varied, the parameter values are as specified in Table 1. For those parameters, $p_{HI} = 0.5026$ and $p_{NE} = 0.5017$.

https://doi.org/10.1371/journal.pntd.0008833.g003
settlement carrying capacity $K_s$ and the transmission rates $a_0$ and $b_0$. In all cases, the sensitivity index is about 0.5 (or $-0.5$ in the case of $\beta$), meaning that 1% increase of the parameter causes $p_{HI}$ to increase (decrease in the case of $\beta$) by about 0.5%. Since $p_{NE}$ increases (decreases) slightly more than $p_{HI}$, the sensitivity index of $p_{HI} - p_{NE}$ and of the incidence rate have reverse signs. The incidence rate is most sensitive to the cost of the ITNs, $C_{ITN}$, and the vector birth rate, $\beta$. A decrease of the ITN cost causes the incidence rate to decrease. The dependence of $\beta$ is more complex. The disease is endemic only for medium values of $\beta$ ($0.009$, $0.068$); there are not enough vectors for low $\beta$ (in fact no vectors for $\beta < \mu$) or not enough infected vectors for high $\beta$. In the endemic state, there is a critical birth rate $\beta_0 \approx 0.018 = \mu + \omega$ where reducing $\beta$ below $\beta_0$, while still having it above $0.009$, may actually increase the incidence rate. See Fig 4C.

Conclusions and discussion

In this paper, we modeled Chagas disease dynamics using the compartmental model developed in [44]. We parameterized the model based on values found in literature. We applied a game-theoretical approach, developed by [23], and determined the optimal voluntary use of

Table 2. The sensitivity analysis. The sensitivity index $SI_y$ of a variable $y$ on a parameter $x$ was calculated as $(\frac{\partial}{\partial x} \cdot \frac{y}{x} )$, see for example [72]. The numbers were rounded to the three decimal places. Parameters are as specified in Table 1. The sensitivity index $-0.5$ means that a 1% increase of a parameter value $x$ will result in the 0.5% decrease of the variable $y$.

| Parameter | $SI_{p_{HI}}$ | $SI_{p_{NE}}$ | $SI_{p_{HI} - p_{NE}}$ | $SI_{I}$ |
|-----------|---------------|---------------|-------------------------|-----------|
| $a_0$     | 0.496         | 0.498         | -1.007                  | -0.502    |
| $b_0$     | 0.496         | 0.498         | -1.007                  | -0.523    |
| $\alpha$  | -0.493        | -0.495        | 1.024                   | 1.522     |
| $\beta$   | -0.495        | -0.497        | 1.007                   | 0.522     |
| $\mu$     | -0.106        | -0.106        | 0.243                   | 0.121     |
| $\delta$  | 0.000         | 0.000         | 0.041                   | 0.041     |
| $\sigma$  | 0.117         | 0.117         | -0.253                  | -0.133    |
| $K_s$     | 0.511         | 0.514         | -0.990                  | -0.488    |
| $K_p$     | -0.002        | -0.002        | -0.030                  | -0.026    |
| $\omega$  | 0.003         | 0.003         | 0.042                   | 0.036     |
| $C_{Chagas}$ | 0            | 0.002         | -0.977                  | -0.975    |
| $C_{ITN}$ | 0             | -0.002        | 1.044                   | 1.042     |

https://doi.org/10.1371/journal.pntd.0008833.t002
insecticide treated nets (ITNs) to prevent the spread of infection through vector bites. We validated our model by predicting incidence rates that closely track the real incidence rates in Latin America, Mexico and Columbia. Our results confirm that individuals behave rationally and weigh the risks of insect bites against the cost of ITNs.

Our model gives two main predictions. We show that to completely eradicate the vector transmission through the voluntary use of ITNs, the cost of ITNs should be as low as possible. We also show that coupling ITN use with other means of vector control to decrease the vector presence in the households is very effective. On the other hand, in agreement with [39], if one cannot reduce the vector’s presence (or the vector birth rate) in the household below a critical threshold, increasing the vector presence may lead to a slightly lower incidence rate.

The use of ITNs has many advantages: it protects against multiple diseases such as malaria, leishmaniasis, and dengue [18], and it can be easily integrated into community health work [58, 76]. Compared to residual insecticide spraying, the use of ITNs does not require qualified spraying teams and it also requires considerably less insecticide [77]. Moreover, [78] showed that residual insecticide spraying was less effective than expected mainly because of moderate insecticide resistance and the limited effectiveness of selective treatment of infested sites only. The vectors can navigate past the nets; but most vectors that traversed the nets were early-stage nymphs, which are less likely to carry T. cruzi [79]. Furthermore, the spread of triatomine insects can be slowed down even if ITNs is used only on animal cages [79].

Our model can be extended in several ways. One can include disease related mortality which was omitted here for the sake of simplicity. A disease related mortality could cause a backward bifurcation and an existence of endemic equilibria even for \( R_0 < 1 \) [80, 81]. One can also relax the assumption about vector migration and allow the vectors to migrate from the settlement. Finally, one can consider transmission other than between vectors and humans. Yet the findings of our simple model agree with more complex models such as [11, 39, 42, 50] which found that the best way to decrease risk of human infection is by decreasing the number of triatomine in a given area and reducing the number of domestic animals.

Although every math model has many limitations, these models can help us to understand diseases and implications of various control measures. We hope that this model helps to serve as a tool in showing the importance of ITN use to prevent Chagas disease and to minimize the domestic transmission in Latin America as stated by the London Declaration.

Supporting information

S1 Matlab Code. The matlab code used to generate the figures is available in S1 Matlab Code. (M)

Author Contributions

Conceptualization: Habeeb Issa, Jan Rychtář, Dewey Taylor, Nancy Umana.

Formal analysis: Cheol Yong Han, Jan Rychtář, Dewey Taylor, Nancy Umana.

Investigation: Cheol Yong Han, Habeeb Issa, Dewey Taylor, Nancy Umana.

Methodology: Jan Rychtář, Dewey Taylor, Nancy Umana.

Resources: Cheol Yong Han, Habeeb Issa.

Software: Cheol Yong Han, Jan Rychtář.

Supervision: Jan Rychtář, Dewey Taylor.
Validation: Dewey Taylor, Nancy Umana.

Writing – original draft: Cheol Yong Han, Habeeb Issa, Jan Rychtář, Dewey Taylor, Nancy Umana.

Writing – review & editing: Jan Rychtář, Dewey Taylor.

References

1. Bartsch SM, Peterson JK, Hertenstein DL, Skrip L, Ndeffo-Mbah M, Galvani AP, et al. Comparison and validation of two computational models of Chagas disease: a thirty year perspective from Venezuela. Epidemics. 2017; 18:81–91. https://doi.org/10.1016/j.epidem.2017.02.004 PMID: 28279459

2. Erazo D, Cordovez J. Modeling the effects of palm-house proximity on the theoretical risk of Chagas disease transmission in a rural locality of the Orinoco basin, Colombia. Parasites & Vectors. 2016; 9 (1):592. https://doi.org/10.1186/s13071-016-1884-8

3. Tarleton RL, Gürler RE, Urbina JA, Ramsey J, Viotti R. Chagas disease and the London declaration on neglected tropical diseases. PLoS Neglected Tropical Diseases. 2014; 8(10). https://doi.org/10.1371/journal.pntd.0003219 PMID: 25299701

4. WHO. Chagas disease (also known as American trypanosomiasis); 2020. https://www.who.int/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis).

5. Olivera MJ, Chaverra KA. New Diagnostic Algorithm for Chagas Disease: Impact on Access to Diagnosis and Out-of-Pocket Expenditures in Colombia. Iranian Journal of Public Health. 2019; 48(7):1379–1381. PMID: 31497563

6. Tarleton RL, Reithinger R, Urbina JA, Kitron U, Gürler RE. The challenges of Chagas disease—grim outlook or glimmer of hope? PLoS Medicine. 2007; 4(12). https://doi.org/10.1371/journal.pmed.0040332 PMID: 18162039

7. Lee BY, Bacon KM, Bottazzi ME, Hotez PJ. Global economic burden of Chagas disease: a computational simulation model. The Lancet Infectious Diseases. 2013; 13(4):342–348. https://doi.org/10.1016/S1473-3099(13)70002-1 PMID: 2395248

8. Hotez PJ, Bottazzi ME, Franco-Paredes C, Ault SK, Periago MR. The neglected tropical diseases of Latin America and the Caribbean: a review of disease burden and distribution and a roadmap for control and elimination. PLoS Neglected Tropical Diseases. 2008; 2(9). https://doi.org/10.1371/journal.pntd.0000300

9. Tanowitz HB, Kirchhoff LV, Simon D, Morris SA, Weiss LM, Wittner M. Chagas’ disease. Clinical Microbiology Reviews. 1992; 5(4):400–419. https://doi.org/10.1128/cmrr.5.4.400 PMID: 1423218

10. Velasco-Hernandez JX. A model for Chagas disease involving transmission by vectors and blood transfusion. Theoretical Population Biology. 1994; 46(1):1–31. https://doi.org/10.1006/tpbi.1994.1017

11. Cruz-Pacheco G, Esteva L, Vargas C. Control measures for Chagas disease, Mathematical Biosciences. 2012; 237(1–2):49–60. https://doi.org/10.1016/j.mbs.2012.03.005 PMID: 22450034

12. Kirchhoff L. Chagas Disease (American Trypanosomiasis) Clinical Presentation. Departments of Internal Medicine (Infectious Diseases) and Epidemiology, Carver College of Medicine and College of Public Health, University of Iowa, USA. 2011;

13. Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. The Lancet. 2010; 375(9723):1388–1402. https://doi.org/10.1016/S0140-6736(10)60061-X

14. Dumonteil E, Ruiz-Piña H, Rodríguez-Félix E, Barrera-Pérez M, Ramírez-Sierra MJ, Rabinovich JE, et al. Re-infestation of houses by Triatoma dimidiata after intra-dom icile insecticide application in the Yucatan peninsula, Mexico. Memórias do Instituto Oswaldo Cruz. 2004; 99(3):253–256. https://doi.org/10.1590/S0074-02762004000300002 PMID: 15273795

15. Dumonteil E, Bottazzi ME, Zhan B, Heffernan MJ, Jones K, Valenzuela JG, et al. Accelerating the development of a therapeutic vaccine for human Chagas disease: rationale and prospects. Expert review of vaccines. 2012; 11(9):1043–1055. https://doi.org/10.1586/erv.12.85 PMID: 23151163

16. Mayo Clinic. Chagas disease; 2020. https://www.mayoclinic.org/diseases-conditions/chagas-disease/symptoms-causes/syc-20356212.

17. WHO. Prevention of Chagas Disease; 2016. https://www.who.int/chagas/disease/prevention/en/.

18. Kroeger A, Ordóñez-Gonzalez o, Behrend M, Alvarez G. Bednet impregnation for Chagas disease control: a new perspective. Tropical Medicine & International Health. 1999; 4(3):194–198. https://doi.org/10.1046/j.1365-3156.1999.43370.x PMID: 10223214
19. Kroeger A, González M, Ordóñez-González J. Insecticide-treated materials for malaria control in Latin America: to use or not to use? Transactions of the Royal Society of Tropical Medicine and Hygiene. 1999; 93(6):565–570. https://doi.org/10.1016/S0035-9203(99)90048-2 PMID: 10717733

20. Ibuka Y, Li M, Vietri J, Chapman GB, Galvaní AP. Free-riding behavior in vaccination decisions: an experimental study. PloS One. 2014; 9(1). https://doi.org/10.1371/journal.pone.0087164 PMID: 24472546

21. Maskin E. Nash equilibrium and welfare optimality. The Review of Economic Studies. 1999; 66(1):23–38.

22. Chang SL, Piraveenan M, Pattison P, Prokopenko M. Game theoretic modelling of infectious disease dynamics and intervention methods: a review. Journal of Biological Dynamics. 2020; 14(1):57–89. https://doi.org/10.1080/17513758.2020.1720322 PMID: 31996099

23. Bauch CT, Earn DJ. Vaccination and the theory of games. Proceedings of the National Academy of Sciences. 2004; 101(36):13391–13394. https://doi.org/10.1073/pnas.0403823101 PMID: 15329411

24. Crawford K, Lancaster A, Oh H, Rychtář J. A voluntary use of insecticide-treated cattle can eliminate African sleeping sickness. Letters in Biomathematics. 2015; 2(1):91–101. https://doi.org/10.30707/LIB2.1 Crawford

25. Klein SRM, Foster AO, Feagins DA, Rowell JT, Erovenko IV. Optimal voluntary and mandatory insect repellent usage and emigration strategies to control the chikungunya outbreak on Reunion Island. Preprint. 2019.

26. Kobe J, Pritchard N, Short Z, Erovenko IV, Rychtář J, Rowell JT. A Game-Theoretic Model of Cholera with Optimal Personal Protection Strategies. Bulletin of Mathematical Biology. 2018; 80(10):2580–2599. https://doi.org/10.1007/s11538-018-0476-5 PMID: 30203140

27. Dorsett C, Oh H, Paulemond ML, Rychtář J. Optimal repellent usage to combat dengue fever. Bulletin of Mathematical Biology. 2016; 78(5):916–922. https://doi.org/10.1137/s1538-0167-17 PMID: 27142427

28. Brettin A, Rossi-Goldthorpe R, Weishaar K, Erovenko IV. Ebola could be eradicated through voluntary vaccination. Royal Society Open Science. 2018; 5(1):171591. https://doi.org/10.1098/rsos.171591 PMID: 29410863

29. Chouhan A, Maiwand S, Ngo M, Putalapattu V, Rychtář J, Taylor D. Game-theoretical model of retroactive Hepatitis B vaccination in China. Bulletin of Mathematical Biology. 2020; 82:80. https://doi.org/10.1007/s11538-020-00748-5 PMID: 32542575

30. Schechekhoff K, Ejaz A, Erovenko IV. A game-theoretical model of optimal clean equipment usage to prevent hepatitis C among injecting drug users. Preprint. 2019.

31. Martinez A, Machado J, Sanchez E, Erovenko IV. Optimal vaccination strategies to reduce endemic levels of meningitis in Africa. Preprint. 2019.

32. Bankuru SV, Kossol S, Hou W, Mahmoudi P, Rychtář J, Taylor D. A Game-theoretic Model of Monkeypox to Assess Vaccination Strategies. PeerJ. 2020; 8:e9272. https://doi.org/10.7717/peerj.9272 PMID: 32607280

33. Cheng E, Gambhirrao N, Patel R, Zhowandai A, Rychtář J, Taylor D. A game-theoretical analysis of Poliomyelitis vaccination. Journal of Theoretical Biology. 2020; 499:110298. https://doi.org/10.1016/j.jtbi.2020.110298 PMID: 32371008

34. Sykes D, Rychtář J. A game-theoretic approach to valuating toxoplasmosis vaccination strategies. Theoretical Population Biology. 2015; 105:33–38. https://doi.org/10.1016/j.tpb.2015.08.003 PMID: 26319752

35. Acosta-Alonzo CB, Erovenko IV, Lancaster A, Oh H, Rychtář J, Taylor D. High endemic levels of typhoid fever in rural areas of Ghana may stem from optimal voluntary vaccination behavior. Proc R Soc A. 2020; p. 20200354. https://doi.org/10.1098/rspa.2020.0354 PMID: 33071586

36. Verelst F, Willem L, Beutels P. Behavioural change models for infectious disease transmission: a systematic review (2010–2015). Journal of The Royal Society Interface. 2016; 13(125):20160820. https://doi.org/10.1098/rsif.2016.0820

37. Nouvellet P, Cucunubá ZM, Gourbière S. Ecology, evolution and control of Chagas disease: a century of neglected modelling and a promising future. In: Advances in Parasitology. vol. 87. Elsevier; 2015. p. 135–191.

38. Rabinovich JE, Rossell O. Mathematical models and ecology of Chagas disease. American Trypanosomiasis Research, PAHO Sci Publ. 1976; 318:245–250.

39. Cohen JE, Gütter RE. Modeling household transmission of American trypanosomiasis. Science. 2001; 293(5530):694–698. https://doi.org/10.1126/science.1060638

40. Inaba H, Sekine H. A mathematical model for Chagas disease with infection-age-dependent infectivity. Mathematical Biosciences. 2004; 190(1):39–69. https://doi.org/10.1016/j.mbs.2004.02.004 PMID: 15172802
41. Slimi R, Eli Yacoubi S, Dumonteil E, Gourbière S. A cellular automata model for Chagas disease. Applied mathematical modelling. 2009; 33(2):1072–1085. https://doi.org/10.1016/j.apm.2007.12.028

42. Coffield DJ Jr, Spagnuolo AM, Shillor M, Mema E, Pelli B, Pruzinsky A, et al. A model for Chagas disease with oral and congenital transmission. PloS One. 2013; 8(6). https://doi.org/10.1371/journal.pone.0067267

43. Acuña-Zegarra MA, Olmos-Liceaga D, Velasco-Hernández JX. The role of animal grazing in the spread of Chagas disease. Journal of Theoretical Biology. 2018; 457:19–28. https://doi.org/10.1016/j.jtbi.2018.08.025 PMID: 30138633

44. Hidayat D, Nugraha ES, Nuraini N. A mathematical model of Chagas disease transmission. In: AIP Conference Proceedings. vol. 1937. AIP Publishing LLC; 2018. p. 020008.

45. Broom M, Rychtář J, Spears-Gill T. The game-theoretical model of using insecticide-treated bed-nets to fight malaria. Applied Mathematics. 2016; 7(09):852–860. https://doi.org/10.4236/am.2016.79076

46. Massad E. The elimination of Chagas’ disease from Brazil. Epidemiology & Infection. 2008; 136(9):1153–1164. https://doi.org/10.1017/S0950268807009879 PMID: 18053273

47. Kroeber A, Villegas E, Ordoñez-Gonzalez J, Pabón E, Scorza JV. Prevention of the transmission of Chagas’ disease with pyrethroid-impregnated materials. The American Journal of Tropical Medicine and Hygiene. 2003; 68(3):307–311. https://doi.org/10.4269/ajtmh.2003.68.307 PMID: 12685636

48. Rassi A Jr, Rassi A, Little WC, Xavier SS, Rassi SG, Rassi AG, et al. Development and validation of a risk score for predicting death in Chagas’ heart disease. New England Journal of Medicine. 2006; 355(8):799–808. https://doi.org/10.1056/NEJMoa053241

49. Nouvellet P, Dumonteil E, Gourbière S. The improbable transmission of Trypanosoma cruzi to human: the missing link in the dynamics and control of Chagas disease. PLoS Neglected Tropical Diseases. 2013; 7(11):e2505. https://doi.org/10.1371/journal.pntd.0002505 PMID: 24244766

50. Gürtler RE, Cecere MC, Castanera MB, Canale D, Lauricella MA, Chuit R, et al. Probability of infection with Trypanosoma cruzi of the vector Triatoma infestans fed on infected humans and dogs in northwest Argentina. The American Journal of Tropical Medicine and Hygiene. 1996; 55(1):24–31. https://doi.org/10.4269/ajtmh.1996.55.1.TM0550010024 PMID: 8702018

51. World Bank. Life expectancy in years; 2020. https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=ZJ.

52. Rabinovich JE. Vital statistics of Triatominae (Hemiptera: Reduviidae) under laboratory conditions. I. Triatoma infestans Klug. Journal of Medical Entomology. 1972; 9(4):351–370. https://doi.org/10.1093/jmedent/9.4.351 PMID: 4559948

53. de Almeida Dias F, Guerra B, Vieira LR, Perdomo HD, Gandara ACP, do Amaral RJV, et al. Monitoring of the parasite load in the digestive tract of Rhodnius prolixus by combined qPCR analysis and imaging techniques provides new insights into the trypanosome life cycle. PLoS Neglected Tropical Diseases. 2015; 9(10).

54. Peterson JK, Bartsch SM, Lee BY, Dobson AP. Broad patterns in domestic vector-borne Trypanosoma cruzi transmission dynamics: synanthropic animals and vector control. Parasites & Vectors. 2015; 8(1):537. https://doi.org/10.1186/s13071-015-1146-1 PMID: 26489493

55. Crawford B, Kribs-Zaleta C. A metapopulation model for sylvatic T. cruzi transmission with vector migration. Mathematical Biosciences & Engineering. 2014; 11(3):471–509. https://doi.org/10.3934/mbe.2014.11.471 PMID: 24506545

56. Tomasin N, Ragone PG, Gourbière S, Aparicio JP, Diosque P. Epidemiological modeling of Trypanosoma cruzi: Low stercorarian transmission and failure of host adaptive immunity explain the frequency of mixed infections in humans. PLoS Computational Biology. 2017; 13(5):e1005532. https://doi.org/10.1371/journal.pcbi.1005532 PMID: 28481887

57. Erlanger TE, Enayati AA, Hemingway J, Mshinda H, Tami A, Lengeler C. Field issues related to effectiveness of insecticide-treated nets in Tanzania. Medical and Veterinary Entomology. 2004; 18(2):153–160. https://doi.org/10.1111/j.0269-283X.2004.00491.x PMID: 15189240

58. Kroeber A, Avíñoa A, Ordoñez-Gonzalez J, Escandon C. Community cooperatives and insecticide-treated materials for malaria control: a new experience in Latin America. Malaria journal. 2002; 1(1):15. https://doi.org/10.1186/1475-2875-1-15 PMID: 12473181

59. Catala de Montenegro S. Estimation of the frequency of host-vector contact in populations of Triatoma infestans (Klug, 1834) under natural climatic conditions. In: Proceedings of the IV Argentine Congress of Protozoology, La Falda, Cordoba, Argentina. vol. 11; 1987. p. 25.

60. Catalá S, Crocco L, Morales G. Trypanosoma cruzi transmission risk index (TcTRI): an entomological indicator of Chagas disease vectorial transmission to humans. Acta Tropica. 1997; 63(3):285–295. https://doi.org/10.1016/S0001-706X(97)00098-3 PMID: 9492913
61. López AG, Crocco L, Morales G, Catalá SS. Feeding frequency and nutritional status of peridomestic populations of *Triatoma infestans* from Argentina. Acta Tropica. 1999; 73(3):275–281. https://doi.org/10.1016/S0001-706X(99)00039-X PMID: 10546845

62. Arevalo A, Carranza JC, Guhl F, Clavijo JA, Vallejo GA. Comparison of the life cycles of *Rhodnius colombiensis* (Moreno, Jurberg & Galvao, 1999) and *R. prolixus* (Stal, 1872) (*Hemiptera, Reduviidae, Triatominae*) under laboratory conditions. Biomedica. 2007; 27:119–129. https://doi.org/10.7775/biomedica.v27i1.255 PMID: 18154252

63. Castañera MB, Aparicio JP, Gürtler RE. A stage-structured stochastic model of the population dynamics of *Triatoma infestans*, the main vector of Chagas disease. Ecological Modelling. 2003; 162(1–2):33–53. https://doi.org/10.1016/S0304-3800(02)00388-5

64. Rabinovich JE, Himschoot P. A population-dynamics simulation model of the main vectors of Chagas’ Disease transmission, *Rhodnius prolixus* and *Triatoma infestans*. Ecological Modelling. 1990; 52:249–266. https://doi.org/10.1016/0304-3800(90)90019-D

65. Spagnuolo AM, Shillor M, Kingsland L, Thatcher A, Toenskoetter M, Wood B. A logistic delay differential equation model for Chagas disease with interrupted spraying. Journal of Biological Dynamics. 2012; 6(2):377–394. https://doi.org/10.1080/17513758.2011.587986

66. Monroy C, Rodas A, Mejia M, Rosales R, Tabaru Y. Epidemiology of Chagas disease in Guatemala: infection rate of *Triatoma dimidiata*, *Triatoma nitida* and *Rhodnius prolixus* (*Hemiptera, Reduviidae*) with *Trypanosoma cruzi* and *Trypanosoma rangeli* (*Kinetoplastida, Trypanosomatidae*). Memorias do Instituto Oswaldo Cruz. 2003; 98(3):305–310. https://doi.org/10.1590/S0074-02762003000300003 PMID: 12986407

67. Cecere MC, Canale DM, Gürtler RE. Effects of refuges on the population dynamics of *Triatoma infestans* in experimental huts under natural climatic conditions in central Argentina. Journal of Applied Ecology. 2003; 40:742–56.

68. Rabinovich JE, Waisnivesky-Colli C, Solarz ND, Gürtler RE. Probability of transmission of Chagas disease by *Triatoma infestans* (*Hemiptera: Reduviidae*) in an endemic area of Santiago del Estero, Argentina. Bulletin of the World Health Organization. 1990; 69(6):737. PMID: 2127392

69. Noor FMM, Gassner A, Terheggen A, Dobie P. Beyond sustainability criteria and principles in palm oil development in Colombia. Tropical Medicine & International Health. 2002; 7(5):450–458. https://doi.org/10.1046/j.1365-3156.2002.00876.x PMID: 12000655

70. Castillo-Neyra R, Barbu CM, Salazar R, Borrini K, Naquira C, Levy MZ. Host-seeking behavior and dispersion of *Triatoma infestans*, a vector of Chagas disease, under semi-field conditions. PLoS Neglected Tropical Diseases. 2015; 9(1):e3433. https://doi.org/10.1371/journal.pntd.0003433 PMID: 25569228

71. Molina C. The good, the finite, and the infinite; 2016. PhD thesis, McMaster University.

72. Arriola L, Hyman JM. Sensitivity analysis for uncertainty quantification in mathematical models. In: Castillo-Neyra R, Barbu CM, Salazar R, Borrini K, Naquira C, Levy MZ. Host-seeking behavior and dispersion of *Triatoma infestans*, a vector of Chagas disease, under semi-field conditions. PLoS Neglected Tropical Diseases. 2015; 9(1):e3433. https://doi.org/10.1371/journal.pntd.0003433 PMID: 25569228

73. Kroeger A, Ayala C, Lara AM. Unit costs for house spraying and bednet impregnation with residual insecticides in Colombia: a management tool for the control of vector-borne disease. Annals of Tropical Medicine & Parasitology. 2002; 96(4):405–416. https://doi.org/10.1179/000349802125001159 PMID: 12171622

74. WHO. Chagas disease in Latin America: an epidemiological update based on 2010 estimates. Weekly Epidemiological Record, Relevé Épidémiologique Hebdomadaire. 2015; 90(06):33–44. PMID: 25671846

75. Kroeger A, Mancheno M, Alarcón J, Pesse K. Insecticide-impregnated bed nets for malaria control: varying experiences from Ecuador, Colombia, and Peru concerning acceptability and effectiveness. The American Journal of Tropical Medicine and Hygiene. 1995; 53(4):313–323. https://doi.org/10.4269/ajtmh.1995.53.313 PMID: 7485681

76. Kroeger A, Ordoñez-Gonzalez J, Añón AJ. Malaria control reinvented: health sector reform and strategy development in Colombia. Tropical Medicine & International Health. 2002; 7(5):450–458. https://doi.org/10.1046/j.1365-3156.2002.00876.x PMID: 12000655

77. Kroeger A, Meyer R, Mancheno M, Gonzalez M, Pesse K. Operational aspects of bednet impregnation for community-based malaria control in Nicaragua, Ecuador, Peru and Colombia. Tropical Medicine & International Health. 1997; 2(6):589–602. https://doi.org/10.1046/j.1365-3156.1997.d01-319.x PMID: 9236827

78. Gurevitz JM, Gaspe MS, Enriquez GF, Provecho YM, Kitron U, Gürtler RE. Intensified surveillance and insecticide-based control of the Chagas disease vector *Triatoma infestans* in the Argentinian Chaco. PLoS Neglected Tropical Diseases. 2013; 7(4). https://doi.org/10.1371/journal.pntd.0002156 PMID: 23593555

79. Levy MZ, Quispe-Machaca VR, Ylla-Velasquez JL, Walle LA, Richards JM, Rath B, et al. Impregnated netting slows infestation by *Triatoma infestans*. The American Journal of Tropical Medicine and Hygiene. 2008; 79(4):528–534. https://doi.org/10.4269/ajtmh.2008.79.528 PMID: 18840739
80. Chitnis N, Cushing JM, Hyman J. Bifurcation analysis of a mathematical model for malaria transmission. SIAM Journal on Applied Mathematics. 2006; 67(1):24–45. https://doi.org/10.1137/050638941

81. Djijou-Demasse R, Abiodun GJ, Adeola AM, Botai JO. Development and analysis of a malaria transmission mathematical model with seasonal mosquito life-history traits. Studies in Applied Mathematics. 2020; 144(4):389–411. https://doi.org/10.1111/sapm.12296