OPTIMAL CONTROL METHODS FOR CHAGAS DISEASE

by

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THESIS

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Abstract

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Chagas disease is the world's most neglected tropical disease. Having a lack of cure makes the primary focus on the disease preventing it and controlling it. This study takes into account three different control measures: bed nets, low-volume insecticide spraying, and improving housing conditions, analyzes their cost effectiveness compared to each other, and determines which combination of the three control measures prevents the most *T. cruzi* infections in a rural Latin American village over a decade.

It was shown that there is a a hierarchical importance in the control measures when preventing the spread of Chagas disease. In order of highest effectiveness, they are bed nets, low-volume insecticide spraying, and improving overall housing conditions. It was found that the most cost-effective scenario occurs when full coverage for bed nets and low-volume insecticide spraying is obtained, followed by devoting the remaining portion of the budget towards improving overall housing conditions. It was shown that if at least 36.30 USD per month is devoted to bed nets, then $R_0 < 1$.

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1. Introduction

Chagas disease, also known as American trypanosomiasis, is a life-threatening illness caused by the protozoan parasite *Trypanosoma cruzi*. *T. cruzi* is spread through a number of different ways. A few leading causes include vertical transmission in hosts, oral transmission, and stercorarian transmission via blood meal, where the vector bites the host and then defecates near the wound. The parasite is contained in the feces of the vector, which is therefore transferred upon defecation onto the host, where it spreads into the body. Nearly ten million individuals throughout Latin America are infected with Chagas disease. Chagas disease causes organ deformity and early death in nearly one third of the infected population. The disease can also be transmitted through organ transplants and blood transfusions.

Preventative measures for Chagas disease focus on controlling vector population density. The main approaches include spraying insecticides, improving the quality of housing, using bed nets, and screening blood donors. There are currently no effective vaccinations to treat Chagas disease. The only drug treatments are for the acute stages of Chagas disease, but they are highly toxic. In fact, the efficacy of these drug treatments has been called into question on a number of occasions [10]. For these reasons, current studies and methods of prevention are focused on vector control and monitoring blood work.

Chagas disease is most prevalent in South America, mainly in people who cannot afford health care. For that reason, this study will focus on optimizing control methods of Chagas disease to describe how those who cannot afford screening or treatment can prevent infection. We will focus on optimizing control methods for Chagas disease using bed nets, spraying insecticides, and improving housing conditions.

There have been numerous studies regarding domestic transmission of Chagas disease. One such study, [19], modeled the long-term population effects insecticide spraying had on *Triatoma infestans*. [3] modeled the overall population dynamics of vectors (both infected and

uninfected), infected hosts, and other mammals in a village over a decade. This allows us to see how *Triatoma infestans* reproduce and spread *T. cruzi* in a small area.

Numerous studies have been conducted over the past few decades regarding control measures for vector populations. In [21], insecticide was sprayed in a large number of communities in Argentina over a twelve year period on a fixed budget. [1, 22] analyzed the cost effectiveness of implementing low-volume insecticide spraying vs not doing anything at all. They also analyzed the efficiency with which certain insecticides can control vector populations, namely Deltamethrin. [15] analyzed the effectiveness of long-lasting insecticidal nets, particularly on preventing contacts between humans and vectors infected with Malaria in Africa. [17] studied the effectiveness of different combinations of control methods, namely spraying insecticides on timed intervals, improving housing conditions, and combining the two. [17] conducted a study that compared different combinations of spraying insecticide and improving housing conditions. Interestingly, they showed that spraying insecticide every few months near the beginning of making housing improvements proved the most effective at maintaining low vector populations for extended periods of time. The study done in [17] was conducted in real time at multiple villages. This study will only focus on modeling spraying at regular intervals throughout the period in question.

Using bed nets is the most affordable control option available to prevent infections. The main purpose of a bed net is to reduce contact with vectors, which would prevent blood meals on hosts and therefore reduce the number of potential infections. Throughout this study, we will assume that a bed net is a Long-Lasting Insecticidal Net (LLIN). We will assume that the use of bed nets affects only the contact rate (and thus potentially vector longevity).

Spraying insecticides is a very common method used to control vector populations. Multiple health organizations have conducted studies on insecticide effectiveness, vector resistance, and its ability to slow infection rates [24, 18]. Unlike bed nets, this is both a preventative and control

measure. It does cost more to spray insecticides in a residence, but it temporarily annihilates the vector population.

Theoretically, the best way to control populations of vectors is to improve overall housing conditions. In rural Latin America, most dwellings are made of materials that would not be acceptable in developed countries. Doing things such as filling in holes in walls, replacing roofing materials, caulking, etc. will decrease the number of points for vectors to enter into a host's dwelling. Doing so will also decrease the population of vectors by reducing the number of hosts available to them. This is the most expensive option available that is being considered in this study. It could very well be an issue for those who cannot afford health care as they might not be able to afford to perform upgrades in their housing situations.

Bed nets, insecticide spraying, and housing improvements are all potential control methods for Chagas disease. This model will analyze each control method on its cost efficiency and its effectiveness to minimize infections given a specific budget. It will do so by creating a dynamical system that models *T. cruzi* which incorporates all three control methods and determines which combination of control measures reduces infections the most.

2. Model

To describe the effects of optimizing control methods for Chagas disease, we will first describe the underlying assumptions. For simplicity purposes, we will only consider a small environment. Our setting will focus on domestic transmission in a rural Latin American village. We will focus on two different populations, the hosts (humans) and vectors (which may or may not be infected by *T. cruzi*). Throughout this paper, the subscripts H and V will correspond to hosts and vectors, respectively.

Variables, notation, and parameters are summarized in Tables 1 and 2. In Table 1, we follow the approach used in [19] of assuming a village with a population of 400 and extrapolating an initial figure for vector population and infection prevalence from published data.

Table 1: Variables and notation for optimization of control methods model.

Var.	Meaning	Units	I.C.	Source
$N_H(t)$	Density of hosts	hosts/village	400	[19]
$S_H(t)$	Density of uninfected hosts	hosts/village	310	[19]
$I_H(t)$	Density of hosts infected with *T. cruzi*	hosts/village	90	[19]
$N_V(t)$	Density of vectors	vectors/village	33995	[19]
$S_V(t)$	Density of uninfected vectors	vectors/village	23049	[19]
$I_V(t)$	Density of vectors infected with *T. cruzi*	vectors/village	10946	[19]

The total host density is given by $N_H = I_H + S_H$, and similarly for N_V. Since vertical transmission of Chagas disease is not present in vectors, birth produces only susceptible vectors. The birth rate of vectors will be accounted for logistically. In this model, however, improving housing conditions will impact the birth rate of vectors. More specifically, improving housing conditions will decrease the carrying capacity by a factor of c.

The dynamics of the system are shown in Figure 1.

The resulting dynamics can be summarized by the following system of ordinary differential equations:

Table 2: Parameter definitions and estimates.

Parm.	Definition	Units	Value	Source
r_H	Maximum growth rate for hosts	per year	9.637e-2	[8]
r_V	Maximum growth rate for vectors	per year	2.20925	[8]
μ_H	Natural mortality rate of hosts	per year	2.57e-5	[4]
μ_V	Natural mortality rate of vectors	per year	3.27e-3	[12]
ω_V	Starvation mortality rate of vectors	per year	0.02857	[16]
β_H	Infection rate for hosts	hosts per vector per year	4.00876e-4	[8]
β_V	Infection rate for vectors	per year	5.424e-3	[8]
K_H	Carrying capacity for hosts	hosts per village	1000	[8]
K_V	Carrying capacity for vectors	vectors per village	37000	[8]
q	Vertical transmission percentage in hosts		0.01	[14]
T	Insecticide spraying time step	days	90	[1]
budget	Allocated budget for control measures	USD/month	355.16	[21]
a	Proportion of vectors not affected by bed nets	———	control parm	
b	Proportion of vectors remaining after spraying insecticide	———	control parm	
c	Proportion of vector carrying capacity remaining under housing improvements	———	control parm	
p_a	Portion of budget allocated to bed nets	———	control parm	
p_b	Portion of budget allocated to insecticides	———	control parm	
p_c	Portion of budget allocated to housing improvements	———	control parm	

$$I'_H(t) = a(p_a)\beta_H S_H(t)\tfrac{I_V(t)}{N_H(t)} - \mu_H I_H(t) + r_H q I_H(t)\Big(1 - \tfrac{N_H(t)}{K_H}\Big)$$

$$S'_H(t) = -a(p_a)\beta_H S_H(t)\tfrac{I_V(t)}{N_H(t)} - \mu_H S_H(t) + r_H(N_H(t) - qI_H(t))\Big(1 - \tfrac{N_H(t)}{K_H}\Big)$$

$$I'_V(t) = a(p_a)\beta_V S_V(t)\tfrac{I_H(t)}{N_H(t)} - m(a(p_a))I_V(t)$$

$$S'_V(t) = -a(p_a)\beta_V S_V(t)\tfrac{I_H(t)}{N_H(t)} - m(a(p_a))S_V(t) + r_V N_V(t)\Big(1 - \tfrac{N_V(t)}{c(p_c)K_V}\Big)$$

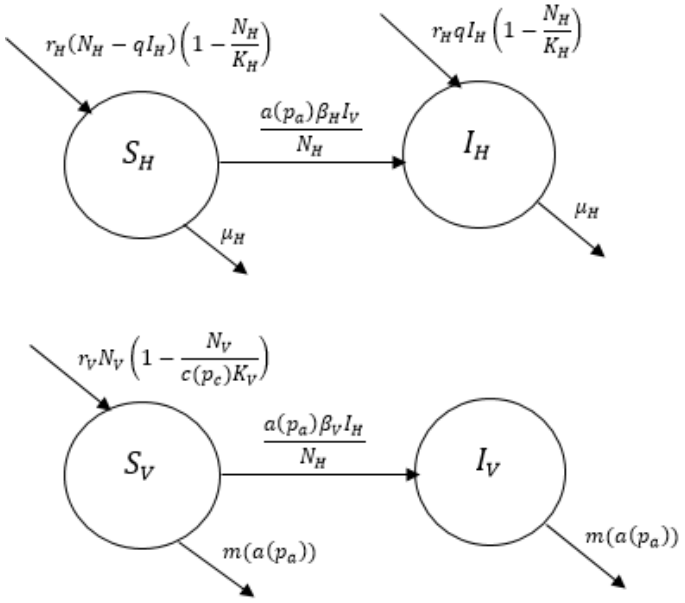

Figure 1: Flow chart showing the dynamics of our system between spraying.

Note that in the above system, the insecticide coefficient is not accounted for. It is assumed for this model that a proportion of the dwellings, depending on p_b, will be sprayed once each time period T, when the vector population will be reset to a proportion b of its current value. This produces a metered model, with the resets given by the equation

$$N_V(nT^+) = bN_V(nT^-), n = 1, 2, 3, ... \tag{1}$$

More detailed information about metering effects on populations can be found in [2].

Each of the coefficients a, b, and c are uniquely determined during each simulation. The coefficient a will be determined using the following equation,

$$a(p_a) = 1 - 0.93 \min\left(1, \frac{p_a}{p_a^*}\right), \tag{2}$$

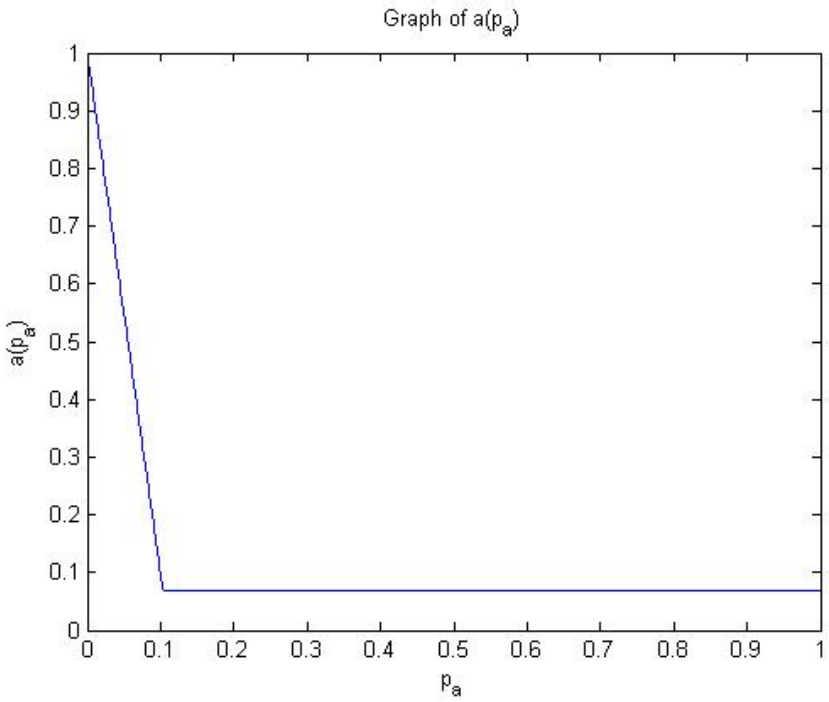

Figure 2: Shows the overall behavior of $a(p_a)$, which is the proportion of vector-host contacts not prevented by bed nets, as a function of the budget proportion allocated to providing the nets.

which can be visualized in Figure 2.

In Figure 2, $a(0) = 1$, p_a^* is the budget proportion at which control measure a (bed nets) is covered for the entire community (to be determined), and 0.93 is the average maximum effectiveness of a bed net at preventing infection when the entire population is utilizing a bed net as a control measure [15].

The behavior of the coefficients b and c will be nearly identical to a, and will be represented by the following equations, respectively:

$$b(p_b) = 1 - 0.976 \min\left(1, \frac{p_b}{p_b^*}\right) \tag{3}$$

$$c(p_c) = 1 - 0.9 \min\left(1, \frac{p_c}{p_c^*}\right) \tag{4}$$

For b, 0.976 is its maximum efficiency when used consistently [1]. For c, 0.9 is its maximum efficiency [17].

The total number of deaths occurring in the vector population is determined both by natural deaths, μ_V, and starvation deaths, ω_V, caused by bed nets. We will denote this by $m(a(p_a))$, where

$$m(a(p_a)) = \frac{\mu_V \omega_V}{\mu_V + a(p_a)(\omega_V - \mu_V)}. \tag{5}$$

The mortality rates given for this equation are accurate for all $a \in [0, 1]$. More specifically, $m(0) = \omega_V$ and $m(1) = \mu_V$. When $a(p_a) \in (0, 1)$, $m(a(p_a))$ yields the appropriate mortality rate for the vectors.

Since studies have been done in the past analyzing control methods for Chagas disease on a budget, namely [21], this study was used to replicate a similar budget. This study had a total budget of 309,426 USD over twelve years, which was distributed over 242 communities found in Moreno, Argentina, each of which contained an average of 2.5 houses per community. Comparatively, since the village in our model consists of 100 houses, taking the monthly average and multiplying by forty yields a monthly control budget of 355.16 USD. Along with cost estimates, this will be used to calculate p_a^*, p_b^*, and p_c^*.

3. Analysis

3.1. Unmetered Model

3.1.1. Population Dynamics

Since population dynamics are separate from infection dynamics, we can look at the resulting equations for the total population of hosts and vectors separately, given by the equations:

$$N_H'(t) = r_H N_H(t)\left(1 - \frac{N_H(t)}{K_H}\right) - \mu_H N_H(t) \tag{6}$$

$$N_V'(t) = r_V N_V(t)\left(1 - \frac{N_V(t)}{c(p_c)K_V}\right) - m(a(p_a))N_V(t) \tag{7}$$

Each equation has an extinction equilibrium and a survival equilibrium. They are $N_H^* = 0$, $N_V^* = 0$,

$$N_H^* = K_H\Big(1 - \frac{\mu_H}{r_H}\Big), \tag{8}$$

and

$$N_V^* = c(p_c)K_v\Big(1 - \frac{m(a)}{r_v}\Big). \tag{9}$$

The extinction equilibrium points are locally asymptotically stable if the maximum growth rate is less than the mortality rate, i.e, if $r_H < \mu_H$ and $r_V < m(a)$. The survival equilibrium points are locally asymptotically stable if the reverse is true for both equations, i.e, $\mu_H < r_H$ and $m(a(p_a)) < r_V$.

Moreover, both equations above are autonomous and their solutions are monotone. Therefore, the respective locally-asymptotic equilibria are in fact globally-asymptotically stable. Since both populations persist in reality, we will henceforth assume that $\mu_H < r_H$ and $m(a(p_a)) < r_V$. This way, the hosts and vectors will approach their respective survival equilibrium points.

3.1.2. Infection dynamics

To study infection dynamics, we consider a simplified system in which population dynamics have reached equilibrium. By substituting $S_H = N_H - I_H$ and $S_V = N_V - I_V$, we can reduce the number of equations in our non-metered dynamical system down to two. Namely, only the infected classes will be remaining. The new system of equations is:

$$I'_H(t) = a(p_a)\beta_H(N^*_H - I_H(t))\frac{I_V(t)}{N^*_H} - \mu_H I_H(t) + r_H q I_H(t)\Big(1 - \frac{N^*_H}{K_H}\Big) \tag{10}$$

$$I'_V(t) = a(p_a)\beta_V(N^*_V - I_V(t))\frac{I_H(t)}{N^*_H} - m(a(p_a))I_V(t) \tag{11}$$

From the previous section, $N^*_H = K_H\big(1 - \frac{\mu_H}{r_H}\big)$ and $N^*_V = c(p_c)K_v\big(1 - \frac{m(a)}{r_v}\big)$. Using the Next-Generation Operator (NGO) method from [11], we were able to calculate R_0 for this system. Specifically,

$$R_0 = \frac{q}{2} + \sqrt{\frac{q^2}{4} + \frac{a(p_a)^2\beta_H\beta_V N^*_V}{\mu_H m(a(p_a))N^*_H}} \tag{12}$$

For simplification purposes, we will use an alternative threshold quantity equivalent to R_0. Namely,

$$\hat{R_0} = \sqrt{\frac{a(p_a)^2\beta_H\beta_V N^*_V}{m(a(p_a))\mu_H(1-q)N^*_H}} \tag{13}$$

Note that $R_0 < 1$ iff $\hat{R_0} < 1$. We will look at the disease-free equilibrium (DFE), (0,0), and endemic equilibrium (EE),

$$\left(\frac{a(p_a)^2\beta_H\beta_V\frac{N^*_V}{N^*_H} - \mu_H(1-q)m(a(p_a))}{\frac{a(p_a)\beta_V}{N^*_H}\big(\mu_H(1-q) + a(p_a)\beta_H\frac{N^*_V}{N^*_H}\big)}, \frac{a(p_a)^2\beta_H\beta_V\frac{N^*_V}{N^*_H} - \mu_H(1-q)m(a(p_a))}{\frac{a(p_a)\beta_H}{N^*_H}\big(a(p_a)\beta_V + m(a(p_a))\big)}\right)$$

of the above system. First, we observe by inspection that the expression for the endemic equilibrium is only positive when $\hat{R_0} > 1$. Second, the NGO definition of $\hat{R_0}$ gives us that the

DFE is locally asymptotically stable when $\hat{R}_0 < 1$. Third, using the Routh-Hurwitz criteria, we can determine local asymptotic stability for the EE. Let J denote the Jacobian of the EE. It was determined that $tr(J) < 0$ and $det(J) > 0$ when $\hat{R}_0 > 1$. For more details, see Appendix A. Thus, when $\hat{R}_0 > 1$, although the DFE is unstable, the EE is locally asymptotically stable.

Now, let's consider global behavior. By Dulac's Criterion, using $\beta = \frac{1}{I_H I_V}$, there are no periodic orbits. Since $I_H \leq N_H^*$ and $I_V \leq N_V^*$, together with the coordinate axes, N_H^* and N_V^* form a bounding box around I_H and I_V. To prove this, first assume that $I_H(t) \geq N_H^*$. Here, $I_H'(t) = a(p_a)\beta_H I_V(t)\Big[1 - \frac{I_H(t)}{N_H^*}\Big] + \mu_H(q-1)I_H(t) < 0$ since $q < 1$ and $\frac{I_H(t)}{N_H^*} > 1$. Second, assume that $I_V(t) \geq N_V^*$. Here, $I_V'(t) = a(p_a)\beta_V(N_V^* - I_V(t))\frac{I_H(t)}{N_H^*} - m(a(p_a))I_V(t) < 0$ since $m(a(p_a))I_V(t) > 0$ and $I_V(t) > N_V^*$. This shows that all solutions tend to an equilibrium point inside the bounding box and don't leave once inside. This eliminates unbounded growth of solutions. Therefore, by the Poincaré-Bendixson Theorem, since we have eliminated unbounded growth and periodic orbits, all solutions of the above system approach an equilibrium. When $\hat{R}_0 < 1$, the disease-free equilibrium is therefore globally asymptotically stable. When $\hat{R}_0 > 1$, the disease-free equilibrium is unstable and the endemic equilibrium is therefore globally asymptotically stable. For both cases, there is at most one saddle point equilibrium, so there are no phase polygons. Therefore, by [20], we can extend the stability criteria of the reduced system above to the overall dynamical system.

3.1.3. Cost Analysis

By substituting $p_c = 1 - p_a$ into (13), $\hat{R}_0$ can be turned into a function of p_a. Along $\big[0, 1\big]$, we can see how $\hat{R}_0$ fluctuates for the unmetered model in Figure 3.

When $0 \leq p_a < p_a^*$, $\hat{R}_0$ is monotonically decreasing. $\hat{R}_0$ reaches its minimum when $p_a = p_a^*$. When $p_a^* < p_a \leq 1$, $\hat{R}_0$ increases slightly since p_c is decreasing.

Let $\hat{p_a} = 0.102189$. In $\big[0, p_a^*\big]$, $\hat{R}_0 = 1$ when $p_a = \hat{p_a}$. The disease is endemic for $p_a < \hat{p_a}$,

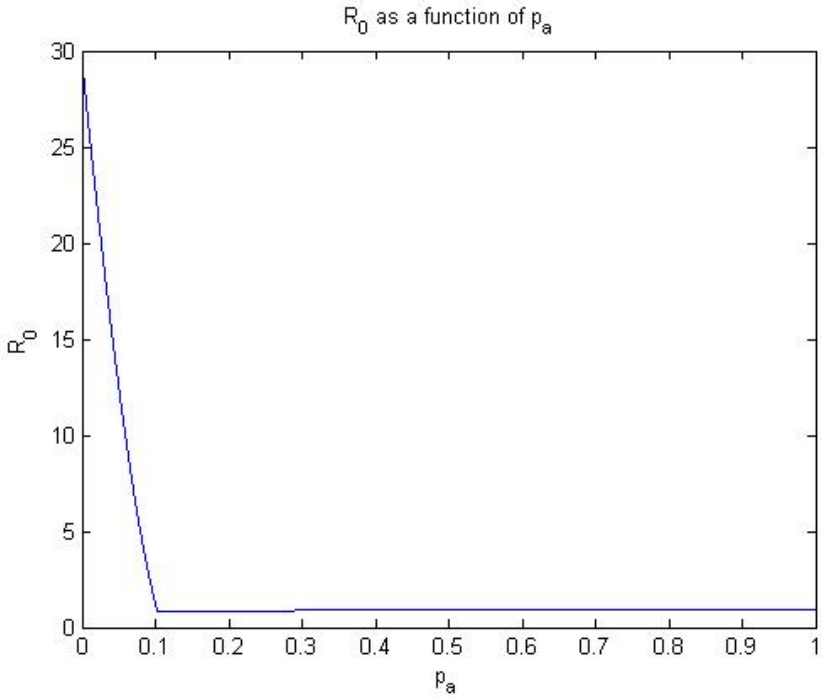

Figure 3: This graph shows the value of $\hat{R}_0$ as a function of p_a. Values were used from Table 2 to generate this graph.

but for $p_a > \hat{p_a}$, $\hat{R}_0 < 1$, with a minimum at p_a^*.

3.2. Metered Model

3.2.1. Effects of Metering

Using the baseline parameter values given in Table 2, the graph of the infected host population for the metered model trends downward, while the graph for the unmetered model trends upward. This difference is due to spraying insecticide at regular intervals, which causes oscillatory behavior. The unmetered graph exhibits stable growth, specifically non-oscillatory growth. The effects of metering on $I'_H(t)$ can be seen in Figure 4.

Using the baseline parameter values given in Table 2 and choosing p_a such that $0 \leq p_a < \hat{p_a}$, $\hat{R}_0 > 1$ when $p_b = 0$ (as verified using (13)). However, when $\hat{p_a} < p_a \leq 1$, $\hat{R}_0 < 1$. This can

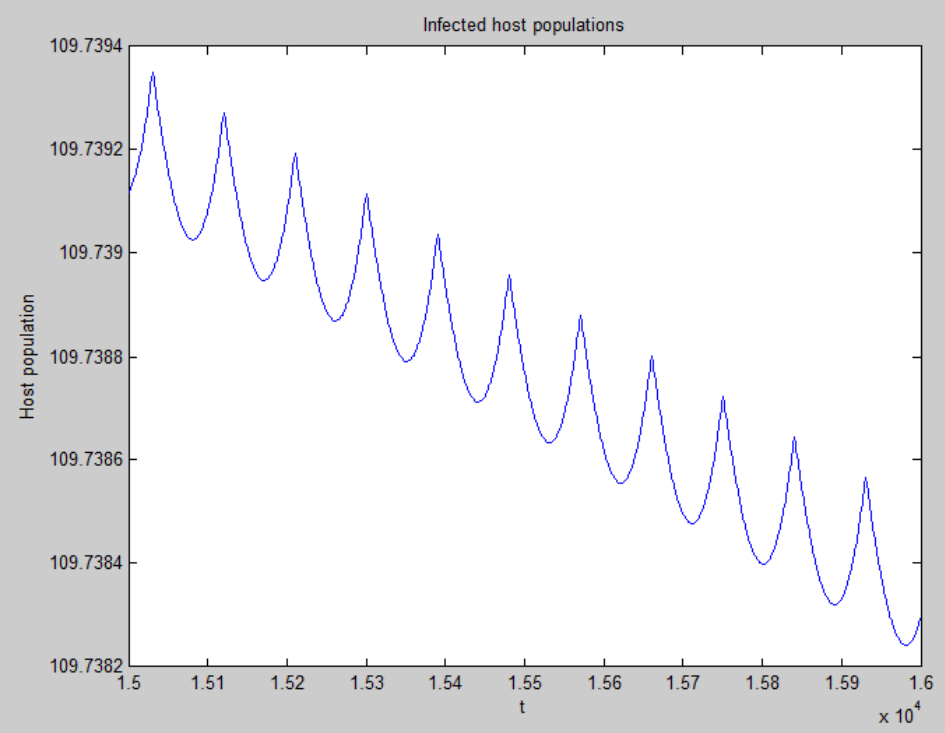

Figure 4: Shows the effects of metering on I_H. The oscillations are due to "spraying" the vector populations every 90 days.

be seen in Figure 5.

This specific example was plotted using the following combination of control measures: $p_a = 0.09, p_b = 0.47, p_c = 0.44$. Here, $\hat{R_0} \approx 3$, $I_H^* \approx 808$, so $\hat{R_0} > 1$ for the unmetered model. However, Figure 5 shows that $\hat{R_0} < 1$ for the metered model.

3.2.2. Cost Analysis

Allocating a monthly budget of only 355.16 USD for an entire village restricts what resources can be allocated towards the control measures. [15] determined that a LLIN cost 6.59 USD per unit and lasts 36 months before it needs to be replaced. Using this data, we can calculate the three-year cost to ensure full coverage of LLINs by:

$$6.59 \, \tfrac{USD}{net} \times 2 \, \tfrac{nets}{house} \times 100 \, \tfrac{houses}{village} = 1318 \, \tfrac{USD}{village}$$

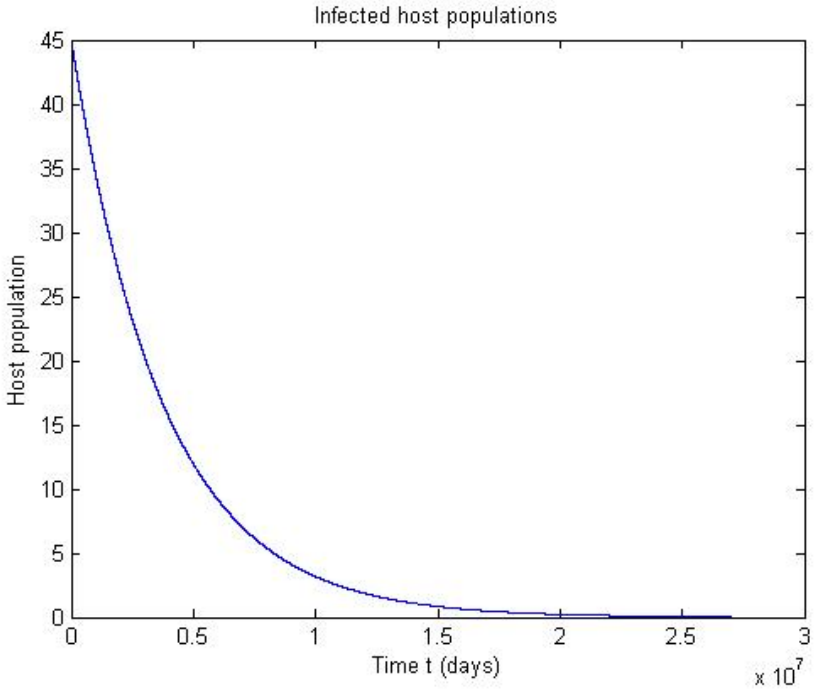

Figure 5: Shows the population of I_H. Parameters from Table 2 were used to generate this curve. This was used to determine the asymptotic behaviors of $\hat{R}_0$ for the metered model.

The monthly allocation of money needed to ensure full coverage of LLINs is given by :

$$\frac{1318}{36} = 36.61 \, \frac{USD}{month}$$

Therefore, p_a^* is given by:

$$p_a^* = \frac{36.61}{355.16} = 0.10308 \tag{14}$$

Similarly, low-volume insecticide spraying costs 8 USD per house and lasts 3 months [22]. Improving housing conditions costs 700 USD per house and was measured to last for 21 months [21]. Taking this into account, we found $p_b^* = 0.7508$ and $p_c^* = 9.385$.

After running 4947 numerical simulations over all possible combinations of budget allocations, the scenarios were ranked in regards to resource allocation. Results were measured by the level of infected hosts after a period of ten years.

Results indicate that in order to achieve the best outcome, you should allocate your budget by setting $p_a = min(p_a^*, 1)$, $p_b = min(1, 1 - p_a^*)$, and $p_c = 1 - p_a - p_b$. That is, bed nets proved most cost-effective, followed by insecticide spraying. For the case when $p_a^* > 1$, full coverage for LLINs is not obtained. For the case when $p_a^* < 1$, but $p_b^* > 1 - p_a^*$, this means that full coverage for LLINs is obtained, but not for insecticide spraying.

The budget used in this study was 355.16 USD per month. With the given costs for each control measure, we have $p_a^* + p_b^* < 1$, but $p_a^* + p_b^* + p_c^* > 1$. In other words, full coverage with LLINs and insecticide spraying is obtained, but fully improving housing conditions for an entire village is impossible. After devoting the portions of your budget for LLINs and insecticide spraying (i.e., p_a^* and p_b^*), devote the remaining portion of the budget towards housing improvements $(1 - p_a^* - p_b^*)$.

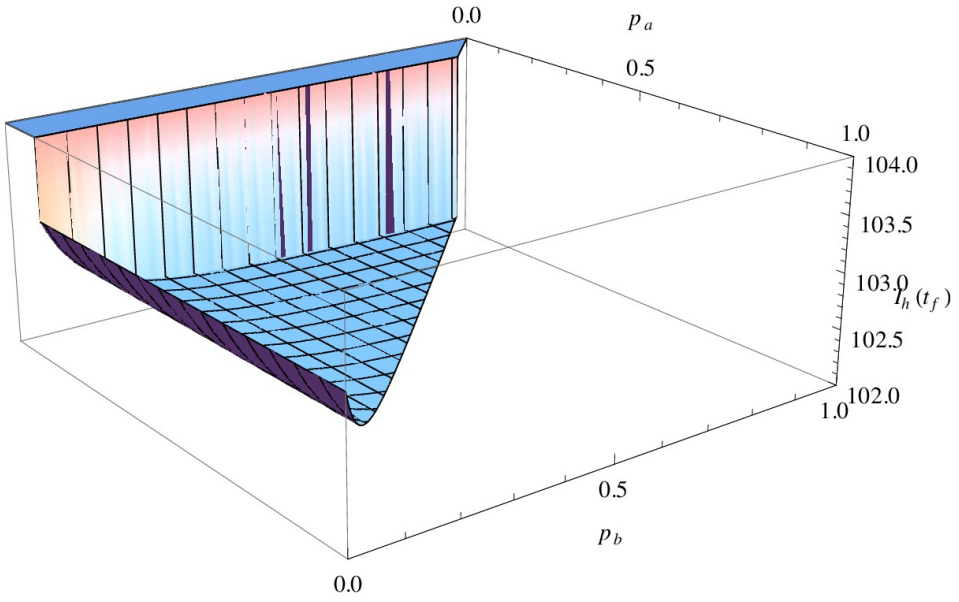

Figure 6: Shows the total infected host population I_H with each combination of control measures and the given estimated budget.

Figure 6 shows that there are high levels of infections when less than p_a^* of the budget is allocated towards bed nets. It also shows that infection levels remain consistent when more than p_a^* of the budget is allocated towards bed nets. This shows that allocating more than p_a^* to the bed nets is not cost-effective.

Due to the high cost of improving housing conditions, a significantly larger budget of 3636.61 USD must be implemented to allow for full coverage of all three control measures. This is nearly ten times the budget used in this model. Results show, however, that the total number of infections only decreases between five and ten percent in the long run compared to the original budget. The differential impact of all the extra housing improvements is minimal, so it's not cost-effective from a public health standpoint (even if it's highly desirable from the perspective of an individual family).

Conversely, infections skyrocketed when full coverage for LLINs is not obtained (i.e., $p_a^* > 1$). It was shown earlier that to ensure full coverage of LLINs, a minimum monthly budget of 36.61 USD must be allocated. For this specific budget, $p_a^* = 1$. With this minimal budget implemented, infections reached a minimum when $p_a = p_a^*$. More specifically, $\hat{R_0} < 1$ if $p_a = 1$. This shows that allocating a minimum budget equivalent to the value of p_a^* is extremely important in the long run in order to reduce the spread of infection.

If $p_b = p_b^*$ and a monthly budget of 303.26 USD is allocated towards control measures, an additional 266.65 USD must be allocated plus the minimum monthly budget from the previous case. For this budget, $p_a^* \approx 0.13$ and $p_b^* \approx 0.87$.This budget shows that $\hat{R_0}$ is at its lowest point when $p_a = p_a^*$ and $p_b = p_b^*$. For all t, $I_H(t)$ for the 303.26 USD per month budget was $\approx 9\%$ lower than $I_H(t)$ for the same t in the 36.61 USD per month budget.

One potential issue with the model is due to the high cost of improving housing conditions. Some potential solutions include finding cheaper materials than used in studies such as [21]. In fact, reducing the overall cost of these materials by approximately ninety-five percent only

caused a five percent decrease in the total infected hosts after each simulation. This confirms that improving housing conditions is the least important control measure out of three focused on in this study, whether or not full coverage for improving housing conditions is met.

4. Conclusions

It was shown that the control measures do in fact have a hierarchical importance when it comes to preventing the spread of Chagas disease. Ordered by the highest effective rate of preventing infections, they are LLINs, followed by insecticide spraying and improving housing conditions.

This model addressed a few different budget scenarios. If $p_a > p_a^*$, the number of infections doesn't decrease since a smaller portion of the budget is being allocated towards the other two control measures. This is a waste of the budget since each host will possess an LLIN at this point. Conversely, if $p_a < p_a^*$, then the infection rate is significantly higher since the contact rate between humans and vectors is not at its lowest. In another case, when $p_a^* < 1$ and $p_b^* > 1 - p_a^*$, the total number of infections is at its lowest point when p_a^* of the budget is allocated towards LLINs and the remaining portion of the budget is allocated towards p_b^*. Another case is when $p_a^* + p_b^* < 1$ and $p_c^* > 1 - p_a^* - p_b^*$, infections reached the lowest point when $p_a^* + p_b^*$ of the budget is allocated towards full coverage of LLINs and insecticide spraying. Finally, if $p_a^* + p_b^* + p_c^* \leq 1$, the full coverage is obtained for all three control measures. Numerical analysis indicated that the number of infections after ten years under a budget large enough to maximize all three control measures was reduced by less than 5% from that obtained when only *a* and *b* are maximized.

These different cost scenarios have shown that the case with the estimated budget when $p_a^* + p_b^* < 1$ and $p_c^* > 1 - p_a^* - p_b^*$ proved most effective at preventing infections in a cost effective manner.

For the model presented in this paper, it was found that $\hat{R_0} > 1$ without control measures. However, it was shown in both the unmetered and metered model that $\hat{R_0} < 1$ when LLINs are applied.

Specifically, it is possible to make $\hat{R_0} < 1$ by ensuring that at least $\hat{p_a}$ of the budget is allocated towards LLINs. More specifically, $\hat{R_0} < 1$ on $\left(\hat{p_a}, 1\right]$.

With the analysis performed on the cost effectiveness of all three control measures, it was shown that increasing the budget ten-fold to improve the housing conditions of each dwelling in the village only minimally reduced infections over a long period of time. If these details were presented in front of a committee, it could be argued that they would not approve the allocation of so much money to improving the conditions of a host's dwelling. Keeping a budget at a relatively small number annually (similar to the initial estimate) is most effective at reducing infections when comparing the cost-effectiveness of all three control measures.

The total number of infections for the estimated realistic budget ($p_a^* + p_b^* < 1$ and $p_c^* > 1 - p_a^* - p_b^*$) show that the total number of infections after ten years was approximately one-third that of other cases when fewer or no control measures reach full coverage. This lines up with other studies performed in Latin America [17, 21]. The effectiveness of LLINs and insecticide spraying are comparable to the levels shown in [15] and [1].

There are a few factors that contribute to the limitations of the budget involved in this study. One such factor is the size of the village and the contributions it makes to its country's GDP. Smaller villages get less budget allocated towards them than larger villages. There are also a large number of villages in a country. If a village makes small contributions relative to its size towards its country's GDP, it will likely not receive enough of the country's budget to control the disease.

Since insecticide can only safely be applied to a dwelling every 90 days without being fatal to a host [1], this limits how frequently a vector population can be controlled. This was the main factor in deciding the metering portion of the model.

Another factor that would contribute to limiting the budget is the cost of creating the control measure, shipping them, and distributing them. It is often the case that shipping and distributing costs are more than double that of creating the control measure [15].

Assumptions made about the model include the budget allocated for the village used in this

study. For specifics on how the budget was obtained, see [21]. Initial conditions were obtained from similar studies [3, 8] to compare results. Costs for each control measure were obtained from studies done using each control measure [1, 15, 21].

Future work includes introducing other control measures such as predators that feed on *Triatoma infestans*. Also, the current model can be extended to incorporate different stages of the vector's life cycle into the model. Vectors have more stages in their life cycle than were assumed for this model. For more information regarding these stages, see [3]. Extending the model to incorporate these different stages would allow for a more accurate representation of the contact rates, death rates, and reproduction rates of vectors.

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Appendix A

Endemic equilibrium of unmetered model

Solving for I_H^* and I_V^*, we set $I_H'(t) = I_V'(t) = 0$ and get the following:

$$0 = a(p_a)\beta_H I_V^* - \frac{a(p_a)\beta_H}{N_H^*} I_H^* I_V^* - (1-q)\mu_H I_H^* \tag{15}$$

$$0 = \frac{a(p_a)\beta_V}{N_H^*} N_V^* I_H^* - \Big[\frac{a(p_a)\beta_V}{N_H^*} I_H^* + m(a(p_a))\Big] I_V^* \tag{16}$$

From (15), we see that:

$$I_H^* = \frac{a(p_a)\beta_H I_V^*}{(1-q)\mu_H + \frac{a(p_a)\beta_H}{N_H^*} I_V^*}. \tag{17}$$

Plugging (17) into (16) yields:

$$0 = \frac{a(p_a)^2\beta_H\beta_V \frac{N_V^*}{N_H^*} I_V^*}{\mu_H(1-q) + \frac{a(p_a)\beta_H}{N_H^*} I_V^*} - \frac{a(p_a)^2\beta_H \frac{\beta_V}{N_H^*} {I_V^*}^2}{\mu_H(1-q) + \frac{a(p_a)\beta_H}{N_H^*} I_V^*} - m(a(p_a))I_V^*. \tag{18}$$

Thus, either $I_V^* = 0$, or we have:

$$0 = \frac{a(p_a)^2\beta_H\beta_V \frac{N_V^*}{N_H^*} - a(p_a)^2\beta_H \frac{\beta_V}{N_H^*} I_V^*}{\mu_H(1-q) + \frac{a(p_a)\beta_H}{N_H^*} I_V^*} - m(a(p_a)). \tag{19}$$

Then we have:

$$0 = a(p_a)^2\beta_H\beta_V \frac{N_V^*}{N_H^*} - a(p_a)^2\beta_H \frac{\beta_V}{N_H^*} I_V^* - m(a(p_a))\Big(\mu_H(1-q) + \frac{a(p_a)\beta_H}{N_H^*} I_V^*\Big). \tag{20}$$

Thus, solving for I_V^* yields:

$$I_V^* = \frac{a(p_a)^2\beta_H\beta_V \frac{N_V^*}{N_H^*} - \mu_H(1-q)m(a(p_a))}{\frac{a(p_a)\beta_H}{N_H^*}\Big(a(p_a)\beta_V + m(a(p_a))\Big)}. \tag{21}$$

Plugging (21) into (17), we obtain:

$$I_H^* = \frac{a(p_a)^2 \beta_H \beta_V \frac{N_V^*}{N_H^*} - \mu_H(1-q)m(a(p_a))}{\frac{a(p_a)\beta_V}{N_H^*}\left(\mu_H(1-q) + a(p_a)\beta_H \frac{N_V^*}{N_H^*}\right)} \tag{22}$$

Appendix B

Jacobian calculations from Infection Dynamics

From (10) and (11), we obtain the Jacobian:

$$J(I_H, I_V) = \begin{bmatrix} -\Big(\mu_H(1-q) + a(p_a)\beta_H \frac{I_V^*}{N_H^*}\Big) & a(p_a)\beta_H\Big(1 - \frac{I_H^*}{N_H^*}\Big) \\ a(p_a)\beta_V\Big(\frac{N_V^* - I_V^*}{N_H^*}\Big) & -\Big(m(a(p_a)) + a(p_a)\beta_V \frac{I_H^*}{N_H^*}\Big) \end{bmatrix}$$

Using the substitutions $\tilde{m} = m(a(p_a))$, $\tilde{\mu} = \mu_H(1-q)$, $\tilde{\beta_V} = a(p_a)\beta_V$, and $\tilde{\beta_H} = a(p_a)\beta_H \frac{N_V^*}{N_H^*}$, then the Jacobian becomes:

$$J(I_H, I_V) = \begin{bmatrix} -\Big(\tilde{\mu} + \tilde{\beta_H} \frac{I_V^*}{N_V^*}\Big) & \tilde{\beta_H} \frac{N_H^*}{N_V^*}\Big(1 - \frac{I_H^*}{N_H^*}\Big) \\ \tilde{\beta_V} \frac{N_V^*}{N_H^*}\Big(1 - \frac{I_V^*}{N_V^*}\Big) & -\Big(\tilde{m} + \tilde{\beta_V} \frac{I_H^*}{N_H^*}\Big) \end{bmatrix}$$

Applying the same substitutions to (21) and (22), we obtain that:

$$I_H^* = \frac{\tilde{\beta_H}\tilde{\beta_V} - \tilde{\mu}\tilde{m}}{\frac{\tilde{\beta_V}}{N_H^*}[\tilde{\mu} + \tilde{\beta_H}]} \tag{23}$$

and that:

$$I_V^* = \frac{\tilde{\beta_H}\tilde{\beta_V} - \tilde{\mu}\tilde{m}}{\frac{\tilde{\beta_H}}{N_V^*}[\tilde{m} + \tilde{\beta_V}]} \tag{24}$$

It is easily seen that $trace(J) < 0$. More specifically,

$$tr(J) = -\Big(\tilde{\mu} + \tilde{m} + \tilde{\beta_H}\frac{I_V^*}{N_V^*} + \tilde{\beta_V}\frac{I_H^*}{N_H^*}\Big) \tag{25}$$

It can also be seen that $det(J) > 0$. More specifically,

$$\begin{aligned} det(J) &= \Big(\tilde{\mu} + \tilde{\beta_H}\frac{I_V^*}{N_V^*}\Big)\Big(\tilde{m} + \tilde{\beta_V}\frac{I_H^*}{N_H^*}\Big) - \tilde{\beta_H}\tilde{\beta_V}\Big(1 - \frac{I_H^*}{N_H^*}\Big)\Big(1 - \frac{I_V^*}{N_V^*}\Big) \\ &= \Big(\tilde{\mu} + \tilde{\beta_H}\frac{I_V^*}{N_V^*}\Big)\Big(\tilde{m} + \tilde{\beta_V}\frac{I_H^*}{N_H^*}\Big) - \tilde{\mu}\tilde{m} \\ &= \tilde{\mu}\tilde{\beta_V}\frac{I_H^*}{N_H^*} + \tilde{m}\tilde{\beta_H}\frac{I_V^*}{N_V^*} + \tilde{\beta_H}\tilde{\beta_V}\frac{I_V^*}{N_V^*}\frac{I_H^*}{N_H^*} \end{aligned}$$