Modeling Chagas disease in Chile: From vector to congenital transmission

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ABSTRACT

Chagasí disease is a human health problem in Latin America. It is highly prevalent in northern Chile between the Arica-Parinacota and Coquimbo regions, with reported incidence of 3–11/100000 inhabitants and mortality of 0.3–0.4/100000. The interruption of vector transmission was reported in 1999 by means of the elimination of the primary vector, *Triatoma infestans*, from human dwellings, thus the epidemiologic dynamics of this disease should be modified. Here we model the dynamics of Chagasí disease based on previous models for vector and congenital transmission, propose a model that includes both transmission forms and perform simulations. We derive useful relationships for the reproductive number (R_0) showing that it may be expressed as the sum of the vector (R_{0V}) and congenital (R_{0C}) contributions. The vector contribution is larger than the congenital one; without the former Chagasí disease vanishes exponentially in two to three generations. Sensitivity analyses showed that the main parameters that intervene are the human bite rate, the density of vectors per human and the mortality rate of the insect vectors. Our model showed that the success of the eradication of Chagasí disease is based on the interruption of domestic transmission. Once this is obtained, the control strategies should focus on avoiding the domiciliation of wild vectors, re-colonization by the primary vector, and an adequate coverage of congenital case treatment.

1. Introduction

Chagasí disease is one of the most important neglected diseases affecting Latin America, considered recently as an emergent disease in America and some countries of Europe (Jackson et al., 2009; MINSAL, 2014). Annual incidence varies between 28000 and 56000 cases (OPS/OMS, 2012) and the mortality between 10000 and 14000 annually (Hotez et al., 2008, 2012), affecting 6–11 million individuals (Cucunubá et al., 2016) with 65–100 million people at risk (Fuentes et al., 2012; MINSAL, 2014). The endemic area in Chile extends between the Arica-Parinacota (18°30′S) and Libertador Bernardo OíHiggins (34°36′S) regions, with 873,415 people at risk. Annual incidence varies between 3/100000 and 11/100000

habitants, and the mortality is about 0.3–0.4/100000 (MINSAL, 2014).

Chagasí disease is produced by the protozoan *Trypanosoma cruzi*, transmitted by blood-sucking bugs of the Triatominae subfamily (Hemiptera: Reduviidae) (Lent and Wygodzinsky, 1979; Schofield, 1994; Carcavallo et al., 1998; Schofield and Galvão, 2009). There are four species in Chile: *Triatoma infestans*, *Mepraia spinolai*, *M. gajardoi* and *M. parapatrica*; *T. infestans* is the domiciliary vector (Shenone et al., 1980, 1989; Apt and Reyes, 1986a,b, 1990; Canals et al., 1991a,b, 1992; Ehrenfeld et al., 1998; Botto-Mahan et al., 2002, 2005a,b) and the main species responsible for the prevalence in this country and some others of South America (Canals et al., 1993, 1998, 1999; Ordenes et al., 1996). There are other forms of transmission such as congenital, oral, organ transplantation and accidental laboratory exposure (Da Silva et al., 1968; Nóbrega et al., 2009; Apt et al., 2008a,b; MINSAL, 2014). However, Uruguay since 1997, Chile since 1999 and Brazil since 2006 have been recognized as countries that eliminated vector transmission of Chagasí disease (Raimundo et al., 2010; MINSAL, 2014) which was a consequence of

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efficient eradication campaigns of the domiciliary vector (Telleria and Tibayrenc 2010; Razzi et al., 2010, 2012).

The epidemiological dynamics of Chagasí disease should be changing in these countries from vector to congenital transmission as a consequence of *T. infestans* elimination, and impacting the reproductive number (R_0) of this disease (Massad, 2008; Raimundo et al., 2010; Cordovez et al., 2014).

Mathematical models have the potential to demonstrate dynamic changes that occasionally may be complex. These models, coupled to the dialog with decision-makers may be a great contribution in the approach to the prevention and control of diseases (Heesterbeek et al., 2015). For Chagasí disease several models considering diverse topics have been developed, contributing to address control measures (Nouvellet et al., 2015). These models consider vector transmission, congenital transmission, chronicity, domestic and wild transmission and migration, among others (Rabinovich and Rossell, 1978; Canals and Cattan, 1992; Inaba and Sekine, 2004; Cherif et al., 2008; Das et al., 2009; Raimundo et al., 2010; Spagnuolo et al., 2011; Rascalou et al., 2012; Coffield et al., 2013; González-Parra et al., 2015; Peterson et al., 2015). The goal of this study was to model the transition from a vector to a congenital transmission of Chagasí disease appropriate for Chile, simulating the dynamics and deriving simple and useful relationships to understand the process and to implement appropriate control measures.

2. Modeling

The model is based on the integration of two previous models of Chagasí disease transmission; the first for vector transmission (Canals and Cattan, 1992) and the second for congenital transmission (Raimundo et al., 2010).

Three interacting populations were considered: the human population (males and females), the populations of domestic and wild animals that constitute the reservoir and the population of *T. infestans*, because the wild vectors have little importance in Chile (Canals et al., 1993, 1998, 1999). The female human population was divided into the following compartments: susceptible adults (S_F), susceptible children (S_f), infected female children born to chagasic mothers (I_{f1}), untreated and infected female children (I_{f2}) and infected women (I_F). The equivalent compartments in males were: S_M, S_m, I_{m1}, I_{m2} and I_M. For animal (A) and vector (V) populations, infected (I_A and I_V. respectively) and susceptible ($A - I_A$ and $V - I_V$, respectively) compartments were considered. The flow diagram of the transmission of Chagas disease is shown in Fig. 1. The following parameters were considered: probability of a chagasic individual reaching and reproduce at reproductive age (m), transfer rate of female children to reproductive age (σ), transfer rate of male children to reproductive age ($\sigma\acute{\imath}$), mortality rates of humans, vectors and animals (μ, μ_v and μ_a, respectively), birth rate of susceptible and infected humans (λ and $\lambda\hat{\imath}$), proportion of females in the population (k), probability of chagasic children born to chagasic mothers (p), treatment rate (ζ), proportion of male and female children treated (r, q), specific mortality rate of Chagas' disease in adults (α_1), specific mortality rate in children (α_2), bite rates in humans (b_h) and animals (b_a), proportion of infectious bites by an infected vector (f), proportion of potentially infectious bites that a susceptible vector makes on an infected host ($f\hat{\imath}$), carrying capacity of vectors in humans (K), intrinsic growth rate of the vector population (r_v) and the ratio between the animal reservoir biomass and human biomass (ν).

Based on Fig. 1, the dynamics of the vector and congenital transmission were formalized by a system of ordinary differential-algebraic equations. For human populations, males and females, following Raimundo et al. (2009) we consider three transitional

stages: newborn pre-vaccine, children growing up and adults. In the case of susceptible humans the first stage makes no sense and was not included. The sub-indexes (m_1, m_2) and (f_1, f_2) indicate transitional stages from birth to the reproductive age in males and females, respectively. For these compartments the equations are:

$$\frac{dI_F}{dt} = (m\sigma)I_{f2} - (\mu + \alpha_1) + \frac{b_h I_V S_{f1}}{N}$$

$$\frac{dI_{f1}}{dt} = \lambda k\grave{p} I_F - (\mu + \zeta) I_{f1}$$

$$\frac{dI_{f2}}{dt} = \zeta(1-q)I_{f1} - (m\sigma + \mu + \alpha_2)I_{f2} + \frac{b_h f I_V S_{f1}}{N}$$

$$\frac{dS_f}{dt} = \grave{\lambda}k(1-p)I_F + \lambda k S_F + \zeta q I_{f1} - (\mu + \sigma)S_f - \frac{b_h f I_V S_{f1}}{N}$$

$$\frac{dS_F}{dt} = \sigma S_f - \mu S_F - \frac{b_h f I_V S_F}{N}$$

$$\frac{dI_M}{dt} = (m\grave{\sigma})I_{m2} - (\mu + \alpha_1)I_M + \frac{b_h f I_V S_M}{N}$$

$$\frac{dI_{m1}}{dt} = \grave{\lambda}(1-k)p I_F - (\mu + \zeta) I_{m1}$$

$$\frac{dI_{m2}}{dt} = \zeta(1-r)I_{m1} - \left(m\grave{\sigma} + \mu + \alpha_2\right)I_{m2} + \frac{b_h f I_V S_{m1}}{N}$$

$$\frac{dS_m}{dt} = \grave{\lambda}(1-k)(1-p)I_F + \lambda(1-k)S_F + \zeta r I_{m1} - \left(\mu + \grave{\sigma}\right)S_m - \frac{b_h f I_V S_m}{N}$$

$$\frac{dS_M}{dt} = \grave{\sigma}S_m - \mu S_M - \frac{b_h f I_V S_M}{N}$$

For the insect vector population we consider a population increasing to its carrying capacity and for the animal reservoir a population proportional to the human population

$$\frac{dV}{dt} = \frac{r_V V(K(A+N) - V)}{K(A+N)}$$

$$A = \nu N$$

With these assumptions the carrying capacity is $V^* = K(A + N) = K(1 + \nu)N$:

For the infected fraction of insects and animals the equations are:

$$\frac{dI_A}{dt} = \frac{b_a f I_V(A\grave{\ } - I_A)}{A} - \mu_a I_A$$

$$\frac{dI_V}{dt} = \left(\frac{b_h f \grave{\imath}_h}{N} + \frac{b_a f \grave{\imath}_A}{A}\right)(V - I_V) - \mu_V I_V$$

The total human population and the infected fraction will be, respectively:

$$N = I_F + I_{f1} + I_{f2} + S_F + S_f + I_M + I_{m1} + I_{m2} + S_M + S_m$$

$$I_h = I_F + I_{f1} + I_{f2} + I_M + I_{m1} + I_{m2}$$

And the population will increase following:

$$\frac{dN}{dt} = \grave{\lambda}I_F + \lambda S_F - \mu N - \alpha_1(I_F + I_M) - \alpha_2(I_{m2} + I_{f2})$$

If there are no infections, considering a birth rate $\Gamma = \lambda N$, the population free of infection would reach a size $N^* = \Gamma/\mu$.

3. Methods

Two methodological approaches were used. First, the model was reduced to the simplest form collapsing by some transition equations and considering some plausible assumptions to obtain simple relationships of practical utility. Since the animal reservoir was considered as proportional to the human population, assuming
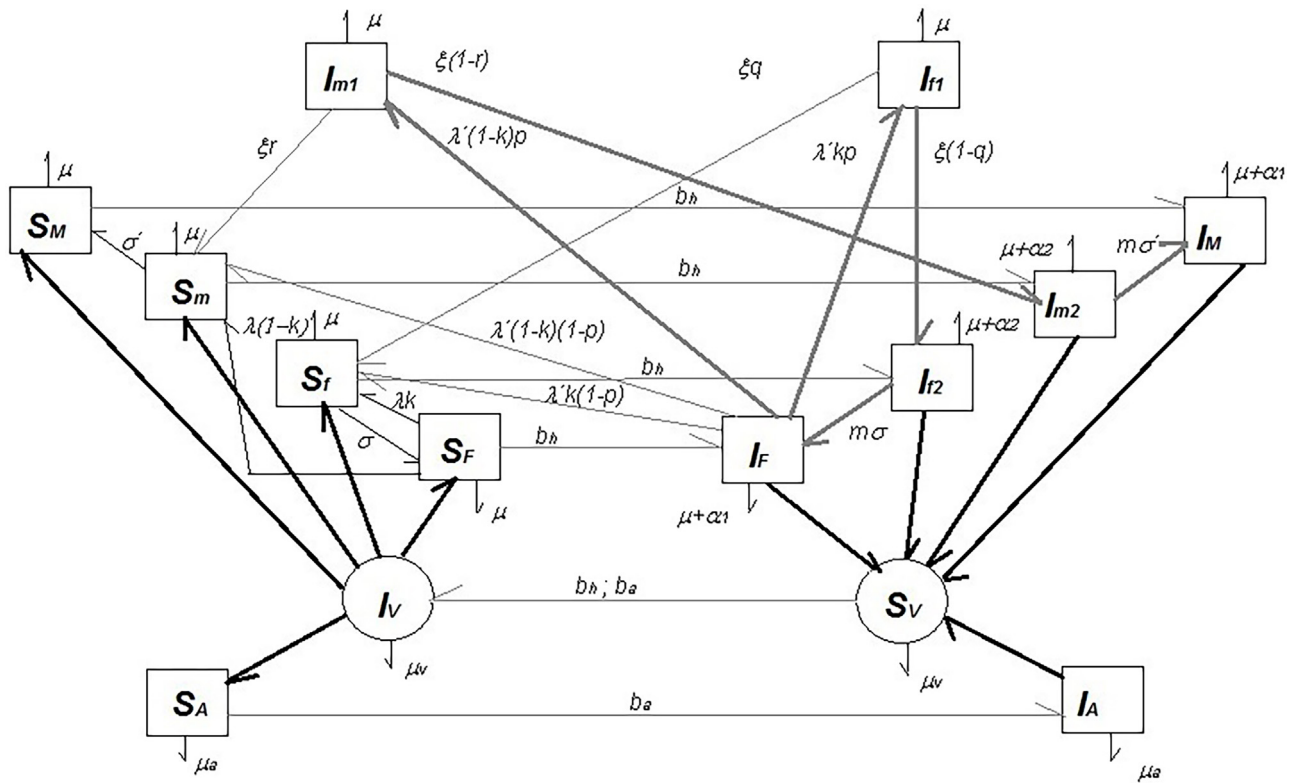
Fig. 1. Flux diagram of the vector and congenital transmission of Chagasídisease. The female human population was divided into the following compartments: susceptible adults (S_F), susceptible children (S_f), infected female children born to chagasic mothers (I_{f1}), untreated and infected female children (I_{f2}) and infected women (I_F). The equivalent compartments in males were: S_M, S_m, I_{m1}, I_{m2} and I_M. For animal (A) and vector (V) populations, infected (I_A and I_V. respectively) and susceptible (S_A and S_V, respectively) compartments were considered. Lines in bold show the vector contacts, the broad gray lines the congenital route, and the fine gray lines the internal transitions. The vectorial mediated transitions are indicated by "b" parameters. All parameters as in the text.

that the insect vector is a generalist species without host preferences and then assuming that the human and animal bite rates are the same ($b_h = b_a = b$) the equation that represents the evolution of infected vectors may be expressed as a function of the human population and the parameter of proportionality (v). Considering that the compartments $I_{f1}, I_{f2}, I_{m1}, I_{m2}$ are transition stages of the same population that end in the infected adult female and male populations, assuming that during these transition stages the parameters are maintained constant and the same for males and females without lags induced by the different reproductive age, and that there are no changes in the bite rate, a single equation for infected humans (I_h) was formulated. From this reduced model R_0 was obtained by the next generation matrix (M_g), a matrix whose elements M_{ij} are the expected number of new cases with state at infection i, generated by one individual who has just been introduced in state at infection j (Diekmann and Heesterbeek 2010; Van Den Driessche and Watmough 2002; Diekmann et al., 2010). The formation of the operator (M_g) involves determining two compartments, infected (F) and non-infected (V), where $M_g = FV^{-1}$ from the model and R_0 is given by the spectral radius (dominant eigenvalue) of the matrix FV^{-1} (Diekmann and Heesterbeek 2010; Van Den Driessche and Watmough 2002; Diekmann et al., 2010). Then a sensitivity analysis was performed, obtaining the elasticities of R_0 with respect to the parameters of interest (θ): $\varepsilon_\theta = \frac{\partial R_0/R_0}{\partial \theta/\theta} = \frac{\theta}{R_0}\frac{\partial R_0}{\partial \theta}$ (Shah and Gupta, 2013; Canals et al., 2015). The elasticity represents the proportional variation of R_0 caused by small proportional variations of θ.

In a second approach, simulations were performed for different values of R_0: 1.52; 1.07; 0.70; 0.41 as the result of variations of the bite rate or the density of insect vectors and with $R_0 = 0.04$, which corresponds to congenital transmission only ($b_h = 0$, or equivalently $d = 0$). The equations of the complete model were integrated numer-

ically by Eulerís method (Runge-Kutta of first order), which offers good resolution considering that $dt = 1$ day and the simulated time was more than 80 years (30,000 days), programmed in EXCEL software. The parameters used and the initial conditions are shown in Tables 1 and 2. All simulations used an initial population of 6000 insects, of which 60 were infected, and a human population of 1,311,000 individuals with 308,000 infected, distributed as in Table 2.

4. Results

In the reduced model the dynamics of infected compartments may be represented by:

$$dI_h/dt = \psi I_h - (\mu + \alpha)I_h + bfI_V(N - I_h)/N$$
$$dI_V/dt = (1 + v)bf'I_h(V - I_V)/N - \mu_V I_V$$

where $\psi = \lambda i m p(1 - q)k$ corresponds to the recruitment rate of congenital patients. In this model $I_F = kI_h$ infected women have a birth rate λi, but to contribute to the adult infected population the proportion should be chagasic (p), they should survive and reproduce at the reproductive age (m) and not be treated ($1 - q$). Thus ψ represents the contribution to congenital Chagasí disease. The vector contribution comes from the infected bite rate that produces I_V infected vectors in a proportion ($N - I_h$)/N of susceptible humans, while ($V - I_V$) susceptible triatomines make ($1 + v$)bfi potentially infectious bites on I_h/N infected humans.

If there is no vector transmission (i.e. $b = 0$), the condition for the existence of Chagas' disease is that: $dI_h/dt > 0$, that is $\psi I_h - (\mu + \alpha)I_h > 0$ or equivalently $R_{oc} = \frac{\psi}{\mu + \alpha} > 1$.

Table 1

Parameter values used in simulations. The references from which the values were estimated are [1] Canals et al. (1991a,b); [2]; Canals et al. (1993); [3] Canals et al. (2016), [4] Canals and Cattan (1992); [5] Raimundo et al., (2009); [6] Canals et al., (1998); [7] Canals et al. (1999); [8] Rabinovich and Rossell (1978). [*] represents estimations based on Chilean data estimated for this paper.

Parameter	Definition	Value	Method	Based on
μh	Human death rate	0.0000457 days^{-1}	Based on life expectancy	[*]
μ_V	Vector death rate	0.008 days^{-1}	From cohort studies	[1–3]
μ_A	Animal death rate	0.00091 days^{-1}	Assuming 3 years of life expectancy	[4]
Λ	Human birth rate	0.00015 days^{-1}	Based on the increase of Chilean population	[*]
$\lambda\hat{\imath}$	Human birth rate of chagasic mothers	0.00015 days^{-1}	Based on reference	[5]
σ	Transfer rate of girls to reproductive status	0.000183 days^{-1}	Based on Chilean data of reproductive age	[*]
$\sigma\hat{\imath}$	Transfer rate of boys to reproductive status	0.000137 days^{-1}	Based on Chilean data of reproductive age	[*]
m	Probability that sexually immature female chagasic children become pregnant	0.9	Based on reference	[5]
K	Proportion of females	0.5	Usual value	[*]
p	Proportion of chagasic children born to chagasic mothers	0.1	Based on reference	[5]
ζ	Treatment rate	0.000274 days^{-1}	Based on reference	[5]
q, r	Proportion of treated male and female children	0.5	Estimated for Chile, based on underestimation of Chagas prevalence	[*]
α_1	Disease-related death rate of chagasic pregnant women	0.0000274 days^{-1}	Based on reference	[5]
α_2	Disease-related death rate of untreated children	0.0000274 days^{-1}	Based on reference	[5]
b_h	Bite rate on humans	variable	Based on reference	[6–8]
b_a	Bite rate on animals	0.0754 days^{-1}	Based on reference	[8]
f	Proportion of infectious bites produced by infected vectors	0.1	Based on reference	[8]
$f\hat{\imath}$	Proportion of infectious bites from the bite on infected host	0.1	Based on reference	[1]
K	Carrying capacity per human or animal	50	Based on previous plausible estimations	[1]
ν	Number of animals per human	0.2	Approximate value	[*]
r_V	Intrinsic rate of increase of vector population	0.014423	Based on reference	[1]

Table 2

Initial conditions for simulations.

I_F	275000
I_{f1}	8250
I_{f2}	8250
S_F	500000
S_f	1500
I_{m1}	8250
I_{m2}	8250
S_m	1500
I_M	0
S_M	500000

On the other hand, if congenital transmission does not exist the model is reduced to:

$$dI_h/dt = -(\mu + \alpha)I_h + bfI_V(N - I_h)/N$$

$$dI_V/dt = (1 + \nu)bf'I_h(V - I_V)/N - \mu_V I_V ,$$

whose next generation matrix (M_g) is:

$$Mg = FV^{-1}\begin{bmatrix} 0 & bf \\ \dfrac{(1+\nu)bf'V*}{N*} & 0 \end{bmatrix} \cdot \begin{bmatrix} \dfrac{1}{\mu+\alpha} & 0 \\ 0 & \dfrac{1}{\mu_V} \end{bmatrix} =$$

$$\begin{bmatrix} 0 & \dfrac{bf}{\mu_V} \\ \dfrac{(1+\nu)bf'V*}{(\mu+\alpha)N*} & 0 \end{bmatrix} .$$

The first Eigenvalue (equivalent to the reproductive number) is $R_{0V} = \frac{(1+\nu)b^2ff'd*}{(\mu+\alpha)\mu_V}$, where V* and N* represent the equilibrium populations free of the disease of the vector and humans, and $d* = V*/N* (=(K(1+\nu))/(\lambda/\mu) = k(1+\nu)\mu/\lambda)$ corresponds to the equilibrium density of insect vectors per human.

Now, if we consider both vector and congenital transmission, the next generation matrix is: $M_g = \begin{bmatrix} \psi & bf \\ \dfrac{(1+\nu)bf'V*}{N*} & 0 \end{bmatrix} \cdot \begin{bmatrix} \dfrac{1}{\mu+\alpha} & 0 \\ 0 & \dfrac{1}{\mu_V} \end{bmatrix} = \begin{bmatrix} \dfrac{\psi}{\mu+\alpha} & \dfrac{bf}{\mu_V} \\ \dfrac{(1+\nu)bf'V*}{(\mu+\alpha)N*} & 0 \end{bmatrix}$, whose first eigenvalue (t) comes from the solution of the characteristic equation:

$$t^2 - \frac{\psi}{\mu+\alpha}t - \frac{(1+\nu)b^2ff'd*}{(\mu+\alpha)\mu_V} = 0, \quad t = \frac{\psi}{2(\mu+\alpha)}$$

$$+ \sqrt{\left(\frac{\psi}{2(\mu+\alpha)}\right)^2 + \frac{(1+\nu)b^2ff'd*}{(\mu+\alpha)\mu_V}} \quad ,$$

The condition of persistence of Chagas disease is t > 1, yielding:

$$R_0 = \frac{(1+\nu)b^2ff'd*}{(\mu+\alpha)\mu_V} + \frac{\psi}{\mu+\alpha} = R_{0V} + R_{0C} > 1.$$

Thus the reproductive number of the system with vector and congenital transmission may be expressed as the sum of the reproductive numbers of the systems with only congenital transmission and only vector transmission.

The reproductive number R_0 showed greater sensitivity to the variations of bite rates and vector densities than variations in mortality rates of vectors and recruitment rate of congenital patients (Figs. 2 and 3). The sensitivity of R_0 increases greatly with small variations of the bite rate (b) and density of vector insects (d) quickly reaching unity. Also the mortality rate of the vector reaches a value close to one with the usual values of vector mortality in Chile (see Table 1). Congenital recruitment also reaches high values of sensitivity but only at high values of ψ. The sensitivity to human mortality may be high only at low mortality values and the effect of the reservoir (ν) only at very high values. The decrease of vector density or equivalently of the bite rate had a clear effect on R_0 (Table 3) with consequences on Chagasí disease dynamics.
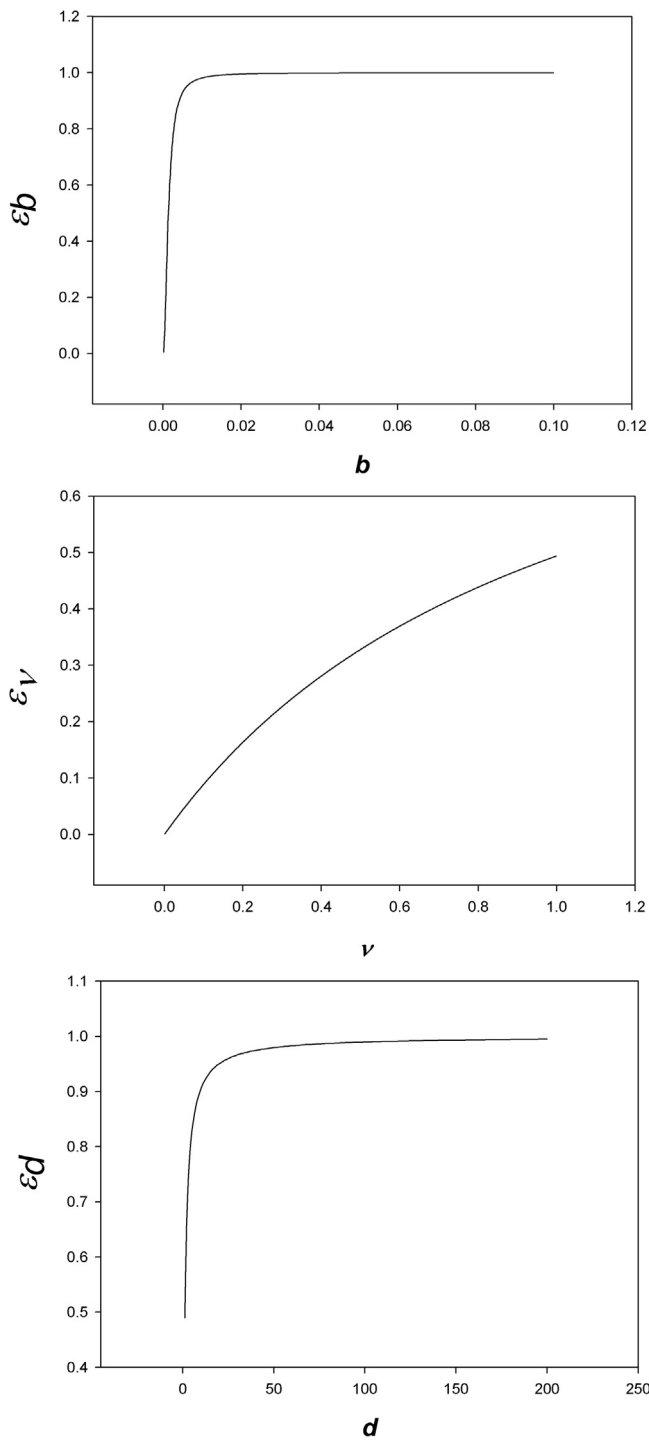
Fig. 2. Variation of elasticities of the bite rate (ε_b), of the animal reservoir (ε_v) and of insect density (ε_d) for different values of b, v and d respectively.
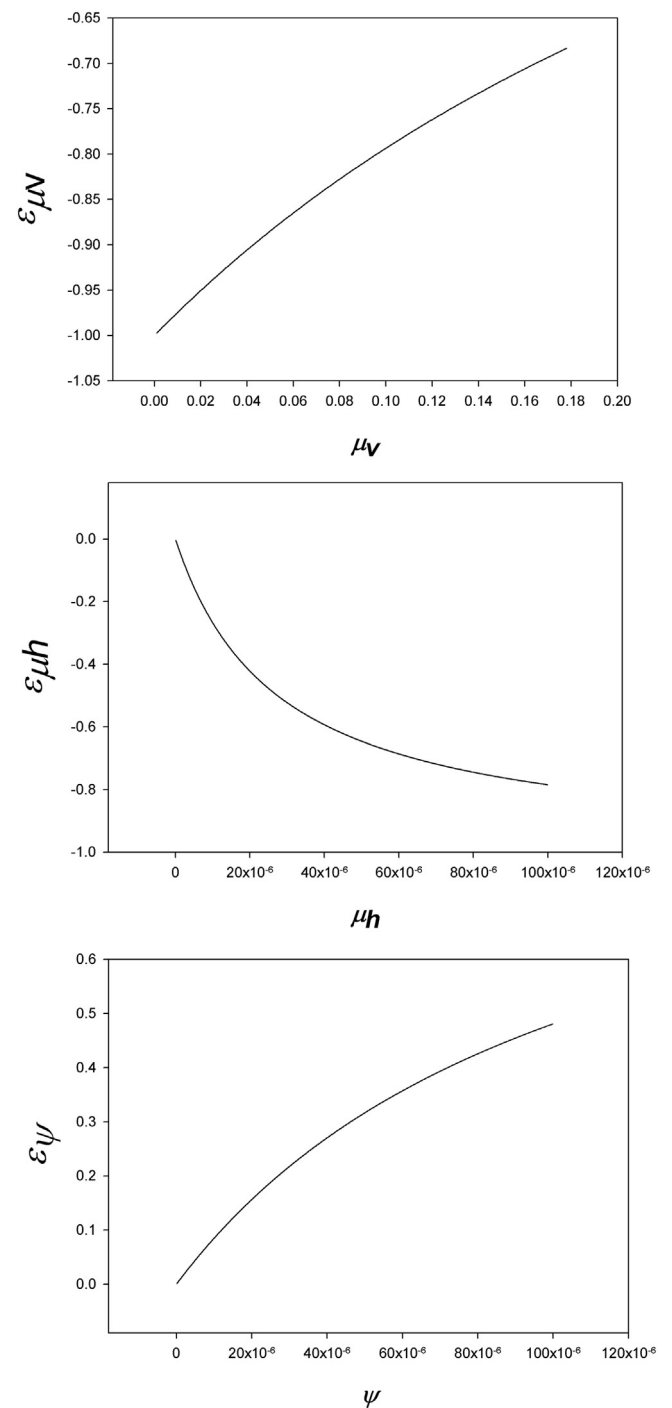

Fig. 3. Variation of elasticities of the mortality rate of vectors ($\varepsilon_{\mu v}$), of the mortality rate of humans ($\varepsilon_{\mu h}$) and of the congenital contribution (ε_{ψ}) for different values of μ_V, μ_H, and ψ, respectively.

Table 3

Effect of reduction of the bite rate (b_h), maintaining the density of insects vector constant ($d = 50$ insects/humans), or the reduction of the vector density, maintaining the bite rate constant ($b_h = 0.0754$ days^{-1}) on the reproductive number.

b_h (days^{-1}); d = 50	d (insects/humans); b_h =0.0754	R_{0V}	R_{0C}	R_0
0.0012	0.0127	1.477	0.042	1.520
0.0010	0.0088	1.025	0.042	1.068
0.0080	0.0057	0.657	0.042	0.699
0.0060	0.0032	0.369	0.042	0.411
0.0000	0.0000	0.000	0.042	0.042

The total infected compartment (I) increases at R_0 values greater than one and decreases with R_0 values less than one. The inverse behavior was shown by the susceptible compartment (Fig. 4). The infected compartments I_F, I_{f2} and I_{m2} in general terms showed a similar behavior. However when R_0 was greater or close to one, after a small population decrease, the I_F fraction increases to its equilibrium value (Fig. 5). In a long-term simulation the prevalence increases to an equilibrium value at $R_0 > 1$, is maintained close to a constant value at $R_0 = 1$, and decreases when R0 < 1. For example at $R_0 = 0.04$ obtained without vector transmission the prevalence falls
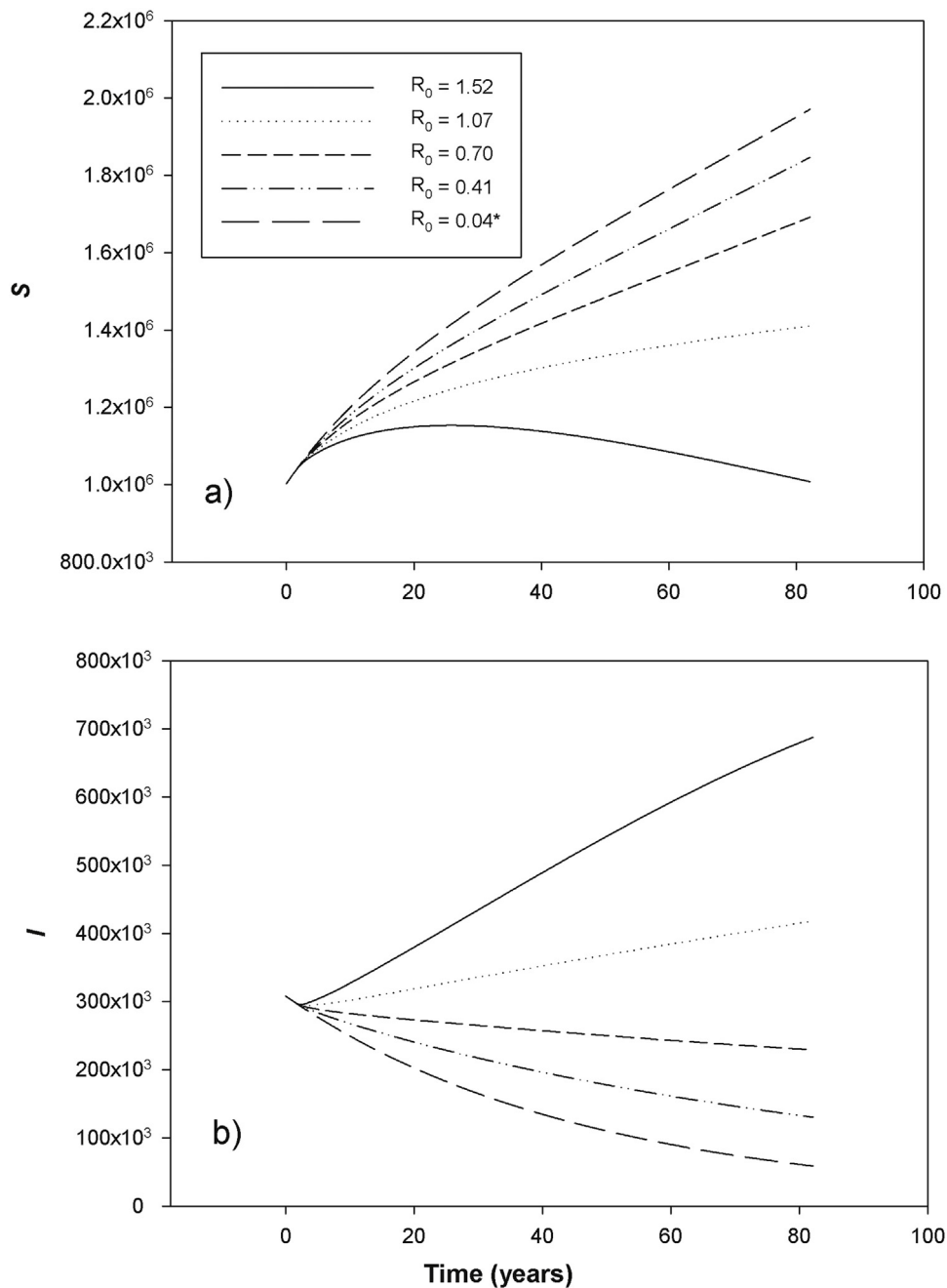
Fig. 4. Evolution on time of susceptible (S), infected (I) and the prevalence of Chagas (Pv) computed as the ratio between the infected human population and the total human population, for the initial conditions showed in Table 2 and for different reproductive numbers (R_0) (from Table 3).

to negligible values at approximately 60 years (two generations) (Fig. 6).

5. Discussion

The model developed here was based on previous models of Canals and Cattan (1992) for the vector and Raimundo et al. (2010) for congenital transmission of Chagasí disease. Vector and congenital are the two main mechanisms of Chagasí disease transmission in North, Central and South America (Telleria and Tibayrenc 2010), although in some places oral transmission has been reported (Silva et al., 1968; Nóbrega et al., 2009). This has not been reported in Chile, thus the model accounts for the main transmission mechanisms. The model considers the human population, the vector population *T. infestans* and the animal population that represents

the non-human reservoir. *T. infestans* is the domestic vector that accounts for 99.4–99.8% of Chagasí disease in Chile (Canals et al., 1993, 1999). In this model the possibility of colonization of human dwellings by wild vectors once *T. infestans* was eradicated was not considered. In this respect, it has been reported that *M. spinolai* may be considered as in the domiciliation phase (Canals et al., 2000; Cattan et al., 2002). Although it can survive in human dwellings (Canals et al., 1994a,b) there are few reports of intra-domiciliary colonies of this species (Frías-Lasserre, 2010; Botto-Mahan et al., 2015). However, the domestic environment can be a sink population and the dispersal of this species into houses can lead to some level of transmission (Rascalou et al., 2012) that was not considered in our model. The other two species have not been reported colo-

nizing human dwellings. This model considers the animal reservoir population as a whole, despite the great diversity of wild and peri-domiciliary vertebrates that have been reported as infected by *T. cruzi*. Several peri-domestic animals such as dogs, cats, rabbits, horses and also several rodents in Chile, and more than 150 mammal species have been described as hosts of *T. cruzi* in America (Schenone et al., 1980; Rozas et al., 2005; Rozas et al., 2007). The parameter ν must be interpreted as an amplification factor of the human reservoir produced by the presence of animal hosts accessible to the insect vectors. It is a parameter difficult to estimate because there are factors not considered such as the host preferences of the vector, a fact reported in several triatomines (Zeledon and Rabinovich, 1984; Schenone et al., 1985; Salvatella et al., 1994; Canals et al., 2001; Molina et al., 2004) and the different carrying capacities that each host may support as a consequence of differences in body size or in behavior. For example several rodents and lagomorphs, although they have small body mass, have nesting habits that favor the access of the insect vectors, while artiodactyls, although they have large body size, have great mobility that makes them difficult for the bugs to access. Despite this, it may be possible to estimate v as some function of animal biomass

Although the complete model includes 8 infected compartments, it was possible to reduce it to two compartments, rescuing the fundamentals of the whole model. Two main assumptions were considered for this. First, the insect vectors bite humans and animals indifferently. Although this assumption is not necessarily true, the reported bite rates on animals and humans are very similar. For example, in *T. infestans* an animal bite rate of $0.0754\,\text{days}^{-1}$ has been reported (Rabinovich & Rossel, 1978), optimum bite rates of $0.1527\,\text{days}^{-1}$, and critical bite rates (i.e. minimum bite rates to allow reproduction and survival) of $0.038\,\text{days}^{-1}$ (Canals et al., 1999) a and bite rate of $0.0799\,\text{days}^{-1}$ for humans (Canals et al., 1998, 1999). These values are also similar to those reported for *Rhodnius prolixus*, between 0.089 and $0.119\,\text{days}^{-1}$ (Rabinovich et al., 1979). Second, the transition stages have homogeneous behavior that may be rescued by its parameters.

The reproductive number of the reduced model includes most of the parameters of the whole model, except those that characterize the "internal" transitions (i.e. from If_1 to If_2 to I_F). Although some parameters are a strong simplification of the reality it has the virtue of providing and easy and understandable formulae for the reproductive number, expressing it as the sum of the reproductive number of the vector and congenital Chagas transmission. From these formulae it may be seen that the existence of congenital Chagas will depend directly on the number of chagasic mothers (kI_h), the birth rate of chagasic mothers (λi), the probability of transmission of Chagasí disease to their children (p), treatment (q) and survival and reproduction at reproductive age (m); all parameters included in ψ. It also depends inversely on the general and Chagas-specific mortality rates ($\mu + \alpha_1$). On the other hand, vector transmission will depend directly on the animal reservoir (ν), the proportion of infectious bites (f and $f\tilde{\imath}$), the vector density per human (d) and the square of the bite rate (b^2); and inversely on ($\mu + \alpha_1$) and the mortality rate of *T. infestans* (μ_V). Also in R_0 we can see that the magnitude of the contribution of vector Chagas is much greater than the congenital one and that the most sensitive parameters are the bite rate (b), vector density (d) and the mortality rate of the vector (μ_V), but operating in the opposite sense. This suggests that the epidemiologic measures must be directed to reduce the bite rate and the density and to increase the mortality of *T. infestans*. There are other recent models that yield other expressions of R_0. For example, Peterson et al. (2015) developed a model to simulate domestic vector-borne transmission, examining the interaction between synanthropic animals and effect of vector control. In this model the authors were interested in the reservoir animal population and the effect of a death rate term accounting for
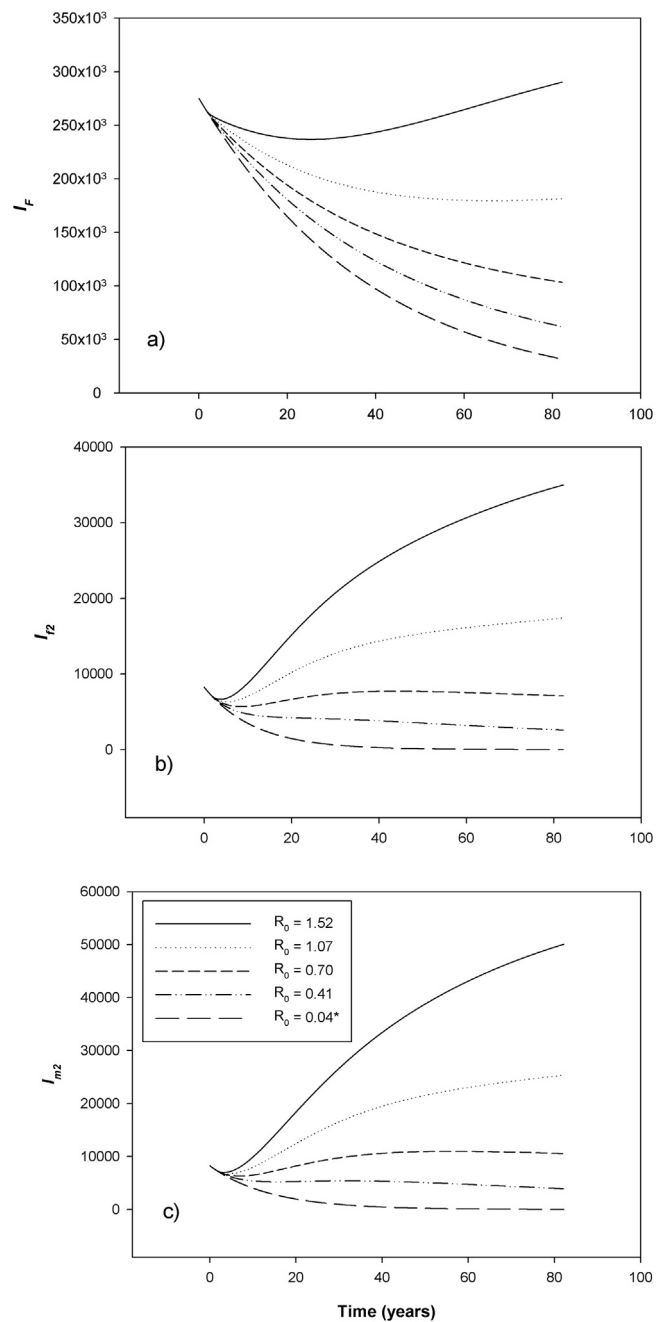

Fig. 5. Evolution on time of infected females (I_F), and infected children; females (I_{f2}) and males (I_{m2}), for the initial conditions showed in Table 2 and for different reproductive numbers (R_0) (from Table 3).

the vector control. They concluded that a reduction of synanthropic animals may slow *T. cruzi* transmission. In our study, in which the animal population is represented by the parameter ν; the lower the value of ν, the lower the value of R_0, agreeing with Peterson et al. (2015). Also Rascalou et al. (2012) analyzed several vector borne diseases including Chagasí disease arriving to a general expression for R_0. In this approach an interesting point was consider the rate of transmission of *T. cruzi* composed of the finding rate, the probability of transmission per contact and the delay between meals (inversely related to the biting rate), with the result that the finding rate had no impact, but the delay between meals had similar or even larger impact than immigrations on R_0, agreeing with our results.
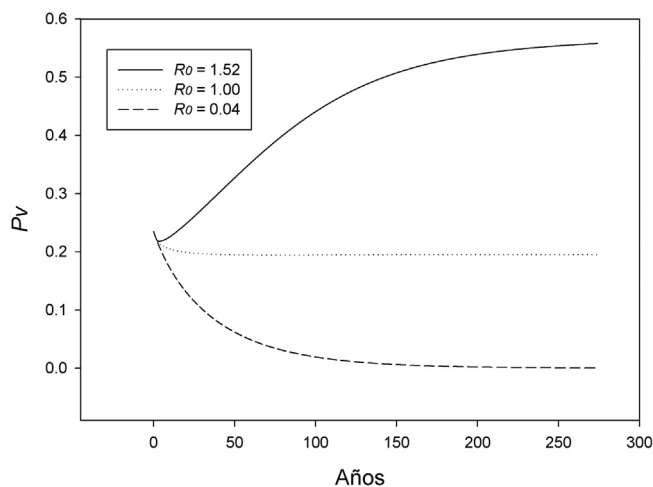
Fig. 6. Long term evolution on time of the prevalence of Chagas (Pv) computed as the ratio between the infected human population and the total human population for three values of R_0.

In all simulations a population with an initial prevalence of 23.5% was considered, which was a frequent value in the hyper-endemic zones of northern Chile (Schenone et al., 1980; Apt and Reyes, 1986a,b, 1990). The maximum *T. infestans* population considered was a value near the carrying capacity described for this species (Rabinovich et al., 1978; Canals et al., 1991a,b, 1993, 1998). For example, with these assumptions, which may be similar to those of human settlements without disinfection, considering a critical bite rate of 0.038 days^{-1} (Canals et al., 1999) and a density of 20 insects per human a $R_0 = 5.97$ is obtained, where the vector contribution is $R_{0V} = 5.92$ (99.2%), a value consistent with a previous report (Canals et al., 1992) and lower than the value of 7.2 reported in Colombia where the main vector is *Rhodnius prolixus* (Cordovez et al., 2014).

The decrease of R_0 mediated by the decrease of the bite rate or by the decrease of the insect density is associated with clear changes in the dynamics of Chagasí disease. The same value of R_0 (for example $R_0 = 1.52$) may be obtained with density $d = 0.0127$ and $b_h = 0.0754$, or equivalently at a bite rate of $b_h = 0.012$ days^{-1} and $d = 50$ (vector at carrying capacity). When the transmission chain is broken ($b_h = 0$ or equivalently $d = 0$), congenital transmission cannot be maintained over time and Chagasí disease will vanish, agreeing with previously reported results Raimundo et al. (2010). Even if no child is medically treated ($q = r = 0$), the contribution of congenital Chagas would be $R_{0C} = 0.084$. It may be expected that cases of Chagas in children will be negligible in 30 years (near one generation) and all human cases in two to three generations.

This model shows that the key factor for the control of the Chagasí disease is breaking the vector transmission chain, which has been reported for Uruguay, Chile and Brazil (MINSAL, 2014; Raimundo et al., 2010). This is particularly relevant when there is a low number of vector species as in Chile (Botto-Mahan et al., 2010). Once the elimination of the domestic vector is obtained, *T. infestans*, two threats are perceived: 1) the existence of wild foci of *T. infestans*, reported recently (Bacigalupo et al., 2006, 2010, 2015) which may favor the reintroduction of this species in the domestic environment and 2) the domiciliation of wild vectors (Canals et al., 2001; Botto-Mahan et al., 2002, 2005a,b, 2010; Botto-Mahan, 2009). Domestic environments may be considered as sink populations that favor some level of transmission (Rascalou et al., 2012; Waleckx et al., 2015a). The elimination of *T.infestans* and the avoidance of a reintroduction of this species and the intrusion of the wild vector is a big task that needs a clear strategy including situational analysis of eco-bio-social determinants of house infestation and maintenance and evaluation of vector control intervention like

the eco-health intervention for Chagas disease in Yucatan, Mexico in which the main vector is *T. dimidiata* (Waleckx et al., 2015b).

Once the transmission chain is broken, since no oral transmission has been reported in Chile, and since 2008 a careful control has been implemented in blood banks (MINSAL 2014), the persistence of Chagasí disease will depend on congenital transmission, which may be reduced to eradication by means of increasing the proportion of newborn treated (q and r). Although congenital transmission cannot be prevented, early diagnosis allows the early treatment of children, reaching 100% cure if the children are treated before one year with Benznidazol or Nifurtimox (Schijman 2006; Toro et al., 2016).

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