Efficiency of self-control strategies on the spread of the insect vector of Chagas disease.

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1 Summary

In this paper we analyze the effect of a new strategy of control of the insect vector for Chagas disease in a rural community. The mathematical analysis is concentrated on the required frequency between controls required to eradicate the insect of the community.

Keywords: *Chagas disease, Spatial stochastic models.*

2 Introduction

Chagas disease or American trypanosomiasis is caused by a protozoan, *Trypanosoma cruzi* Chagas, transmitted mainly by *Triatoma infestans* (Klug). The disease is widely distributed in South America, mainly in Argentina, Bolivia, Brazil, Chile, Paraguay, Peru and Uruguay. The incurable lesions of Chagas disease develop in one third of those infected, estimated 10-20 years after the initial acute phase. These include chronic cardiophaty (27% of infected), chronic digestive lesions (6%) and neurological disorders (3%). Individuals with severe chronic disease become progressively sick and die generally as a result of heart failure. It is estimated that 25 % of the total population of Central and South America are at risk, with one million new cases each

year. It is also estimated that the disease produces 45,000 deaths annually, and that 16-18 million people are currently infected. Of these, 2-3 million may have already developed chronic complications and over 3 million are still in the incubation period. (WHO, 1997)

Success in eradication of Chagas disease depends mainly in the eradication of its vectors. It is estimated that half of the cases of the disease were transmitted by the vector *T. infestans* (Gorla, 1989). The type of construction of a house is determinant for the environment of *T. infestans*, thus control strategies are based mainly in insecticide spraying in houses. In Argentina, this type of control was done in the past through periodic campaigns from official institutions but recently, this changed and now households are provided with the necessary tools to perform a periodic control.

Using a program to simulate the spread of the vector through a community of houses, we observed that the "self-control" was less efficient than a periodic campaign, even if the control was done at random intervals whose expected value was much smaller than that of the campaigns. The problem seems to arise from the heterogeneity in the times of spraying in the community. In this paper we analyze among other factors, how the frequency of control affects the probability of erradication of the vector from the community.

3 Review

Rabinovich (1985) Developed a deterministic model consisting of three differential equations describing changes in vector and host populations and the relationship between the two. The model was used to evaluate three types of control: spraying, through house improvement and biological control due to the parasitoid *Ooencyrtus trinidadensis*. The effectiveness of the control strategies were evaluated in terms of (1) the number of vectors per house, (2) the proportion of infected vectors, (3) the number of infected people and (4) a safety

factor to measure the number of weeks between infected bites. It was concluded that a satisfactory control could be achieved by annual spraying, household collection of bugs or by a combination of house improvements, but it appeared that a dramatically better control could be achieved by use of biological control, as long as the assumptions made on the form of attack of the parasitoid were fulfilled. Rabinovich *et. al.* (1990) analyzed numerically a population-dynamics model for the two main vectors of Chagas disease: *T. infestans* and *Rhodnius prolixus.* The model included the infection of bugs with the parasite *T. cruzi*, human and animal infection from bugs, migration between houses and the environment as well as the type of house. The main parameters affecting stability behavior of the vector populations were (a) the threshold nymphal density at which irritation of the host starts, (b) female density, (c) number of hosts available and (d) the emigration rate. Parameters (a) and (b) combined were determinant in the stability behavior of the vector population, from a stable point equilibria to a limit cycle. Velasco-Hernández (1992) showed that if density dependent factors are ignored the equilibrium is asymptotically stable, whereas if this is included as well as stage-structure in the cycle life of the vector, limit cycle solutions may be obtained.

Regarding dispersion patterns of *T. infestans,* Schofield (1985) studied its dispersive flight and derived expressions for the distribution function of flight duration and distance. Both a linear flight as well as a Brownian motion pattern were considered. Simple expressions for the probability of infestation of a specified target house from a specified source house, as well as the probability that a particular house will not be infected by a given house in a fixed period of time were derived.

4 A model for spread of the vector of Chagas disease.

The dynamics of the spread of the vector of Chagas disease depends on several factors, for instance the type of houses and their distribution in the community as well as the type of control used. The localization of the houses and the presence of natural barriers affects the dispersion of the insect, whereas the structure of the houses affects the "carrying capacity" of the insect in every house, thus conferring more or less "infectiveness" to houses. On the other hand, the type of control could be either a periodic campaign in all houses of the community or a self-control, in which every household is provided with the tools to perform a chemical control. In this case the control is performed at random intervals. The time between applications could have a different distribution for every house, and they are assumed to be independent within and between houses.

Heterogeneity in control affects the possibility of a total eradication in the community: after performing stochastic simulations in communities with different degrees of incidence of the vector, it was found that even if the control was performed in every house at random (small) intervals from a common exponential distribution, the insect could not be eradicated because there were always susceptible houses.

Since heterogeneity in control seems to be a driving factor, and given that this is the current -official- strategy to follow, this analysis concentrates in the calculation of the probability of eradication with self-control under different scenarios, including heterogeneity in control and in the carrying capacity of houses.

In our model there are four possible states for a particular house: susceptible, latent, infective and treated. Susceptible houses can be occupied by *T. infestans* at any time. Latent houses have *T. infestans* but their density is too low and competition among them is not strong, and it is assumed that the emigration rate of *T. infestans* is zero. This houses become infective at

rate δ, and then each produces *T. infestans* at a given rate α_i, $i = 1, 2, 3, \ldots, d$, where α_i is a house property. Control is performed in every latent or infective house at rate μ_j, $j = 1, 2, 3, \ldots c$, here μ_j is also a household property. Both α_i and μ_j could be associated or not.

Control has an efficiency p_0 which means that in a proportion p_0 of houses treated the *T. infestans* will be eradicated. Once a house is treated it remains immune for a random period of time and loses immunity at rate ν, becoming susceptible again. In real life situations, infection depends not only on the current number of infective and susceptible houses, but also in the different migration categories of the infective houses. Moreover, the localization of both type of houses in the community is important since the probability that an infected house will infect a susceptible house depends on the distance between the two houses.

5 The expected number of secondary infections.

The interest in the calculation of the expected value for the number of secondary cases of infections per infective individual is related to the evolution of basic branching process: consider a process of this type in which an individual gives birth to k individuals with probability P_k, $k \geq 0$, and let θ be the probability that a population that starts with one individual will go to extinction. Thus the following equality holds:

$$\theta = \sum_{k=0}^{\infty} \theta^k P_k \tag{4.1}$$

It can be shown that if $\mathbf{E}\{k\} \leq 1$ then $\theta = 1$. Therefore the branching process has a *threshold* value at 1. Several authors (see Bartlett (1955) and Kendall (1956)) have shown that approximating epidemic process or in general linear birth death processes is reliable provided that $N \to \infty$. The basic assumption when approximating an epidemic process with a branching

process is that the expected number of secondary infections is the same regardless of the current state of the process (infected, removed, latent, etc.), which does not hold especially if shortage of susceptibles reduces significatively the expected number of newly infections.

Perhaps the most illustrative example on how the reduction in the number of susceptible individuals affects the dynamics of a process, even if the average offspring size is greater than one, is provided by Durret and Levin (1992) with the basic contact process in one dimension. In this process there is a linear array of cells, some of them being occupied. An occupied cell occupies its two surrounding cells if it survives, which occurs with probability $(1-q)$. Every cell reproduces at discrete steps, thus, starting with one occupied cell, the expected number of occupied cells at the next step is $3(1-q)$. Although it seems enough that a q-value smaller than 2/3 will guarantee a survival of the population, this is not true due to a shortage of free cells in the next step which reduces the average offspring size. Numerical evaluations give a threshold value for $q \approx 0.47$, for an average offspring size of 1.59.

Thus, for finite populations, the average number of infections per individual has to be greater than one for the epidemic to survive. This average has been called the *threshold value* and for SIR models, it has been numerically estimated to be (See Nåsell, 1995) of approximately $1 + K_r/N^{\frac{1}{3}}$ with K_r a positive constant that depends of the initial population size.

A great deal of effort has been done in the calculation of the *threshold value* for different epidemic models. One fact that is frequently overlooked in epidemic processes is that a necessary and sufficient condition for the epidemic to extinct whithout reaching a large number of infections, is that the expected number of secondary infections caused by an infective individual among a large population of susceptibles be smaller than 1, regardless of the *threshold value*. This is of particular interest for practical applications, since very rarely the control measures are so precise to be directed to reach the boundaries of the threshold Thus, in practice, it will suffice

to guarantee an expected number of new infections smaller than one. In addition, for moderately large populations the threshold value approaches to 1 fast.

Then, if the infection rate is λ and X, the duration of the infection period has distribution $f(x)$ with $\mathbf{E}[X] = \mu^{-1}$ then the distribution of the number of secondary infections K is

$$P[K = k] = \int_0^\infty \frac{e^{\lambda t}(\lambda t)^k}{k!} f(t)\, dt,$$

here, we assume that infections occur at the points of a Poisson process with rate λ. The expected value of the number of infections is then

$$\mathbf{E}[\mathbf{E}[K|X]] = \mathbf{E}[\lambda x] = \lambda \mathbf{E}[X] = \lambda/\mu. \tag{4.2}$$

Thus, as long as contacts occur according to a Poisson process, the expected number of secondary cases of infection depends on the distribution of X only through its first moment. The assumption of exponential distribution between contacts can be relaxed, but in this case $\mathbf{E}[K|X]$ becomes $M(x)$, the renewal function evaluated at x. Since $M(x)$ is linear in x only if contacts occur at the points of a Poisson process, (4.2) does not hold anymore.

As previously stated, if the expected number of secondary infections caused for an initial infective individual in a population of susceptibles, under a given strategy, is less than one, the epidemics will die out and the strategy can be considered appropriate. The parameters in the model are defined formally:

$\alpha_i =$ Migration rate of females of *T. infestans* in a house with migration category i, $i = 1, 2, \ldots d$.

$\mu_j =$ Control rate in a house with control category j, $j = 1, 2, \ldots c$.

$\delta =$ rate at which a latent house becomes infective.

ν = rate at which a treated house becomes susceptible.

p_0 = Probability of eradication in a house is treated.

Here it is assumed that a latent and infective houses are prone to control. This is because it is assumed that in a given household the decision on whether treating or not depends on detecting the presence of *T. infestans*. It is important to remark what happens in the model to the proportion $(1 - p_0)$ of houses in which the *T. infestans* could not be eradicated in a given treatment period: if the house is infective and the treatment is effective, then the house undergoes an immune period with mean ν^{-1} followed by a susceptible state. If the treatment fails, then it is assumed that the population of *T. infestans* is only decreased and it will enter a latent state again after going trough the immune period. The same applies to latent houses.

If we assume that a migrating *T. infestans* that has survived will always find a susceptible house, then the infection rate of a house on migration category i is $\lambda_i = \phi\alpha_i$, where ϕ is the proportion of female migrating insects that survives to make a colony.

The distribution of the number of houses under each emigration category α_i and control category μ_j is also relevant for the outcome of the epidemic. Two cases are considered: a) a single category for both emigration and density, b) three categories for emigration and control each, whose distribution in the community is either dependent or independent. The last case is motivated because of the suspicion that houses with higher migration rate are associated with lower control rate.

5.1 Assessing the efficiency of the strategy: the case of a single migration and control categories.

In this case, all houses have the same rate α of production of *T. infestans* – and thus there is a common infectivity λ – and in every latent or infective house the control is performed at rate μ. Let K be the number of infected houses during the infectious life of the infected house. Recall that due to defective treatments then the house could become latent again after a period of immune period. Using first step analysis we have:

$$\mathbf{E}[K] = \mathbf{E}[K|T < L]P(T < L) + \mathbf{E}[K|T > L]P(T > L),$$

where $T < L$ stands for the event "A treatment occurs before the latent period ends" and $T > L$ the complementary event. If latency is exponentially distributed then

$$P(T < L) = \mu/(\mu + \delta),$$

$$P(T > L) = \delta/(\mu + \delta), \tag{4.3}$$

and

$$\mathbf{E}[K|T < L] = \mathbf{E}[K](1 - p_0),$$

$$\mathbf{E}[K|T > L] = \lambda/\mu + \mathbf{E}[K](1 - p_0)\,, \tag{4.4}$$

the first equality in (4.4) because by assumption, with probability $(1 - p_0)$ the vector in the house will not be completely eradicated, and the house will be infective again after some finite time. Therefore,

$$\mathbf{E}[K] = \mathbf{E}[K](1 - p_0)\ P(T < L) + \Big[\lambda/\mu + \mathbf{E}[K](1 - p_0)\Big] P(T \geq L),$$

which simplifies to

$$\mathbf{E}[K] = P(T > L)\frac{\lambda}{\mu p_0}, \quad p_0 > 0 \tag{4.5}$$

that is,

$$\mathbf{E}[K] = \frac{\delta\,\lambda}{(\delta+\mu)\,\mu\,p_0}, \quad p_0 > 0 \tag{4.6}$$

Clearly, for a control strategy to work properly, one needs

$$\mu > \frac{1}{2}\left(\frac{\sqrt{\delta}\,\sqrt{p_0\,\delta + 4\lambda}}{\sqrt{p_0}} - \delta\right). \tag{4.7}$$

If the efficiency p_0 is 1, then

$$\mu > \frac{1}{2}\left(\sqrt{\delta}\sqrt{\delta + 4\lambda} - \delta\right).$$

Non exponential distribution for the Latency.

Now consider the case in which the duration of the Latency is not exponential, but instead we use a distribution with non-constant hazard rate, and investigate how this affects (4.7). Consider the case in which the duration of the latency period follows a Gamma(r,r δ), so that the mean is still δ^{-1}. While (4.5) remains unchanged, (4.3) is now:

$$P(T > L) = \left(\frac{\mathrm{r}\,\delta}{\mathrm{r}\,\delta + \mu}\right)^{\mathrm{r}},$$

thus $P(T > L;\ \mathrm{r} > 1)$ is smaller than $P(T > L; \mathrm{r} = 1)$. If $\mathrm{r} < 1$ the relationship is reversed. The expected number of infections becomes then:

$$\mathbf{E}[K] = \left(\frac{\mathrm{r}\delta}{\mathrm{r}\delta + \mu}\right)^{\mathrm{r}} \frac{\lambda}{\mu p_0}, \quad p_0 > 0. \tag{4.9}$$

The probability of extinction under complete efficiency.

If $\mathbf{E}[K] > 1$, it is important to asses the probability that the spread of the vector will be stopped. Here, we assumed a Gamma distribution for the duration of the latency period and that $p_0 = 1$.

Starting in the latency period, the house may enter the infectious period and then undergo a treatment. Let X be the time to next treatment in a latent house, and Y the duration of the latency state (under no control). Let $g(x)$ and $f(y)$ be the respective probability density functions.

Define V the duration of the infectious period, where

$$V = \begin{cases} x - y & x > y \\ 0 & x \leq y \end{cases}$$

Defining the density function of V as $h(v)$, we have:

$$h(v) = \int_0^\infty g(y + v) f(y)\, dy$$

$$= \int_0^\infty \mu e^{-\mu(y+v)} f(y)\, dy$$

$$= \mu e^{-\mu v}\, \mathbf{E}[e^{-\mu y}]$$

$$= \mu e^{-\mu v}\, \mathbf{M}_Y(-\mu).$$

Using (4.9), we have that probability mass function of K, the number of infections per infective individual is:

$$P(K=k) = \int_0^\infty P(K=k|V=v)h(v)\, dv + I_{[k=0]}P[V=0]$$

$$= \int_0^\infty \frac{e^{-\lambda v}(\lambda v)^k}{k!} \mu e^{-\mu v}\, \mathbf{E}[e^{-\mu y}] dv + I_{[k=0]}P[V=0]$$

which simplifies to:

$$P(K=k) \;=\; \mathbf{E}[e^{-\mu y}]\; \frac{\mu}{\lambda} \left(\frac{\lambda}{\lambda+\mu}\right)^{k+1} + I_{[k=0]}P[V=0]. \tag{4.10}$$

If $Y \sim \exp(\delta)$ then

$$\mathbf{E}[e^{-\mu y}] = \delta/(\delta+\mu)\,,$$

$$P[V=0] = P[T<L] = \mu/(\mu+\delta).$$

Then (4.10) becomes:

$$P(K=k) = \frac{\mu}{\lambda}\, \frac{\delta}{\delta+\mu} \left(\frac{\lambda}{\lambda+\mu}\right)^{k+1} + I_{[k=0]} \frac{\mu}{\mu+\delta}.$$

Using (4.1) we have

$$\theta = \frac{\mu}{\mu+\delta} + \sum_{j=0}^{\infty} \frac{\mu}{\lambda} \frac{\delta}{\delta+\mu} \theta^j \left(\frac{\lambda}{\lambda+\mu}\right)^{j+1}.$$

Solving for θ gives:

$$\theta = \text{Min}\left\{1, \frac{\mu(\delta+\lambda+\mu)}{\lambda(\delta+\mu)}\right\}. \tag{4.11}$$

Numerical evaluations of relevant expressions in this section will be performed later.

5.2 Assessing the efficiency of strategies: the case of several migration and control categories.

If there are several migration categories, the population is heterogeneous with respect to the infectiveness. Also, it is heterogeneous in the control time, and it is expected that both types of heterogeneity influence the optimum control rate.

Let $C(i,j)$ the proportion of houses in migration category i and control category j. Then

$$\mathbf{E}[K] = \sum_i \sum_j C(i,j) \frac{\delta \lambda_i}{(\delta+\mu_j)\mu_j p_0}, \quad p_0 > 0.$$

If $p_0 = 1$,

$$P(Extinction) = \sum_i \sum_j C(i,j) \theta_{ij},$$

where θ_{ij} is given by (4.11) with $\lambda = \lambda_i$ and $\mu = \mu_j$. Note that if $C(i,j) = p_i\, q_j$, where p_i is the proportion of houses with migration category i and q_j is that of the houses in control category j, then both factors (migration and control) are independent, and we have

$$\mathbf{E}[K] = \sum_i \sum_j p_i\, q_j \frac{\delta\, \lambda_i}{(\delta+\mu_j)\, \mu_j\, p_0}, \quad p_0 > 0$$

$$= \sum_i p_i\, \lambda_i \sum_j q_j \frac{\delta}{(\delta+\mu_j)\, \mu_j\, p_0}, \quad p_0 > 0$$

6 Numerical evaluations.

Numerical calculations require some degree of information on the parameters, and there are very few field studies with the aim of estimating the parameters involved here. Regarding migration parameters, these have been mostly under controlled conditions, and the "latency" period depends heavily on the type of house. Furthermore, no information is available on the distribution of the migration and control categories, and it is reasonable to expect this to be highly variable with geographicak regions. Here, we attempt to provide with a general framework that allows for input of adecuate parameters.

Castañera [G] has estimated the female migration rate δ to be approximately 0.68 per day (Lit), and the duration of latency to be approximately 180 days, but there is no information on the probability of survival of the migrating females. Here we use this migration rate and assume the survival probability to be one, and vary the frequency of control as well as the latency period.

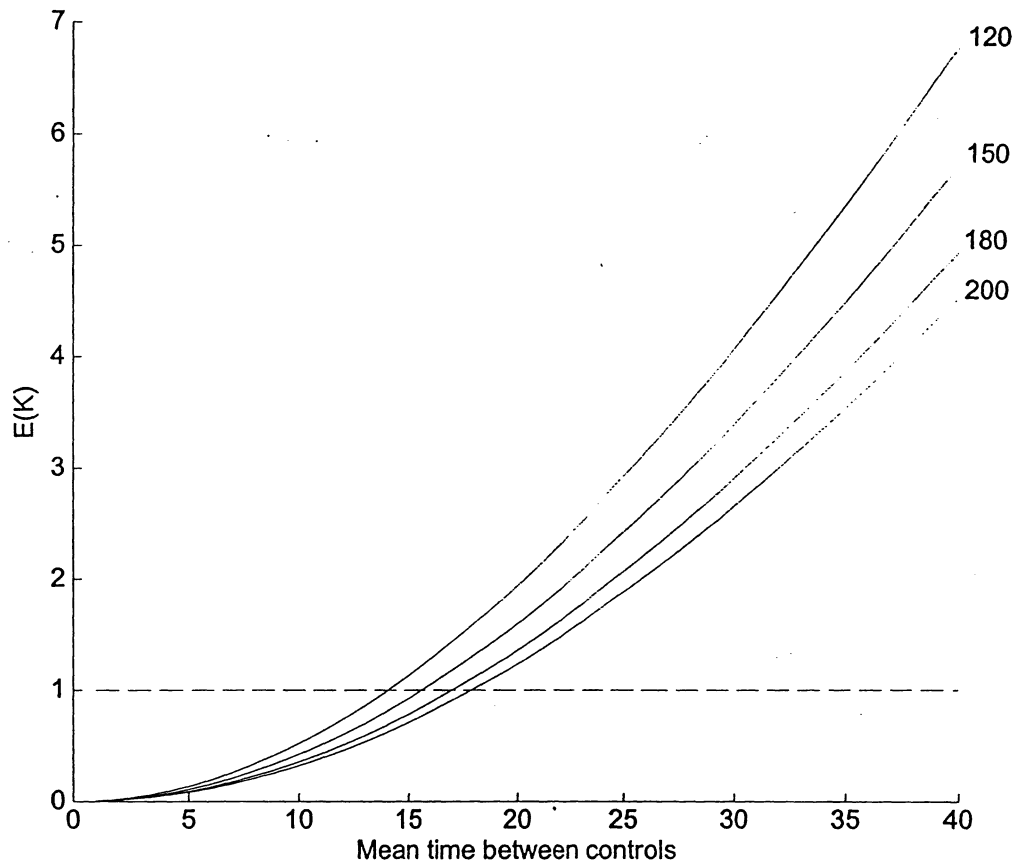

Figure 4.1 Mean time between controls required to achieve $\mathbf{E}[K] < 1$ for $p_0 = 1$ and $\lambda = 0.68$. Numbers to the right indicates duration of latency. Latency is assumed to be Exponentially distributed.

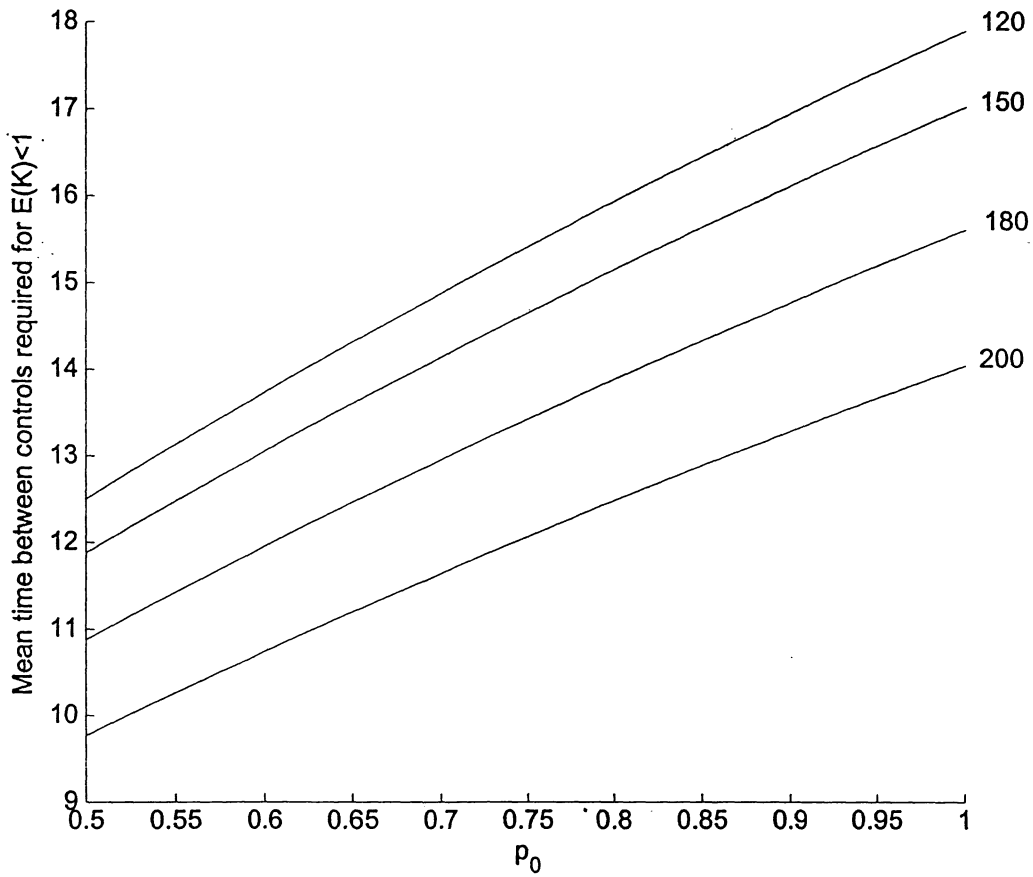

Figure 4.2 Effect of p_0 on the frequency of control required to achieve $\mathbf{E}[K] < 1$ for $\lambda = 0.68$. Numbers to the right indicates duration of latency.

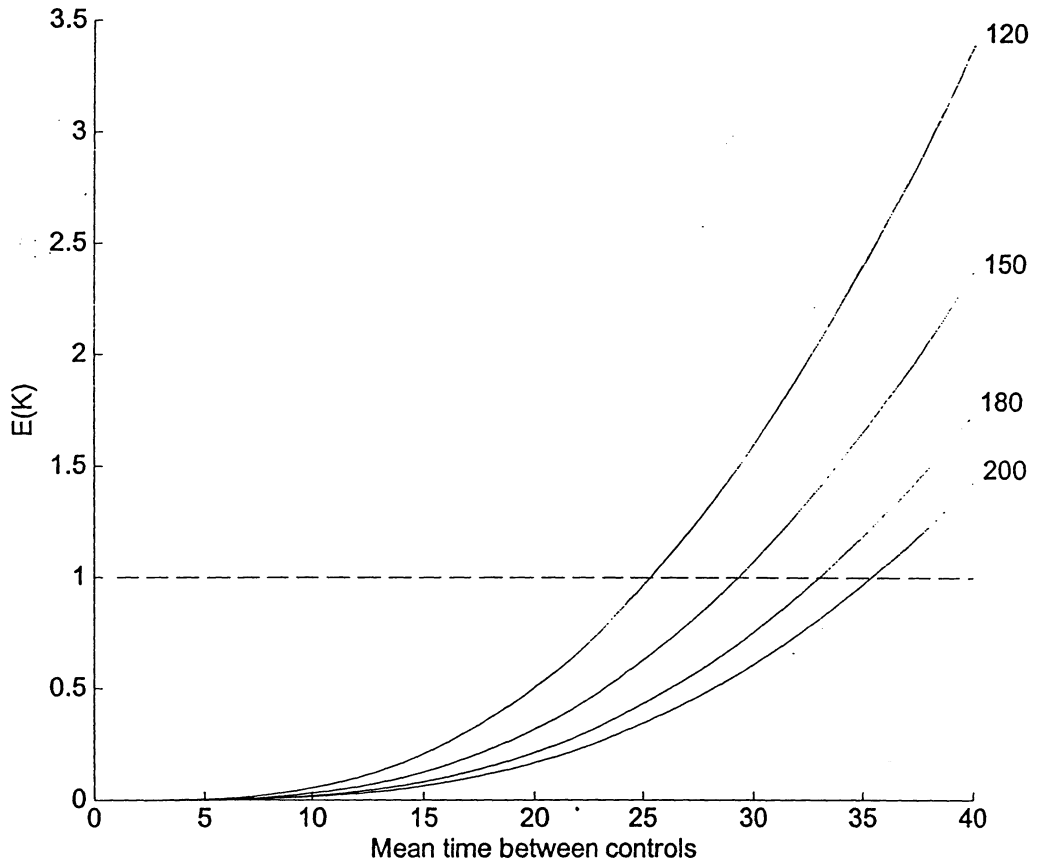

Figure 4.3 Mean time between controls required to achieve $\mathbf{E}[K] < 1$ for $p_0 = 1$ and $\lambda = 0.68$. Numbers to the right indicates duration of latency. Latency is assumed to be Gamma(3,3 δ).

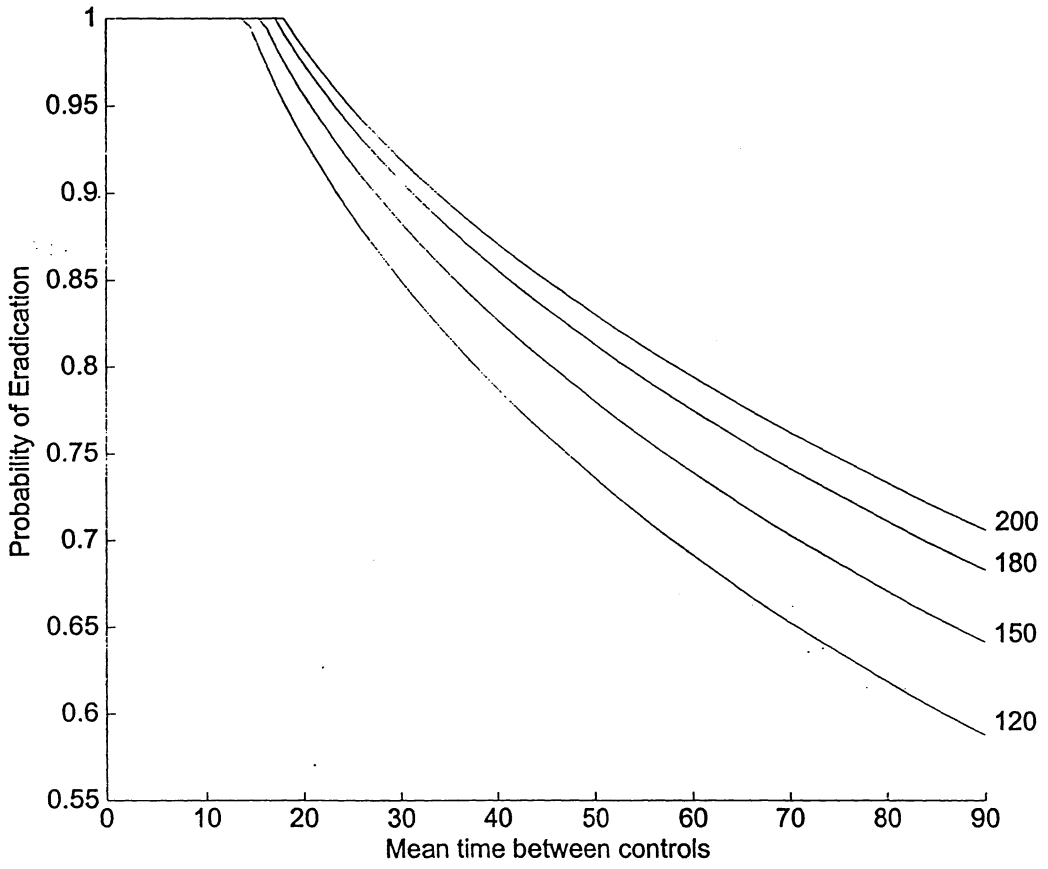

Figure 4.4 Effect of the time between controls on the probability of eradication. Numbers to the right indicates duration of latency. Latency is assumed to be Exponentially distributed.

Fig 4.1 shows how $\mathbf{E}[K]$ is affected by the frequency of control and latency according to (4.6). Four durations of latency were used: 120, 150, 180 and 200 days, whereas the frequency of control varies between 1 and 40 days. In this simulations p_0 is set to one. The dotted line marks the value $\mathbf{E}[K] = 1$. It can be seen that the range of control for these values has to be around two weeks in order $\mathbf{E}[K] < 1$.

Fig. 4.2 also shows the effect the efficiency p_0 on the frequency of control required to achieve $\mathbf{E}[K] < 1$, for an exponential distribution of latency. Fig. 4.3 is similar to 4.1 except that here the latency fololows a Gamma distribution. This is expression (4.9) with a Gamma(3,3 δ) distribution of the latency, with δ^{-1}set to 120, 150, 180 and 200 days. The mean durations are the same than for Fig 4.1 but the variances are one third smaller. Using this parameters the expected time between two treatments can be increased by a factor of two.

Fig 4.4 depicts how the probability of erradication θ is affected by the duration of latency and frequency of control, according to 4.11, under complete efficiency of treatment ($p_0 = 1$) and a migration rate $\lambda = 0.68$. The latency durations were assumed exponential with means $\delta^{-1} = 120$, 150, 180 and 200 days. As expected, the four lines start at $\theta = 1$ and start decreasing when the frequency of control makes $\mathbf{E}[K] > 1$, which matches the value shown in Fig. 4.1. In general, it can be seen that the expected time between treatments has to be smaller than 30 days for the probability of erradication to be about 95 percent, for latency durations smaller than 200 days. Fig 4.4 shows the frequency required to make $\mathbf{E}[K] < 1$ as a function of p_0, with δ and λ fixed. From 4.6 this function is

$$f(p_0) = 2\left(\frac{\sqrt{\delta}\,\sqrt{p_0\,\delta + 4\lambda}}{\sqrt{p_0}} - \delta\right)^{-1}$$

for δ small, the previous expression can be approximated with

$$f(p_0) = \sqrt{\frac{p_0}{\delta \lambda}}$$

7 Discussion

For the set of parameters used, the model predicts that very small intervals between treatments are required in order to eradicate the vector from a community. Even if the tratement is completely efficient at the household level ($p_0 = 1$), the average time between controls is smaller than two weeks, which is impractical for most communities. If a campaign is more effective than self control depends strongly on the coverage of the campaign and the efficiency in every house. If the goal is to reduce the loss of human lives and costs, altough a single campaign could be more expensive than self-control, on the long run it could be the opposite. It seems that an alternative could be to achieve some level of coordination in the households regarding the time of self-control, which will make it similar to a campaign, but the feasibility of this depends on particular characteristics of the communities, and detailed studies are required.

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