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Abbreviations

CD	Chagas disease
CI	Confidence intervals
ELISA	Enzyme-linked immunosorbent assay
EEA	European Economic Area
EU	European Union
IgE	Immunoglobulin E
LR	Logistic regression
OR	Odds ratio
T. cruzi	*Trypanosoma cruzi*
PR	Prevalence rate
SD	Standard deviation
SoHO	Substances of human origin
Ref.	Reference group
SD	Standard deviation
Sig.	Statistically significant
WHO	World Health Organization

Executive summary

Background

Mass population movements have accounted for the emergence of Chagas disease (CD) outside endemic regions, including the European Union/European Economic Area (EU/EEA). The parasite responsible for causing CD, *Trypanosoma cruzi* (*T. cruzi*), can be transmitted through substances of human origin (SoHO), such as blood transfusions and organ transplantations [1], posing a risk to the recipients. This, together with congenital transmission, is of increasing concern in non-endemic countries.

Objective

To identify which factors are consistently associated with a higher risk of carrying a *T. cruzi* infection in people residing in non-endemic countries.

Methods

A comprehensive search of Medline (including PubMed) and EMBASE databases was conducted covering the period between January 2000 and June 2022 to identify observational cohort and cross-sectional studies that reported any factor associated with carrying a *T. cruzi* infection in non-endemic countries. Screening, data extraction, and critical appraisal (Joanna Briggs Institute tools) were undertaken by two independent study authors. Due to the heterogeneous nature of the data, vote-counting and narrative syntheses were undertaken.

Results

Thirty-three cross-sectional and 18 observational cohort studies were identified, resulting in coverage of a total population of approximately 132 million people. Synthesis highlighted the following factors as being associated with higher odds of carrying a *T. cruzi* infection in non-endemic countries: being born in endemic countries (Latin American countries); having stayed in endemic countries; having a history of living in rural areas of endemic countries; having a history of living in specific housing conditions in endemic countries (mud houses or those with thatched rooves); a history of blood transfusion in endemic countries; older age in people with other factors associated with *T. cruzi*; maternal origin from endemic countries; having a family history of CD; and generic knowledge of CD prior to testing for *T. cruzi* infection.

Conclusions

The assessment of the aforementioned factors will increase the ability to detect people infected with *T. cruzi*, supporting the eligibility assessment of SoHO donors, and implement public health measures.

Background

Chagas disease (CD) is caused by the protozoan parasite *Trypanosoma cruzi* (*T. cruzi*) [2] and is endemic in 21 countries of continental Latin America [3]. The course of CD consists of an acute and chronic phase and, if it remains untreated, can cause severe health complications [4]. Apart from the vector-borne transmission through the triatomine bug, which constitutes the main route of transmission in countries endemic for CD, *T. cruzi* can be also transmitted through ingesting food or drinks contaminated with the parasite; through laboratory accidents; congenitally; or via substances of human origin (SoHO), such as blood transfusions and organ transplantations [1]. The latter two routes of transmission are of increasing concern in the context of non-endemic areas (e.g. the EU/EEA).

Although CD is treatable, and curable in the early stage, it is mainly asymptomatic at acquisition and remains unrecognised in most cases [5]. As a consequence, most individuals infected with *T. cruzi* remain untreated for several years. Although the overall prevalence of CD is low in endemic countries, the consequences for infected people can be severe, and infected asymptomatic people can transmit the disease either congenitally or via SoHO. Identifying evidence-based individual and contextual factors associated with a *T. cruzi* infection could assist, aid, and/or support in eligibility assessment of SoHO donors and the identification of other people at risk of carrying *T. cruzi* infection.

This systematic review aims to provide the evidence regarding the demographic, environmental, and epidemiological or other characteristics associated with carrying *T. cruzi* infection in at-risk individuals residing in areas non-endemic for CD [6]. The characteristics associated with *T. cruzi* infection are referred to as risk factors in this report.

Methods

This study was conducted adhering to the Joanna Briggs Institute (JBI) methods for risk factor reviews and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7]. A prospective protocol for the systematic review has been previously published in PROSPERO [CRD42022338572] [8].

Eligibility criteria

Population

Eligible participants for the studies included in this review were males and females of the general population of all ages residing in non-endemic countries. People infected via congenital transmission were considered eligible for inclusion only if they were not born in endemic countries outlined by the World Health Organization (WHO) [3].

Exposure

Eligible risk factors included, but were not restricted to: mother born in an endemic country; birth country; travel to- or residency in CD-endemic countries and length of travel; place of residency; number/duration visits/residency; housing material during visits/residency and presence of domestic animals; contact with the vector; age; sex; sociodemographic; race/ethnicity, education; prior treatment for CD; and history of blood transfusion/transplantation in endemic countries.

Outcome

The outcome of interest was infection with *T. cruzi*. Infection with *T. cruzi* includes people who were proven to be infected with *T. cruzi* via a test but were either asymptomatic or unaware of their infection if symptomatic. We also included a diagnosis of CD as the outcome measure, which included people who were proven to be infected with *T. cruzi* and were symptomatic. Finally, we also included studies in which authors stated people were infected with *T. cruzi* or had CD, without giving any details of testing or diagnosis of the disease, respectively.

Study design

Randomised controlled trials (including quasi), observational cohort, case-control and cross-sectional studies were eligible for inclusion. Studies that focussed on patients infected with *T. cruzi* only without providing any comparison with healthy individuals were also eligible, but the findings from these descriptive studies are reported separately. Case reports, conference abstracts, and studies conducted in endemic countries were excluded.

Search strategy and information sources

A comprehensive search strategy of two databases (Medline and EMBASE) from 1 January 2000 to 29 June 2022 was developed to identify eligible studies (Annex 1). No language restrictions were applied. Reference lists of retrieved papers were scanned.

- MEDLINE(R) In-Process & Other Non-Indexed Citations and MEDLINE(R) (Ovid), including PubMed;
- EMBASE (Ovid).

All potentially relevant citations were downloaded to Endnote X8 Reference Manager bibliographic software (version 8.0; Clarivate Analytics, Philadelphia, PA, United States (US)).

Selection process, data collection process and data items

Selected studies were imported into Rayyan online software and de-duplicated [9]. Two reviewers conducted screening of studies independently for relevance based on titles/abstracts and full texts, with disagreements resolved through discussion.

A pre-piloted data extraction form was used to extract relevant data. One reviewer extracted data, with a second reviewer independently checking 50% of the extracted records. This is a deviation from the original protocol, which stated that two reviewers would independently extract data; no discernible differences were identified between the reviewers, with 100% agreement being achieved, justifying the deviation.

Data extracted consisted of the following categories: i) studies' details, country and setting(s) where the study was conducted, study design, and date when the data were collected; ii) descriptive statistics regarding population characteristics, such as sex, age, country of origin, socio-economic characteristics, country of residence, comorbidities, number and length of travel, migration status (i.e. short- or long-term), history of family CD, evidence of congenital

transmission of *T. cruzi*, housing conditions, history of transfusion/transplantation; and iii) data on risk factors associated with carrying a *T. cruzi* infection were expressed either quantitatively (e.g. crude proportions, prevalence rates [PR], odds ratios [OR], relative risks [RR], regression coefficients plus measures of variance where available) or qualitatively (i.e. narrative presentation of risk factors). Where data were not reported in the text but provided in graphs, the web plot digitizer tool was used to extract the data [10].

Study risk of bias assessment

The methodological quality of the included studies with an analytical design was assessed by a single reviewer, using the JBI critical appraisal tools [11]. A second reviewer independently checked at least 50% of the included studies, while a third reviewer acted as the final arbiter where disagreements were evident. JBI critical appraisal tools target the following categories: i) inclusion criteria; ii) measurement of condition/exposure of interest; iii) confounding factors and how they were treated; iv) assessment of outcomes; and v) statistical analysis and reasons for attrition [11]. None of the studies were excluded based on their appraisal.

Effect measures and synthesis method

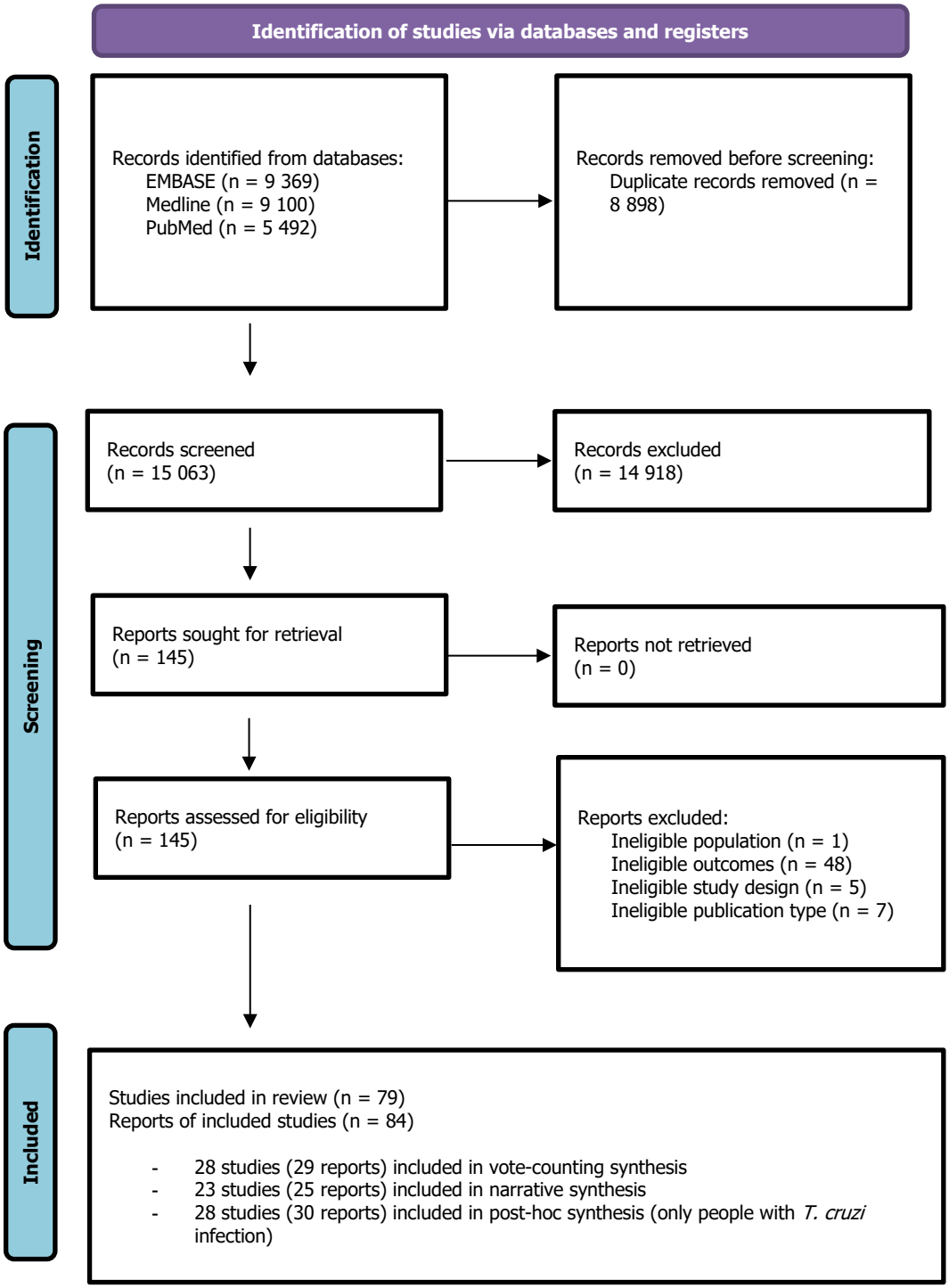
Due to the large heterogeneity in setting, recruited populations and comparison groups, effect sizes were summarised using the vote-counting synthesis method based on the direction of effects [12]. Findings from the vote-counting synthesis are presented using cross-study visual displays [13]. Where OR were reported, forest plots were generated using the packages "dplyr" [14], "ggplot2" [15], and "gridExtra" [16] in RStudio [17]. Where odds ratios were not reported but the necessary data were available, ORs were computed and included in the vote-counting synthesis. Studies that did not report measures of association between risk factors and *T. cruzi* infection were not included in the vote-counting synthesis, and data from these studies were narratively synthesised. Studies that focussed on *T. cruzi*-infected patients only without providing any comparison with healthy individuals were synthesised separately. Sources of heterogeneity were explored by conducting subgroup analyses based on: i) geographical location of the study (EU/EEA, Switzerland); and ii) SoHO (blood donors) in general and within EU/EEA.

Results

A total of 23 961 articles were retrieved, of which 8 898 were duplicates. Overall, 14 918 articles were excluded following title and abstract screening, and 61 were excluded following the full-text screen; as a result, 79 studies (from 84 reports, as some studies were published in several reports) were included in the systematic review (Figure 1A). Studies excluded during the full-text screening can be found in Annex 5. Fifty-one studies (from 54 published reports) were included in the synthesis, with 28 studies included in the vote-counting synthesis and 23 studies in the narrative synthesis (Table 1A in Annex 2).

The remaining 28 studies used a descriptive design which only included people with *T. cruzi* infection or diagnosed with CD, and therefore could not be included in subsequent syntheses due to a lack of a comparator group (Table 2A in Annex 2). From the 51 studies included in the synthesis, 33 studies (35 reports) used a cross-sectional design [18-52] and 18 studies (19 reports) used an observational cohort design [53-70]. Approximately 132 million individuals were included in this review, with study sample sizes ranging from 41 [34] to 131 529 240 [62] (median: 596).

Figure 1A. PRISMA flow diagram of the selected studies



Characteristics of the included studies

Overall, 42 studies were conducted in EU/EEA countries (France, Germany, Italy, and Spain) and Switzerland. Six studies were conducted in the US [21,29,36,56,61,62], two studies were conducted in Canada [51,65], and one study was conducted in Japan [70]. In nine studies, the population consisted of blood donors [21,24,26,33,41,43,56,65,70].

Risk of bias and critical appraisal of the included studies

Overall, 33 cross-sectional and 18 observational cohort studies were critically appraised (Annex 3). In general, most cross-sectional and cohort studies were judged to be adequately reported. Most of the poor ratings in the cross-sectional studies pertained to the way the sample was defined and how confounder factors were treated. Most poor ratings in cohort studies pertained to the identification of confounding factors and how the confounder factors were treated.

Vote-counting synthesis

Overall, data drawn from 28 studies were used for the vote-counting synthesis (Annex 4). The vote-counting synthesis highlighted 11 key factors which were assessed for their association with carrying a *T. cruzi* infection in non-endemic countries:

1) Being born in an endemic country: Overall, 19 studies reported data on the association between country of origin and *T. cruzi* infection. Among these, 16 studies reported data regarding the association between Bolivia as country of origin and *T. cruzi* infection [18,19,22,23,30-32,39-41,44,46,52,60,69,71]. In all 16 studies, being born in Bolivia was associated with higher odds of carrying a *T. cruzi* infection (Annex 4) compared to being born in other Latin American countries [18,19,30-32,39,40,44,52,69,71] or compared to being born in any other country (Latin American and non-endemic) [22,23,41,60]. In one of these studies, Bolivian or Brazilian nationality was associated with higher odds of carrying a *T. cruzi* infection compared to being born in other Latin American and non-endemic countries [60]. Apart from two studies [31,39] all effect sizes were statistically significant (considering $p<0.05$). The association between Bolivia as a country of origin and *T. cruzi* infection remained statistically significant among the three studies which adjusted for other factors in their analysis [18,46,52].

Four studies reported the association of a Latin American country other than Bolivia as country of origin and *T. cruzi* infection [29,36,39,69]. Two of these studies reported data on the association of El-Salvador as country of origin and *T. cruzi* infection [29,36], one study on Paraguay [69] and one study on Colombia and Argentia [39]. El-Salvador as the country of origin was associated with higher odds for *T. cruzi* infection compared to other Latin American countries [29,36] and non-endemic countries [29] with these effects remaining statistically significant also in one study which adjusted for other risk factors [36]. Originating from Paraguay was associated with higher odds for carrying a *T. cruzi* infection compared to other LA countries [69]. Colombia and Argentina were also associated with increased odds of *T. cruzi* infection when compared to Ecuador with this effect not being significant (considering $p<0.05$) [39]. One study reported a positive association between being born outside the EU and having a *T. cruzi* infection among children born from mothers infected with *T. cruzi* with this effect being non-significant (considering $p<0.05$) [53].

2) Stay in endemic countries: One study conducted in blood donors showed that individuals living in a non-endemic country who had spent three or more months in an endemic country were significantly more likely to have *T. cruzi* infections (considering $p<0.05$) [21]. The association between a stay of three or more months in endemic countries and *T. cruzi* infection was also reported for the donors born in non-endemic countries indicating that the association persists regardless of birth country [21].

3) History of living in rural areas of endemic countries: Overall, 13 studies reported data regarding the association between the history of living in rural areas of endemic countries and carrying a *T. cruzi* infection [18,19,21,23,25,31,32,36,38,46,47,52,71]. In all but one study [31], a history of living in rural areas was associated with higher odds of carrying a *T. cruzi* infection compared to a history of living in urban areas, with these effects being statistically significant in nine studies (considering $p<0.05$) [18,19,21,23,25,32,38,47,71].

4) History of living in poor housing conditions in endemic countries: 12 studies reported data regarding the association between the history of living in poor housing conditions in endemic countries and *T. cruzi* infection [18,19,21,25,32,36,37,39,45,47,52,71]. In all studies, a history of living in mud houses was associated with higher odds of carrying a *T. cruzi* infection compared to living in houses made of other materials (such as bricks, Annex 4). Apart from three studies [36,45,52], these effects were statistically significant (considering $p<0.05$). These effects remained statistically significant even in those studies that adjusted for other risk factors [18,19,52]. Three studies also reported data regarding the association between the history of living in houses with thatched rooves and *T. cruzi* infection compared to rooves made of other materials [21,32,36]. In all studies, a history of living in houses with thatched rooves was positively associated with *T. cruzi* infection with these effects being statistically significant. In the only study where adjustment for other factors was conducted, the effects became non-significant ($p>0.05$) [36].

5) Contact with the vector in an endemic country or at the border: Overall, seven studies reported data regarding the association between the experience of a contact (including bites or having seen the vector) with the vector in an endemic country or in a region at the border of an endemic country and *T. cruzi* infection (19, 21, 25, 30, 32, 36, 45). In all studies, experience of any contact with the vector was associated with *T. cruzi* infection with these effects being statistically significant in six studies (considering $p<0.05$) [19,21,25,30,32,46]. In two cases [19,25], those effects remained statistically significant even in the studies adjusting for other risk factors.

6) History of blood transfusion/transplantation in endemic countries: Overall, nine studies reported data regarding the association between history of transfusion/transplantation in endemic countries and *T. cruzi* infection [18,23,25,30,39,45-47,52]. In all but three studies [18,46,52], previous blood transfusion compared to no previous transfusion in endemic countries was associated with increased odds of being infected with *T. cruzi* with this effect being statistically significant in two studies (considering $p<0.05$) [23,30].

7) Age: Overall, 15 studies reported data regarding the association between age and *T. cruzi* infection [18,22,23,25,29,30,37,39,45-47,52,53,60,62]. In all studies, older age was associated with *T. cruzi* infection, among individuals with other factors associated with *T. cruzi* infection, irrespective of the age categorisation used, with these effects being statistically significant in eleven studies (considering $p<0.05$) [18,22,23,29,30,37,39,45,52,60,62].

8) Maternal origin from an endemic country: A single study assessed the relationship between maternal origin and *T. cruzi* infection and showed that individuals with mothers' born in endemic countries have higher odds of carrying an infection of *T. cruzi* compared to individuals whose mothers did not originate from endemic countries with this effect being statistically significant (considering $p<0.05$) [21]. This study also assessed the relationship between the grandmother's origin and *T. cruzi* infection and found an association between having a grandmother born in an endemic country and *T. cruzi* infection with this effect being statistically significant [21].

9) Family history of CD: Overall, 13 studies reported data regarding the association between family history of CD (a history of CD in a family member or relative) and *T. cruzi* infection [18,19,23,25,29-31,36,38,39,44-46]. In all studies, a family history of CD was associated with carrying a *T. cruzi* infection, with 11 studies reporting statistically significant associations (considering $p<0.05$) [18,19,23,25,29-31,38,39,44,46]. In two studies which adjusted for other risk factors, these effects remained statistically significant [18,25]. Three of the 13 studies specifically reported a positive association between having a mother with CD or a *T. cruzi* infection and carrying a *T. cruzi* infection [25,30,38].

10) Prior generic knowledge of CD: Overall, eight studies reported data regarding the association between a generic knowledge of CD prior to being tested and carrying a *T. cruzi* infection [25,32,36,38,44-47]. In all studies, a prior knowledge of CD was associated with higher odds of *T. cruzi* infection compared to individuals with no prior generic knowledge of CD with these effects being statistically significant in five studies (considering $p<0.05$) [32,36,44,46,47].

11) Sex: Overall, 17 studies reported data regarding the association between sex and *T. cruzi* infection [18,22,23,25,29,31,33,36,37,44-47,52,53,56,60]. In all but four studies [44-47], being female was associated with higher odds of having a *T. cruzi* infection compared to males among individuals with other factors associated with *T. cruzi* infection, with these effects being statistically significant (considering $p<0.05$) in two studies [37,60].

Table 1. Summary of key risk factors which were assessed for their association of *Trypanosoma cruzi* infection in non-endemic countries

Risk factor for *T. cruzi* infections	Number of studies	Number of studies showing statistically significant association ($p<0.05$)
Being born in an endemic country (of which Bolivia)	19 (16)	17 (14)
Stay in endemic country	1	1
History of living in rural areas	13	9
History of living in poor housing conditions	12	9
Contact with the vector	7	6
History of blood transfusion in endemic countries	9	2
Being older	15	11
Mother or grandmother born in endemic country	1	1
Having a family history of Chagas disease	13	11
Prior generic knowledge of Chagas disease	8	5
Being female	17	2

Narrative synthesis

Overall, data drawn from the 23 studies that did not report measures of association between risk factors and *T. cruzi* infection were narratively synthesised (Annex 2) [20,24,26–28,34,35,43,48,49,51,54,55,57-59,61,63-68,70]. The majority of the infected people were from Latin American countries, with most of them born in Bolivia [20,24,26–28,34,35,43,48,49,54,57-59,63,64,68,70]. However, studies also reported cases of infection in people who were born in Argentina [43,54,55,58,59,65,66,68], Brazil [26,54,68], Chile [55,68], Colombia [26,55], Ecuador [43,54,55,58,59,68], Guatemala [61], El Salvador [24,55,61], Honduras [55,68], Mexico [54,61], Nicaragua [55], Paraguay [54,55,58,65,66,68], Peru [55], Canada (born from mothers born in Latin American countries and having travelled to Latin America) [65], and Italy (having travelled in Latin American countries) [26,54] or worked in Latin American countries [26]).

In almost half the studies, *T. cruzi* infection was more prevalent in females [20,27,28,34,35,55,57,58,63,64,67]. However, most of these studies focused on the outcome of pregnancy in women at risk of infection or infected with *T. cruzi*, including prenatal screening [20,35,55,57,58,63,67]. In the studies where the focus was not pregnant women, a majority of the infected people were female [27,28,34,64]. In three studies, the proportion of CD patients with a history of blood transfusion in countries endemic for CD was approximately 10% [28,34,68]. In one study on patients [61], one confirmed CD case was a woman from El Salvador who had received a kidney donation from her mother; however, the mode of transmission could not be determined.

In five studies that exclusively assessed blood donors [24,26,43,65,70], most of the positive cases were in people born in endemic countries, those who were born in non-endemic countries had extensive travels or stayed in Latin America [26,65] and, in one of these two studies [65], in addition to travels in Latin America, mothers of the infected people were born in endemic countries. In one study conducted in at-risk patients, the only positive infection among travellers was a short-term traveller who consumed crude-sugar cane juice during a foodborne outbreak of CD in Brazil [54].

In two studies, most patients with *T. cruzi* infection had a history of living in rural areas of endemic countries [28,68]. In two studies, most people infected with *T. cruzi* had a history of living in poor housing conditions [34,66]. Two studies reported data regarding the minimum years spent in non-endemic countries before being diagnosed with CD indicating a minimum of seven years [27,55].

Congenital transmission of *T. cruzi* was reported in three studies [20,57,67], where vertical transmission rates ranged from 2.6% to 5%. In most studies, all cases of vertical transmission occurred in mothers who were from Bolivia.

Subgroup analyses

From a total of 51 studies, nine were conducted in non-endemic countries other than EU/EEA countries or Switzerland, namely six in the US [21,29,36,56,61,62], two in Canada [51,65], and one in Japan [70]. There were no differences in the reported factors associated with *T. cruzi* between individuals residing in EU/EEA countries and Switzerland and those residing in non-endemic countries outside the EU/EEA and Switzerland.

From a total of 51 studies, nine studies reported data regarding the risk factors of blood donors [21,24,26,33,41,43,56,65,70], with five studies conducted in Italy or Spain and four studies in the US, Canada or Japan. There were no differences in the risk factors for carrying a *T. cruzi* infection between blood donors in general and the rest of the individuals. In most studies on blood donors conducted in EU/EEA the *T. cruzi*-positive blood donors in EU/EEA were from Latin American countries, and those who were born in EU/EEA had travelled to endemic countries (where one man travelled through Mexico and donated blood three years later; the other man worked in Mexico and Brazil and donated blood six months later) [26].

Findings from single-arm studies

Data from the 28 studies, which only included people infected with *T. cruzi* (i.e. no comparator group), comprised of 7 490 individuals. In most studies, the majority of patients were born in Latin American countries and were immigrants in non-endemic countries. In 18 of the studies, most patients were from Bolivia (Table 2A, Annex 2; Annex 6). Additional factors associated with *T. cruzi* infection were contact with the vector, history of transfusion in endemic countries, and vertical transmission, where all cases of vertical transmission occurred in mothers who were from Bolivia, except for in one study, where the cases of congenital *T. cruzi* transmission occurred in children originating from Latin American countries but born in Europe who had never travelled abroad where the mother country of origin was not stated.

Discussion

This systematic review identified the following risk factors associated with carrying a *T. cruzi* infection in non-endemic countries: i) being born or having stayed in Latin American countries; ii) having a history of living in rural areas in endemic countries; iii) having a history of living in poor housing conditions in endemic countries; iv) having received blood transfusions in endemic countries; v) older age among individuals with other factors associated with *T. cruzi* infection; vi) maternal origin from endemic country; vii) having a family history of CD; and viii) having a generic knowledge of CD prior to testing.

Since CD is endemic in the Americas, migration of people from Latin American countries increases the numbers of individuals in non-endemic countries at risk of carrying a *T. cruzi* infection. In this review, being born in an Latin American endemic country, was associated with *T. cruzi* infection, with Bolivia being the most common country that was assessed in the included studies. Where studies considered multiple Latin American countries of origin, the strongest associations were reported for individuals being born in Boliva, however associations between *T. cruzi* infection and country of origin were reported for several other Latin American countries than Bolivia. Bolivia is in the heart of the Gran Chaco region which remains a hotspot for vectorial transmission by *Triatoma infestans*, the main vector of *T. cruzi* [1,72]. Although the prevalence of CD has declined in endemic countries since the 1990s, Bolivia remains the country with the highest prevalence in 2019 [73]. It is unknown whether the overrepresentation of Bolivia in the studies included in this review might have diluted the association between other Latin American countries and *T. cruzi* infection. It should be noted that while a limited number of studies considered the association with *T. cruzi* infection for either other Latin American countries or endemic countries as a whole, being born in an endemic country was always associated with *T. cruzi* infection when compared to non-endemic countries.

No studies in this review reported data regarding association between travelling to endemic area and *T. cruzi* infection. However, in the studies included in the narrative syntheses, all positive cases in people born in non-endemic countries reported travelling to or residence in endemic countries [26,54,65]. The risk related to travelling cannot be excluded as a result. Furthermore, one study showed that having spent three or more months in an endemic country was associated with higher risk for being infected with the parasite, including for individuals born in non-endemic countries, suggesting that having spent time in an endemic country is a predictor for *T. cruzi* infection [21].

The triatome bug vector is most associated with rural areas in endemic countries where it lives in cracks and holes in the walls of poorly constructed houses, in thatched rooves or in various outdoor settings [2,3]. This review found a history of living in poor housing conditions in endemic countries, for example, in houses with walls made of mud or with a thatched roof, consistently associated with *T. cruzi* infections. In addition, having a history of living in rural areas in endemic countries was a consistent factor associated with *T. cruzi* infection. These findings are therefore likely to reflect a higher risk for exposure of the vector and *T. cruzi* infection. In the studies included in this review, there was also some evidence of an association between previous contact with the vector in an endemic country and *T. cruzi* infection which is in concordance with the aforementioned factors. However, close contact with the vector could be also considered a potential confounder due to having previously been in or in close proximity to an endemic country. Also, there is the potential for vector presence in neighbouring non-endemic countries as *T. cruzi* infection has been reported in mammalian reservoirs (i.e. Texas, US [32]).

In our review, another factor associated with confirmed positive *T. cruzi* infection was the knowledge of CD prior to being tested. Indeed, this can increase the awareness of the disease itself and it can increase the number of tested people and as a consequence the number of positive cases. General knowledge of CD could also imply that these individuals are more likely to have lived in an affected area and consequently with increased risk for becoming infected.

Blood transfusions can be a transmission route for CD. This review found having received transfusions in endemic countries was associated with *T. cruzi* infection. Since the 1990s, endemic countries have provided a coordinated public health response to prevent and control CD, which includes the implementation of universal serological screening of blood donors, which has been well-adopted in Latin American countries with reduction in transfusion transmitted infections [3,74]. None of the studies that reported an association between previous blood transfusion in endemic countries and infections caused by the parasites, revealed the year for transfusion for the participants. Thus, it is not possible to conclude whether *T. cruzi* infection was related to a transfusion received before the implementation of universal screening in Latin American countries or because of residual infectivity due to limited sensitivity of the screening tests [74].

Our review has shown that older age is associated with *T. cruzi* infection among individuals with other factors associated with *T. cruzi* infection. This could be attributed to two main factors: 1) a longer exposure period to the *T. cruzi* parasite infection 2) older generations might have been born during a time when there were limited control programs and screening initiatives in place in endemic countries. None of the studies used a specific year of birth or a range of years as thresholds within which most *T. cruzi* -infected individuals were born.

One study showed that individuals in non-endemic countries with mothers or grandmothers born in endemic countries have an increased odds of carrying a *T. cruzi* infection with these effects being statistically significant

[21]. This is the only study that provided data regarding the association between maternal origin and *T. cruzi* infection. Given that all the studies in this review included immigrants coming from endemic countries, almost all the included participants had at least some members living or having lived in endemic countries, which might explain the lack of studies reporting data regarding the association between mothers or grandmothers born in endemic countries and *T. cruzi* infection.

In this review, a family history of CD is associated with higher odds of *T. cruzi* infections. This category could include a maternal history of CD, siblings' history of CD, grandmaternal history of CD and relatives' history of CD and was in most of the studies labelled as 'family history of CD'. A family history might reflect the environment that one shares with other family members or can be due to congenital transmission of *T. cruzi* from an infected mother. Only three of the studies specifically reported the association of having a mother who is infected with *T. cruzi* with *T. cruzi* infection [25,30,38].

Three studies from the narrative synthesis were identified that assessed the impact of congenital transmission of *T. cruzi*, reporting that the rate ranged from 2.6% to 5%, with all cases of congenital transmission occurring in mothers who were from Bolivia [20,57,67]. Considering that congenital transmission is an increasing concern in non-endemic countries, further studies should specifically address and evaluate pregnant women at risk of *T. cruzi* and strategies to control congenital transmission. No studies in this systematic review were identified that assessed vertical transmission of *T. cruzi* via breast-feeding. In general, data on this route of transmission are scarce and transmission through breastfeeding (precluded contamination of infected blood) is not considered clearly proven [75].

In endemic countries, there is usually no difference in *T. cruzi* infection between sexes. However, in this review we found women more infected than men among the individuals with other factors associated with *T. cruzi* infection. However, women tend to be overrepresented in the examined population due to the way researchers have selected participants (i.e. pregnant women from endemic countries). It should also be noted that the odds ratio in the majority of studies regarding the association between woman and *T. cruzi* infection was low with only a few studies being statically significant.

Currently in many countries in EU/EEA, selective testing of *T. cruzi* in SoHO donors occurs, primarily based on the outcome of questionnaires [76,77], which has been shown to be nearly as effective as, and less costly than universal donor testing [78]. Other EU/EEA countries defer risk groups [76,77]. Results from this systematic review could be considered when implementing prevention measures supporting in identifying donors at risk to reduce SoHO-transmission in non-endemic countries [77].

Strengths and limitations

This systematic review has several strengths. Firstly, it was carried out conforming to the PRISMA statement and employed gold-standard methods in conducting and reporting the findings. Secondly, to the best of our knowledge this is the largest systematic review that has synthesised data on factors associated with infection with *T. cruzi* in individuals residing in non-endemic countries.

However, this review inevitably also has some limitations. First, although we used a robust search strategy, grey literature was not searched. However, based on the number of studies and participants included in this review, it is highly unlikely that any unpublished data could have significantly changed the direction of the observed effects; however, it could have revealed other effects not reported in the included studies. It is possible that the population samples included in the studies in this review were not representative of the general population or that less-commonly studied risk factors were not identified.

Finally, reporting bias cannot be excluded, with results not considered statistically significant (i.e. not reaching the arbitrary p-value threshold) not being reported. Second, due to the heterogeneity in populations and comparison groups included in this review, a meta-analysis was precluded. Third, some of the included studies were underpowered, while scarcity of data was evident in respect of specific risk factors. It can be presumed, therefore, that the true effect of specific risk factors has not been detected in the context of underpowered studies. Although vote-counting synthesis is not based on the statistical significance of effects, the predictive validity of risk factors with zero or few cases within underpowered studies should be interpreted under this limitation. In a similar vein, multiple comparisons were undertaken in several studies included in this review without p-value thresholds being adjusted (e.g. Bonferroni correction). Given that we cannot exclude the possibility that type I error has occurred in studies reporting multiple comparisons, p-values within the context of those studies should be interpreted with caution.

Conclusions and potential implications

In this review, we provide a robust description of the factors associated with a higher probability of *T. cruzi* infections and the frequency and consistency of the reporting of these factors in the literature. *T. cruzi* infection can pose a significant health risk to individuals; being aware of the factors that are consistently associated with *T. cruzi* infection could therefore increase the understanding of which individuals might be at risk of carrying a *T. cruzi* infection in non-endemic countries.

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Annex 1. Search strategies

Note: The search strategy used was conducted for a wider review on Chagas disease and therefore includes terms that are not relevant to identifying risk factors.

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#1	Randomised controlled trials as Topic/	156 180
#2	Randomised controlled trial/	571 576
#3	Random allocation/	106 857
#4	Randomised controlled trial.pt.	571 576
#5	Double blind method/	172 239
#6	Single blind method/	32 018
#7	Clinical trial/	535 453
#8	exp Clinical Trials as Topic/	375 111
#9	controlled clinical trial.pt.	94 918
#10	clinical trial$.pt.	604 379
#11	multicenter study.pt.	322 894
#12	RCT.tw.	27 852
#13	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12	1 534 590
#14	(clinic$ adj25 trial$).ti,ab.	555 215
#15	((singl$ or doubl$ or treb$ or trip$) adj (blind$ or mask$)).tw.	189 443
#16	Placebos/	35 916
#17	Placebo$.tw.	236 801
#18	(allocat$ adj3 random$).tw.	42 170
#19	(Phase I or Phase II or Phase III or Phase IV).mp.	166 774
#20	#14 or #15 or #16 or #17 or #18 or #19	927 628
#21	exp case control studies/	1 332 398
#22	exp cohort studies/	2 364 720
#23	Retrospective.tw.	668 369
#24	Longitudinal.tw.	294 733
#25	Cross sectional.tw.	455 038
#26	cohort analy$.tw.	10 421
#27	Epidemiological studies/	9 124
#28	case control.tw.	144 242
#29	Prevalence.tw.	729 577
#30	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29	3 806 695
#31	(non-equivalent control group or post-testing or pretesting or pre-test post-test design or pretest post-test control group design or quasi-experimental methods or quasi-experimental study or time-series or risk-taking or risk-taking or risk taking or passive immunity or immune response).mp. or time series analysis.tw.	271 830

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#32	(((nonequivalent or non-equivalent) adj3 control$) or post-test$ or post test$ or pre test$ or pre-test$ or quasi-experiment$ or quasi experiment$ or time-series).mp. or time series.tw.	79 301
#33	#31 or #32	302 872
#34	#13 or #20 or #30 or #33	5 467 442
#35	exp Clinical Laboratory Techniques/ or exp Diagnostic Tests, Routine/ or "Reproducibility of Results"/ or exp "Sensitivity and Specificity" / or exp Humans / or exp ROC Curve /	21 634 531
#36	Index adj5 test$.mp.	15 187
#37	Reference adj5 standard$.mp.	76 155
#38	Gold$ adj5 standard$.mp.	84 756
#39	Target adj5 condition$.mp.	6 364
#40	Diagnosis.tw.	1 718 543
#41	Screening.tw.	611 908
#42	Clinical adj5 pathway$.mp.	11 743
#43	Triag$.tw.	25 249
#44	Test$ adj5 accurac$.mp.	24 542
#45	#35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44	22 092 436
#46	#34 or #45	22 710 701
#47	T cruzi.tw.	9 321
#48	Trypanosoma cruzi/	12 948
#49	Chagas disease/	12 696
#50	Chagas disease.tw.	12 808
#51	Trypanosoma cruzi.tw.	15 087
#52	American trypanosomiasis.tw.	742
#53	Chagas$ adj3 disease.tw.	13 264
#54	T cruzi adj10 lineage$.mp.	208
#55	T cruzi adj10 infect$.mp.	4 075
#56	Chagas adj15 transmi$.mp.	1 340
#57	T cruzi adj15 transmi$.mp.	737
#58	Tissue$ adj5 transplant$.mp.	26 953
#59	Tissue$ adj5 donor$.mp.	48 934
#60	Organ$ adj5 recipient$.mp.	10 072
#61	Blood adj5 recipient$.mp.	5 230
#62	Cell$ adj5 recipient$.mp.	21 274
#63	Tissue$ adj5 recipient$.mp.	2 068
#64	Organ$ adj5 infect$.mp.	30 566
#65	Blood adj5 infect$.mp.	34 967
#66	Cell$ adj5 infect$.mp.	175 584

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#67	Tissue$ adj5 infect$.mp.	44 003
#68	Organ$ adj10 transplant$. mp.	64 336
#69	SoHO.mp.	258
#70	exp Blood Donors/ or exp Humans / or exp Tissue Donors/ or exp Antibodies, Monoclonal/ or exp Organ Transplantation/ or exp Biological Assay /	20 683 951
#71	MPHO.mp.	5
#72	Allogenic adj5 transpl$.mp.	2 861
#73	Donor$ adj10 material.mp.	2 180
#74	Blood adj5 donor$.mp.	45 738
#75	Organ$ adj5 donor$.mp.	17 361
#76	Cell$ adj5 donor$.mp.	39 472
#77	Tissue$ adj5 donor$.mp.	48 934
#78	Oral$ adj15 transmi$.mp.	5 241
#79	Vector$ adj15 transmi$.mp.	15 007
#80	Congenital adj15 transmi$.mp.	3 272
#81	Organ$ adj5 transmi$.mp.	5 331
#82	Blood adj5 transmi$.mp.	9 790
#83	Cell$ adj5 transmi$.mp.	18 119
#84	Tissue$ adj5 transmi$.mp.	3 909
#85	Blood adj5 transfusion.mp.	102 138
#86	Cornea adj5 tissue$.mp.	1 642
#87	Sclera adj5 tissue$.mp.	625
#88	Valve adj5 tissue$.mp.	3 012
#89	Skin adj5 tissue$.mp.	34 372
#90	Bone adj5 tissue$.mp.	62 099
#91	Tendon adj5 tissue$.mp.	3 969
#92	Cartilage adj5 tissue$.mp.	13 263
#93	Epiderm$ adj5 tissue$.mp.	4 270
#94	Cord adj3 blood.mp.	32 517
#95	Oocyte adj3 cell$.mp.	2 827
#96	Sperm adj3 cell$.mp.	7 022
#97	Stem adj3 cell$.mp.	421 558
#98	Bone adj3 marrow.mp.	287 036
#99	Blood adj3 plasma.mp.	45 696
#100	Blood adj3 platelet$.mp.	93 705
#101	Erythrocyte$.mp.	237 586

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#102	Heart$.mp.	1 384 957
#103	Cardiac.mp.	845 200
#104	Kidney$.mp.	934 305
#105	Renal.mp.	745 032
#106	Lung$.mp.	955 589
#107	Pulmonary.mp.	745 667
#108	Liver.mp.	1 197 258
#109	Hepatic.mp.	338 069
#110	Intestin$.mp.	554 165
#111	Pancrea$.mp.	363 300
#112	Bowel.mp.	177 717
#113	Viscera$.mp.	89 306
#114	#47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57	23 724
#115	#58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #92 or #93 or #94 or #95 or #96 or #97 or #98 or #99 or #100 or #101 or #102 or #103 or #104 or #105 or #106 or #107 or #108 or #109 or #110 or #111 or #112 or #113	22 851 340
#116	Risk adj5 factor$.mp.	1 322 084
#117	Endemic adj5 countr$.mp.	9 713
#118	Risk adj5 exposure$.mp.	48 520
#119	Birth adj3 place$.mp.	4 315
#120	Domestic adj5 animal$.mp.	25 405
#121	Birth adj3 countr$.mp.	3 039
#122	Famil$ adj3 birth$.mp.	2 016
#123	Length adj5 travel.mp.	173
#124	Duration adj3 travel.mp.	330
#125	Place adj5 residen$.mp.	7 603
#126	Countr$ adj5 residen$.mp.	2 268
#127	Urban adj3 area$.mp.	43 421
#128	Rural adj3 area$.mp.	51 638
#129	Congenital.mp.	379 371
#130	Length adj5 stay.mp.	157 953
#131	History adj5 transfusion.mp.	2 034
#132	History adj5 transplant$.mp.	3 386
#133	non-endemic adj5 countr$.mp	737
#134	Parasite$ adj5 exposure$.mp.	1 648
#135	Infection$ adj5 exposure$.mp.	11 536

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#136	Famil$ adj5 exposure$.mp	3 977
#137	#116 or #117 or #118 or #119 or #120 or #121 or #122 or #123 or #124 or #125 or #126 or #127 or #128 or #129 or #130 or #131 or #132 or #133 or #134 or #135 or #136	1 967 376
#138	Predict$ adj5 model$.mp.	210 801
#139	Microscop$.mp.	1 084 049
#140	Immunoglobulin G/ or exp Serologic Tests/ or Risk Factors/ or Immunoglobulin M/	1 243 214
#141	Serodiagnos$.mp.	19 325
#142	Serologic.mp.	47 791
#143	Sero-logic$.mp.	14
#144	exp Polymerase Chain Reaction/cl, is, mt, re, st, sn, td [Classification, Instrumentation, Methods, Radiation Effects, Standards, Statistics & Numerical Data, Trends]	81 307
#145	Antibod$ adj10 test$.mp.	86 446
#146	Antigen$ adj10 test$.mp.	60 095
#147	Process$ adj10 method$.mp.	119 430
#148	Risk adj10 transmi$.mp.	36 952
#149	Sensitivit$.tw.	932 780
#150	Specificit$.tw.	548 555
#151	Red adj3 cell$.mp.	116 034
#152	Diagnostic adj3 test$.mp.	77 192
#153	Screening adj3 test$.mp.	47 426
#154	Prevent$ adj10 test$.mp.	29 450
#155	H?ematocrit.mp.	55 874
#156	HCT.mp.	18 487
#157	Ht.mp.	71 576
#158	Immunochromatograph$.mp.	4 310
#159	ICT.mp.	6 952
#160	Electrochemiluminescence.mp.	4 538
#161	ECLIA.mp.	564
#162	PCR.mp.	584 235
#163	Nucleic adj3 acid$.mp.	308 328
#164	Strout adj3 method.mp.	11
#165	Immunoblot$.mp.	107 683
#166	Western adj3 blot$.mp.	383 953
#167	exp Persistent Infection/ or exp Retrospective Studies/ or exp Enzyme-Linked Immunosorbent Assay/ or exp Seroepidemiologic Studies/	1 211 340
#168	ELISA.mp.	191 129
#169	ChLIA.mp.	16

Ovid MEDLINE(R) ALL 1946 to 29 June 2022		Number of hits
#170	CMIA.mp.	348
#171	Chemiluminescen$ adj5 Immunoassay$.mp.	3 789
#172	Chemiluminescen$ adj5 microparticle.mp.	538
#173	CLIA.mp.	1 516
#174	H?emagglutination.mp.	47 368
#175	Chemiluminescen$.mp.	24 530
#176	138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175	6 061 377
#177	115 or 137 or 176	24 674 483
#178	46 and 114	15 227
#179	177 and 178	14 223
#180	limit 179 to yr="2000 -Current"	9 100

PubMed		Number of hits
#1	(((Chagas disease OR T cruzi OR Trypanosoma cruzi OR American trypanosomiasis[MeSH Major Topic]) OR (T cruzi[Title/Abstract] OR Chagas disease[Title/Abstract] OR Trypanosoma cruzi[Title/Abstract] OR American trypanosomiasis[Title/Abstract])) AND (tissue[Text Word] OR tissues[Text Word] OR transplant[Text Word] OR transplants[Text Word] OR transplantation[Text Word] OR organ[Text Word] OR organs[Text Word] OR blood[Text Word] OR infection[Text Word] OR infections[Text Word] OR SoHO[Text Word] OR donors[Text Word] OR MPHO[Text Word] OR allogenic[Text Word] OR cell[Text Word] OR cells[Text Word] OR transmission[Text Word] OR cornea[Text Word] OR sclera[Text Word] OR valve[Text Word] OR skin[Text Word] OR bone[Text Word] OR bones[Text Word] OR tendon[Text Word] OR cartilage[Text Word] OR cord[Text Word] OR oocyte[Text Word] OR sperm[Text Word] OR stem[Text Word] OR plasma[Text Word] OR platelet[Text Word] OR platelets[Text Word] OR marrow[Text Word] OR erythrocytes[Text Word] OR heart[Text Word] OR cardiac[Text Word] OR renal[Text Word] OR kidney[Text Word] OR kidneys[Text Word] OR lungs[Text Word] OR lung[Text Word] OR pulmonary[Text Word] OR liver[Text Word] OR hepatic[Text Word] OR pancreas[Text Word] OR pancreatic[Text Word] OR bowel[Text Word] OR visceral[Text Word] OR intestines[Text Word] OR intestine[Text Word] OR intestinal[Text Word] OR risk[Text Word] OR endemic[Text Word] OR non-endemic[Text Word] OR exposure[Text Word] OR residence[Text Word] OR residency[Text Word] OR congenital[Text Word] OR rural area[Text Word] OR urban area[Text Word] OR family[Text Word] OR travel[Text Word] OR stay[Text Word] OR microscopy[Text Word] OR blood tests[Text Word] OR serological[Text Word] OR assay[Text Word] OR assays[Text Word] OR antigen[Text Word] OR antigens[Text Word] OR antibody[Text Word] OR antibodies[Text Word] OR processing[Text Word] OR specificity[Text Word] OR sensitivity[Text Word] OR diagnostic[Text Word] OR screening[Text Word] OR ICT[Text Word] OR hematocrit[Text Word] OR ECLIA[Text Word] OR PCR[Text Word] OR RT-PCR[Text Word] OR polymerase[Text Word] OR nucleic[Text Word] OR immunoblot[Text Word] OR blot[Text Word] OR blotting[Text Word] OR strout[Text Word] OR ELISA[Text Word] OR CMIA[Text Word] OR ChLIA[Text Word] OR CLIA[Text Word] OR Hemagglutination[Text Word] OR Chemiluminescence[Text Word])) NOT (case report[Title/Abstract] OR review[Title/Abstract] OR literature review[Title/Abstract] OR meta-analysis[Title/Abstract] OR meta analysis[Title/Abstract] OR letter[Title/Abstract] OR historical letter[Title/Abstract] OR narrative review[Title/Abstract] OR historical articles[Title/Abstract] OR expert opinion[Title/Abstract])	21 158
#2	//the same as above but with date restriction (Filters: from 2000 – 2022)//	14 180
#3	(((((Chagas disease OR T cruzi OR Trypanosoma cruzi OR American trypanosomiasis[MeSH Major Topic]) OR (T cruzi[Title/Abstract] OR Chagas disease[Title/Abstract] OR Trypanosoma cruzi[Title/Abstract] OR American trypanosomiasis[Title/Abstract])) AND (tissue[Text Word] OR tissues[Text Word] OR transplant[Text Word] OR transplants[Text Word] OR transplantation[Text Word] OR organ[Text Word] OR organs[Text Word] OR blood[Text Word] OR infection[Text Word] OR infections[Text Word] OR SoHO[Text Word] OR donors[Text Word] OR MPHO[Text Word] OR allogenic[Text Word] OR cell[Text Word] OR cells[Text Word] OR transmission[Text Word] OR cornea[Text Word] OR sclera[Text Word] OR valve[Text Word] OR skin[Text Word] OR bone[Text Word] OR bones[Text Word] OR tendon[Text Word] OR cartilage[Text Word] OR cord[Text Word] OR oocyte[Text Word] OR sperm[Text Word] OR stem[Text Word] OR plasma[Text Word] OR platelet[Text Word] OR platelets[Text Word] OR marrow[Text Word] OR erythrocytes[Text Word] OR heart[Text Word] OR cardiac[Text Word] OR renal[Text Word] OR kidney[Text Word] OR kidneys[Text Word] OR lungs[Text Word] OR lung[Text Word] OR pulmonary[Text Word] OR liver[Text Word] OR hepatic[Text Word] OR pancreas[Text Word] OR pancreatic[Text Word] OR bowel[Text Word] OR visceral[Text Word] OR intestines[Text Word] OR intestine[Text Word] OR intestinal[Text Word] OR risk[Text Word] OR endemic[Text Word] OR non-endemic[Text Word] OR exposure[Text Word] OR residence[Text Word] OR residency[Text Word] OR congenital[Text Word] OR rural area[Text Word] OR urban area[Text Word] OR family[Text Word] OR travel[Text Word] OR stay[Text Word] OR microscopy[Text Word] OR blood tests[Text Word] OR serological[Text Word] OR assay[Text Word] OR assays[Text Word] OR antigen[Text Word] OR antigens[Text Word] OR antibody[Text Word] OR antibodies[Text Word] OR processing[Text Word] OR specificity[Text Word] OR sensitivity[Text Word] OR diagnostic[Text Word] OR screening[Text Word] OR ICT[Text Word] OR hematocrit[Text Word] OR ECLIA[Text Word] OR PCR[Text Word] OR RT-PCR[Text Word] OR polymerase[Text Word] OR nucleic[Text Word] OR immunoblot[Text Word] OR blot[Text Word] OR blotting[Text Word] OR strout[Text Word] OR ELISA[Text Word] OR CMIA[Text Word] OR ChLIA[Text Word] OR CLIA[Text Word] OR Hemagglutination[Text Word] OR Chemiluminescence[Text Word])) AND (randomised[Title/Abstract] OR randomized[Title/Abstract] OR random[Title/Abstract] OR allocation[Title/Abstract] OR experimental[Title/Abstract] OR quasi experimental[Title/Abstract] OR quasi-experimental[Title/Abstract] OR cross-sectional[Title/Abstract] OR trial[Title/Abstract] OR clinical[Title/Abstract] OR Phase I[Title/Abstract] OR Phase II[Title/Abstract] OR Phase III[Title/Abstract] OR Phase IV[Title/Abstract] OR multicentre[Title/Abstract] OR multicenter[Title/Abstract] OR placebo[Title/Abstract] OR blinding[Title/Abstract] OR case control[Title/Abstract] OR retrospective[Title/Abstract] OR longitudinal[Title/Abstract] OR cross sectional[Title/Abstract] OR cohort[Title/Abstract] OR diagnostic[Title/Abstract] OR comparative[Title/Abstract] OR	7 245

	parallel[Title/Abstract] OR pragmatic[Title/Abstract] OR epidemiological[Title/Abstract] OR prevalence[Title/Abstract] OR non-equivalent[Title/Abstract] OR equivalent[Title/Abstract] OR inferiority[Title/Abstract] OR non-inferiority[Title/Abstract] OR post-test[Title/Abstract] OR posttest[Title/Abstract] OR pretest[Title/Abstract] OR pre-test[Title/Abstract] OR accuracy[Title/Abstract] OR gold standard[Title/Abstract] OR reference standard[Title/Abstract] OR time series[Title/Abstract] OR time-series[Title/Abstract] OR index test[Title/Abstract] OR triage[Title/Abstract] OR clinical pathway[Title/Abstract])) NOT ((case report[Title/Abstract] OR review[Title/Abstract] OR literature review[Title/Abstract] OR meta-analysis[Title/Abstract] OR meta analysis[Title/Abstract] OR letter[Title/Abstract] OR historical letter[Title/Abstract] OR narrative review[Title/Abstract] OR historical articles[Title/Abstract] OR expert opinion[Title/Abstract]))	
#4	//the same as above but with date restriction (Filters: from 2000 – 2022)//	5 492

EMBASE 1974 to 2022 Week 25		**Number of hits**
#1	exp "randomized controlled trial (topic)"/	228 910
#2	Randomized controlled trial/	713 589
#3	exp randomization/	94 269
#4	randomized controlled trial.ti,ab.	122 007
#5	exp double blind procedure/	196 010
#6	exp clinical trial/ or exp controlled study/ or exp single blind procedure/	9 682 876
#7	controlled clinical trial.ti,ab.	22 406
#8	clinical trial$.ti,ab.	627 655
#9	multicenter study.ti,ab.	48 502
#10	RCT.tw.	47 230
#11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	10 188 007
#12	(clinic$ adj25 trial$).ti,ab.	785 406
#13	((singl$ or doubl$ or treb$ or tripl$) adj (blind$ or mask$)).ti,ab.	264 587
#14	exp placebo/	381 750
#15	placebo.ti,ab.	342 288
#16	(allocat$ adj3 random$).ti,ab.	52 141
#17	(Phase I or Phase II or Phase III or Phase IV).mp.	213 466
#18	12 or 13 or 14 or 15 or 16 or 17	1 406 018
#19	exp case control study/	207 230
#20	exp cohort analysis/	855 002
#21	exp retrospective study/	1 261 407
#22	exp longitudinal study/	174 161
#23	exp cross-sectional study/	489 032
#24	cohort analy$.ti,ab.	16 699
#25	case control.ti,ab.	188 861
#26	prevalence.ti,ab.	1 034 739
#27	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	3 397 911
#28	(non-equivalent control group or post-testing or pretesting or pretest posttest design or pretest posttest control group design or quasi-experimental methods or quasi-experimental study or time-series or risk-taking or risktaking or risk taking or passive immunity or immune response).mp. or time series analysis.ti,ab.	524 431
#29	(((nonequivalent or non-equivalent) adj3 control$) or post-test$ or post test$ or pre test$ or pre-test$ or quasi-experiment$ or quasi experiment$ or time-series).mp. or time series.ti,ab.	116 617
#30	28 or 29	562 975
#31	11 or 18 or 27 or 30	12 501 112
#32	exp diagnosis/ or exp diagnostic test/ or exp diagnostic test accuracy study/ or exp "sensitivity and specificity"/	7 491 724
#33	(Index adj5 test$).mp.	22 093
#34	(Reference adj5 standard$).mp.	46 309
#35	(Gold$ adj5 standard$).mp.	147 557
#36	(Target adj5 condition$).mp.	7 642
#37	diagnosis.ti,ab.	2 490 758
#38	screening.ti,ab.	854 786

EMBASE 1974 to 2022 Week 25		Number of hits
#39	(Clinical adj5 pathway$).mp.	24 655
#40	Triag$.ti,ab.	39 165
#41	(Test$ adj5 accurac$).mp.	210 840
#42	32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41	8 945 393
#43	31 or 42	18 149 239
#44	T cruzi.ti,ab.	10 409
#45	exp Trypanosoma cruzi/	16 857
#46	exp Chagas disease/	17 053
#47	Chagas Disease.ti,ab.	14 263
#48	Trypanosoma cruzi.ti,ab.	16 195
#49	American trypanosomiasis.ti,ab.	758
#50	(Chagas$ adj3 disease).ti,ab.	14 730
#51	(T cruzi adj10 lineage$).mp.	240
#52	(T cruzi adj10 infect$).mp.	4 634
#53	(Chagas adj15 transmi$).mp.	2 080
#54	(T cruzi adj15 transmi$).mp.	870
#55	44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54	28 097
#56	(Tissue$ adj5 transplant$).mp.	27 600
#57	(Tissue$ adj5 donor$).mp.	10 772
#58	(Organ$ adj5 recipient$).mp.	15 483
#59	(Blood adj5 recipient$).mp.	9 551
#60	(Cell$ adj5 recipient$).mp.	32 906
#61	(Tissue$ adj5 recipient$).mp.	3 252
#62	(Organ$ adj5 infect$).mp.	42 079
#63	(Blood adj5 infect$).mp.	54 922
#64	(Cell$ adj5 infect$).mp.	220 393
#65	(Tissue$ adj5 infect$).mp.	68 075
#66	(Organ$ adj10 transplant$).mp.	102 786
#67	SoHO.mp.	294
#68	MPHO.mp.	18
#69	(Allogenic adj5 transpl$).mp.	15 508
#70	(Donor$ adj10 material).mp.	5 665
#71	(Blood adj5 donor$).mp.	72 033
#72	(Organ$ adj5 donor$).mp.	45 826
#73	(Cell$ adj5 donor$).mp.	66 514
#74	(Tissue$ adj5 donor$).mp.	10 772
#75	(Oral$ adj15 transmi$).mp.	7 135
#76	(Vector$ adj15 transmi$).mp.	18 477
#77	(Congenital adj15 transmi$).mp.	3 363
#78	(Organ$ adj5 transmi$).mp.	4 735
#79	(Blood adj5 transmi$).mp.	10 204

EMBASE 1974 to 2022 Week 25		Number of hits
#80	(Cell$ adj5 transmi$).mp.	23 880
#81	(Tissue$ adj5 transmi$).mp.	5 209
#82	(Blood adj5 transfusion).mp.	176 780
#83	(Cornea adj5 tissue$).mp.	3 131
#84	(Sclera adj5 tissue$).mp.	727
#85	(Valve adj5 tissue$).mp.	4 404
#86	(Skin adj5 tissue$).mp.	47 273
#87	(Bone adj5 tissue$).mp.	88 997
#88	(Tendon adj5 tissue$).mp.	5 960
#89	(Cartilage adj5 tissue$).mp.	18 433
#90	(Epiderm$ adj5 tissue$).mp.	5 414
#91	(Cord adj3 blood).mp.	57 218
#92	(Oocyte adj3 cell$).mp.	3 438
#93	(Sperm adj3 cell$).mp.	8 437
#94	(Stem adj3 cell$).mp.	654 902
#95	(Bone adj3 marrow).mp.	500 322
#96	(Blood adj3 plasma).mp.	56 397
#97	(Blood adj3 platelet$).mp.	25 291
#98	Erythrocyte$.mp.	348 514
#99	Heart$.mp.	2 674 667
#100	Cardiac.mp.	1 070 991
#101	Kidney$.mp.	1 427 454
#102	Renal.mp.	961 467
#103	Lung$.mp.	1 828 147
#104	Pulmonary.mp.	841 936
#105	Liver.mp.	1 673 368
#106	Hepatic.mp.	454 440
#107	Intestin*.mp.	804 565
#108	Pancrea$.mp.	543 344
#109	Bowel.mp.	288 690
#110	Viscera$.mp.	121 837
#111	56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110	9 722 553
#112	exp risk factor/	1 225 895
#113	(Endemic adj5 countr$).mp.	12 960
#114	(Risk adj5 exposure$).mp.	65 904
#115	(Birth adj3 place$).mp.	5 763
#116	(Domestic adj5 animal$).mp.	24 112
#117	(Birth adj3 countr$).mp.	3 868
#118	(Famil$ adj3 birth$).mp.	2 417
#119	(Length adj5 travel).mp.	215

EMBASE 1974 to 2022 Week 25		Number of hits
#120	(Duration adj3 travel).mp.	434
#121	(Place adj5 residen$).mp.	9 597
#122	(Countr$ adj5 residen$).mp.	2 939
#123	(Urban adj3 area$).mp.	99 437
#124	(Rural adj3 area$).mp.	96 604
#125	Congenital.mp.	641 536
#126	(Length adj5 stay).mp.	282 314
#127	(History adj5 transfusion).mp.	3 527
#128	(History adj5 transplant$).mp.	8 809
#129	(non-endemic adj5 countr$).mp.	1 008
#130	(Parasite$ adj5 exposure$).mp.	1 930
#131	(Infection$ adj5 exposure$).mp.	16 097
#132	(Famil$ adj5 exposure$).mp.	6 982
#133	112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132	2 358 397
#134	(Predict$ adj5 model$).mp.	273 329
#135	Microscop$.mp.	1 320 158
#136	exp serology/	192 653
#137	Serodiagnos$.mp.	41 824
#138	Sero-logic$.mp.	75
#139	Serologic.mp.	35 988
#140	(polymerase adj3 chain).mp.	1 157 994
#141	(Antibod$ adj10 test$).mp.	109 998
#142	(Antigen$ adj10 test$).mp.	65 137
#143	(Process$ adj10 method$).mp.	193 074
#144	(Risk adj10 transmi$).mp.	48 812
#145	Sensitivit$.tw.	1 202 027
#146	Specificit$.tw.	706 124
#147	(Red adj3 cell$).mp.	158 251
#148	(Diagnostic adj3 test$).mp.	327 216
#149	(Screening adj3 test$).mp.	120 597
#150	(Prevent$ adj10 test$).mp.	43 119
#151	H?ematocrit.mp.	83 671
#152	HCT.mp.	40 085
#153	Ht.mp.	100 705
#154	Immunochromatograph$.mp.	6 596
#155	ICT.mp.	10759
#156	Electrochemiluminescence.mp.	9 967
#157	ECLIA.mp.	1 458
#158	PCR.mp.	849 889
#159	(Nucleic adj3 acid$).mp.	168 298
#160	(Strout adj3 method).mp.	19

EMBASE 1974 to 2022 Week 25		**Number of hits**
#161	Immunoblot$.mp.	167 962
#162	(Western adj3 blot$).mp.	544 267
#163	exp enzyme linked immunosorbent assay/	433 445
#164	ELISA.mp.	327 981
#165	ChLIA.mp.	78
#166	CMIA.mp.	872
#167	(Chemiluminescen$ adj5 Immunoassay$).mp.	14 670
#168	(Chemiluminescen$ adj5 microparticle).mp.	1 350
#169	CLIA.mp.	4 972
#170	H?emagglutination.mp.	32 902
#171	Chemiluminescen$.mp.	43 257
#172	134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171	5 915 900
#173	43 and 55	15 440
#174	111 or 133 or 172	15 029 779
#175	173 and 174	11 299
#176	limit 175 to yr="2000 -Current"	9 369

Annex 2. Characteristics of included studies

Table 1A. Characteristics of included studies using an analytical design

These studies include both patients with a T. cruzi infection and healthy individuals who were at risk of T. cruzi infection.

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
[53] Alcántara Román et al., 2018*	Spain (northern Barcelona)	Observational cohort	192; 117 seropositive mothers with 300 descendants (192 descendants had serological results); 100% mothers & 48% (144/300) descendants; 2005–2016	- mean age (yr, SD): 21.31 (±7.4) - 23/192 seropositive (11.98%; 95% CI 8.1–17.3%)	<u>Serological status of descendants based on socio-demographic factors</u> - Age (<14 yrs; *T. cruzi*-positive): 7/70; Age (>14 yrs; *T. cruzi*-positive): 16/122, p=0.52 (NS) - Sex (male; *T. cruzi*-positive): 11/96; Sex (female; *T-cruzi*-positive): 12/96, p=0.82 (NS) - Born in EU (yes; *T. cruzi*-positive): 5/51; Born in EU (no; *T. cruzi*-positive): 18/141, p=0.58 (NS) - Accessibility of descendants for testing (yes; *T. cruzi*-positive): 16/139; Accessibility of descendants for testing (no; *T. cruzi*-positive): 7/53, p=0.74 (NS) <u>Computed OR (95%CI), p-value</u> - Sex (ref.: male): 1.1 (0.46, 2.64), p=0.82 (NS) - Age (ref.: <14yr): 1.35 (0.53, 3.48), p=0.52 (NS) - Born in EU (ref.: No): 0.74 (0.26, 2.11), p=0.57 (NS)
[54] Angheben et al., 2011	Italy (Verona & Florence)	Observational cohorts	<u>Retrospective review</u> 867; at-risk individuals (migrants, adoptees, expatriates, travellers, born to seropositive mothers); 48.6%; 1998–2010 <u>Screening programme</u> 214 pregnant women, 28 specimens from blood donors, 70 HIV-positive LA migrants; at-risk subjects (pregnant women, blood donors & HIV-positive subjects of LA origin or born to a LA mother); NR;	<u>Retrospective review</u> - mean age (yr): 26.2 (range: 1–85 yr) - 36/867 (4.2%) were seropositive <u>Screening programme</u> - Pregnant women: mean (yr), range: 32 (14–44); Blood donors: 39 (21–55), HIV-positive patients: 38 (22-56) - 3/214 (1.4%) pregnant women were seropositive; No blood donors were seropositive; None of the HIV-positive patients were seropositive	<u>Country of origin of seropositive (retrospective review)</u> - 77.7% were from Bolivia; the rest from LA & CA countries (only one patient was from Italy); - 83.4% were migrants, 13.8% were adopted children <u>Country of origin of seropositive (Screening programme)</u> - 3 seropositive pregnant women were from LA countries (2 from Bolivia & 1 from Paraguay)

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
			1998–2010		
[18] Antinori et al., 2018	Italy (Milan)	Cross-sectional	501 (471 adults & 30 children); adults & children from LA countries; 63%; 2013–2014	- median age: 39 yr (IQR= 32-48.7) - median age: 10.5 yr (IQR 8.2-14) - CD: 48/501 (prevalence: 9.6%)	- 43/48 (89.6%, p<0.0001, Sig.) were from Bolivia; 4 from El Salvador; 1 from Argentina - Age in yrs (median, IQR): 41 (1-66), p= 0.405(NS) - Females: 16/48(33.3%), p=0.448(NS) - Department of origin: Santa Cruz (50%), p<0.0001 (***Sig.***) - Had lived in rural areas: Yes (81.2%), p<0.0001 (***Sig.***) - Had lived in mud houses: Yes (79.2%), p<0.0001 (***Sig.***) - Had received transfusion: Yes (8.8%), p= 0.569 (NS) - Has a relative with CD: Yes (22.9%), p<0.0001 (***Sig.***) <u>Univariate analysis (OR, 95%CI, p-value)</u> - Age (each yr more): 1.01 (0.99, 1.04), p=0.314 (NS) - Sex (ref.: male): 1.28 (0.67, 2.44), p= 0.449 (NS) - Country of origin (ref.: all but Bolivia): 21.80 (8.43, 56.35), p<0.0001 (***Sig.***) - Department of origin (ref.: Provinces outside Bolivia): Santa Cruz = 17.99 (7.96, 40.66), p <0.0001 (***Sig.***); Cochabamba = 12.96 (5.42, 30.96), p<0.0001 (***Sig.***); La Paz = 0.98 (0.05, 18.92), p= 0.991 (NS) - Having lived in rural areas (ref.: No): 3.99 (1.88, 8.44), p<0.001 (***Sig.***) - Having lived in mud houses (ref.: No): 4.64 (2.25, 9.56), p <0.0001 (***Sig.***) - Previous transfusions (ref.: No): 0.70 (0.21,

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					2.37), p= 0.571 (NS) - Having a relative with CD (ref.: No): 24.22 (7.86, 74.57), p <0.0001 (***Sig.***) <u>Multivariate analysis (aOR, 95%CI, p-value)</u> - Age (each yr more): 1.05 (1.02, 1.09), p= 0.004 (***Sig.***) - Country of origin (ref.: all but Bolivia): 8.80 (2.10, 36.87), p= 0.003 (***Sig.***) - Department of origin (ref.: Provinces outside Bolivia): Santa Cruz= 3.72 (1.02, 13.64),p= 0.047 (***Sig.***); Cochabamba= 2.09 (0.56, 7.78), p=0.272 (NS); La Paz= 0.18 (0.01, 4.06), p= 0.278 (NS) - Having lived in mud houses (ref.: No): 2.68 (1.17, 6.13), p= 0.019 (***Sig.***) - Having a relative with CD (ref.: No): 12.77 (2.96, 55.06), p= 0.001 (***Sig.***)
[19] Avila Arzanegui et al., 2013	Spain (Basque Country)	Cross-sectional	158; LA pregnant women; 100%; 2008–2010	- mean age (SD): 28.5 yr (±5.3) - 19/158 (prevalence: 12%)	- 16 (84.2%) came from Bolivia, 2 from Paraguay and 1 from Brazil <u>Univariate Analysis (OR, 95%CI, p-value)</u> - Natural of Bolivia: 8.55 (2.39, 30.56), p=0.001 (***Sig.***) - Residence in rural area: 3.80 (1.44, 10.02), p=0,007 (***Sig.***) - Residence in house with adobe: 9.79 (3.55, 27.31), p=0.001 (***Sig.***) - Contact with vector: 15.84 (3.52, 71.09), p=0.001 (***Sig.***) - Family history of CD: 3.33 (1.22, 9.064), p=0,018 (***Sig.***) - Family history of sudden death: 3.30 (1.02, 10.68), p=0.046 (***Sig.***) *The relationship with the following variables were NS (ORs are NR): Previous surgery; transfusion; clinical manifestations; family history of cardiopathy;

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					family history of constipation; primiparity; spontaneous abortion; age; time of residence in Spain. Multivariate Analysis (B, 95%CI, p-value) - Residence in house with adobe: 5.275 (1.773, 15.693), p=0.003 (***Sig.***) - Contact with vector: 9.543 (2.018, 45.121), p=0.004 (***Sig.***)
[20] Barona-Vilar et al., 2012	Spain (Valencian Community)	Cross-sectional	1 975; pregnant women from endemic countries and their newborns; 100%; 2009–2010	- mean age in yr (SD): 29 (6) - 11.4% prevalence (overall) - Prevalence in SA countries were higher than CA countries (11.8% vs. 2.5%, p<0.01) (***Sig.***) - In SA countries, the prevalence of the was higher in women born in countries from the Southern Cone than from the Andean Region (24.8% vs. 0.1%, p<0.0001) (***Sig.***) - The highest prevalence was observed in women from Bolivia compared to other countries in this region (34.1%) (p<0.0001) (***Sig.***)	- 94.7% (214/226) of the detected cases in this study corresponded to Bolivian mothers - 8 newborn infants (all from Bolivian mothers) were diagnosed with cCD (vertical transmission rate of 3.7%)
[55] Basile et al., 2019	Spain (Catalonia)	Observational cohort	33 469; Pregnant women; 100%; 2010–2015	- NR - 818/33 469 (prevalence: 2.44) - prevalence rate: 2.8 positive cases per 100 pregnancies screened - Rates were highest in women from Bolivia (15.79)	Maternal risk factors for vertical transmission of the infection (aOR, 95%CI, p-value) - Age < 33 yr (ref.: ≥ 33 yr): 1.3 (0.35, 5.28), p=0.693 (NS) - No previous treatment (ref.: yes): 6.67 (0.78, 876.89), p=0.093 (NS) - Country of birth (ref.: Bolivia): Paraguay 1.30 (0.17, 10.15), p=0.801 (NS) - Clinical form of CD (ref.: intermediate): Heart 14.40 (2.11, 87.67), p=0.009 (***Sig.***) - Siblings completing follow-up (ref.: Negative): 22.79 (3.75, 161.54), p=0.001 (***Sig.***) - Yr living in Catalonia (ref.: >7): 1.76 (0.42, 10.05), p=0.453 (NS)
[56] Cantey et al., 2012*	US	Observational cohort	1084 (37 included in the follow-up study);	- NR - 1084/29 million	- 15/37 consists of concordant group

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
			blood donors; NR; 2006–2010	(prevalence: 1 in 26,700 donations)	(positive by two tests); 100% were born in US; 60% female; 67% were non-Hispanic white; 33% were Hispanic; in none of the case mother was born in an endemic country - 2/15 received blood product in US; 8/15 travel to endemic country; 3/15 travel to rural area of an endemic country - 15/15 have resided in a state with *T. cruzi* vector or infected mammalian reservoir with 11/17 living in rural area within these states; 7/15 have worked outdoors in those states; 10/15 had outdoor leisure activity in those states. Computed summary statistics: OR (95%CI), p-value - Sex (ref.: male): 3.07 (0.78, 13.16), p=0.1 (NS)
[21] Custer et al., 2012	US	Cross-sectional	1 183 076 donors (2 940 491 allogeneic donations)/230 completed the risk-factor questionnaire; Blood donors; NR; 2007–2009	- NR - Prevalence: 1 in 13 292 donors (95% CI, 1:13,269-1:13,317) - 63/221 were confirmed cases (risk-factors questionnaire)	- 37/89 (41.6%) of confirmed positive donors were female; 68.5% were first-time donors; 30.3% & 34.8% aged between 25-39 & 40-54 respectively; 75.3% were Hispanics; 28.1% were born in US, 36% in Mexico, 25.8% in CA or SA. Associations between positive donors' characteristics & risk factors (OR, 95%CI, p-value) - Lived in a rural area of endemic countries: 38.6 (15.1, 102.5), p<0.0001 (***Sig.***) - Lived in house with a thatched roof: 15.8 (4.8, 66.1), p<0.0001 (***Sig.***) - Lived in a house made of mud or earth: 20.1 (7.6, 58.3), p<0.0001 (***Sig.***) - Been bitten by kissing bug: 76.1 (11.1, 3173), p<0.0001 (***Sig.***) - Mother born in endemic countries: 26.0 (11.3, 60.4), p<0.0001 (***Sig.***) - Grandmother born in endemic countries: 18.7

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(8.4, 41.8), p<0.0001 (***Sig.***) <u>Multivariable predictors' model (OR, 95%CI, p-value)</u> - Donation history: 1.7 (0.6, 4.8), p=0.4 (NS) - ≥3 months in endemic country (yes): 9.7 (3.0-31.8), p<0.001 (***Sig.***) - Hispanic ethnicity (yes): 7.4 (2.4, 22.7), p<0.001 (***Sig.***)
[22] Da Costa-Demaurex et al., 2019	Switzerland (Lausanne)	Cross-sectional	1 010; at-risk groups (migrants, travellers, pregnant women); NR; 2011–2012	- median (IQR): 34 yr (25–46) - Prevalence: 16/1 010 (1.6%, 95% CI: 0.9–2.6%) - Prevalence among migrants: 16/698, (2.3%, 95% CI: 1.3–3.7%) & among Bolivians 14/78, (18%, 95% CI: 10.2–28.3%)	- Median age (IQR): 45 yr (IQR 36–52) - All positive cases were in people born in Latin America <u>Predictors for positivity (OR, 95%CI, p-value)</u> - Bolivian origin: 95 (19, 484), p<0.001 (***Sig.***) - Tested in the community: 56 (14, 219), p<0.001 (***Sig.***) - Tested in the community (when being Bolivian): 23 (2, 243), p<0.001 (***Sig.***) - Age >35 yr: 3.4 (1.1, 10.5), p=0.03 (***Sig.***) - Female sex: 1.2 (0.4, 3.2), p=0.76 (NS)
[23] Di Girolamo et al., 2016*	Italy (Bologna)	Cross-sectional	151; being born in an endemic country/having spent >3 months in endemic areas/being born from a mother born in an endemic country; 62.91%; 2010–2013	- mean age (SD): 37.5(13.1) - 12/151 (prevalence: 7.94%)	- Out of 12, 10 were Bolivians and 2 were Argentinians - 75% were females - 92% aged >35 yr - 58% lived in rural area - 42% had cases of CD within the family - 33% had blood transfusion in the country of origin - 7 were in the indeterminate phase <u>Computed summary statistics: OR (95%CI), p-value</u> - Sex (ref.: male): 1.67(0.46, 8.25), =0.42 (NS) - Age (ref.: ≤35yr): 7.22 (1.32, 181.31), p=0.019

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(***Sig.***) - Country of origin (ref.: other than Bolivia): 23.47 (4.81, 114.38), p=0.0001 (***Sig.***) - Residence area (ref.: urban): 3.36(0.98, 12.36), p=0.03 (***Sig.***) - Cases of CD in family (ref.: No): 14.88(3.63, 60.95), p=0.0002 (***Sig.***) - History of blood transfusion in the country of origin (ref.: No): 7.68 (1.9, 31.08), p=0.004 (***Sig.***)
[24] El Ghouzzi et al., 2010	France (Paris)	Cross-sectional	30 837 (31 956 donations); Blood donors born in LA and/or whose mother had been born in LA and/or returned from traveling in LA more than 4 months; NR; 2007–2008	- NR - Prevalence (overall): 9.7 in 100 000 donors. - Prevalence (among donors from LA): 0.31%	- 3 positive donors (1 born in Bolivia & 2 born in El Salvador)
[25] Favila Escobio et al., 2015*	Spain (Majorca)	Cross sectional	251; adult Bolivians; 42.2%; 2011–2012	- Mean age (SD): 34.62 (9.3) - Prevalence: 19.1% (CI95%: 14.06-24.19) (48/251)	<u>Province of origin</u> - La Paz/Santa Cruz/Cochabamba/Chupisaca-Potosi-Tarija (versus other provinces less risk): p=0.08 (NS) Time since leaving Bolivia - <4 yr (versus ≥4 yr): p=0.82 (NS) Area - Rural (versus urban): p=0.004 (***Sig.***) House - Mud (versus brick): p=0.01 (***Sig.***) Mother serology - Positive (versus negative): p<0.001 (***Sig.***) CD in relatives - Yes (versus No): p=0.001 (***Sig.***) Have seen the insect - Yes (versus No): p<0.001 (***Sig.***) Experience of transfusion - Yes (versus No): p=0.89 (NS) Previous CD results

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					- Positive (versus negative): p=0.002 (***Sig.***) Previous CD treatment - Yes (versus No): p=0.006 (***Sig.***) <u>Adjusted model OR (95%CI), p-value</u> - Sex (ref.: male): 2.09 (95%CI: 0.9-4.59) (NS) - Family history of CD (ref.: No): 2.65 (95%CI: 1.19-5.76) (***Sig.***) - Contact with the vector (ref.: no): 4.79(95%CI: 1.37-16.70) (***Sig.***) <u>Computed OR (95%CI), p-value</u> - Sex (ref.: male): 1.81 (0.96, 3.42), p=0.06 (NS) - Time since leaving Bolivia (ref.: <4yr): 0.88(0.31, 2.51), p=0.82 (NS) - Area (ref.: urban): 2.6 (1.33, 5.08), p=0.005 (***Sig.***) - House (ref.: brick-made): 2.45 (1.2, 5), p=0.01 (***Sig.***) - Mother serology (ref.: Negative): 8.33 (2.65, 26.13), p=0.0003 (***Sig.***) - CD in relatives (ref.: No): 3.45 (1.67, 7.14), p=0.0008 (***Sig.***) - Contact with the vector (ref.: No): 5 (1.89, 13.19), p=0.001 (***Sig.***) - Experience of transfusion (ref.: No): 1.06 (0.4, 2.77), p=0.89 (NS) - Previous Chagas results (ref.: No): 10.23 (1.85, 56.48), p=0.007 (***Sig.***) - Previous CD treatment (ref.: No): 12.8 (1.3, 125.94), p=0.02 (***Sig.***)
[57] Flores-Chavez et al., 2011	Spain (Madrid)	Observational cohort	3 839; pregnant women from LA; 100%; 2008–2010	- NR - prevalence (overall): 3.96% (152/3,839) - prevalence was 10% for only pregnant Bolivian women & 6% for pregnant	- 95.4% (145/152) of seropositive mothers were from Bolivia - four infected children were detected (all born to Bolivian mothers)

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
				Bolivian women & pregnant women from other countries with clinical and epidemiological background	- Overall rate of cCD transmission: 2.6%
[58] Francisco-González et al., 2018	Spain (Madrid)	Observational cohort	1 244; LA pregnant women; 100%; 2013–2015	- NR - Prevalence 3.2% (95%CI: 2.4-4.4%) (40/1244) - Prevalence in Bolivian women was 16.3% (95% CI: 12.6-20.8%)	- 85% of the pregnant women with positive serology for *T. cruzi* were from Bolivia (the rest from Paraguay, Ecuador and Argentina) - 40 newborns born to mothers with positive CD serology (vertical transmission rate 2.8%, 95% CI: 0-15%)
[26] Gabrielli et al., 2013	Italy (Rome)	Cross-sectional	128; at-risk blood donors (born and/or coming from LA countries); 42.2%; 2010–2012	- Mean age (range): 37.5 yr (19-66 yr) - 5/128 (3.9%) were positive to at least one serological test	- The seropositive individuals were three LA immigrants from Brazil, Bolivia and Colombia and two Italian The Italians were: '…a 38-year-old man, a backpacker globetrotter who, during 2008–2009, travelled through Mexico and in 2012 offered a first blood donation', and the second was '…a 46-year-old engineer researcher, who worked in Mexico and, more recently, in impervious internal areas of Brazil, where he stayed until 2011 (six months before his first blood donation that evidenced his positivity to ICT)'. The blood of this donor proved PCR-positive and showed a very mild parasitaemia in Giemsa-stained thick blood smears.
[59] Giménez-Martí et al., 2006	Spain (Valencia)	Observational cohort	432 sera; immigrant population of SA; 52%; 2001	NR	- Positive results: Bolivia 31.7% (13/41), Argentina 12.5% (1/8), Colombia 6.5% (12/185) and Ecuador 2.2% (4/185) - The samples positive for both techniques came mostly from Bolivia (13/16)
[27] Gómez i Prat et al., 2019	Spain (Barcelona)	Cross-sectional	271; mostly Bolivian immigrants; 71.2%; 2017	- median age (IQR): 38 yr (31–44) - prevalence: 8.9% (24/271)	- Out of 24 infected people, 23 were Bolivians and 1 was Argentinian - 41.7% of positive participants aged 50-59 yr - 75% (18/24) of positive participants have lived in Spain >10 yr - 75% (18/24) of the positive results were in

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					women
[28] Gonzalez Martinez et al., 2009	Spain (Barcelona)	Cross-sectional	216; patients from LA; NR; 2004–2006	- NR - prevalence: 21.3% (46/216)	- 38/216 (82.6%) were women - 42 (91%) were originally from Bolivia (the rest from Brazil, Honduras and Chile) - 44/216 (95.7%) had lived in a rural area - 11/216 (24%) had lived in other endemic countries - 5/216 (10.9%) they had received blood transfusions
[60] Guggenbühl Noller et al., 2020	Germany	Observational cohort	5 991; Routine patients; ≈40%; 2000–2018	- mean age (SD): 39.1 (16.7) - prevalence: 1.4% (81/5991)	- 47/81 patients found positive (58.0%) were evaluated - 15/43 (34.9%) CD cases were diagnosed for the first time - 35/80 (43.8%) patients were females of childbearing age - Most prevalent nationality was Bolivian n = 20/35 (57.1%) (where data were available) LR (OR, 95%CI, p-value) in a subset of patients (n=1596) - Sex (ref.: females): 0.17 (0.03, 0.60) (***Sig.***) - Brazilian/Bolivian nationality (ref.: other): 273.48 (51.68, 5059.88) (***Sig.***) - Age (ref.: previous yr): 1.03 (1.01, 1.06) (***Sig.***)
[29] Hernandez et al., 2019*	US (Los Angeles County)	Cross-sectional	189; relatives of patients with CD; 59.3%; NR	- NR - prevalence: 7.4% (14/189)	- 10/14 seropositive individuals (71.4%) were over 40 - El Salvador had the highest prevalence (9/55, 16.4%, p= 0.005) (***Sig.***) - Siblings (7/28, 25%, p=0.001) (Sig.) & parents (2/5, 40%, p< 0.045) (***Sig.***) had the highest prevalence - 4/138 (2.9%) participants who had a parent with CD were seropositive Computed OR (95%CI), p-value

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					- Sex (ref.: male): 1.25 (0.4, 3.91), p=0.69 (NS)
[61] Hyson et al., 2021	US (Colorado)	Observational cohort	1 156; hospital patients (pre-transplant screening); 39%; 2006–2020	- median age: 59 - prevalence: 1.99% (23/1156)	- 52% with positive *Trypanosoma cruzi* IgG were born in an endemic country with 3/23 were confirmed positive (all 3 from were born in LA) - 13/23 (54%) were born in CD endemic regions: 6 in Mexico, 3 in El Salvador, and from 1 each in Honduras, Guatemala, Colombia, Bolivia (9 of these unconfirmed) - 11 cases came from the solid organ transplant clinics, 3 from the bone marrow transplant clinic, 2 from the infectious disease clinic, 2 from the inpatient general medicine service, & 5 from the inpatient cardiology service.
[62] Ikedionwu et al., 2020	US (whole country database)	Observational cohort	131 529 240; women of reproductive age admitted to hospital; 100%; 2002–2017	- NR - prevalence: 3.7 cases per million hospitalisations (487/131 529 240)	- Aged 15–24 yr: 6.8% cases; aged 35–49 yr: 76.6% of cases Adjusted LR (OR, 95%CI, p-value) - Age (ref.: 15–24 yr): 1.76 (0.7, 4.38), p=0.23 (NS) (25–34 yr); 9.39 (4.18, 21.07), p<0.0001 (***Sig.***) (35–49 yr) - Race (ref.: White): 0.45 (0.06, 3.43), p=0.44 (NS) (Black); 25.85 (5.64, 118.5), p<0.0001 (***Sig.***) (Hispanic); 5.16 (1.07, 24.94), p=0.04 (***Sig.***) (Other) - Zip income quartile (ref.: Highest quartile): 0.25 (0.12, 0.52), p<0.0001 (***Sig.***) (lowest); 0.37 (0.18, 0.78), p=0.01 (***Sig.***) (2nd quartile); 0.24 (0.11, 0.52), p<0.0001 (***Sig.***) (3rd quartile)
[30] Jackson et al., 2010*	Switzerland (Geneva)	Cross-sectional	1 012; adult LA migrants; 83%; 2008	- mean age (SD): 37.2 (11.3) - prevalence (95%CI): 12.8% (10.8– 14.9), (130/1 012) - prevalence among Bolivians: 26.2% (22.3–	- Three positive non-Bolivian patients had lived in Bolivia for several years LR (unadjusted OR, 95%CI) (n=1012) - Age (ref.: ≤35): 2.7

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
				30.1), 127/1012	(1.8, 4) (age>35) (***Sig.***) - Sex (ref.: male): 1.04 (0.6, 1.7) (NS) - Origin (ref.: other): 61.7 (19.5, 195.3) (Bolivia) (***Sig.***) - Mother with *T. cruzi* infection: 5.9 (3.4, 10.3) (***Sig.***) - Previous triatomine bite: 7.1 (3.9, 12.0) (***Sig.***) <u>LR (adjusted OR, 95%CI) (n=378)</u> - Age (ref.: ≤35): 6.1 (2.2, 16.7) (age>35) (***Sig.***) - Sex (ref.: male): 1.04 (0.3, 3.4) (NS) - Origin (ref.: other): 31.7 (7.2, 139.5) (Bolivia) (***Sig.***) - Mother with *T. cruzi* infection: 6.5 (1.9, 22.8) (***Sig.***) - Previous triatomine bite: 1.8 (0.7, 4.6) (NS) <u>Computed OR (95%CI), p-value</u> - Previous transfusion (ref.: no): 2.3(1.49, 3.73), p=0.0002 ***(Sig.)***
[31] Lescure et al., 2009**	France (Paris)	Cross-sectional	254; at-risk LA population; 59.8%; 2008–2009	- median age (range): 33 (11–63) - prevalence: 23.6% (60/254)	- 87.4% were of Bolivia origin <u>LR (OR, 95%CI)</u> - Sex (ref.: male): 0.76 (0.48, 1.45) (NS) - Origin (ref.: other): 2.14 (0.68, 4.30) (Bolivia) (NS) - Zone (ref.: rural): 1.02 (0.52, 1.83) (urban) (NS) - Personal antecedents of CD (ref.: no): 3.23 (1.08, 4.27) (***Sig.***) - Family antecedents of CD (ref.: no): 1.84 (1.08, 3.52) (***Sig.***)
[63] Llenas-Garcıa et al., 2021	Spain (Valencian community)	Observational cohort	1 178; pregnant LA women; 100% ; 2013–2018	- NR - prevalence: 2.2% (26/1 178) - prevalence in Bolivian women: 18.7% (21/112)	- Mean age (SD): 33.7 (3.9) yr - The highest prevalence was observed in Bolivian women.
[32] Llenas-Garcıa et al.,	Spain (Madrid)	Cross-sectional	154; HIV-1/HIV-2 LA adults; 24.5%;2008–	- mean age (SD): 36.9 (±8.4)	- Country of origin of cases (confirmed by 2

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
2012*			2009	- prevalence: 2.6% (4/154); prevalence (confirmed by both ELISA & IFAT): 1.9% (3/154)	tests): 2 Bolivian women & 1 Argentinian man Factors associated with CD diagnosis (PR, 95%CI, p-value) - Male sex: 0.16 (0.015, 1.76), p= 0.151 (NS) - Bolivian origin: 23.67 (2.31, 242.52), p= 0.016 (***Sig.***) - Had seen vectors at home: 27.2 (2.69, 274.84), p= 0.012 (***Sig.***) - Previous CD test: 24.73 (2.43, 251.74), p= 0.015 (***Sig.***) - Secondary education: 0.11 (0.01, 1.17), p= 0.084 (NS) - Rural origin: NP, p=0.023 (***Sig.***) - Travel to their home country: NP, p=0.091 (NS) - Adobe-made house: NP, p=0.001 (***Sig.***) - Thatch-roofed house: NP, p<0.0001 (***Sig.***) - Knowledge of CD: NP, p=0.019 (***Sig.***) - Knowledge of vectors: NP, p=0.009 (***Sig.***) Computed OR (95%CI), p-value - Country of origin (ref.: other than Bolivia): 28.2 (2.35, 338.33), p=0.008 (***Sig.***)
[33] Mangano et al., 2020*	Italy (Tuscany)	Cross-sectional	1 985; at-risk blood donors; 39.6%; 2016–2018	- NR - prevalence: 0.5% (95%) CI: 0.3–0.9) (10/1 985)	% Seropositivity (95% CI) - Females: 0.8 (0.4, 1.7) - Age (18–29): 1.4 (0.6, 3.2) - LA: 1.0 (0.3, 3.5) The groups above were over-represented among seropositive donors, however there were no significant differences. Computed OR (95%CI), p-value - Sex (ref.: male): 2.28

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(0.64, 8.13), p=0.2 (NS)
[34] Manzardo et al., 2008	Spain (Barcelona)	Cross-sectional	41; at-risk immigrants from tropical areas; 62.6%; 2001–2004	- Median age (range): 28 (0.6, 80.6) - prevalence: 34% (14/41)	- 9/14 positives were women - All positives were Bolivian (42.2% from Santa Cruz de la Sierra & 35.7% from Cochabamba) - 5/14 had been living in clay houses; 4/14 had family history of CD; 2/14 had blood transfusion in their country of origin; 1/14 was a child whose mother had positive serology for CD
[35] Martinez de Tejada et al., 2009	Switzerland (Geneva)	Cross-sectional	305; LA pregnant women; 100%; 2008	- mean age (SD): 30.4 (5.7) - prevalence: 2% (6/305); prevalence (Bolivians): 8.8%	- All seropositive women were of Bolivian origin - All patients were at the stage of chronic/indeterminate phase of the disease - 6 newborns (two of them were found positive)
[36] Meymandi et al., 2017	US (Los Angeles County)	Cross-sectional	4 755; LA–born residents; 65.5%; 2008–2014	- 31-40: 25.4%; 41–50: 36.3; 51–60: 27% - prevalence: 1.24% (95% CI = 0.93–1.55%), (59/4755); Prevalence was higher in Salvadorans (3.45%)	<u>CD Prevalence (95% CI), p-value</u> - Age range (18–30): 0.61 (0, 1.30), p=0.277 (NS) - Age range (31–40): 1.08 (0.49, 1.67), p=0.550 (NS) - Age range (41–50): 1.57 (0.98, 2.16), p=0.129 (NS) - Age range (51–60): 1.21 (0.62, 1.80), p=0.888 (NS) - Sex (male): 1.18 (0.65, 1.71), p=0.711 (NS) - Sex (female): 1.30 (0.90, 1.70) - Education (less than High school): 1.45 (1.03, 1.87), p=0.121 (NS) - Education (≥High school): 0.90 (0.43, 1.37) - Country of origin (Mexico): 0.79 (0.48, 1.10), p<.001 (***Sig.***) - Country of origin (Oaxaca, Mexico): 4.65 (0.20, 9.10), p=0.004 (***Sig.***) - Country of origin (Zacatecas, Mexico): 2.20 (0.29, 4.11), p=0.028 (***Sig.***) - Country of origin

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(Jalisco, Mexico): 0.63 (0.08, 1.18), p=0.650 (NS) - Country of origin (other, Mexico): 0.53 (0.22, 0.84), p=0.026 (***Sig.***) - Country of origin (El Salvador): 3.45 (2.19, 4.71), p<0.001 (***Sig.***) - Country of origin (Guatemala): 0.63 (0, 1.34), p=0.275 (NS) - Country of origin (Other): 1.04 (0, 2.21), p=0.758 (NS) - Lived in rural area/farm: 1.85 (0.77, 2.93), p=0.110 (NS) - Thatched roof: 2.70 (1.13, 4.27), p=0.002 (***Sig.***) - Mud: 1.47 (0.73, 2.21), p=0.290 (NS) - Adobe: 1.28 (0.82, 1.74), p=0.372 (NS) - Zero housing factors: 0.77 (0.0, 1.63), p=0.411 (NS) - 1 housing factor present: 1.13 (0.60, 1.66), p=0.516 (NS) - 2 housing factors present: 0.72 (0.09, 1.35), p=0.446 (NS) - 3 housing factors present: 3.46 (1.10, 5.82), p=0.001 (***Sig.***) - Remembers triatomine bites: 1.40 (0.58, 2.22), p=0.574 (NS) - Prior CD diagnosis: 50.0 (21.7, 78.3), p<0.001 (***Sig.***) - Family history sudden death: 0.68 (0, 1.62), p=0.371 (NS) - Family history heart disease: 1.54 (0.68, 2.4), p=0.332 (NS) - Family history CD: 6.45 (0, 15.1), p= 0.054 (NS) - Heard of CD: 3.30 (1.54, 5.06), p<0.001 (***Sig.***) <u>Multivariable analysis of risk factors (aOR, 95%CI,</u>

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					p-value) - Salvadoran origin: 6.2 (2.8, 13.5), p<0.001 (***Sig.***) - Female sex: 1.2 (0.6, 2.6), p=0.619 (NS) - Lived in thatched roof house: 2.0 (0.9, 4.4), p=0.099(NS) - All 3 housing risk factors (thatched roof, mud, adobe): 2.5 (1.0, 6.4), p=0.048 (***Sig.***) - Lived in rural area/farm: 1.3 (0.6, 3.0), p=0.503 (NS) - Heard of CD: 2.4 (1.0, 5.8), p=0.047 (***Sig.***) - Less than high school education: 2.1 (0.9, 5.2), p=0.092 (NS) - Recalls triatomine bites: 1.3 (0.6, 2.9), p=0.523 (NS)
[64] Monge-Maillo et al., 2015	Spain (Madrid)	Observational cohort	357; LA immigrants; 44.9%; 2000–2009	- NR - prevalence: 48.1% (172/357)	- The most frequent country of origin was Bolivia (95.9%; 165/172) - Most patients were females (67.4%; 116/172)
[71] Munoz, Coll et al., 2009	Spain (Barcelona)	Observational cohort	1 350; LA pregnant women; 100%; 2005–2007	- NR - prevalence: 3.4% (95% CI, 2.43%, 4.73%), (46/1350) - Prevalence (cCD infection): 7.3% (1.5%, 19.9%) (3/41)	- All the infected women were at the indeterminate stage of the infection - 45 women delivered a total of 46 infants & 3 cases of cCD infection were identified Risk factors (OR, 95%CI), p-value - Country of origin (Bolivia): 106.5 (35.7, 356.2), p<0.001 (***Sig.***) - History of living in mud houses: 7 (3.55, 13.8), p<0.001 (***Sig.***) - History of living in rural areas: 7.51 (4.02, 14.04), p<0.001 (***Sig.***)
[37] Munoz, Gómez i Prat et al., 2009	Spain (Barcelona)	Cross-sectional	489; adult LA immigrants; 68.9%; 2004–2007	- mean age (SD): 34(±11) - prevalence: 41% (202/489)	- 7% (14/202) had received transfusions in their country of origin - all patients were in the chronic phase of disease LR (OR, 95%CI), p-value - Sex (ref.: male): 1.70

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(1.03; 2.81), p= 0.038 (***Sig.***) - Age (ref.: <25 yr): 3.01 (1.67; 5.43) (25–50 yr), p=0.001(***Sig.***); 2.94 (1.08; 8) (>50 yr), p=0.001 (***Sig.***) - Localization (ref.: above equator): 24.09 (11.21; 51.78), p<0.0001 (***Sig.***) - Mud (ref.: No): 4.32 (2.60; 7.16), p<0.0001 (***Sig.***)
[38] Navarro et al., 2017*	Germany (Munich)	Cross-sectional	43; citizens of Bolivian origin; 67.4%; 2013–2014	- Mean age (SD): 39 (17.2) - Prevalence: 9.3% (95%CI: 0.26%, 18.35%)	<u>Associations between CD diagnosis & risk factors (p-value)</u> - Rural origin (p=0.017) - Born to a mother with CD (p=0.003) <u>Computed OR (95%CI), p-value</u> - Sex (ref.: male): 1.5(0.14, 15.87), p=0.73 (NS)
[66] O'Brien et al., 2014 Linked: [65] O'Brien et al., 2012	Canada	Observational cohort	7 255; blood donors at-risk; NR; 2009–2011	- NR - prevalence: 0.18% (13/7 255)	- 11/13 were born in an endemic country (nine in Paraguay and two in Argentina); 4 donors had mothers or grandmothers born in Russia - Most of the positive donors had lived in a house with a dirt floor and/or mud walls - The two donors that had been born in Canada but had not lived in CA/SA had both had mothers born in SA (they also had extensive travels to SA)
	Canada	Observational cohort	6 470; blood donors; NR; 2009–2011	- prevalence: 0.03% (2/6470) - prevalence (overall): 0.1% (15/13725)	- Both donors had risk factors including birth in South America (Argentina and Paraguay) and living in a rural area in a house with a dirt floor.
[39] Ortí Lucas et al., 2009	Spain (Valencia)	Cross-sectional	400; LA pregnant women; 100%; 2005–2007	- mean age (SD): 25.9 (± 5) - prevalence: 10.4% (40/383); - prevalence (confirmed with IFI test): 9.7%	- The highest prevalence was recorded in women from Bolivia (20/77, 26%), Brazil (2/8, 25%), Nicaragua (1/5, 20%)

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
				(37/383)	LR of risk factors for CD diagnosis (B, 95%CI, p-value) - Age: 0.853 (0.745, 0.976), p= 0.021 (***Sig.***) - Family history of CD: 33.717 (8.327, 136.528), p<0.0001 (***Sig.***) - Type of house (adobe): 0.045 (0.001, 1.811), p= 0.1 (NS) - History of transfusion: 2.448 (0.816, 7.349), p= 0.11 (NS) - Country of origin Bolivia (ref.: Ecuador): 7.629 (0.882, 65.999), p= 0.65 (NS) - Country of origin Colombia (ref.: Ecuador): 2.967 (0.246, 35.792), p= 0.392 (NS) - Country of origin Argentina (ref.: Ecuador): 3.147 (0.265, 37.346), p= 0.364 (NS) - Country with low prevalence (<10%): 7.444 (0.366, 151.312), p= 0.191 (NS) - Country with high prevalence (>10%): 3.028 (0.294, 31.211), p= 0.253 (NS)
[67] Otero et al., 2012	Spain (Barcelona)	Observational cohort	633; Pregnant women at-risk; 100%; 2008–2010	- mean age (SD): 29.5 (6) - prevalence: 3.5% (95%CI: 2.2, 5.2) (22/1473) - Prevalence (Bolivian women): 14.5% (95%CI: 10.4–19.4%)	- One case of cCD infection was identified, yielding a vertical transmission rate of 5%
[52] Pane et al., 2018*	Italy (Rome)	Cross-sectional	368; LA migrants; 71.7%; 2014	- median age (IQR): 42 (33–51) - prevalence: 8.69% (32/368)	- 27/32 came from Bolivia Risk factors (p-value) - Subjects with a positive serological test for *T. Cruzi* were of older age (p = 0.015) (***Sig.***) - Born in Bolivia (p < 0.001) (***Sig.***) - History of living in mud houses (p = 0.001) (***Sig.***) - Residence in rural environment (p=0.249) (NS) - Previous blood transfusion in endemic countries (p=0.243) (NS)

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					- Blood donation in Italy (p=1) (NS) <u>Multivariable LR (OR, 95%CI), p-value</u> - Age, by 10 yr increase: 1.98 (1.25, 2.86), p=0.002 (***Sig.***) - Sex (ref.: male): 1.59 (0.57, 4.42), p=0.375 (NS) - Subjects born in Bolivia (ref.: No): 22.09 (7.34, 66.44), p< 0.001 (***Sig.***) - Residence in mud houses (ref.: No): 12.13 (1.57, 93.77), p=0.017 (***Sig.***) <u>Computed (univariate) OR (95%CI), p-value</u> - Sex (ref.: male): 1.78 (0.71, 4.47), p=0.21 (NS) - Country of origin (ref.: other than Bolivia): 15.21 (5.68, 40.74), p<0.0001 (***Sig.***) - Rural residence (ref.: urban): 1.62 (0.7, 3.72), p=0.25 (NS) - Residence in mud houses (ref.: No): 13.89 (1.87, 103.17), p=0.01 (***Sig.***) - Blood donation in Italy (ref.: No): 0.74 (0.09, 5.83), p=0.77 (NS)
[40] Paricio-Talayero et al., 2008*	Spain (Valencian Community)	Cross-sectional	624; pregnant LA women; 100%; 2005–2007	- mean age (SD): 28.3 yr (5.8) - prevalence: 4.7% (95% CI: 3, 6.3) (29/624)	<u>Country of origin (%, 95%CI)</u> - Bolivia: 17.5 (11.2; 23.9) - Ecuador: 1.5 (0, 3.6) - Colombia: 1.5 (0, 3.6) <u>Computed OR (95%CI), p-value</u> - Country of origin (ref.: other than Bolivia): 17.06(6.39, 45.55), p<0.0001 (***Sig.***)
[68] Perez-Ayala et al., 2011	Spain (Madrid)	Observational cohort	1 146; LA immigrants; NR; 2003–2009	- NR - prevalence: 31% (357/1 146)	- 346/357 (97%) were from Bolivia; the rest were from Paraguay, Argentina, Brazil, Ecuador,

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					Honduras and from Chile - 83.5% recalled having seen the vector in their homes - 78.7% had lived in rural areas. - 59% patients had a relative with CD - In 17.92% vertical transmission was a possibility (mother with CD) - 10% patients had received a previous blood transfusion.
[41] Piron et al., 2008* Linked: [42] Piron et al., 2007	Spain (Catalonia)	Cross-sectional	1 774; donors at-risk (born or transfused in endemic areas/whose mother was born in endemic area; 49%; 2005–2006	- mean age (SD): 35 (11) - prevalence: 0.62% (11/1 774) - prevalence (among Bolivians): 10.2%	- 6/11 positive donors were from Bolivia; the rest from Argentina , Ecuador, and Paraguay & one Spaniard who had been living in Venezuela for 27 yr - 3/11 had lived in rural areas; 3/10 (one missing) had lived in house with adobe. - None of the 37 donors born of a mother native to an endemic area (of an endemic country) and none of the donors transfused in an endemic area (n = 21) (of an endemic country) were positive for *T. Cruzi* Computed OR (95%CI), p-value - Country of origin (ref.: other than Bolivia): 37.24 (10.23, 135.53), p<0.0001 (***Sig.***)
[43] Piron et al., 2006	Spain (Catalonia)	Cross-sectional	630; blood donors from CA/LA; NR; 2005	- NR - prevalence: 0.95% (6/630)	- 4 were from Bolivia; the rest from Ecuador & Argentina - 3/6 were females; 2/6 had lived in a rural area; 2/6 had lived in a house with adobe - None had received a blood transfusion in the country
[44] Ramos et al., 2015	Spain (Alicante)	Cross-sectional	176; LA immigrants; 68.3%; 2012–2014	- median age (IQR): 38 (30.5, 53.0) - Prevalence: 2.3% (95%CI	- all patients were from Bolivia; all were at the intermediate stage of the disease

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
				0.9, 5.7%) (5/176)	Univariate analysis (OR, 95%CI), p-value - Male: 3.36 (0.54, 20.69), p=0.17 (NS) - Eosinophilia: 1.65 (0.18, 15.44), p=0.65 (NS) - Hyper IgE: 1.97 (0.32, 12.14), p=0.46 (NS) - History of relatives with CD: 5.48 (0.86, 35.03), p=0.046 (***Sig.***) - Living in a rural environment: 2.24 (0.36, 13.94), p=0.37 (NS) Multivariate analysis (OR, 95%CI), p-value - History of relatives with CD: 1.10 (0.05, 25.49), p= 0.96 (NS)
[69] Ramos, Milla et al., 2012	Spain (Elche)	Observational cohort	545; LA pregnant immigrants; 100%;2006–2010	- median age (range): 28.9 (16–45) - prevalence: 1.28% (95% CI: 0.06, 2.56) (7/545) - prevalence (among Bolivians): 10.26% (95% CI: 4.06, 23.58) - prevalence (among Paraguayans): 6.52% (95%CI: 2.24, 17.5)	- 4/7 were Bolivian (OR 19.1, 95% CI: 14.6, 79.7); 3/7 were from Paraguay (OR 8.4, 95%CI: 2.1, 35.8) - no cases of cCD transmission were detected (95% CI 0–43)
[45] Ramos, Ponce et al., 2012**	Spain (Elche)	Cross-sectional	201 (128 Paraguayans & 73 Bolivians); Paraguayans & Bolivians; 56.7%; 2009–2010	- median (range): 30 (2–78) - Prevalence: 6.46% (13/201) - Prevalence (among Bolivians): 9.59% (95% CI: 4.72, 18.5%) - Prevalence (among Paraguayans): 4.69% (95% CI: 2.17, 9.85%)	Factors associated with *T. cruzi* infection (p-value where reported) - Sex (NS) - Age expressed as median (p=0.03) (***Sig.***) - Mud houses (NS) - Knowledge about CD (NS) - History of relatives with CD (NS) - History of transfusion (NS) - Constipation (NS) - Dysphagia (NS) Computed OR (95%CI), p-value - Country of origin: 2.15 (0.69, 6.68), p=0.18 (NS) - Sex (ref.: male): 0.88 (0.28, 2.72), p=0.82 (NS) - Age (ref.: <30yr): 3.33 (0.88, 12.49), p=0.07

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(NS) - Experience living in mud houses: 1.89 (0.59, 6.01), p=0.27 (NS) - History of relatives with CD: 1.4 (0.36, 5.4), p=0.61 (NS) - History of transfusion: 3.05(0.32, 28.22), p=0.32 (NS) - Knowledge about CD (ref.: no): 1.33 (0.39, 4.49), p=0.64 (NS)
[46] Ramos-Sesma et al., 2021	Spain (Alicante)	Cross-sectional	596 (496 adults & 100 aged less than 18); LA individuals; 59.8%; 2016–2018	- median (adults) (IQR): 41 (34–50) - Prevalence (adults): 10.9% (95% CI: 8.3, 14.5%) (54/496)	- no cases of CD in individuals aged less than 18 - 53/54 were Bolivians <u>Factors associated with *T. cruzi*-positive serology (OR, 95%CI)</u> - Male: 1.65 (0.92, 2.82) - Age (yr): 1.02 (1, 1.53) - Time in Spain: 0.97 (0.92, 1.02) - Education (Primary school): 2.10 (1.16, 2.78) - Country of birth (Bolivia): 104 (14.2, 761) - Living in rural area: 1.36 (0.43, 4.28) - Triatomines seen at home: 9.0 (2.03, 39.9) - Blood transfusion recipient: 0.69 (0.15, 3.19) - Relatives with CD: 3.95 (1.53, 10.2) - Having heard about CD: 19.5 (2.57, 148) - Previously underwent CD serology: 5.61 (2.91, 10.8) <u>Factors associated with *T. cruzi*-positive serology (aOR, 95%CI), p-value</u> - Male: 1.58 (0.77, 3.23), p=0.21 (NS) - Age (yr): 1.02 (0.99, 1.06), p=0.11 (NS) - Time in Spain: 1.01 (0.93, 1.08), p=0.89 (NS) - Primary school: 2.40 (1.14, 5.06), p=0.021

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					(***Sig.***) - Country of birth (Bolivia): 102 (13, 781), p<0.001 (***Sig.***) - Previously underwent CD serology: 2.12 (0.98, 4.50), p=0.054 (NS)
[47] Roca et al., 2011*	Spain (Barcelona)	Cross-sectional	766; LA patients over 14 yr admitted to hospital; 60.05%; 2007–2009	- NR - Prevalence: 2.87% (95%CI: 1.6, 4.12%) (22/766) - Prevalence (among Bolivians): 16.53% (95%CI: 9.6, 23.39%)	- 21/22 positive cases were in people from Bolivia - All the patients were in the chronic phase of CD Factors associated with infection status (p-value) - Sex (NS) - Age (yr) (NS) - Journeys to country of origin in last 12 months (NS) - Had lived in rural areas: (p<0.001) (***Sig.***) - Had lived in adobe houses: (p<0.001) (***Sig.***) - Had received transfusion in country of origin (NS) - Had heard of CD in country of origin (p<0.001) (***Sig.***) - Knew someone with CD (p<0.001) (***Sig.***) <u>Computed (univariate) OR (95%CI), p-value</u> - Sex (ref.: male): 0.79 (0.33, 1.85), p=0.59 (NS) - Journeys to country of origin in last 12 months (ref.: No): 0.54 (0.21, 1.41), p=0.21 (NS) - Residence (ref.: urban): 6.8 (2.47, 18.64), p= 0.0002 (***Sig.***) - Residence in adobe houses (ref.: no): 14.79 (4.91, 44.58), p< 0.0001 (***Sig.***) - Transfusion in country of origin (ref.: no): 2.05 (0.59, 7.18), p=0.25 (NS) - Knew someone with CD (ref.: no): 33.11 (10.96, 100.07), p< 0.0001 (***Sig.***) - Country of origin (ref.: other than Bolivia):

[Ref.] Study ID	Country	Study design	N (overall); population type; Female (%); Data collection date	Age (mean/median/range) in overall sample; prevalence	Risk factors associated with *T. cruzi* infection
					126.39 (16.82, 949.61), p< 0.0001 ***(Sig.)***
[48] Salvador et al., 2018	Spain (Barcelona)	Cross-sectional	42; adults who have undergone solid organ transplantation & have been born/lived > 1 yr in an endemic country; 52.4%; 2016	- median age (range): 50.5 (23–73) - prevalence: 7.1% (95%CI: 2.5, 19.1) (3/42)	- All cases were Bolivians
[70] Sayama et al., 2019	Japan	Observational cohort	13 298; at-risk blood donors (born/raised/travel in LA); 26.9%; 2004–2012 & 2013–2016	- NR - prevalence: 0.088% (12/13 298)	- 3/12 were found positive by both ELISA & CLIA - The 2 positive cases were from Bolivia & 1 from Brazil
[49] Soriano Arandes et al., 2009	Spain (Barcelona)	Cross-sectional	224 (108 children & 116 women); women of child-bearing age & the paediatric immigrant population from LA/born in Spain with their mothers coming from endemic areas; 2006–2007	- median for children (range): 8.95(2 months, 14) - median for adult women (range): 30.2(15, 45) - prevalence (overall): 11.16% (25/224)	- All positive cases in adults were from Bolivia
Linked: [50] Soriano et al., 2007			168; children and non-pregnant women immigrants from SA & CA; 2006–2007	- median for children (range): 8.95(2 months, 14) - median for adult women (range): 30.2(15, 45) - prevalence (overall): 10.11% (17/168) - prevalence (using both ELISA & recombinant, overall): 3.65% - prevalence (using both tests' women only): 4.25% (4/98) - prevalence (children): 10% (7/70)	
[51] Steele et al., 2007	Canada	Cross-sectional	102; LA refugees & immigrants; 54.9%; NR	- range (25-34): 35.3%; range (35-44): 19.6%; range (16–24): 18.6%; - Prevalence : 0.98% (95%CI: 0.02, 5.3%) (1/102)	- The infected person had lived in Argentina > 10 years and had lived in a thatched-roof dwelling > 5 years; she also had a family history of heart disease. No blood transfusions/donations were reported.

CD: Chagas disease; cCD: Congenital Chagas disease; CI: Confidence interval; CLIA: chemiluminescent immunoassay; ELISA: enzyme-linked immunosorbent assay; EU: European Union; HIV: human immunodeficiency virus; IFAT: immunofluorescence antibody test; IgE: immunoglobulin E; IQR: interquartile range; LA: Latin America; LR: Logistic regression; NP: Not provided; NR: Not-reported; NS: non-significant; Ref.: reference; SA: South America; SD: standard deviation; Sig.: statistically significant; OR: Odds ratio; PR: Prevalence rate; T. cruzi: Trypanosoma Cruzi.
Rows highlighted in grey denote those studies included in the vote-counting synthesis.
**Summary statistics were computed based on the provided data.*
***Effect sizes were computed by using web plot digitizer.*

Table 2A. Characteristics of included single-arm studies

These studies only included T. cruzi-infected individuals. References to studies are in Annex 6.

Study ID	Country	N patients; Population; Female (%); Date of data collection	Study design	Outcomes of interest
Aguirre-Salegui et al., 2017	Spain (Basque Country)	104; adults admitted to hospital; 81.7%; 2010–2015	Observational cohort (retrospective)	- main diagnosis at discharge CD (10/104) - Non-significant associations between organ involvement and sex - 60.6% of the patients were born in Bolivia (63/104)
Cobo et al., 2016	Spain	72; LA immigrants; NR; 2004–2013	Observational cohort (retrospective)	- 65/72 were from Bolivia
Di Girolamo et al., 2010	Italy	483; LA immigrants admitted to hospital; 63%; 2005–2008	Observational cohort (retrospective)	- 114 were citizens of endemic countries and 369 were persons born in endemic countries
Dodd et al., 2019	US	585; donors; NR; 2007–2015	Observational cohort (retrospective)	- Younger donors in the rest of US/areas with sylvatic cycles compared to Southern California ($p<0.0001$) - Hispanics compared to non-Hispanics, were more likely to reside in Southern California than other areas with sylvatic cycles (OR, 15.9; 95% CI, 4.7, 53.8; $p < 0.0001$) or the rest of the United States (OR, 16.6; 95% CI, 4.8, 57.7; $p < 0.0001$) - Donors who did not provide their ethnicity compared to non-Hispanics were more likely to reside in Southern California than other areas with sylvatic cycles (OR, 5.7; 95% CI, 1.6, 20.5; $p = 0.0045$) or the rest of the United States (OR, 13.2; 95% CI, 3.4, 51.7; $p < 0.0001$) - Hispanics compared to donors who did not provide their ethnicity were nearly three times more likely (OR, 2.8; 95% CI, 1.7, 4.6; $p = 0.0001$) to reside in Southern California than other areas with sylvatic cycles - Statistically significant more donors resided in substandard housing ($p<0.0001$) and lived in rural areas ($p=0.015$) in Southern California compared to the rest of US/areas with sylvatic cycles - Statistically significant more donors in Southern California with Mother born or lived in Mexico, Central America, or South America ≥ 1 yr compared to the rest of US/areas with sylvatic cycles ($p=0.001$) - Statistically significant more donors in Southern California with maternal grandmother born or lived in Mexico, Central America, or South America compared to the rest of US/areas with sylvatic cycles ($p<0.0001$). - Statistically significant more donors in Southern California had born/resided in endemic areas of Latin America ≥ 1 yr compared to the rest of US/areas with sylvatic cycles ($p<0.0001$)

Study ID	Country	N patients; Population; Female (%); Date of data collection	Study design	Outcomes of interest
Espinosa-Pereiro et al., 2019	Spain	833; patients; 67.34%; 2002–2015	Observational cohort (retrospective)	- 94.11% were born in Bolivia
Field et al., 2010	Travellers from different European countries	94; European travellers; NR; 2008	Cross-sectional	- The majority were exposed in Bolivia (95.7%; n = 90) - The majority imported into Spain (97.9%; n = 92) by immigrant travellers (98.9%; n = 93).
Francisco-Gonzalez et al., 2019	Spain	122; seropositive-infected pregnant women; 100%; 2012–2016	Observational cohort (retrospective)	- Ninety-nine (81.1%) were from Bolivia; the rest from LA and central America countries - Three newborns with vertical transmission (cCD transmission rate of 2.75%, 95% CI: 0.57%–8.8%). In all the cases, mothers' country of origin was Bolivia
Garcia et al., 2015	US (Texas)	17; *T. Cruzi*-positive blood donors; 41.1%; 2007–2012	cross-sectional	- 76.5% (10/17) Hispanic origin - 36% (6/17) potential locally acquired infections (5 born in US and one in Mexico) - The 5 born in the US did not report significant histories of travel to endemic countries
Gautret et al., 2012 Linked: Perez-Molina et al., 2011	European countries	184; immigrants to Europe; NR; 2008–2010	Observational cohort (prospective)	- 94 patients (2008); 30 patients (2009); 60 (2010) - 58/60 patients in 2010 were Bolivian immigrants
Gobbi et al., 2014	Italy	332; patients with Chagas; 73.9%; 2005–2013	Observational cohort (retrospective)	- 61% reported living in rural areas - 73.2% reported living in mud houses - 6.9% of them reported history of blood transfusion in endemic countries - 97% of patients came from rural high-prevalence Bolivian environments (especially from Santa Cruz and Cochabamba Departments)
González Sanz et al., 2020	UK	60; positive *T. cruzi* serology attending the Hospital for Tropical Diseases; 70%; 1995–2018	Observational cohort (retrospective)	- 75% were from Bolivia (the rest were from endemic countries of South America) - 52% of the patients were diagnosed in their home countries; 9, 15% were diagnosed in Spain; 20, 33% were diagnosed in the UK - 86% of diagnosed women were of childbearing age
Herrador et al., 2015	Spain	1729 (546 re-admissions); Chagas patients hospitalised; 74%; 1997–2011	Observational cohort (retrospective)	- Median age was 35 yr (range 0–87); 69.8% were 16-45 age group - The most frequent main diagnostics associated with CD were related to pregnancy, giving birth or postpartum complications (36.6%), heart and circulatory conditions (15.3%) and digestive system conditions (9.1%).
Imai et al., 2019	Japan	6; patients with suspected CD	NR	- Median age was 53.5 years - 5 patients were immigrants from LA

Study ID	Country	N patients; Population; Female (%); Date of data collection	Study design	Outcomes of interest
		based on clinical findings; 66.6%; 2012–2017		(Brazil, 3; Bolivia, 2), and 1 was Japanese (cCD infection and was born in Japan to a Bolivian mother) - Chronic-phase CD was diagnosed in 5 patients
Jackson et al., 2012	Switzerland	137; LA migrants with CD; 84.7%; 2011	Cross-sectional	- 94.2% were from Bolivia; the rest from Argentina & Brazil - Median (range) age: 43 (25–69) - 111 (81%) were in the indeterminate phase, 25 (18.3%) had signs of *T. cruzi* cardiopathy and 1 (0.7%) had digestive tract involvement - 83.3% were living without residency permit; 72.3% were living without health insurance - 74.5% were overweight, 25.5% were obese (25.5%) and 63.5% had excessive waist circumference
Leiby et al., 2008	US (California)	51; *T. cruzi* seropositive donors; 51%; 1997–2000	Observational cohort (retrospective)	- Most (80%) of whom were born in Mexico (n=25) or El Salvador (n=16) - Donors ages' at enrolment ranged from 42 to 62 yr, and they had immigrated from 9 to 37 yr earlier - 86% reported that they had lived in a substandard house; 64% had seen triatomine bugs; 27% had bitten by triatomine bugs
Martinez-Perez et al., 2016	Spain	149; *T. Cruzi* patients; 67.7%; 2009–2011	Cross-sectional	- Most of those, who had DTU determined, were coming from Bolivia (n=98) - No association between DTU and geographical region was found (NS)
Norman et al., 2010	Spain	95; *T. Cruzi*-positive immigrants; 65.2%; 1989–2007	Observational cohort (retrospective)	- Mean age (range): mean age 36 yr, range: 16–69 yr - 94.7% (90/95) were from Bolivia; the rest from LA/CA countries - 79 patients were from rural areas, 76 patients recalled having seen the vector in their homes in their countries of origin, 15 patients had received a blood transfusion in endemic countries and for 7 patients vertical transmission was a possibility (mother with known positive *T. cruzi* serology).
O'Brien et al., 2008	Canada	0; donors at-risk; NR; 2006	Cross-sectional	<u>Exposures reported as risky</u> - travel to any endemic country of LA/SA - cumulative time in risk area (more or less than 6 months)
Pinazo et al., 2014	Spain	71; individuals from *T. cruzi*-endemic areas; 83.1%; NR	Observational cohort (prospective)	- 92.9% (66/71) were from Bolivia; the rest were from Argentina & Paraguay - Mean age (SD): 36(9)

Study ID	Country	N patients; Population; Female (%); Date of data collection	Study design	Outcomes of interest
Rodriguez-Guerineau et al., 2014	Spain & Switzerland	45 (35 in Spain & 10 in Switzerland); People with age <18 yr; 48.9%; 2004–2012	Observational cohort (retrospective)	- Mean age (range): 4 yr (1months to 18 yr) - 41 originated from Bolivia; the rest from Argentina & Nicaragua - 18/45 (≈40%) were born in Europe and 27 (≈60%) in LA - 2/45 (4.4%) were diagnosed during the acute phase; 43/45 (95.6%) were in the chronic phase of the infection - 2 cases responding to the criteria of an acute cCD infection; transplacental transmission was the route of infection for those children born in Europe who never travelled abroad.
Romay-Barja et al., 2019	Spain (Madrid)	46; Bolivian citizens who had undertaken their Chagas screening; 57.6% (in the overall sample n=166); 2017	Cross-sectional	- 63% (30/46) were women; 50% (23/46) aged 35–44 yr; 41.3% (19/46) came from a rural area of Santa Cruz or Cochabamba; 50% (23/46) had lived in an adobe house; 89% (41/46) had seen vectors
Salvador et al., 2017	Spain (Barcelona)	202; blood donors; 59.9%; 2005–2015	Cross-sectional	- 156/202 were born in Bolivia (the rest from LA countries)
Salvador et al., 2015 Linked to:	Spain	38; Chagas patients with and any kind of immunosuppressive condition; 65.8%; 2007–2014	Observational cohort (retrospective)	- Median age (age range): 37(0-66) - 35/38 (92.1%) were from Bolivia - Median time of residence in Spain: 6 (1–12) yr - Acute *T. cruzi* infection was detected in two Spanish patients
Salvador et al., 2014		1274; Chagas patients; 67.5%; 2007–2012	Observational cohort (prospective)	- Mean age, yr: 37.7 (18–81) - 97% were from Bolivia; all but one from the rest from LA & CA countries (one from Spain) - Time of diagnosis since arrival in Spain (yr): 5.1 (0–38) - 8.6% were blood donors; 83.9% were screened at hospital
Sanchez-Montalva et al., 2021	Spain	1 (& 2 with discordant results); 78.8%; 2017	Cross-sectional	- 1 patient had visited Bolivia (the two discordant had visited Bolivia and Argentina respectively) <u>Exposures reported as risky</u> - Beverages associated with CD oral infection - Staying at a house built of adobe; reported palm tree roof; reported wooden walls; reported cane walls - Self-reported insect bites; reported observation of triatomine bugs - No participant referred blood transfusion, hospitalization or surgical procedures during the trip
Soriano-Arandes et al., 2014	Spain	42; *T. cruzi*-infected pregnant women; 100%; 2011	Cross-sectional	- 90.5% (38/42) were Bolivian - 67% of pregnant women were in the chronic phase & indeterminate form - 74% of cases were diagnosed during gestation, 21% were diagnosed before gestation, and none was diagnosed during delivery - cCD transmission rate of 6.9%
Tilli et al., 2020	Italy	598 (65 cases in children aged below 15); Patients admitted to hospital due to	Observational cohort	- 249/598 aged between 25-44; 248/598 aged between 45-64

Study ID	Country	N patients; Population; Female (%); Date of data collection	Study design	Outcomes of interest
		NTDs; 70%; 2011–2016	(retrospective)	- 121/598 were Italian citizens; 477/598 (80%) were foreign citizens - CD was more frequently diagnosed in women (M/F ratio 0.43) - Bolivians had an average hospitalization rate for CD in the considered period higher than 500 per 100,000, with 441 diagnoses - Amoebiasis (unspecified) was the most common non-NTD diagnosis associated with CD (139/598).
Valerio-Sallent et al., 2012	Spain	139; seropositive *T. cruzi* patients; 61.2%; 2007–2011	Observational cohort (prospective)	- Mean age: 37.79 - 94.2% patients of Bolivian origin
Zammarchi et al., 2017	Italy	19; NTD cases admitted to hospital; 63.2%; 2000–2015	Observational cohort (retrospective)	- Mean age (yr): 39 - 2 female patients were diagnosed in virtue of a screening test performed during pregnancy; 2 patients were diagnosed thanks to a screening test before beginning of immunosuppression therapy, 4 were diagnosed as they were relatives (sons) of a positive mother, 2 because of the presence of compatible clinical features of chronic disease, and other subjects (9) were voluntarily tested.

CA: Central America; CD: Chagas disease; DTU: Discrete typing units; LA: Latin America; NTDs: Neglected Tropical Diseases; T. cruzi: Trypanosoma Cruzi

Annex 3. Critical appraisal of included studies

Table 3A. Critical appraisal of studies using an analytical cross-sectional design

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Antinori et al., 2018	Y	Y	Y	Y	Y	Y	Y	Y
Avila Arzanegui et al., 2013	Y	Y	Y	Y	Y	Y	Y	Y
Barona-Vilar et al., 2012	Y	Y	Y	Y	Y	NA	Y	Y
Custer et al., 2012	Y	Y	Y	Y	Y	Y	Y	Y
Da Costa-Demaurex et al., 2019	Y	Y	U	Y	Y	NA	Y	Y
Di Girolamo et al., 2016	Y	Y	Y	Y	Y	N	Y	Y
El Ghouzzi et al., 2010	Y	Y	Y	Y	Y	NA	U	Y
Favila Escobio et al., 2015	Y	Y	Y	Y	Y	Y	Y	Y
Gabrielli et al., 2013	Y	Y	Y	Y	Y	U	U	Y
Gómez i Prat et al., 2019	U	Y	Y	Y	Y	NA	Y	Y
Gonzalez Martinez et al., 2009	Y	Y	Y	Y	Y	NA	Y	Y
Hernandez et al., 2019	U	Y	Y	Y	Y	NA	Y	Y
Ikedionwu et al., 2020	Y	Y	Y	Y	Y	Y	Y	Y
Jackson et al., 2010	Y	Y	Y	Y	Y	Y	Y	Y
Lescure et al., 2009	Y	Y	Y	Y	Y	U	Y	Y
Llenas-Garcıa et al., 2012	Y	Y	Y	Y	Y	NA	Y	Y
Mangano et al., 2020	Y	Y	Y	Y	Y	NA	Y	Y
Manzardo et al., 2008	U	N	Y	Y	Y	NA	Y	Y
Martinez de Tejada et al., 2009	U	Y	Y	Y	Y	U	Y	Y
Meymandi et al., 2017	U	Y	Y	Y	Y	Y	Y	Y
Munoz, Gómez i Prat et al., 2009	Y	Y	Y	Y	Y	Y	Y	Y
Navarro et al., 2017	Y	Y	Y	Y	Y	NA	Y	Y
Ortí Lucas et al., 2009	U	Y	Y	Y	Y	U	Y	Y
Pane et al., 2018	U	Y	Y	Y	Y	Y	Y	Y
Paricio-Talayero et al., 2008	Y	Y	Y	Y	N	NA	Y	Y
Piron et al., 2008	Y	Y	Y	Y	Y	NA	Y	Y
Piron et al., 2006	Y	Y	Y	Y	N	NA	Y	Y
Ramos et al., 2015	U	Y	Y	Y	Y	Y	Y	Y
Ramos, Ponce et al., 2012	U	Y	Y	Y	Y	NA	Y	Y
Ramos-Sesma et al., 2021	Y	Y	Y	Y	Y	Y	Y	Y
Roca et al., 2011	U	Y	Y	Y	Y	NA	Y	Y

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Soriano-Arandes et al., 2009	Y	Y	Y	Y	N	NA	Y	Y
Steele et al., 2007	Y	Y	Y	Y	Y	NA	Y	Y

NA: not applicable; N: no; U: unclear; Y: yes.

JBI critical appraisal checklist for analytical cross-sectional studies: Y
Q1: Were the criteria for inclusion in the sample clearly defined?
Q2: Were the study subjects and the setting described in detail?
Q3: Was the exposure measured in a valid and reliable way?
Q4: Were objective, standard criteria used for measurement of the condition?
Q5: Were confounding factors identified?
Q6: Were strategies to deal with confounding factors stated?
Q7: Were the outcomes measured in a valid and reliable way?
Q8: Was appropriate statistical analysis used?

Table 4A. Critical appraisal of studies using an analytical cohort design

Studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Alcántara Román et al., 2018	Y	Y	Y	Y	N	NA	Y	NA	Y	NA	Y
Angheben et al., 2011	Y	Y	Y	Y	N	NA	Y	NA	NA	NA	Y
Basile et al., 2019	Y	Y	Y	Y	Y	NA	Y	NA	NA	NA	Y
Cantey et al., 2012	Y	Y	Y	Y	Y	NA	Y	NA	NA	NA	Y
Flores-Chavez et al., 2011	Y	Y	Y	N	NA	NA	Y	NA	NA	NA	Y
Francisco-González et al., 2018	Y	Y	Y	N	NA	NA	Y	NA	NA	NA	Y
Giménez-Martí et al., 2006	Y	Y	Y	N	NA	NA	Y	NA	NA	NA	Y
Guggenbühl Noller et al., 2020	Y	Y	Y	Y	Y	NA	Y	NA	NA	NA	Y
Hyson et al., 2021	Y	Y	Y	N	NA	NA	Y	NA	NA	NA	Y
Llenas-Garcıa et al., 2021	Y	Y	Y	Y	Y	NA	Y	NA	NA	NA	Y
Monge-Maillo et al., 2015	U	U	U	U	U	NA	U	NA	NA	NA	Y
Munoz, Coll et al., 2009	Y	Y	Y	Y	U	NA	Y	Y	NA	NA	Y
O'Brien et al., 2012	Y	Y	Y	Y	N	NA	Y	NA	NA	NA	Y
Otero et al., 2012	Y	Y	Y	U	NA	NA	Y	Y	NA	NA	Y
Perez-Ayala et al., 2011	Y	Y	Y	Y	NA	NA	Y	Y	N	NA	Y
Ramos, Milla et al., 2012	Y	Y	Y	Y	Y	NA	Y	NA	NA	NA	Y
Sayama et al., 2019	Y	Y	Y	Y	NA	NA	Y	NA	NA	NA	Y

NA: not applicable; N: no; U: unclear; Y: yes.

JBI critical appraisal checklist for analytical cohort studies:
Q1: Were the two groups similar and recruited from the same population?
Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?
Q3: Was the exposure measured in a valid and reliable way?
Q4: Were confounding factors identified?
Q5: Were strategies to deal with confounding factors stated?
Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
Q7: Were the outcomes measured in a valid and reliable way?
Q8: Was the follow up time reported and sufficient to be long enough for outcomes to occur?
Q9: Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
Q10: Were strategies to address incomplete follow up utilized?
Q11: Was appropriate statistical analysis used?

Annex 4. Graphical representation and synthesis of the data

Table 5A. Presentation of results for those studies included in the vote-counting synthesis

[Ref.] Study ID	Study design; Final sample (*T. cruzi* positive)*	Age[a]	Sex[b]	Country of origin[c]	Stay in endemic country	Mother/ grand-mother born in endemic country[d]	History of living in rural areas of endemic countries[e]	History of living in mud/adobe houses[f]	History of living in house(s) with thatched roof[g]	History of family/ relatives CD[h]	History of transfusions/ transplantation in endemic countries[i]	Contact with the vector (Inc. bites)[j]	Other infection(s)/ health issues[k]	Prior generic knowledge of CD
[53]Alcántara Román et al., 2018	Observational cohort; 192 (descendants of seropositive mothers) (23)	▲ [<14yr (ref.) vs >14yr]	▲	▲ [Born in EU (ref.) vs born outside EU]	-	-	-	-	-	-	-	-	-	-
[18]Antinori et al., 2018**	Cross-sectional; 501 (48)	▲	▲	▲	-	-	▲	▲	-	▲	▼	-	▲	-
		▲	-	▲	-	-	-	▲	-	▲	-	-	-	-
[19]Avila Arzanegui et al., 2013**	Cross-sectional; 158 (19)	-	-	▲	-	-	▲	▲	-	▲	-	▲	-	-
		-	-	-	-	-	-	▲	-	-	-	▲	-	-
[56]Cantey et al., 2012	Cross-sectional; 37 (15)	-	▲	-	-	-	-	-	-	-	-	-	-	-
[21]Custer et al., 2012	Cross-sectional; 221 (63)	-	-	-	▲	▲	▲	▲	▲	-	-	▲	▲	-
[22]Da Costa-Demaurex et al., 2019	Cross-sectional; 1010 (16)	▲ [<35yr (ref.) vs >35yr]	▲	▲	-	-	-	-	-	-	-	-	-	-
[23]Di Girolamo et al., 2016	Cross-sectional; 151 (12)	▲ [≤35yr (ref.) vs >35yr]	▲	▲	-	-	▲	-	-	▲	▲	-	-	-

[Ref.] Study ID	Study design; Final sample (*T. cruzi* positive)*	Age[a]	Sex[b]	Country of origin[c]	Stay in endemic country	Mother/ grand-mother born in endemic country[d]	History of living in rural areas of endemic countries[e]	History of living in mud/adobe houses[f]	History of living in house(s) with thatched roof[g]	History of family/ relatives CD[h]	History of transfusions/ transplantation in endemic countries[i]	Contact with the vector (Inc. bites)[j]	Other infection(s)/ health issues[k]	Prior generic knowledge of CD
[25]Favila Escobio et al., 2015	Cross-sectional; 251 (48)	▲	▲	-	-	-	▲	▲	-	▲	▲	▲	-	▲
		-	▲	-	-	-	-	-	-	▲	-	▲	-	-
[60]Guggenbühl Noller et al., 2020	Observational cohort; 1596 (NR)	▲	▲	▲	-	-	-	-	-	-	-	-	-	-
[29]Hernandez et al., 2019	Cross-sectional; 189 (14)	▲ [<40yr (ref.) vs >40yr]	▲	▲ [other(ref.) vs El Salvador]	-	-	-	-	-	▲	-	-	-	-
[62]Ikedionwu et al., 2020	Observational cohort (cross-sectional data); 131529240 (hospitalisations) (487)	▲ [15–24yr (ref.) vs 35-49yr]	-	-	-	-	-	-	-	-	-	-	-	-
[30]Jackson et al., 2010	Cross-sectional; 1012 (130)	▲ [<35yr (ref.) vs >35yr]	-	▲	-	-	-	-	-	▲	▲	▲	-	-
[31]Lescure et al., 2009	Cross-sectional; 254 (60)	-	▲	▲	-	-	▼	-	-	▲	-	-	▲	-
[32]Llenas-Garcıa et al., 2012	Cross-sectional; 154 (4)	-	▲	▲	-	-	▲	▲	▲	-	-	▲	▲	▲
[33]Mangano et al., 2020	Cross-sectional; 1985 (10)	-	▲	-	-	-	-	-	-	-	-	-	-	-
		▲	▲	▲ [other(ref.) vs El Salvador)]	-	-	▲	▲	▲	▲	-	▲	▲	▲

[Ref.] Study ID	Study design; Final sample (*T. cruzi* positive)*	Age[a]	Sex[b]	Country of origin[c]	Stay in endemic country	Mother/ grand-mother born in endemic country[d]	History of living in rural areas of endemic countries[e]	History of living in mud/adobe houses[f]	History of living in house(s) with thatched roof[g]	History of family/ relatives CD[h]	History of transfusions/ transplantation in endemic countries[i]	Contact with the vector (Inc. bites)[j]	Other infection(s)/ health issues[k]	Prior generic knowledge of CD
[36]Meymandi et al., 2017**	Cross-sectional; 4755 (59)	-	▲	▲ [other(ref.) vs El Salvador]	-	-	▲	-	▲	▲	-	▲	▲	▲
[71]Munoz, Coll et al., 2009	Prospective; 1350 (46)	-	-	▲	-	-	▲	▲	-	-	-	-	-	-
[37]Munoz, Gómez i Prat et al., 2009	Cross-sectional; 489 (202)	▲ [<25yr(ref.) vs 25-50yr & >50yr]	▲	-	-	-	-	▲	-	-	-	-	-	-
[38]Navarro et al., 2017	Cross-sectional; 43 (4)	-	▲	-	-	-	▲	-	-	▲	-	-	-	-
[39]Ortí Lucas et al., 2009	Cross-sectional; 383 (40)	▲	-	▲	-	-	-	▲	-	▲	▲	-	-	-
[52]Pane et al., 2018**	Cross-sectional; 368 (32)	▲	▲	▲	-	-	▲	▲	-	-	▼	-	-	-
		▲ (by 10yr increase)	▲	▲	-	-	-	▲	-	-	-	-	-	-
[40]Paricio-Talayero et al., 2008	Cross-sectional; 624 (29)	-	-	▲	-	-	-	-	-	-	-	-	-	-
[41]Piron et al., 2008 Linked to: [42]Piron et al., 2007	Cross-sectional; 1774 (11)	-	-	▲	-	-	-	-	-	-	-	-	-	-
[44]Ramos et al., 2015**	Cross-sectional; 176 (5)	-	▼	▲	-	-	-	-	-	▲	-	-	▲	▲
		-	-	-	-	-	-	-	-	▲	-	-	-	-

[Ref.] Study ID	Study design; Final sample (*T. cruzi* positive)*	Age[a]	Sex[b]	Country of origin[c]	Stay in endemic country	Mother/ grand-mother born in endemic country[d]	History of living in rural areas of endemic countries[e]	History of living in mud/adobe houses[f]	History of living in house(s) with thatched roof[g]	History of family/ relatives CD[h]	History of transfusions/ transplantation in endemic countries[i]	Contact with the vector (Inc. bites)[j]	Other infection(s)/ health issues[k]	Prior generic knowledge of CD
[69]Ramos, Milla et al., 2012	Prospective; 545 (7)	-	-	▲	-	-	-	-	-	-	-	-	-	-
[45]Ramos, Ponce et al., 2012	Cross-sectional; 201 (13)	▲	▼	-	-	-	-	△	-	△	△	-	▲	△
[46]Ramos-Sesma et al., 2021**	Cross-sectional; 496 (54)	△	▽	▲	-	-	△	-	-	▲	▽	▲	▲	▲
		△	▽	▲	-	-	-	-	-	-	-	-	△	-
[47]Roca et al., 2011	Cross-sectional; 766 (22)	△	▽	-	-	-	▲	▲	-	-	△	-	-	▲

Effect direction: upward arrow in black = association between the variable of interest (demographic/epidemiological/social factors) and the status of T. cruzi-positive/CD patient is statistically significant; upward arrow in grey = association between the variable of interest (demographic/epidemiological/social factors) and the status of T. cruzi-positive/CD patient is non-statistically significant; downward arrow in black = association between the variable of interest (demographic/epidemiological/social factors) and the status of T. cruzi-negative/CD-free individuals is statistically significant; downward arrow in grey = association between the variable of interest (demographic/epidemiological/social factors) and the status of T. cruzi-negative/CD-free individuals is non-statistically significant.

Statistical significance threshold adopted: p<0.05.

Arrows smaller in size indicate studies with small sample size in relation to the predictors tested (e.g. n<100 for 10 outcomes variables tested) and outcomes with zero events in the variables of interest.

** Comparison reference group: T. cruzi-negative/CD-free individuals*

*** Upper and lower rows indicate ORs generated from the univariate & multivariate analyses, respectively.*

[a] Comparison ref.: year before (unless otherwise stated)

[b] Comparison ref.: male (unless otherwise stated)

[c] Comparison ref.: other than Bolivia (unless otherwise stated)

[d] Comparison ref.: none of mother/grandmother was born in an endemic country

[e] Comparison ref.: no experience in living in rural areas (unless otherwise stated)

[f] Comparison ref.: no experience in living in mud/adobe houses (unless otherwise stated)

[g] Comparison ref.: no history of living in house(s) with thatched roof

[h] Comparison ref.: no history of family/relatives CD (unless otherwise stated)

[I] Comparison ref.: no history of transfusion/transplantation in endemic countries

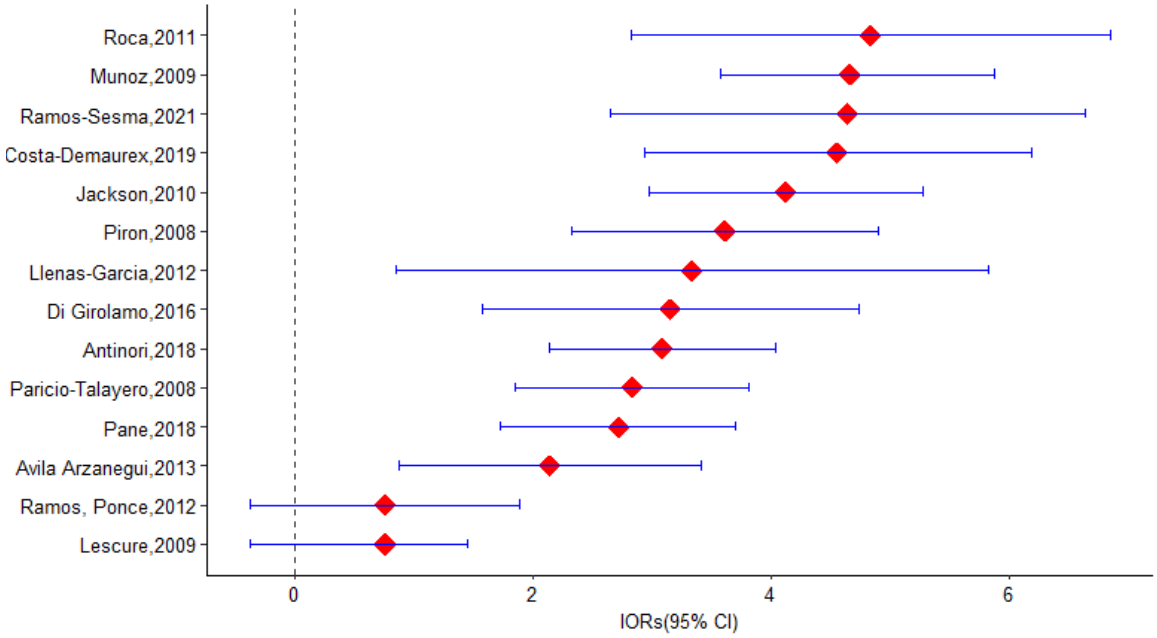
[j] Comparison ref.: no contact (any type) with the vector

[k] Comparison ref.: no other infections/health issues

Graphical representation of odds ratios (ORs)

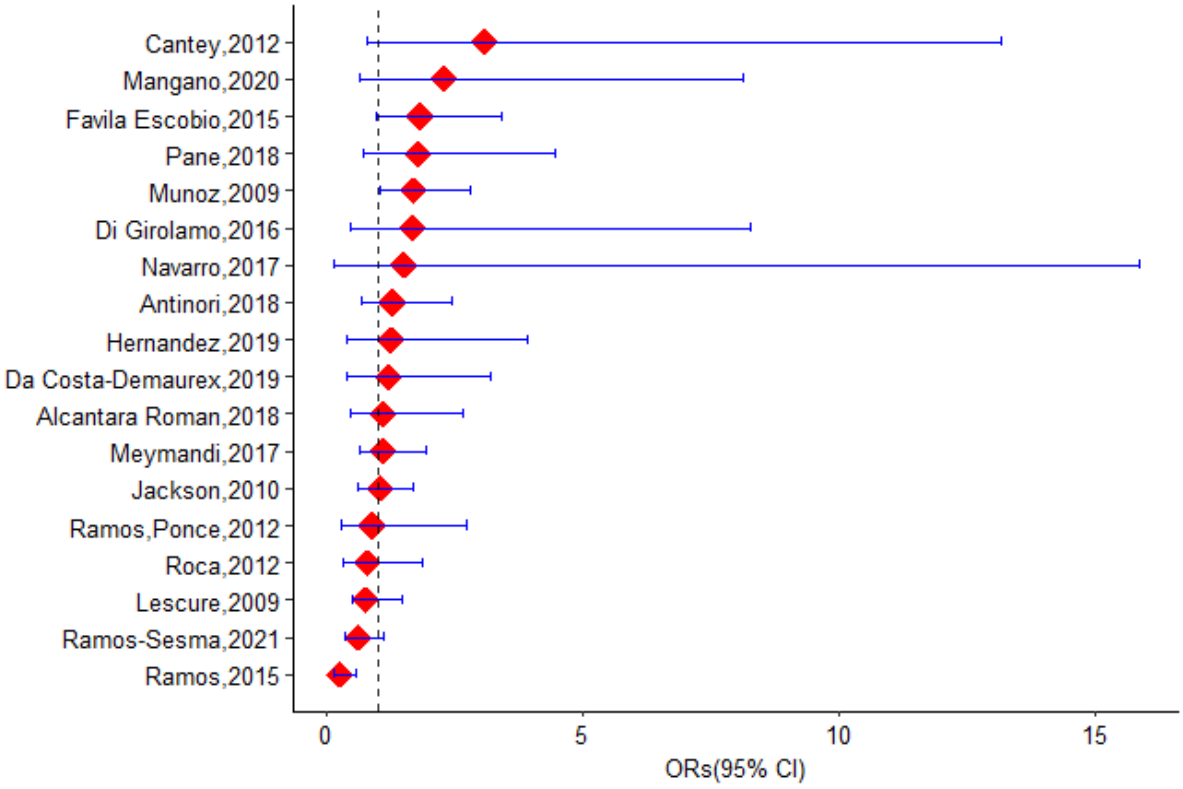
Effect sizes are reported in reverse order according to their magnitude. Higher ORs indicate increased probability to be diagnosed with *T. cruzi* infection.

Figure 2A. Associations between Bolivia as country of origin and *Trypanosoma cruzi* infection*



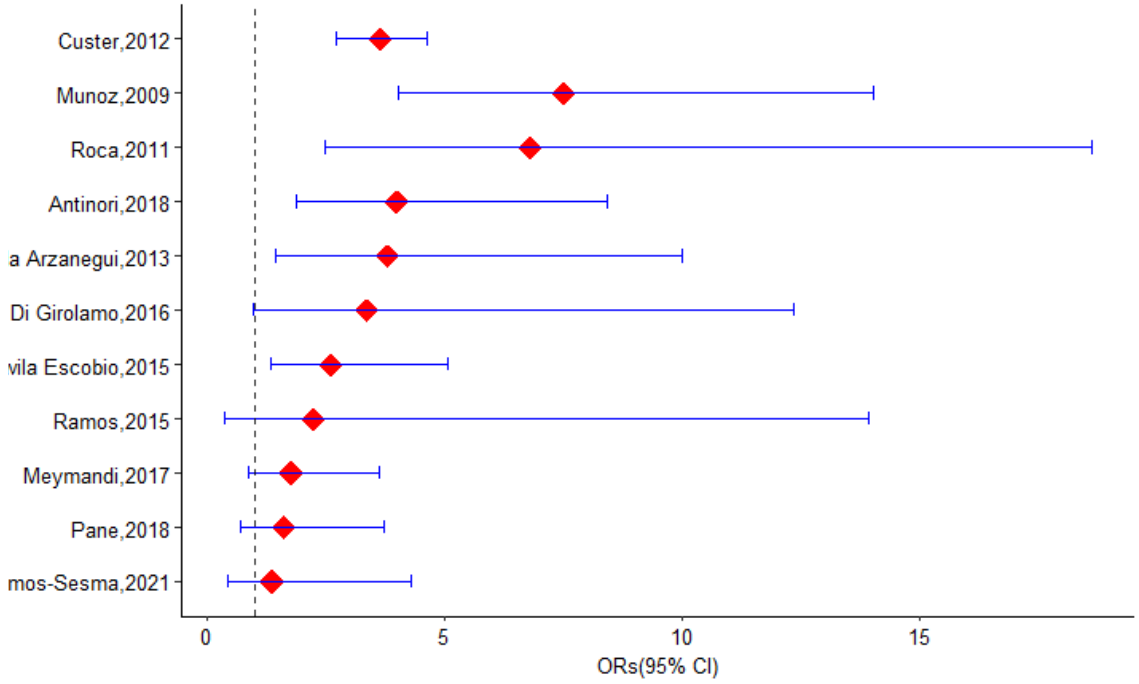
** Log ORs are presented in order to improve the readability of the forest plot.*

Figure 3A. Associations between sex (female) and *Trypanosoma cruzi* infection



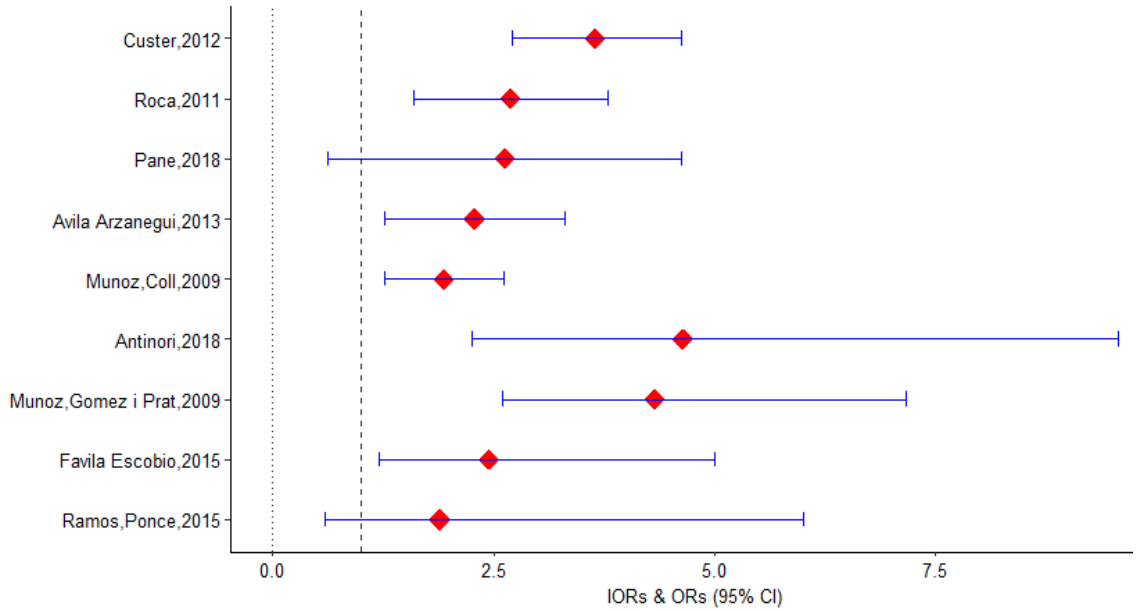
CI: confidence interval; OR: odds ratio

Figure 4A. Associations between history of living in rural areas of endemic countries and *Trypanosoma cruzi* infection**



*** Log OR are presented for the first study in order to improve the readability of the forest plot.*

Figure 5A. Associations between history of living in mud/adobe houses and *Trypanosoma cruzi* infection***



**** Log ORs are presented for the first five studies in order to improve the readability of the forest plot.*

Annex 5. Studies excluded at the full text stage

Title	Year	Authors	Reasons for exclusion
Factors associated with risk behavior in travelers to tropical and subtropical regions	2015	Aldea M, et al.	outcomes out of scope
Family cluster of Chagas disease among Bolivian immigrants in Italy: High rate of maternal-fetal transmission	2022	Antinori S, et al.	outcomes out of scope
Chagas disease and blood transfusion: an emerging issue in non-endemic countries	2011	Assal A, et al.	outcomes out of scope
Chagas disease in European countries: the challenge of a surveillance system	2011	Basile L, et al.	outcomes out of scope
Screening for imported diseases in an immigrant population: experience from a teaching hospital in Barcelona, Spain	2014	Bocanegra C, et al.	outcomes out of scope
Screening Program for Imported Diseases in Immigrant Women: Analysis and Implications from a Gender-Oriented Perspective	2020	Boga J, et al.	outcomes out of scope
The risk for Chagas' disease in the Midwestern United States organ donor population is low	2004	Bryan CF, et al.	outcomes out of scope
Parasitic Infections in Internationally Adopted Children: A Twelve-Year Retrospective Study	2022	Chiappini E, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
The Catalonian Expert Patient Programme for Chagas Disease: An Approach to Comprehensive Care Involving Affected Individuals	2017	Claveria Guiu I, et al.	outcomes out of scope
Prevalence of *Trypanosoma cruzi* infection in blood donors	2020	Da Costa AC, et al.	outcomes out of scope
Chagas disease in France: estimated number of infected persons and cardiac diseases in 2009, by risk groups	2009	Dejour Salamanca D, et al.	outcomes out of scope
Chagas Disease Screening in Maternal Donors of Publicly Banked Umbilical Cord Blood, United States	2016	Edwards JM, et al.	publication type out of scope
"It's Like a Phantom Disease": Patient Perspectives on Access to Treatment for Chagas Disease in the United States	2018	Forsyth CJ, et al.	study design out of scope
One Health Interactions of Chagas Disease Vectors, Canid Hosts, and Human Residents along the Texas-Mexico Border	2016	Garcia MN, et al.	outcomes out of scope
Trypanosoma cruzi screening in Texas blood donors, 2008–2012	2016	Garcia MN, et al.	publication out of scope
Chemiluminescent Microparticle Immunoassay for the Diagnosis of Congenital Chagas Disease: A Prospective Study in Spain	2021	Gil-Gallardo L, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
COVID-19: an opportunity of systematic integration for Chagas disease. Example of a community-based approach within the Bolivian population in Barcelona	2022	Gómez I Prat J, et al.	study design out of scope
Comparative evaluation of community interventions for the immigrant population of Latin American origin at risk for Chagas disease in the city of Barcelona	2020	Gómez I Prat J, et al.	outcomes out of scope
Likely Autochthonous Transmission of *Trypanosoma cruzi* to Humans, South Central Texas, USA	2017	Gunter SM, et al.	publication type out of scope
Chagas Disease Infection Prevalence and Vector Exposure in a High-Risk Population of Texas Hunters	2020	Gunter SM, et al.	publication type out of scope
High prevalence of persistent parasitic infections in foreign-born, HIV-infected persons in the United States	2011	Hochberg NS, et al.	outcomes out of scope
Assessing the Prevalence of Risk Factors for Neglected Tropical Diseases in Brazos County, Texas	2017	Horney J, et al.	outcomes out of scope
Donor-derived *Trypanosoma cruzi* infection in solid organ recipients in the United States, 2001–2011	2013	Huprikar S, et al.	outcomes out of scope
Updated Estimates and Mapping for Prevalence of Chagas Disease among Adults, United States	2022	Irish A, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
Chagas disease in Switzerland: history and challenges	2011	Jackson Y, et al.	study design out of scope
Congenital transmission of Chagas disease in Latin American immigrants in Switzerland	2009	Jackson Y, et al.	publication type out of scope
Chagas disease in Australia and New Zealand: risks and needs for public health interventions	2014	Jackson Y, et al.	study design out of scope
Prevalence of chronic infections and susceptibility to measles and varicellazoster virus in Latin American immigrants	2016	Jackson Y, et al.	outcomes out of scope
Chagas disease: screening tests evaluation in a blood military center, prevalence in the French Army	2007	Kerleguer A, et al.	outcomes out of scope
Results of lookback for Chagas disease since the inception of donor screening at New York Blood Center	2013	Kessler DA, et al.	outcomes out of scope
The early implementation of Trypanosoma cruzi antibody screening of donors and donations within England: preempting a problem	2012	Kitchen AD, et al.	outcomes out for scope
Chagas disease prevalence in pregnant women: migration and risk of congenital transmission	2016	Kolliker-Frers RA, et al.	outcomes out of scope
Trypanosoma cruzi in Los Angeles and Miami blood donors: impact of evolving donor demographics on seroprevalence and implications for transfusion transmission	2002	Leiby DA, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
Frequency of *Trypanosoma cruzi* parasitemia among infected blood donors with a potential association between parasite lineage and transfusion transmission	2017	Leiby DA, et al.	outcomes out of scope
Evidence of *Trypanosoma cruzi* infection (Chagas' disease) among patients undergoing cardiac surgery	2000	Leiby DA, et al.	outcomes out of scope
Diagnostic evaluation of military blood donors screening positive for *Trypanosoma cruzi* infection	2018	Marcus JE, et al.	outcomes out of scope
Anti-*Trypanosoma cruzi* antibody detection in eastern Andalusia (Spain)	2014	Marin C, et al.	outcomes out of scope
Seroprevalence of five neglected parasitic diseases among immigrants accessing five infectious and tropical diseases units in Italy: a cross-sectional study	2017	Martelli G, et al.	outcomes out of scope
Chagas Disease Prevalence in a Cohort of Neurocysticercosis Patients in a Non-Endemic Setting	2022	McAleese KR, et al.	outcomes out of scope
Emerging infectious diseases in pregnant women in a non-endemic area: Almost one out of four is at risk	2021	Modi G, et al.	outcomes out of scope
Anti-*Trypanosoma cruzi* antibodies in Latin American migrants in transit through the Mexico–USA border	2018	Montes-Rincon LM, et al.	population out of scope
Risk factors and primary prevention of congenital Chagas disease in a nonendemic country	2013	Murcia L, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
Treatment of Infected Women of Childbearing Age Prevents Congenital *Trypanosoma cruzi* Infection by Eliminating the Parasitemia Detected by PCR	2017	Murcia L, et al.	outcomes out of scope
Targeted screening and health education for Chagas disease tailored to at-risk migrants in Spain, 2007 to 2010	2011	Navarro M, et al.	outcomes out of scope
Estimating chagas disease prevalence and number of underdiagnosed, and undertreated individuals in Spain	2022	Navarro M, et al.	outcomes out of scope
Prevalence of antibodies to *Trypanosoma cruzi* among solid organ donors in Southern California: a population at risk	2006	Nowicki MJ, et al.	outcome out of scope
The prevalence of Chagas disease among Latin American immigrants with pacemakers in Los Angeles, California	2017	Park S, et al.	publication type out of scope
Gastro-intestinal Chagas disease in migrants to Spain: prevalence and methods for early diagnosis	2011	Perez-Ayala A, et al.	outcomes out of scope
Six-year review of +Redivi: a prospective registry of imported infectious diseases in Spain	2017	Perez-Molinam JA, et al.	outcomes out of scope
Prevalence of Chagas disease and strongyloidiasis among HIV-infected Latin American immigrants in Italy - The CHILI study	2022	Rodari P, et al.	outcomes out of scope

Title	Year	Authors	Reasons for exclusion
Congenital Chagas disease in a non-endemic area: Results from a control programme in Bergamo province, Northern Italy	2018	Rodari P, et al.	outcomes out of scope
Serological screening of Chagas disease in an immigrant population in Asturias, Spain proceeding from Chagas-endemic areas	2009	Rodriguez-Guardado A, et al.	publication type out of scope
Factors associated with Chagas screening among immigrants from an endemic country in Madrid, Spain	2020	Romay-Barja M, et al.	outcomes out of scope
Trypanosoma cruzi cross-reactive antibodies longitudinal follow-up: A prospective observational study in hematopoietic stem cell transplantation	2015	Saba ES, et al.	outcomes out of scope
Anti-*Trypanosoma cruzi* cross-reactive antibodies detected at high rate in non-exposed individuals living in non-endemic regions: seroprevalence and association to other viral serologies	2013	Saba ES, et al.	outcomes out of scope
Organ donor screening practices for *Trypanosoma cruzi* infection among US Organ Procurement Organizations	2011	Schwartz BS, et al.	outcome out of scope
Risk Factors and Screening for *Trypanosoma cruzi* Infection of Dutch Blood Donors	2016	Slot E, et al.	outcomes out of scope
Developing a CASPER Survey to Assess the Prevalence of Risk Factors for Neglected Tropical Diseases in Texas	2017	Smitherman S, et al.	study design out of scope

Title	Year	Authors	Reasons for exclusion
Schistosomiasis, strongyloidiasis and Chagas disease: the leading imported neglected tropical diseases in Italy	2019	Zammarchi L, et al.	outcomes out of scope
Chagas Disease Screening Using Point-of-Care Testing in an At-Risk Obstetric Population	2021	Zamora LE, et al.	outcomes out of scope
Seroprevalence of Chagas infection in the donor population	2012	Zaniello BA, et al.	outcomes out of scope

Annex 6. References of included studies using a single-arm design

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