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Review

Prevalence of Chagas disease in Brazil: A systematic review and meta-analysis

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ABSTRACT

Chagas disease is a major public health problem in Brazil and Latin America. During the last years, it has become an emerging problem in North America and Europe due to increasing international migration. Here we describe the prevalence of Chagas disease in Brazil through a systematic review. We searched national and international electronic databases, grey literature and reference lists of selected articles for population-based studies on Chagas disease prevalence in Brazil, performed from 1980 until September 2012. Forty-two articles with relevant prevalence data were identified from a total of 4985 references. Prevalence ranged from 0% to 25.1%. Most surveys were performed in the Northeast region, especially in the state of Piauí. We observed a high degree of heterogeneity in most pooled estimates ($I^2 > 75\%$; $p < 0.001$). The pooled estimate of Chagas disease prevalence across studies for the entire period was 4.2% (95% CI: 3.1–5.7), ranging from 4.4% (95% CI: 2.3–8.3) in the 1980s to 2.4% (95% CI: 1.5–3.8) after 2000. Females (4.2%; 95% CI: 2.6–6.8), >60 year-olds (17.7%; 95% CI: 11.4–26.5), Northeast (5.0%; 95% CI: 3.1–8.1) and Southeast (5.0%; CI: 2.4–9.9) regions and mixed (urban/rural) areas (6.4%; 95% CI: 4.2–9.4) had the highest pooled prevalence. About 4.6 million (95% CI: 2.9–7.2 million) of people are estimated to be infected with *Trypanosoma cruzi*. The small number of studies and small-scale samples of the general population in some areas limit interpretation, and findings of this review do not necessarily reflect the situation of the entire country. Systematic population-based studies at regional and national level are recommended to provide more accurate estimates and better define the epidemiology and risk areas of Chagas disease in Brazil.

Contents

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1. Introduction

Chagas disease is a Neglected Tropical Disease (NTD) and a major public health problem in Latin America (Moncayo and Silveira, 2009). During the last years, the disease has received increasing attention as an emerging problem in North America and Europe due to international migrations from endemic areas to non-endemic areas (Gascon et al., 2010; Schmunis and Yadon, 2010). There are about of 8–10 million infected people in Latin America (Schmunis and Yadon, 2010; WHO, 2010), with an annual death toll of about 14,000 (WHO, 2010).

After significant reduction of vector and transfusional transmission of *Trypanosoma cruzi* in Brazil, the number of cases with the acute form of Chagas disease has been reduced dramatically (Silveira, 2011a). Reduced specific mortality and increased survival of infected individuals is a consequence of better knowledge about the natural history of the disease and improved clinical and surgical care (Martins-Melo et al., 2012e; Martins-Melo and Heukelbach, 2013; Ramos Jr. et al., 2010). Recent estimates point to 2–3 million infected people in Brazil (Akhavan, 2000; Dias, 2007; Ramos Jr. et al., 2010), with about 6000 deaths annually (Martins-Melo et al., 2012a,b,d).

However, systematic data about the magnitude of Chagas disease in the general population and its distribution in Brazil's regions are not available (Camargo et al., 1984; Silveira et al., 2011). Such information is needed to optimize health resources allocation towards improvement on disease detection, treatment and control. In the present study we estimate the prevalence of Chagas disease in Brazil through a systematic review and meta-analysis of available population-based studies.

2. Materials and methods

2.1. Study area

Brazil, South America's largest country, has a total territory of 8.5 million km^2 and an estimated population of 194 million (2012). The country is divided into five geographic regions (South, Southeast, Central-West, North, and Northeast), 27 Federative Units (26 States and one Federal District) and 5570 municipalities. Despite the economic improvements that have given the country new international recognition and projection, there are still tremendous social and economic inequalities, evidenced by differing human development indexes (HDI) among regions and rural/urban areas (*Instituto Brasileiro de Geografia e Estatística – IBGE*; http://www.ibge.gov.br).

2.2. Literature search

We performed a systematic review of available literature to identify relevant publications about prevalence data of Chagas disease in Brazil. A comprehensive search was conducted in the electronic databases PubMed, Web of Science, Scopus, LILACS and SciELO (covering all dates from the creation of each database up to September 31, 2012), using the following keywords and their combinations: "Chagas disease", "*Trypanosoma cruzi*", "American trypanosomiasis", "prevalence", "epidemiology" and "Brazil". Different combinations were used for each electronic database in order to narrow the amount of results retrieved, but at the same time maximizing the number of relevant studies. At that point, no restrictions were made regarding date of publication, study design, or language of publication. Additional strategies included reviews of journals/periodicals not indexed in the above mentioned electronic databases, internet searches for "grey literature" and screening of reference lists of selected studies. If necessary, the corresponding authors of relevant studies were contacted. Brazilian experts in the field were contacted to detect other potential unpublished studies.

2.3. Selection criteria and data extraction

Reference Manager bibliographic software version 11.0 (Thomson Reuters, New York, NY, United States of America) was used to catalogue the initial literature search results and to manage citations. Titles and abstracts were assessed, and respective papers examined in full for prevalence survey data.

We included studies if all of the following inclusion criteria were met: survey date after 1980; conducted in Brazil; population-based study; number of *T. cruzi*-infected individuals and size of study population available; and use of conventional serological tests for confirmation of infection by *T. cruzi* (e.g., indirect immunofluorescence assay [IFA], enzyme-linked immunosorbent assay [ELISA] and indirect hemagglutination assay [IHA]). We included studies after 1980, as the last major national survey of seroprevalence of *T. cruzi* infection in the general population in Brazil was performed 1975–1980 (Camargo et al., 1984; Silveira et al., 2011).

The following studies were excluded: based on secondary data; duplicated data; no clear definition of methods, especially sampling; non-population based studies such as hospital-based data, clinical studies, case series and case control studies. In the case of repeated surveys in the same population, most recent and/or more complete data were included.

Prevalence data of Chagas disease were extracted from included studies. Prevalence of Chagas disease was defined as the frequency of cases by *T. cruzi* infection in a given population at a given period of time. The information on the study and population characteristics were extracted of all relevant studies, including the author's name, study period, survey geographic location, sample size, age group, number of positive cases, and type of serological test utilized.

2.4. Statistical analysis

Data analysis was carried out in different steps. First, mean prevalences were calculated for grouped data in sub-periods (1980–1989, 1990–1999 and after 2000) and region of residence (Brazilian states and regions), using the sum of the numbers of cases in all studies considered, divided by the sum of the number of participants. The 95% confidence interval (95% CI) was computed using exact binomial method. If the study did not report the year of data collection, the year of publication was used. Then, pooled prevalence estimates for Chagas disease in the general population and their 95% CI were calculated using the random-effects model meta-analysis (Hedges and Vevea, 1998). Heterogeneity between-study was evaluated through Cochran's Q test (reported as χ^2 and p values) and I^2 statistic, which describes the percentage of variation between studies (values of 25%, 50%, and 75% show low,

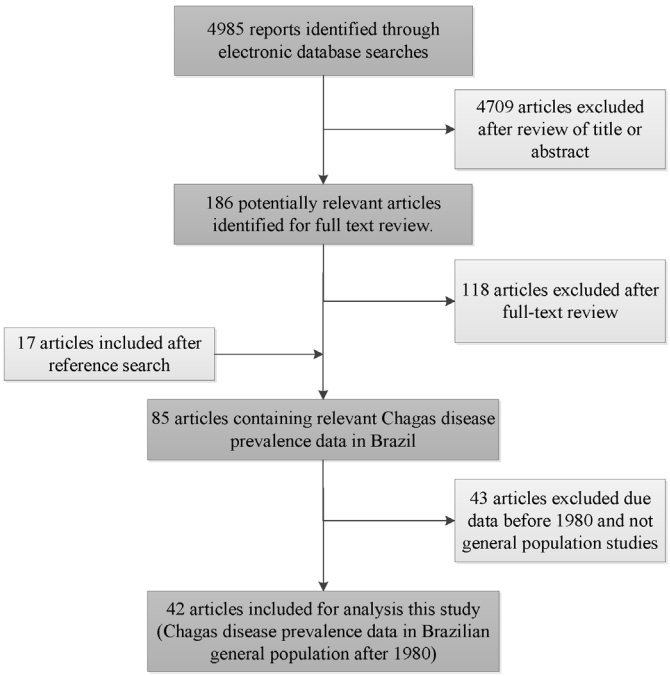

Fig. 1. Flow chart of selection of studies.

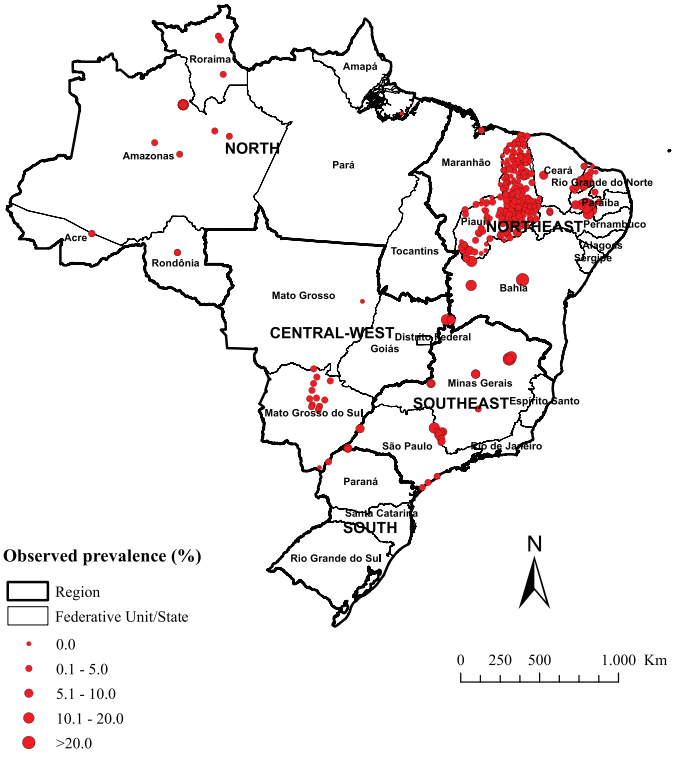

Fig. 2. Spatial distribution of observed Chagas disease prevalence in population-based surveys.

moderate, and high degrees of heterogeneity, respectively) (Higgins et al., 2003; Huedo-Medina et al., 2006). Subgroup analyses included were performed to investigate potential sources of heterogeneity among studies and included the following variables: geographical region, sex, age group (0–9, 10–19, 20–29, 30–39, 40–49, 50–59, >60 years), sample size, survey period, urban or rural area, and type of serological test. Data are presented including prevalence with corresponding 95% CI for each study and the overall random-effects pooled estimate. To estimate the current number of *T. cruzi* infected individuals at national level, we used the pooled prevalence estimate in 2000s and population data from the Brazilian Institute of Geography and Statistics (*IBGE*), based on the 2010 National Population Census.

Data were analyzed using Stata software version 11.2 (Stata Corporation, College Station, United States of America) and Comprehensive Meta-Analysis software version 2.0 (Biostat, Englewood, United States of America). A map detailing prevalence at study sites was created, using ArcGIS software version 9.3 (Environmental Systems Research Institute, Redlands, CA, United States of America).

3. Results

3.1. Literature search results

Of 4895 articles identified, 42 were considered eligible for the review (Aras et al., 2002; Arruda et al., 1984; Bento et al., 1984; Bento et al., 1989; Bento et al., 1992; Bezerra et al., 1983; Boia et al., 1999; Borges-Pereira et al., 2001; Borges-Pereira et al., 2002; Borges-Pereira et al., 2006; Borges-Pereira et al., 2008; Brito et al., 2012; Carvalho et al., 2011a; Carvalho et al., 2003; Carvalho et al., 2011b; Coimbra et al., 1992; Corrêa et al., 2011; Coura et al., 1995a; Coura et al., 1995b; Coura et al., 2002; Dantas-Maia et al., 2007; Dias et al., 2002a; Diotaiuti et al., 2000; Escolano et al., 1989; Figueredo-Silva et al., 1991; Fonsêca et al., 2012; Gazin et al., 2004; Lima et al., 2012; Luitgards-Moura et al., 2005; Machado et al., 1998; Magalhães et al., 2011; Massaro et al., 2008; Montoya et al., 2003; Passos et al., 1997; Peñaranda-Carrillo et al., 2002; Pereira and Coura, 1986; Pereira and Coura, 1987; Silva et al., 2009; Silva et al., 2010; Silva and Goldenberg, 2008; Tachibana et al., 1999; Valente et al., 1998) (Fig. 1). These included a total of 125,580 individuals, with 5229 cases (4.2%) of *T. cruzi* infection.

3.2. Characteristics of studies

The studies were conducted between 1980 and 2011 in 18 Brazilian states. The majority was conducted in the Northeast region (42.9%). Most data were collected in the 1990s and after 2000 (38.1%), and were from rural areas (47.6%). The sample size ranged from 73 to 36,399 individuals (mean: 2990; standard deviation [SD±]: 6679; median: 684.5). The combination of two or more different serological tests for the diagnosis of *T. cruzi* infection was used in 64.3% of studies. Prevalence of Chagas disease varied from 0% to 25.1%. Detailed characteristics of the included studies on the prevalence of Chagas disease are presented in Appendix A.

3.3. Geographical and temporal distribution of study sites

A total of 319 study sites were identified; 310 were unique survey locations, most of them in Piauí state in the northeast of the country. Spatial distribution and observed prevalence by location are depicted in Fig. 2.

An overview of the identified surveys with relevant Chagas disease prevalence data is presented in Table 1. Most studies were performed in the Northeast region. Some states contain a large number of survey locations, while from other states no Chagas disease surveys were published. Most of the surveys were done after 2000. Distribution of surveys within the different time periods ranged from state to state. While some states only have surveys for one or two periods, other states are well covered over time.

The mean prevalence was 4.2% (95% CI: 4.1–4.3) for the entire period. In the 1980s, prevalence was 4.0% (95% CI: 3.8–4.2), 7.0%

Table 1
Overview of Chagas disease prevalence data included in the analysis.

Region/State	Number of locations		Survey period						Prevalence (%)
	Total	Unique	1980–1989		1990–1999		>2000		Mean (CI 95%)
			n	Prevalence % (95% CI)	*n*	Prevalence % (95% CI)	*n*	Prevalence % (95% CI)	
North region	15	12	–	–	5	9.9 (8.6–11.3)	10	2.1 (1.8–2.5)	4.2 (3.7–4.7)
Acre	2	2	–	–	–	–	2	0.8 (0.4–1.6)	0.8 (0.3–1.6)
Rondônia	2	1	–	–	–	–	2	1.6 (0.6–3.2)	1.6 (0.6–3.2)
Amazonas	7	5	–	–	3	11.4 (9.9–13.0)	4	3.5 (2.7–4.3)	7.0 (6.2–7.8)
Roraima	3	3	–	–	–	–	3	1.4 (0.9–2.0)	1.4 (0.9–2.0)
Pará	1	1	–	–	1	0.0 (0.0–1.4)	–	–	0.0 (0.0–1.4)
Amapá	–	–	–	–	–	–	–	–	–
Tocantins	–	–	–	–	–	–	–	–	–
Northeast region	260	257	15	8.7 (8.1–9.3)	9	10.1 (9.2–11.0)	236	2.5 (2.4–2.7)	4.0 (3.8–4.2)
Maranhão	1	1	1	4.6 (2.7–7.2)	–	–	–	–	4.6 (2.7–7.2)
Piauí	222	219	4	14.0 (11.9–16.4)	1	14.3 (10.3–19.1)	217	2.3 (2.2–2.5)	2.7 (2.5–2.9)
Ceará	3	3	–	–	1	5.7 (4.8–6.7)	2	1.9 (1.3–2.6)	4.2 (3.6–4.8)
Rio Grande do Norte	16	16	–	–	–	–	16	5.9 (5.0–7.0)	5.9 (5.0–7.0)
Paraíba	9	9	9	8.1 (7.4–8.8)	–	–	1	1.4 (0.3–4.0)	7.8 (7.2–8.5)
Pernambuco	6	6	–	–	6	9.1 (7.2–11.2)	–	–	9.1 (7.2–11.2)
Alagoas	–	–	–	–	–	–	–	–	–
Sergipe	–	–	–	–	–	–	–	–	–
Bahia	2	2	1	11.0 (7.9–14.8)	1	25.1 (21.9–28.5)	–	–	20.4 (18.0–23.0)
Southeast region	27	27	16	2.9 (2.8–3.1)	7	12.4 (11.5–13.3)	4	2.8 (1.9–3.9)	4.1 (3.9–4.3)
Minas Gerais	8	8	1	12.6 (1.8–19.9)	6	13.6 (12.5–14.1)	1	2.1 (1.1–3.5)	12.1 (11.3–12.9)
Espírito Santo	–	–	–	–	–	–	–	–	–
Rio de Janeiro	–	–	–	–	–	–	–	–	–
São Paulo	19	19	15	2.1 (2.0–2.3)	1	10.1 (8.8–11.5)	3	3.9 (2.3–6.2)	2.6 (2.4–2.8)
South region	1	1	–	–	–	–	1	2.0 (0.5–7.6)	2.0 (0.5–7.6)
Paraná	1	1	–	–	–	–	1	2.0 (0.5–7.6)	2.0 (0.5–7.6)
Santa Catarina	–	–	–	–	–	–	–	–	–
Rio Grande do Sul				–	–	–	–	–	–
Central-West region	16	16	–	–	15	4.7 (4.4–5.0)	1	0.0 (0.0–4.9)	4.7 (4.4–5.0)
Mato Grosso	1	1	–	–	1	0.0 (0.0–2.2)	–	–	0.0 (0.0–2.2)
Mato Grosso do Sul	16	16	–	–	12	1.8 (1.6–2.1)	1	0.0 (0.0–4.9)	1.8 (1.6–2.1)
Goiás	2	2	–	–	2	12.3 (11.5–13.2)	–	–	12.3 (11.5–13.2)
Distrito Federal	–	–	–	–	–	–	–	–	–
Total Brazil	319	310	31	4.0 (3.8–4.2)	36	7.0 (6.7–.7.3)	252	2.5 (2.3–2.6)	4.2 (4.1–4.3)

Details given on the number of surveys per survey year, survey locations, and mean observed prevalence (expressed in %) given per region (5) and states (27). – = data not found or not applicable because there were no relevant papers for this region/state. 95% CI: 95% confidence intervals calculated using exact binomial method.

(95% CI: 6.7–7.3) in the 1990s, and 2.5% (95% CI: 2.3–2.6) after 2000. The mean prevalence ranged between states, from 2.1% (São Paulo) to 14.0% (Piauí) in the 1980s, and 0% (Pará and Mato Grosso) and 25.1% (Bahia) in the 1990s, and between 0% (Mato Grosso do Sul) and 5.9% (Rio Grande do Norte) after 2000.

3.4. Overall prevalence of Chagas disease

Pooled prevalence estimates for the 42 studies included in the meta-analysis are presented in Table 2. Substantial heterogeneity was observed in most pooled estimates, which remained even after subgroup analysis ($I^2 > 75\%$ and $p < 0.001$). The pooled estimate of Chagas disease prevalence across studies for the entire period was 4.2% (95% CI: 3.1–5.7), ranging from 4.4% (95% CI: 2.3–8.3) in the 1980s, 7.2% (95% CI: 4.6–11.0) in the 1990s, to 2.4 (95% CI: 1.5–3.8) after 2000. Sub-analysis by geographical region revealed wide variations in prevalence. The highest estimated regional prevalence was 5.0% (95% CI: 3.1–8.1) in the Northeast and 5.0% (95% CI: 2.4–9.9) in the Southeast region.

Information about sex distribution was available for 19 studies. Prevalence estimates were slightly higher for females (4.2%; 95% CI: 2.6–6.8) than for males (4.1%; 95% CI: 2.6–6.6). In general, prevalence was higher in advanced age groups. The highest prevalence of 17.7% (95% CI: 11.4–26.5) was found in the >60 age group, while the lowest (1.1%; 95% CI: 0.5–2.4) in the 0–9 year-olds.

Pooled Chagas disease prevalence was higher in surveys conducted in mixed urban/rural locations (6.4%; 95% CI: 4.2–9.4) and with sample sizes of 500–1000 individuals (6.8%; 95% CI: 4.2–10.9). The pooled prevalence of studies conducted exclusively in urban areas was 6.0% (95% CI: 3.0–11.4).

Using the population data of the 2010 National Population Census (190.8 million people) and extrapolating our findings to the Brazilian general population, we estimated that in 2010 there were about 4.6 million (95% CI: 2.9–7.2 million) of people infected with *T. cruzi* in Brazil.

4. Discussion

We performed the first systematic nationwide assessment of Chagas disease prevalence in the last three decades. We describe prevalence estimates in Brazil derived from available population-based data. The data evidence high prevalence in endemic regions, especially in urban areas and the elderly. Chagas disease prevalence varied over time, with lowest levels since 2000.

Currently, only acute cases of Chagas disease are of compulsory notification in Brazil, and there are no nationwide data on the magnitude of the disease (Martins-Melo et al., 2012b; Ramos Jr. et al., 2010; Ramos Jr. and Carvalho, 2009). Thus, analysis of population-based studies at both national and regional level is needed to estimate the magnitude of the disease and to describe areas of active transmission (Camargo et al., 1984; Ostermayer et al., 2011; Passos and Silveira, 2011; Silveira, 2011b; Silveira et al., 2011). The only nationwide survey of prevalence of Chagas disease in the Brazilian rural general population was conducted between

Table 2
Pooled prevalence estimates of Chagas disease, stratified by subgroups.

Characteristics	Number of studies	Range[a]	Pooled Chagas' disease prevalence				Heterogeneity	
			Case	Population	Prevalence (%)	95% CI	I^2 (%)	*P*-value (Cochran's *Q*)
Overall prevalence	42	0.0–25.1	5229	125,580	4.2	3.1–5.7	99.1	<0.001
Survey period								
1980–1989	10	0.6–21.7	1746	43,993	4.4	2.3–8.3	99.3	<0.001
1990–1999	16	0.0–25.1	2261	32,185	7.2	4.6–11.0	98.9	<0.001
>2000	16	0.0–9.9	1222	49,402	2.4	1.5–.3.8	97.5	<0.001
Sex[b]								
Male	19	0.0–27.0	1421	41,132	4.1	2.6–6.6	98.5	<0.001
Female	19	0.0–25.9	2139	48,214	4.2	2.6–6.8	99.0	<0.001
Age group (years)[b]								
0–9	19	0.0–17.1	176	22,180	1.1	0.5–2.4	95.6	<0.001
10–19	20	0.0–15.4	293	22,735	1.6	0.8–3.1	95.9	<0.001
20–29	20	0.0–24.6	321	14,339	3.5	1.9–6.4	95.8	<0.001
30–39	19	0.0–33.3	635	11,308	7.2	4.6–12.6	97.8	<0.001
40–49	19	0.0–45.8	798	8604	11.9	7.3–18.7	97.2	<0.001
50–59	18	1.2–58.8	781	6528	17.5	11.1–26.3	97.0	<0.001
≥60	19	0.0–66.7	924	8052	17.7	11.4–26.5	97.5	<0.001
Region of Brazil								
North	10	0.0–13.7	311	7435	2.9	1.5–5.8	96.6	<0.001
Northeast	18	0.6–25.1	2183	54,701	5.0	3.1–8.1	99.1	<0.001
Southeast	9	1.3–18.5	1768	42,752	5.0	2.4–9.9	99.5	<0.001
Central-West	4	0.0–12.7	965	20,592	2.2	0.4–14.5	99.6	<0.001
South	1	–	2	100	2.0	0.5–7.6	0.0	1
Survey area								
Rural	20	0.0–21.7	2000	80,208	3.2	2.1–4.8	98.4	<0.001
Urban	7	1.8–13.7	1282	24,760	6.0	3.0–11.4	99.2	<0.001
Urban/Rural	10	0.8–25.1	1671	15,480	6.4	4.2–9.4	98.0	<0.001
Peri-urban	1	–	13	1076	1.2	0.7–2.1	0.0	1
NS	4	0.6–11.0	258	3668	4.7	2.2–10.0	95.0	<0.001
Sample size								
<100	2	0.0–3.0	3	172	2.4	0.9–6.7	0.0	0.321
100 – 499	13	0.0–14.3	147	3444	3.1	1.8–.5.2	87.8	<0.001
500 – 1000	11	0.6–25.1	702	7567	6.8	4.2–10.9	97.3	<0.001
>1000	16	0.8–18.5	4377	125,192	4.0	2.5–9.4	99.6	<0.001
Serological test								
IFA	15	0.0–21.7	2707	83,631	3.8	2.2–6.4	99.4	<0.001
IFA/IHA	2	5.7–11.0	178	2794	7.9	4.1–14.7	92.8	<0.001
IHA/ELISA	1	–	14	675	2.1	1.2–3.5	0.0	1
ELISA/IFA	15	0.0–18.5	723	8978	3.8	2.3–6.4	96.6	<0.001
ELISA/IFA/IHA	9	0.8–25.1	1607	29,502	5.1	2.6–9.7	99.3	<0.001

We calculated pooled proportions with a random-effects model. We used the I^2 statistic to estimate heterogeneity between pooled studies. 95% CI: 95% confidence interval. IFA: indirect immunofluorescence assay; ELISA: enzyme-linked immunosorbent assay; IHA: indirect hemagglutination; NS: not specified.

[a] Observed prevalence in studies.

[b] Standardization of age groups and sex utilized in some studies.

1975 and 1980, which estimated an overall prevalence of 4.2%, corresponding to 6.5 million infected people (Camargo et al., 1984; Silveira et al., 2011).

To evaluate the impact of control measures and to estimate the importance of congenital transmission of *T. cruzi* infection, recently (2001–2008) a new national survey with children from 0 to 5 years of age was conducted, with a prevalence of 0.03%. This low prevalence in preschool children indicates control of transmission by the main vector (*Triatoma infestans*) in Brazil (Ostermayer et al., 2011). In fact, the proportion of new cases of Chagas disease has been dramatically reduced in the last 30 years, due to systematic surveillance and control in endemic areas in Brazil (Ramos Jr. et al., 2010; Silveira, 2011a; Silveira and Dias, 2011). Occasionally, there was a trend of ageing of patients with Chagas disease, with the highest prevalence and mortality verified in more advanced age groups (Martins-Melo et al., 2012c,e). This transition can be explained mainly due to a cohort effect, a consequence of exposure to *T. cruzi* infection in the past (Lima-Costa et al., 2004). The increased survival of individuals with Chagas disease will pose health professionals to other challenges, due to the association and interaction with other chronic diseases, such as hypertension and diabetes mellitus (Martins-Melo et al., 2012a,e). Additionally, it broadens the possibility of association with HIV infection or other immunosuppressive conditions (e.g., transplantation), with the potential reactivation of Chagas disease (Almeida et al., 2011; Martins-Melo et al., 2012c).

Our study indicates that the persisting Chagas disease prevalence in some endemic areas reflects the need of sustainability of control programmes, avoiding a recrudescence of the vector transmission of disease (Abad-Franch et al., 2013; Ramos Jr. and Carvalho, 2001). There was a high prevalence in some studies performed in the Amazon region, an area previously considered non-endemic (Barata et al., 1988). Currently, this region is responsible for the largest amount of cases of acute Chagas' disease, mainly by oral transmission through the consumption of natural products such as the palm products of *açaí* juice, *juçara* juice and *bacaba* (Dias and Amato Neto, 2011; PAHO, 2009). This mode of transmission and emerging public health concerns for safe foods, encourage surveillance activities aimed at pasteurizing the products and controlling the export of untreated juice and other products to other regions and out of the country (Dias and Amato Neto, 2011; PAHO, 2009). In fact, the main forms of

transmission of *T. cruzi* infection, vectorial and transfusional, are controlled (Moraes-Souza and Ferreira-Silva, 2011; Silveira and Dias, 2011). With the strengthening of the control programmes in Brazil, transmission via the main domiciliary vector (*T. infestans*) was controlled and almost 100% of blood donors are screened serologically (Massad, 2008). The transmission control reduced substantially the number of new cases and deaths from Chagas disease in endemic areas (Martins-Melo et al., 2012a; Ramos Jr. et al., 2010; Silveira, 2011a). Currently, the majority of reported cases of acute Chagas disease in Brazil are caused by oral transmission (Silveira, 2011a).

The decrease of Chagas disease prevalence over the past years is also related to campaigns against Chagas disease on the American Continent by the World Health Organization (WHO) and the Pan American Health Organization (PAHO). These initiatives were performed in cooperation with regional national authorities since the 1990s, such as the creation of the Initiative of Southern Cone countries (Moncayo and Silveira, 2009; WHO, 2010).

Changes in the incidence, prevalence and mortality are also consequences of improvements of socio-economic conditions and migration (Moncayo and Silveira, 2009; Dias, 2013). Over many years, Chagas disease was considered a health problem in endemic rural areas of Latin America (Coura and Borges-Pereira, 2010; Moncayo and Silveira, 2009). The rural-urban migration in recent decades displaced millions of infected people to urban areas, where vector transmission does not occur, causing a change in the epidemiological pattern of Chagas disease. The disease has been transformed into an urban infection that can also be transmitted through blood transfusion and congenital route (Moncayo and Silveira, 2009; Silveira, 2011a). In Brazil, it is estimated that about 70–90% of people affected by Chagas disease are now living in urban areas (Dias, 2007), which is reflected in our study by the fact that high prevalences were observed in surveys conducted in urban areas.

Blood transfusion was the main mechanism of dissemination of the disease in endemic areas along the 1980s and 1990s (Moraes-Souza and Ferreira-Silva, 2011). High prevalence of Chagas disease in urban centres and the inexistence of control programmes resulted in the 1970s in about 20,000 new cases annually in Brazil by transfusion transmission of *T. cruzi* (Moraes-Souza and Ferreira-Silva, 2011). Improved coverage of screening of blood donors substantially reduced the rate of blood-borne transmission (Dias and Amato Neto, 2011; Moraes-Souza and Ferreira-Silva, 2011). Congenital transmission still occurs at considerable levels in Brazil, except in the state of Rio Grande do Sul, which has the largest rate of vertical transmission, as indicated by data collected in a recent survey on seroprevalence in children under five years of age (Ostermayer et al., 2011).

Chagas disease is mainly enzootic hindering elimination and is a major threat to re-introduction in regions where control has been achieved (Coura and Borges-Pereira, 2010). Furthermore, there is no vaccine available to prevent the disease and, although acute infections can be treated, the lack of symptoms during the acute phase leads to delayed diagnosis and makes the epidemiological surveillance a difficult routine (Bwititi and Browne, 2012). Thus, control of Chagas disease remains a challenge for public health, and probably will remain so for many years (Abad-Franch et al., 2013; Massad, 2008; Ramos Jr. and Carvalho, 2001). New control strategies for oral transmission (in the Amazon region) and secondary vectors such as *Triatoma brasiliensis* and *Triatoma pseudomaculata* (in the Northeast region) must be implemented and assessed systematically (Martins-Melo et al., 2012a; Massad, 2008). In addition, adequate access to health services and social assistance should be guaranteed for the large number of individuals afflicted with chronic Chagas disease during the last decades (Ramos Jr. and Carvalho, 2009).

Our study has some limitations. First, data showed a large degree of heterogeneity among studies, and the findings do not necessarily reflect the real situation of the entire country. There is clearly not yet sufficient evidence to estimate Chagas disease prevalence in the general population at national level, and additional population-based studies are needed. The studies were conducted mainly in endemic areas for Chagas disease and were under-represented in others. The regional differences of data availability may have led to an overestimation of the estimates and precluded a more thorough analysis. An alternative would be the use of more robust statistical methods, such as Bayesian geostatistical models (Diggle et al., 1998), that combine disease data with sociodemographic and environmental data to predict risk, and extrapolate the burden of infection, even in regions where there are few data (Chammartin et al., 2013). This was verified in studies with schistosomiasis data in Africa (Schur et al., 2011; Schur et al., 2013) and soil-transmitted helminthiases in South America (Chammartin et al., 2013). However, due to the heterogeneous distribution of Chagas' disease in Brazil, the model must take into consideration socio-demographic and environmental factors, distribution of vectors and reservoirs, human migration and level of the human action on nature (Dias, 2007; Dias et al., 2002c).

Other limitations are a consequence of incomplete or inaccurate information provided in the publications. For example, many studies did not stratify data by sex and age groups were not stratified in a standardized manner. Despite a comprehensive search, it is likely that some studies conducted have not been found because they are not published in indexed journals, and consequently end up not being cited by other authors. Non-publication bias may have caused an overestimation of prevalences. In addition, studies were conducted between 1980 and 2012. This long time period was necessary because of the limited availability of data on in some areas in Brazil, but limits interpretation to some degree. There were also variations of diagnostic tests used in different studies. Despite the predominance of the use of the combination of two or more test to confirm the diagnosis of chronic Chagas disease according to standard of the WHO/PAHO, some studies used only one diagnostic test.

Despite the discussed limitations, the results of this study clearly call to action on research and surveillance of Chagas disease in Brazil. There is an urgent need to conduct national and regional surveys of seroprevalence in order to obtain more reliable information, and to identify high risk areas. However, interruption of transmission by its main domestic vectors reduced political interest and operational budgets (Massad, 2008), and the need for continued surveillance and intervention becomes less appreciated at the political level. There is also a general tendency to underestimate potential re-emergence of vector-borne and emerging infections (Dias et al., 2002b).

Acute Chagas disease is often asymptomatic and not diagnosed and notified. This naturally weakens the surveillance system, reinforcing further the impression that the transmission does not occur (Abad-Franch et al., 2013). The Ministry of Health of Brazil has been discussing the possibility of compulsory notification of chronic forms (Martins-Melo et al., 2012a), considering the burden of chronic diseases in the country and the fact that reactivation of Chagas disease in the presence of HIV infection is considered an AIDS-defining condition in Brazil (Ramos Jr., 2004). This study provides further evidence for the need for introduction of chronic forms as notifiable disease.

5. Conclusions

Despite interruption of main vector and blood-borne transmission, considerable Chagas disease prevalence is observed in

Brazil's endemic areas, with declines in the last decades. The infected population is ageing and increasingly urbanized. Systematic population-based studies at regional and national level are needed to provide more accurate estimates, identify high risk areas and to plan and assess systematic control measures in Brazil.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.actatropica.2013.10.002.

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