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Eurosurveillance

Europe's journal on infectious disease epidemiology, prevention and control

Special edition: Chagas disease in Europe

September 2011

This special edition of *Eurosurveillance* reviews diverse aspects of Chagas disease that bear relevance to Europe. It covers the current epidemiological situation in a number of European countries, and takes up topics such as blood donations, the absence of comprehensive surveillance, detection and treatment of congenital cases, and difficulties of including undocumented migrants in the national health systems. Several papers from Spain describe examples of local intervention activities.

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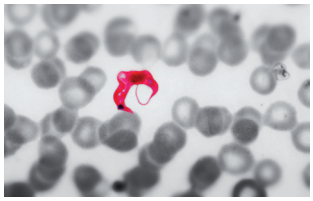

This is a micrograph of *Trypanosoma cruzi* in a blood smear using Giemsa staining technique.

This protozoan parasite, *T. cruzi*, is the causative agent for Chagas disease, also known as "American trypanosomiasis". It is estimated that 16 - 18 million people are infected with Chagas disease, and of those infected, 50,000 will die each year.

The hidden Chagas disease burden in Europe

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Chagas disease in non-endemic countries - that is, in countries outside Latin America with exceptional or no vectorial transmission such as in Europe - has come to light since the beginning of 2000. The emergence of the disease in those countries was mainly linked to population mobility, notably migration. During the last century, Chagas disease cases were detected in non-endemic countries in North America (Canada and the United States) and the Western Pacific Region (mainly Australia and Japan), and only more recently in Europe [1,2].

The history of Chagas disease in Europe can be divided in three significant periods. The initial period, started at the beginning of the 1980s, when the first Chagas disease case in Europe was published [3], 72 years after Carlos Ribeiro Justiniano Chagas discovered the disease in Brazil [4]. Since then, successive sporadic publications have started to draw attention to the existence of Chagas disease cases in different European countries and the existence of the responsible parasite *Trypanosoma cruzi*. These publications describe infection transmission in Europe through different non-vectorial routes such as transfusional, congenital and laboratory-accident transmission, as well as sporadically through the arrival of infected travellers such as tourists, people visiting friends and relatives and adopted children [5].

The year 2000 marked the beginning of a second period, characterised by an increase in the number of cases reported in the scientific literature in many European countries [6]. According to the International Organization for Migration an important increase of migration between Europe and Latin America, predominantly to southern European countries, and mainly to Spain, was documented. Major causes contributing to this migration phenomenon were the economic hardship caused by the recession and high poverty levels in Latin America and tightening of visa regimes in the United States after 2001. The close cultural and historic ties of Latin American countries to Europe and the possibility for many Latin Americans to appeal to dual nationality because they frequently have European ancestors, have also facilitated population mobility in that direction. Demographically, the migrant population was young, with high rates of labour force participation and relatively high rates of educational attainment, with great capacity to integrate into European societies. Additionally, they represented a prime example of the current worldwide trend towards the feminisation of migration, which is relevant in the context of Chagas disease because of the possibility of congenital transmission from infected mothers. Finally, there was also a significant number of undocumented migrants, and that irregular migration posed a significant challenge to governments [7].

The year 2007 marked the beginning of a third period in the history of Chagas disease in Europe, characterised by various initiatives launched at different levels. In July 2007, the World Health Organization (WHO) and the Pan American Health Organization (PAHO) convened a meeting entitled *Revisiting Chagas disease: from a Latin American health perspective to a global health perspective*, with participants of 28 Latin American and non-Latin American countries where the disease was present. A major outcome of the meeting was to highlight the presence of *T. cruzi* infection outside Latin America in the so-called non-endemic countries and an initiative to deal with Chagas disease in non-endemic countries, supplementing the existing intergovernmental initiatives for the control of Chagas disease in Latin America [8].

With the main objectives of assessing the burden of Chagas disease as a public health problem in non-endemic countries and formulating an appropriate response, the WHO organised a series of meetings in 2008 and 2009 that culminated in the Informal Consultation on the Control and Prevention of Chagas disease in Europe, in the first profiles of European countries with Chagas disease cases and the first statement acknowledging that the disease has emerged as an important public health challenge [5,9].

In May 2010 the 63rd World Health Assembly approved the new resolution WHA63.20 which recognises the increased number of cases of Chagas disease in countries where the disease is not endemic and states that all transmission routes have to be tackled. It further promotes the integration of patients with acute and

chronic clinical forms of Chagas disease into primary health services and calls for a mobilisation of national and international, public and private financial and human resources, for the promotion of intersectorial efforts and collaboration, and for the facilitation of networking between organisations and partners [10]. The 63rd World Health Assembly also called for the establishment of an initiative of non-endemic countries aiming at interconnecting all those regions and countries that have patients. Finally, in October 2010, the first WHO report on neglected tropical diseases included Chagas disease as one of the 17 listed diseases [2].

From the point of view of the legal framework, the first official reference to Chagas disease at the European Union level was made in the European Commission's Directive 2004/23/CE [11] amending Directive 2002/98/CE [12] of the European Parliament and Council (2003) on quality and safety of blood, which concerns technical criteria relating to blood and blood donations. Annex III of the directive defines the admission criteria for blood donors or blood types and the minimal exclusion criteria for donations from donors who have or had parasitological diseases; the exclusion of Chagas disease carriers is specified. Other European directives, including 2005/62/CE, establish norms to be followed by institutions when carrying out blood transfusions with blood imported from other countries. In February 2006, the European Parliament published a new directive 2006/17/CE [13] on the donation and control of human tissues and cells, which referred to Chagas disease. The directive relates to the screening of donors based on their epidemiological history and travel to endemic areas. Aligned with European Union directives, France, Spain and the United Kingdom implemented national measures to control transfusional transmission of Chagas disease [14,15].

The present timely special edition of *Eurosurveillance*, published in two parts, is a useful instrument to review and update diverse aspects of Chagas disease in Europe related to topics such as the current epidemiological situation, primary and secondary prevention of *T. cruzi* infection, including congenital cases, control of transmission by transfusion and organ transplantation, care of patients, information, education and communication instruments, and the information and surveillance systems in place in countries within and outside of the European Union.

Basile et al. [16] review the epidemiological situation of the nine European countries with the highest estimated prevalence of *T. cruzi* infection, and the difficulties of dealing with a frequently silent and under- or misdiagnosed disease for which neither acute nor chronic cases are captured by compulsory notification. They point out the need for and challenge of an information and surveillance system in Europe that considers also the number of undocumented migrants. The lack or inconsistency of accurate epidemiological numbers of people with *T. cruzi* infection or Chagas disease can perpetuate the vicious circle of a silent and, in a way, silenced disease.

Along the same lines, the characteristics of patients attended and documented in the EuroTravNet provide precious information on the epidemiological and clinical profile of most of patients, together with the urgent necessity of implementing active measures to increase detection and access to diagnosis and treatment [17]. Other very interesting examples describing possible mechanisms to increase detection and care, and to make the disease more visible, are offered in articles from Italy and Switzerland [18,19]. These are countries with high absolute and relative numbers of *T. cruzi*-infected people, especially in certain regions or cantons. They have even seen reported acute cases of congenital transmission or oral transmission in a tourist coming back from a short trip to an endemic country. The need of an interdisciplinary approach, from the medical to the sociological sciences, taking into account all involved actors, including the patients themselves, is appointed as the unique solution to break the disease silence [20].

In terms of the possibility of implementing secondary prevention of congenital transmission linked to an information system in Europe, two pioneer experiences from Spain illustrate faced challenges and successful strategic measures to enhance the number of screened mothers and limit the number of lost patients in the after birth follow-up [21,22]. Nevertheless, as described by Navarro et al., implementing a protocol for the screening of pregnant women and the early diagnosis of infected newborns and their siblings requires also an essential component of information, education and communication (IEC), adapted to the emotional meaning Chagas disease for the affected population and their knowledge about it [23]. Moreover, any IEC component should include all involved actors, from health personnel to patients, including local non-governmental associations. Also from Spain comes a significant study by Valerio et al. reviewing the epidemiological data of *T. cruzi* infection and Chagas disease clinical chronic manifestations, especially in groups at risk of being infected. These studies evidence that it is essential to know the characteristics of the migrated population in terms of age, country of origin and exposition to infection, in order to propose adequate cost-effective protocols for laboratory and clinical screening and diagnosis, patient care and preventive and control measures [23,24].

It is necessary to move ahead with the description of Chagas disease in Europe. At-risk groups of migrants who lived in endemic areas before Chagas disease control measures were implemented in Latin America can have a high prevalence of infection and disease. But it is also logical to think that Chagas disease in non-endemic countries, with a reduced possibility of reinfection or co-infections with other parasitic diseases, with high standards of hygiene and nutritional status,

could be characterised by a lower morbidity and mortality. We are convinced that this special issue will stimulate further lively discussions around this disease, but also the implementation of the necessary measures to make it visible, stop transmission and provide care to patients in Europe.

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A note from the editors: Chagas disease – neglected in Europe?

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The idea for this special edition first came to us during a presentation at a conference that stimulated an unusually lively discussion in the audience about whether or not it was relevant for European countries to consider Chagas disease in blood donors.

In response to our call for papers [1] we received submissions from several European countries. After peer-review, we now publish a double issue with a set of articles that deal with diverse aspects of the disease such as:

- blood, organ and tissue donation,
- socio-economic aspects,
- clinical characteristics,
- congenital infection,
- screening programmes,
- and treatment.

Chagas disease has been classified as one of the neglected tropical diseases [2]. With this special edition we wanted to offer an opportunity for authors to present thought-provoking ideas as well as provide practical examples of initiatives to control Chagas disease in a non-endemic setting and prevent transmission. We hope that it will stimulate further lively discussions around this disease and what it means for public health in Europe

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Chagas disease in Italy: breaking an epidemiological silence

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Chagas disease, a neglected tropical disease that due to population movements is no longer limited to Latin America, threatens a wide spectrum of people (travellers, migrants, blood or organ recipients, newborns, adoptees) also in non-endemic countries where it is generally underdiagnosed. In Italy, the available epidemiological data about Chagas disease have been very limited up to now, although the country is second in Europe only to Spain in the number of residents from Latin American. Among 867 at-risk subjects screened between 1998 and 2010, the Centre for Tropical Diseases in Negrar (Verona) and the Infectious and Tropical Diseases Unit, University of Florence found 4.2% patients with positive serology for Chagas disease (83.4% of them migrants, 13.8% adoptees). No cases of Chagas disease were identified in blood donors or HIV-positive patients of Latin American origin. Among 214 Latin American pregnant women, three were infected (resulting in abortion in one case). In 2005 a case of acute Chagas disease was recorded in an Italian traveller. Based on our observations, we believe that a wider assessment of the epidemiological situation is urgently required in our country and public health measures preventing transmission and improving access to diagnosis and treatment should be implemented.

Introduction

Chagas disease is a protozoan zoonosis caused by *Trypanosoma cruzi*, with a widespread distribution from the south of the United States to Mexico and Central and South America. In endemic countries it is responsible for the highest estimated burden of neglected tropical diseases, affecting 8 to 10 million people [1]. As a consequence of migration flows, the disease has been recorded also in non-endemic countries and is becoming a global health problem [2]. In Europe, about 59,000-108,000 cases of Chagas disease are estimated [3] . Italy has a large number of Latin American resident migrants, second in Europe only to Spain, as a result of various migratory waves to Argentina, Brazil, Chile, Uruguay and Venezuela through the last 200 years, until the direction of migration reversed in the 1970s [3].

The majority of Latin American migrants reached Italy in the past ten years, with a growing trend [4] . Migrants from different countries tend to have a patchy distribution in Italian Regions, with a major concentration in the north and in Rome. For instance most Bolivians live in Bergamo Province, Lombardy, Ecuadorians in Liguria Region and Peruvians in big cities such as Milan, Florence and Rome [4].

This new epidemiological scenario prompted the Centre for Tropical Diseases in Negrar (CTDN) and the Infectious and Tropical Diseases Unit, University of Florence, Florence (ITDUF) to join to better define the epidemiological situation and to promote prevention and control programmes focused on Chagas disease

and other neglected diseases. In this paper we present the first data obtained by the two Centres in their daily clinical practice and screening programmes targeted to at-risk population in Italy.

These findings should throw light on a disease so far unnoticed in our country. We tried to follow the recent indications by the European network representatives of Non-Endemic Countries Initiative on data collection, risk assessment and control of blood tranfusions, appropriate and sustainable detection strategies for at-risk populations (children, women of child-bearing age, immunodeficient patients), and access to diagnosis and treatment [5].

Methods

Prevalence estimation of *Trypanosoma cruzi* infection and Chagas disease in Latin American migrants living in Italy

The expected number of *T. cruzi*-infected Latin American migrants living in Italy was calculated using the estimated total number of migrants from endemic countries and the average *T. cruzi* infection rate in the country of birth according to either Schmunis et al. [2] or the Panamerican Health Organization (PAHO) [6]. For their estimations, Schmunis et al. used seroprevalences of Chagas disease in Latin American countries in 1990. Their values are generally higher than the PAHO data, which refer to the year 2005, when the situation had improved thanks to disease control initiatives in Latin America.

The source for the number of Latin American legal migrants in Italy on 1 January 2008 was the Italian National Statistics Institute [7]. Data on undocumented migrants were obtained from the Report on Immigration published by Caritas/Migrantes [4] and from the Regional Agencies of Migration. Literature data were also used [3] .

Regarding the estimation of progression from indeterminate to chronic cardiac Chagas disease, a conservative rate of 20% was used [2].

Diagnosis and screening programmes

The two Centres systematically offered Chagas disease testing to all patients with epidemiological risk (such as migration, adoption from or travel to endemic countries, or being born to a Latin American mother), who attended their services for any reason in the study period. The period considered was April 1998 to April 2010 for CTDN and January 2007 to December 2009 for ITDUF.

The first part of the study consisted of a retrospective review of the patient files, in an anonymous way. The second part concerned screening of pregnant women, blood donors and human immunodeficiency virus (HIV)-positive subjects of Latin American origin or born to a Latin American mother. Patients' consent was obtained before testing.

Migrants, travellers and expatriates

Migrants from and travellers to endemic countries, regardless of the duration of travel, were considered eligible when returning from Central and South American countries, excluding the Caribbean where Chagas disease is not endemic. Children born to Latin American mothers were also included. Expatriates were defined as individuals resident in Chagas disease-endemic countries for occupational purposes.

Adopted children

Adopted children were studied as part of a collaboration of CTDN and ITDUF with services for health promotion of adopted children at the Paediatric Division of Sacro Cuore Hospital, Negrar and Anna Meyer Children's University Hospital, Florence, respectively. Adoptees' access to care differs from that of other immigrants in Italy in that there are specialised centres that offer testing for diseases present in the country of birth.

Pregnant women

In 2008, CTDN and ITDUF implemented a screening programme targeted to Latin American pregnant women at Sacro Cuore Hospital, Negrar, and Careggi University Hospital, Florence, in collaboration with the respective Maternal and Child Health Departments. In 2009 the screening included also pregnant women attending the Obstetrics and Gynaecology Clinic at L. Mangiagalli Hospital in Milan. Women were offered to be tested during a prenatal visit, or latest during pre-partum.

Blood donors

All but one donor included in the study were enrolled at the Immunohaematology and Transfusion Unit, Careggi University Hospital, Florence, which began screening donors for Chagas disease in 2008. Only migrants from endemic areas or children born to Latin American mothers were screened.

HIV/AIDS

From January 2008 to April 2010, HIV-positive Latin American migrants attending or referred to ITDUF, the Infectious Disease Division of the University Hospital of Verona and the Infectious Diseases Division at San Raffaele Hospital, Milan were offered to be serologically tested for antibodies against *T. cruzi*. The three centres are important reference centres for the management and treatment of HIV-positive patients.

Laboratory methods

Serology for *T. cruzi* was performed using a combination of two tests: an immunochromatographic assay (Chagas Quick Test, Cypress Diagnostics, Belgium) and an ELISA based on recombinant antigens (BioELISA Chagas, Biokit S.A., Spain) or *T. cruzi* lysate, (DRG CHAGAS IgG, Germany). In some cases serum samples were tested by two ELISAs. In case of discordant result, a third assay was performed, as recommended by the World Health Organization (WHO) [8]. In case of infants born to *T. cruzi*-infected women, serological evaluation

was performed at birth, at one and eight months of age. At each evaluation, blood samples were submitted to parasitological testing (microscopic examination of microhaematocrit) and nested or real-time PCR with primers TCZ1/TCZ2 and TCZ3/TCZ4) [9] and serological evaluation. Molecular diagnosis was performed at the Laboratory of Parasitology, Faculty of Pharmacy, at the University of Barcelona, Spain or at the Public Health Sciences Department at La Sapienza University in Rome, Italy. Infants were considered infected in case of microscopic detection of *T. cruzi* or PCR positivity or seropositivity at eight months of age.

Results

Estimated *Trypanosoma cruzi* infection rate and Chagas disease in Latin American migrants living in Italy

The results are summarised in Table 1. At the end of 2007, around 400,000 Latin American migrants were estimated to be resident in Italy, the most represented countries being Brazil, Ecuador and Peru. According to the seroprevalence of Chagas disease in the country of origin reported by Schmunis et al.[2] or PAHO [6], 11,217–12,578 or 5,902–6,572 *T. cruzi*-infected migrants were expected to live in Italy at the beginning of 2008. In the most pessimistic scenario of progression to the cardiac form, up to 2,516 individuals were estimated to be affected by chronic cardiac Chagas disease in the same period.

Patients attending the two centres

Overall, 867 individuals attending CTDN and ITDUF were tested. The mean age of the population was 26.2 years (range: 1–85 years). A slight predominance of males (51.4%) was observed. Countries of origin and categories of the patients are shown in Table 2. In 1.2% of cases, classification was not possible for missing information.

Overall, 36 of 867 patients (4.2%) had a positive result of *T. cruzi* serology. The largest part of the seropositive individuals were migrants (83.4%), followed by adopted children (13.8%). One was a short-term Italian traveller to Brazil (Santa Catarina). None of 100 expatriates were positive and none of the six newborns from seropositive mothers had a positive test eight months after birth.

Migrants

In the study period, 266 migrants were tested, 147 of whom (65%) were women. The mean age of this population was 34 years (range: 4–83 years). The distribution of nationalities is shown in Table 3. Among the 30 migrants infected by *T. cruzi*, 23 were from Bolivia, two from Argentina, two from Paraguay, one from Brazil, one from Ecuador, and one from Mexico.

Expatriates

None of the 100 tested expatriates was seropositive for *T. cruzi*. In the retrospective analysis, it was not possible to know the host country/ies for a considerable

Table 1

Estimated *Trypanosoma cruzi* infection rate and cardiac chronic Chagas disease in Latin American migrants Italy, on 1 January 2008

Countries	Number of migrants	*T.cruzi* infection rate in countries of origin *Seroprevalences according to Schmunis et al [2]; PAHO [6]*	Estimated number of *T.cruzi* infected migrants *Seroprevalences according to Schmunis et al [2]; PAHO [6]*	Estimated chronic cardiac Chagas disease cases in migrants
Argentina	16,294	8.2%; 4.1%	1,336; 668	267; 53
Bolivia	19,000–27,000	15.4%; 6.8%	2,926–4,158; 1,292–1,836	585–832; 117–166
Brazil	150,000	1.3%; 1%	1,950; 1,500	390; 78
Chile	4,372	2.8%; 1%	122; 43	24; 5
Colombia	19,832	3.9%; 1%	773; 198	155; 31
Costa Rica	446	4.3%; 0.5%	19; 2	4; 1
Ecuador	73,235–80,000	1.2%; 1.7%	879–960; 1245–1360	176–192; 35–38
El Salvador	6,096	6.1%; 3.4%	372; 207	74; 15
Guatemala	532	7.9%; 2%	42; 11	8; 2
Honduras	632	5.8%; 3.1%	37; 20	7;1
Mexico	5,724	0.7%; 1%	40; 57	8;2
Nicaragua	373	1.7%; 1.1%	6; 4	1; 0
Panama	384	9%; 0.006%	35; 0	7; 1
Paraguay	1,246	9.3%; 2.5%	116; 31	23; 5
Peru	76,406–78,000	3%; 0.7%	2,292–2,340; 535–546	458–468; 92–94
Uruguay	1,956	1.2%; 0.7	23; 14	5; 3
Venezuela	6,235	4%; 1.2%	249; 75	50; 15
Others	144	Not calculated	Not calculated	Not calculated
Total	**417,493–438,656**		**11,217–12,578; 5,902–6,572**	**2,243–2,516; 1,180–1,314**

proportion of subjects in this group (72%) from whom the data collection forms reported only 'residence in Chagas disease endemic countries'. Details of the country were available for 28 patients, Brazil and Bolivia being the most represented countries with 11 and 4 individuals, respectively (Table 3). The mean age was 46.9 years (range: 2–85 years). Males were represented with 58%.

Travellers

During the study period, only 28 travellers were screened (six in Florence and 22 in Negrar) with one positive result. This case was a patient with acute Chagas disease returning from a short journey (less than one week) to Santa Catarina, Brazil during the 2005 food-borne outbreak (caused by sugar-cane juice) of Chagas disease in that region. (personal communication, Francesca Prati, 2005). He confirmed having consumed crude sugar-cane juice. The patient was successfully treated (to our knowledge). We do not have more detailed clinical information for this case.

Adopted children

Overall, 457 adopted children were tested, corresponding to 52.7% of the study population (mean age: 7.1 years; range: 2 months–33 years). Five children, all adopted from Bolivia, were found to be seropositive for *T. cruzi* (mean age: 5 years, range: 4–6 years). This corresponded to 7% of all Bolivian adopted children included in the study (n=71).

Screening programmes for pregnant women, blood donors and HIV-positive subjects

Pregnant women

A total of 214 pregnant women (mean age: 32 years, range: 14–44 years) were screened. The countries of origin are reported in Table 4. Three women (1.4%) had a positive result, two from Bolivia and one from Paraguay. One aborted spontaneously in the 16th week (the cause has not been investigated). The other two cases did not transmit the infection. Anti-trypanosomal treatment was offered to all infected women after breastfeeding. The *T. cruzi* infection rate among the subgroup of women of Bolivian origin was 29% (two of seven).

Blood donors

A total of 28 specimens were obtained from subjects at risk for *T. cruzi* infection. Half of them were men with a mean age of 39 years (range: 21–55 years). The countries of origin for donors are reported in Table 4. All tested donors had negative results for *T. cruzi* infection.

Table 2

Seroprevalence of *Trypanosoma cruzi* antibodies in the study participants[a], by country of origin and category, April 1998–April 2010 (n=876)

	Number of individuals n (% of all 867)	Seropositive patients: n (% of 36 seropositive patients)
Country of origin		
Argentina	17 (2)	2 (5.5)
Bolivia	157 (18)	28 (77.7)
Brazil	255 (29.4)	1 (2.8)
Chile	35 (4)	0 (0)
Colombia	120 (13.8)	0 (0)
Costa Rica	10 (1.2)	0 (0)
Ecuador	17 (2)	1 (2.8)
Guatemala	5 (0.6)	0 (0)
Italy	11 (1.3)	1 (2.8)
Mexico	16 (1.9)	1 (2.8)
Nicaragua	1 (0.1)	0 (0)
Paraguay	3 (0.4)	1 (2.8)
Peru	91 (10.4)	0 (0)
Uruguay	1 (0.1)	0 (0)
Venezuela	12 (1.4)	0 (0)
Unknown[b]	116 (13.4)	1 (2.8)
Classification		
Migrants	266 (30.7)	30 (83.4)
Adoptees	457 (52.7)	5 (13.8)
Expatriates	100 (11.5)	0 (0)
Travellers	28 (3.2)	1 (2.8)
Born to seropositive mother	6 (0.7)	0 (0)
Unknown	10 (1.2)	0 (0)

a Individuals evaluated between April 1998 and April 2010 at the Centre for Tropical Diseases, Negrar and between January 2007 and December 2009 at the Infectious and Tropical Diseases Unit, Florence.

b Patients originating from or having visited an unspecified Chagas disease-endemic area.

Table 3

Nationalities (or country of residence for expatriates) of study participants[a], April 1998–April 2010 (n=825)

Country	Migrants (n=266)	%	Adoptees (n=457)	%	Expatriates (n=100)	%
Argentina	14	5.3	1	0.2	2	2
Bolivia	75	28.2	71	15.5	4	4
Brazil	80	30	157	34.4	11	11
Chile	1	0.4	34	7.4	0	0
Colombia	22	9.7	98	21.4	0	0
Costa Rica	1	0.4	9	2	0	0
Ecuador	8	3.5	6	1.3	3	3
Guatemala	0	0	3	0.7	1	1
Mexico	10	3.8	4	0.9	1	1
Nicaragua	0	0	0	0	1	1
Paraguay	3	1.3	0	0	0	0
Peru	26	9.8	65	14.2	0	0
Uruguay	1	0.4	0	0	0	0
Venezuela	5	2.2	1	0.2	5	5
Unknown	21	7.9	8	1.8	72	72

a Individuals evaluated between April 1998 and April 2010 at the Centre for Tropical Diseases, Negrar and between January 2007 and December 2009 at the Infectious and Tropical Diseases Unit, Florence. Travellers, infants born from seropositive mothers and not classified subjects are not represented.

HIV/AIDS

Seventy HIV-positive Latin American migrants were screened, of whom 78% were men with a mean age of 38 years (range: 22-56 years). Their countries of origin are reported in Table 4. Patients from Brazil and Peru, countries with a low prevalence of Chagas disease, represented more than a half of the sample. None of the patients had an indeterminate or positive test *T. cruzi* infection. In the group of HIV-positive migrants studied at ITDUF (n=43), 14 had in their clinical history a nadir of a CD4+ T lymphocyte count below 200/µl.

Discussion

Epidemiology of Chagas disease in Italy

In the past decade, Chagas disease has been increasingly reported in non-endemic countries as a result of improved case finding and growing migration flows. Moreover, the lack of effective control measures and preparedness in most European countries facilitated the emergence of congenital or transfusion-related cases [3].

In Europe, Spain and Italy are the most popular destinations for Latin American migrants. Officially, 275,671 Latin Americans were resident in Italy on 1 January, 2008 [7], most from Peru, Ecuador and Brazil. According to a previous estimate 4,337 to 4,610 were expected to be infected [10]. However, these figures were based on official data on Latin American migrant populations and probably underestimate the true prevalence. Depending on the seroprevalence rates used for the estimations, we can expect that there were between 5,902 and 12,578 cases of Chagas disease in Italy in 2008, in a Latin American population of up to 440,000 individuals (a number that includes undocumented migrants).

Table 4

Nationalities of patients enrolled in screening programmes of pregnant women, blood donors and HIV-positive subjects, January 2008 to April 2010 (n=312)

Country	Pregnant women n=214	Blood donors n=28	HIV-positive subjects n=70
Argentina	6 (2.8%)	0	9 (12.9%)
Bolivia	7 (3.3%)	0	0
Brazil	20 (9.4%)	8 (28.5%)	26 (37.1%)
Chile	4 (1.8%)	4 (14.3%)	1 (1.4%)
Colombia	7 (3.3%)	3 (10.7%)	3 (4.3%)
Costa Rica	1 (0.5%)	0	0
Ecuador	25 (11.7%)	1 (3.6%)	4 (5.7%)
El Salvador	14 (6.5%)	1 (3.6%)	0
Honduras	3 (1.4%)	0	0
Guatemala	0	0	0
Mexico	4 (1.8%)	0	2 (2.9%)
Nicaragua	1 (0.5%)	0	0
Paraguay	1 (0.5%)	0	0
Peru	118 (55.1%)	5 (17.9%)	21 (30%)
Uruguay	1 (0.5%)	1 (3.6%)	1 (1.4%)
Venezuela	2 (0.9%)	3 (10.7%)	2 (2.9%)
Unknown	0	2 (7.1%)	1 (1.4%)

Few extensive evaluations of the Chagas disease infection rate in Latin American migrants in non-endemic countries have been published up to now, with the exception of Bolivians. For this reason, we used population prevalence rates in the countries of origin in 1990 [2] and 2005 [6]. The results were highly discordant. The more pessimistic scenario according to Schmunis et al. [2] prevalences would estimate about 12,000 Chagas disease cases in Italy in 2008.

Migrants from Bolivia are considered to be particularly at risk of Chagas disease [2, 11-14]. In the Lombardy Region alone, the Bolivian community counts about 20,000 people, most undocumented [15]. A majority of Latin American migrants in Italy are women [4], 65% in our study and similar to results from Spain and Switzerland [11, 12]. This aspect can contribute to a silent vertical diffusion of Chagas disease.

Patients attending the two Centres

In both Centres, activities of Chagas disease diagnosis, treatment and follow-up have rapidly grown in the last few years. For instance, only 28 serological tests were carried out at CTDN before 2005, and 548 thereafter. In patients attending the two Centres, an overall infection rate of 4.2% was found, higher than in other European countries, except Spain [12]. This result suffers from a selection bias because reference centres attract at-risk patients and promote the testing of relatives, and from an inhomogeneous population (18.4% were Bolivians).

Migrants

The infection detection rate among migrants (of whom 28.2% were Bolivians) was 11.3%. Among Bolivians, 30.7% of individuals had a positive serological result, which is in accordance with other studies [11,12]. It has already been established [11] that Bolivian origin should be regarded as a predictive factor for *T. cruzi* infection.

The high prevalence of seropositive migrants raises the question of whether to screen all Latin Americans (excluding those originating from the Caribbean). Cost-effectiveness studies are needed in this context, in order to better design public health interventions.

Adopted children

Data on seroprevalence of Chagas disease among adopted children in European countries are lacking. Dejour-Salamanca et al. estimate for France that 235 (between 165 and 384 depending on the prevalence used for calculation) of 19,389 adopted children might have had Chagas disease in the period from 1980 to 2007. Since 2004, less than 500 children have been adopted every year, therefore an extensive screening programme on adoptees could identify six cases per year [16].

In Italy, from the beginning of 2000 to the end of 2009, 6,826 children were adopted from Latin American countries. They came mainly from: Colombia (n=2,787 adoptions), Brazil (n=2,265), Bolivia and Peru (n=475 each), Chile (n=409) and Guatemala (n=114). The mean age of adoptees on arrival to Italy was 5,7 years [17]. Continent- or country-specific data on age were not available. Taking into account the infection prevalence of 7% detected in our sample of Bolivian adoptees, the PAHO estimation (8/100,000 annual incidence rate) for the other nationalities [6], and the mean age at adoption, we estimate 36 adopted children with Chagas disease in Italy at the end of 2009 (33 Bolivians and three with other backgrounds).

Only five cases have been diagnosed until now in adopted children, to our knowledge. The overall detection rate among all adoptees screened by our two centres was 0.9%. Adopted children are a vulnerable population, at risk of stigmatisation. However, we believe that Chagas disease screening should be made available to all, considering the high efficacy of treatment at young age [18].

Chagas disease and travellers

Among 28 screened travellers, one had a positive serological result. This was a patient with acute food-borne Chagas disease after a short journey to Santa Catarina, Brazil in 2005, where 50,000 people had probably been exposed to contaminated sugar-cane juice [19]. Before our study, in 1997 a first acute case acquired in Brazil had been reported in Italy [3].

Sporadic cases of acute or chronic Chagas disease in travellers have been reported in France, Austria and Japan [3,20]. Chagas disease is potentially transmissible to travellers. Oral transmission, which can involve travellers, has been frequently recorded in recent years and is related to a more evident and severe form of the disease in the acute phase. Given that it is often asymptomatic in the early phase, the diagnosis may be easily missed. In case of chronic manifestation of the disease, the previous travel history may be overlooked.

Although international travel plays only an anecdotal role in imported Chagas disease, these cases can potentially be severe and misdiagnosed. Staff at travel clinics should be trained to consider Chagas disease prevention when giving travel advice as well as to recognise the early symptoms of acute Chagas disease when examining patients returning from Latin American countries.

Screening programmes

Chagas disease in pregnant women and newborns

In Europe, the prevalence of *T. cruzi* infection in Latin American women of child-bearing age varies from 3.4% to 9.7% [21,22]. The lower prevalence in our series, also in comparison with the overall prevalence in migrants, is probably due to the low proportion of Bolivian nationals among the pregnant women we screened.

In Italy, there are no systematic screening programmes at national level, but ITDUF and Tuscany Region have started a specific programme, while the CTDN is currently testing all Latin American women presenting at their hospital for delivery or prenatal visit. This is an important issue, if we consider that in 2007 alone, 30 pregnant women were estimated to be infected in Italy and therefore might have given birth to two children with Chagas disease [3]. Moreover, it has recently been demonstrated in Spain that testing pregnant women for Chagas disease is cost-effective [23].

We did not identify any children who acquired Chagas disease from the mother. Nevertheless, maternal transmission is one of the most important factors to deal with in the control of the disease. The reported transmission rates from infected pregnant women to newborns vary from 1% to more than 10% in endemic countries [24] and from 2.7% to 7% in Europe [21,22]. In case a newborn is affected by Chagas disease, prompt treatment should be initiated. In Italy, no protocols for diagnosis and treatment of Chagas disease in newborns have been implemented so far.

Chagas disease and transfusion of blood and blood components or organ, cell and tissue transplantation

In endemic countries, blood transfusion is probably the second most common way of dissemination of the disease [25]. Parasitaemia can persist for several years after infection [25], therefore a patient can transmit the disease several times. In non-endemic countries, transmission of Chagas disease by blood transfusion has been reported [3]. In Europe, Spain, France and the UK have specific policies for testing at-risk donors. There is still an open debate about the most cost-effective strategy for donor screening in non-endemic countries [26,27].

Italy has not yet established a transfusional transmission prevention programme for Chagas disease; a questionnaire asks about prior diagnoses of tropical diseases (in case of Chagas disease the donor is permanently excluded) or travel to tropical countries (in that case, the donor is only temporarily excluded for three months and thereafter can donate blood without undergoing to any further screening for *T. cruzi* infection). With our limited survey we did not identify any infected donor. However, we think that new policies for donor screening are necessary in Italy. The issue of Chagas disease screening is presently being discussed at the National Blood Centre (personal communication, Giuliano Grazzini, 29 April 2011).

Chagas disease can also be transmitted through organ, cells or tissue donation [28]. In Italy, only patients who have already been diagnosed with Chagas disease are excluded from donation. It is common practice to seek a second opinion from by an infectious disease specialist in transplant medicine before organs are used from donors who are considered to be potentially infected with *T. cruzi*. At present, access to urgent diagnosis for

T. cruzi infection is unavailable. In the forthcoming revision of the infectious disease prevention guidelines in transplant medicine, Chagas disease prevention will be discussed (personal communication, Paolo Grossi, 29 April 2011).

Chagas disease and HIV Infection

A further at-risk population, prone to severe manifestations of the disease, are HIV-positive persons. Chagas disease in HIV-positive patients has been predominantly described in those with advanced disease (CD4+ T cell counts below 200 cells/ml), and the infection was included in the group of AIDS-defining illness in Brazil and by PAHO [29].

In HIV-positive patients, the most relevant clinical manifestations of Chagas disease result from reactivation of a chronic *T. cruzi* infection [30]. The central nervous system is the most commonly affected site, in approximately 75% of cases, with clinical signs of acute meningoencephalitis or space-occupying lesions, rapid clinical progression and a high fatality rate of 79% [30,31] The heart is the second most commonly affected organ (25% to 44% of cases) [31,32]. Peripheral blood parasitaemia, and also cerebrospinal fluid invasion, are very common in those subjects [32].

The treatment of reactivated Chagas disease is based on the standard drugs benznidazole or nifurtimox. However, the duration of therapy has not been established in HIV/AIDS patients; longer courses of treatment followed by secondary prophylaxis (at least until immune reconstitution has been achieved) [33] or chronic suppressive therapy are likely to be required [31]. Spanish guidelines recommend treatment of Chagas disease in HIV-positive patients with positive PCR for *T. cruzi* in the blood [33]. Some experts suggest primary prophylaxis for infected individuals with a CD4+ T cell count lower than 200 cells per µL [31].

Many cases have been reported of Chagas disease reactivation in HIV-positive patients, most of them from Latin America [31], while data from Europe are very limited. To our knowledge, only one case of a meningoencephalitis in a 35 year-old Argentinian man living in Spain, has been published and only two serological screening programmes have been carried out, both in Spain, in HIV-positive people of Latin America origin, finding prevalences of *T. cruzi* infection between 2% and 10.5% [34,35].

Although we did not identify any case of Chagas disease in the HIV-positive population screened, we found a high proportion of patients with a history of low CD4+ T cell counts under 200/ml, which deserves consideration. We believe that all HIV-positive patients with epidemiological risk should be tested for Chagas disease as stated in the Brazilian guidelines [36].

Conclusions

The present study on Chagas disease epidemiology is the first ever conducted in Italy. Together with previous estimations [10], it outlines a worrisome scenario, although the picture is still largely incomplete. Chagas disease can be considered an emerging problem in Italy. We believe that our country should urgently improve the access to diagnosis and treatment and implement an efficient approach to case finding and transmission control. A network of Centres working on Chagas disease should be set up to stimulate research, inform and educate both healthcare providers and the public, and offer a qualified service for disease management.

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Chagas disease in Switzerland: history and challenges

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Chagas disease, endemic in Latin America, is an emerging health problem in Europe affecting an estimated 80,000 persons. Around 60,000 Latin American migrants live in Switzerland, and cases of Chagas disease have been reported since 1979. As of June 2011, 258 cases have been diagnosed, mostly adults in the indeterminate phase of the chronic stage of the disease. Vertical transmission has been identified and there is a high potential for blood- and organ-borne transmission in the absence of systematic screening. Major challenges include (i) raising awareness among migrants and healthcare professionals, (ii) developing national protocols for screening and treatment targeting high-risk groups such as pregnant woman, newborns, migrants from highly endemic areas (e.g. Bolivia), and immunocompromised migrants, (iii) preventing blood- and organ-borne transmission by appropriate screening strategies, (iv) taking into account the social vulnerability of individuals at risk in the design and implementation of public health programmes, and (v) facilitating contacts with the communities at risk through outreach programmes, for example in churches and cultural groups

Introduction

The parasite *Trypanosoma cruzi*, the causative agent of Chagas disease, has been affecting humans for at least 9,000 years, but Europe has experienced the emergence of this disease as a significant health issue only very recently [1,2]. In humans, *T. cruzi* is responsible for a chronic infection causing potentially lethal cardiac damages in up to 30% of cases. It was traditionally confined to the Americas, resulting in a high social and financial burden primarily in rural areas [3]. In the absence of *T. cruzi* vectorial transmission outside Latin America, Chagas disease in non-endemic countries is predominantly an imported infection, affecting migrants more than travellers [4]. Besides, transplacental and blood-borne transmissions have been reported in Europe [5,6]. In 2010, the World Health Organization (WHO) estimated that 80,000 persons could be infected in Europe, making Chagas disease one of the predominant emerging parasitic infections in the continent [2].

In Switzerland, a small country of 7.8 million inhabitants, foreigners accounted for 22.4% of the total population in 2010. Currently, 35,000 Latin American migrants originating from the 21 countries endemic for Chagas disease are legal residents in Switzerland. This figure does not include adopted children or migrants who have received the Swiss citizenship. Moreover, since the 1990s, a large number of Latin American migrants have been settling in Europe without residence permit and are not recorded in the official registries. For example, 1,229 residents of Bolivian origin were officially registered in Switzerland in 2009, but migrants associations estimate that around 9,000 Bolivians live in the canton of Geneva alone, most of them undocumented (F. Anda, Association des Boliviens de Genève, June 2010, personal communication). A large majority of recent Latin American migrants are women employed in the domestic industry. Thus, it can be estimated that the real number of Latin American migrants at risk of having Chagas disease currently living in Switzerland may be as high as 60,000 to 90,000 [2]. Undocumented migrants are legally entitled to access the Swiss healthcare system by purchasing a health insurance. Yet, the expensive premium (EUR 200–300 per month), lack of knowledge of the system and administrative barriers prevent the vast majority of them from contracting an insurance, thus making access to care difficult, especially outside the main urban areas, where communities and support groups are less organised.

The first recorded case of Chagas disease in Switzerland dates back to 1979 [7]. Since then, the number of cases recorded has increased in parallel with the growth of the population at risk, alongside higher awareness among health professionals and with improved access to reliable diagnostic tools [8,9]. Several studies have documented the emergence and transmission of Chagas disease in Latin American communities in Switzerland [5,10,11]. Here, we review epidemiological, clinical and social data on all cases of Chagas disease diagnosed and recorded in Switzerland.

Methods

We used several sources of information to identify cases and their characteristics before aggregation: (i) the clinical databases of two studies done in Geneva in 2008: a community-based cross-sectional study in adult Latin American immigrants over the age of 16 years [10] and a prospective study in pregnant Latin American women attended at the Geneva University Hospitals [11], (ii) the database of all cases seen at the Geneva University Hospitals and (iii) information collected from the main laboratories performing diagnosis of *T. cruzi* infection, the major Swiss healthcare institutions and experts active in international health and infectious diseases in Switzerland. To optimise data collection, an internet search for published cases was conducted using two major electronic databases (Pubmed and Embase). The keywords 'Switzerland', 'Chagas disease', and '*Trypanosoma cruzi*' were used. To avoid duplication of cases from different sources, the date of birth, nationality, sex and place of diagnosis and treatment were cross-checked. Cases were defined as any individual in whom *T. cruzi* testing was positive, either by serology (≥9 month after birth in newborns), nucleic-acid assay or microscopy. Up to 2008, the Swiss Tropical Institute in Basel was the only Swiss laboratory performing serology for *T. cruzi* infection (in-house indirect immunofluorescent assay), haemoculture and nucleid acid assay (in-house PCR). Since 2008, Geneva University Hospitals have been using two different serological tests (ELISA cruzi, Biomerieux, Brazil and Chagas Stat-Pak, Chembio Diagnostic Systems, United States). Moreover, several Swiss reference laboratories perform microscopical examination in blood and tissues. Since 2008, screening programmes in Geneva have focused on Latin American individuals who fulfil one or more of the following criteria: Bolivian origin, relative of a patient with Chagas disease, suggestive symptoms, recipient of a blood transfusion in the home country, or pregnancy.

Table 1

Socio-demographic characteristics of patients with Chagas disease, Switzerland, January 1979–June 2011 (n=258)

	N (%) or median (range)
Sex	
Female	215 (83.3)
Male	43 (16.7)
Age	41 (0–77)
Children (<16 years)	9 (3.5)
Country of origin	
Argentina	6 (2.3)
Bolivia	241 (93.4)
Brazil	8 (3.1)
Chile	2 (0.8)
Colombia	1 (0.4)
Lack of valid residency permit (undocumented)[a]	171 (97.1)

[a] Denominator=176.

Results

Number of cases and place of diagnosis

From 1979 to June 2011, a total of 258 persons have been diagnosed with *T. cruzi* infection in Switzerland. All but five patients were diagnosed in Geneva.

Time variation of frequency of cases and clinical features

From 1979 to 2007, in the absence of screening programmes, 11 cases of *T. cruzi* infection had been identified including eight symptomatic cases: five with cardiac, one with cardiac and digestive complications, and two congenital infections with placental abnormalities [5,7-9]. After screening programmes were initiated in Geneva, 247 cases were diagnosed from January 2008 to June 2011, with a lower proportion of symptomatic cases (53 of the 231 clinically evaluated patients).

Socio-demographic characteristics

Table 1 shows the socio-demographic characteristics of the 258 patients. The median age was 41 years and women were overrepresented with 83% of cases. The vast majority of patients were Bolivians (n=241). Information on whether they had a residence permit was available for 176 patients. Most of those (n=171) were living in Switzerland without a residence permit and without health insurance.

Mode of transmission and clinical staging

Congenital transmission (acute phase) was diagnosed in four newborns, all of them from Bolivian mothers. In addition, five children between 1 and 11 years of age were diagnosed at the early indeterminate phase of the chronic stage. Table 2 shows the clinical staging of the 258 patients. One fatal case occurred following a fulminant *T. cruzi* infection reactivation in an immunosuppressed patient who had received a heart transplant [10].

Diagnosis

All patients in the indeterminate phase of the chronic stage and one newborn (aged nine months) were

Table 2

Clinical staging of patients with Chagas disease, Switzerland, January 1979–June 2011 (n=258)

Stage	N (%)
Acute – congenital	4 (1.6)
Acute – reactivation	1 (0.4)
Chronic – early indeterminate	5 (2)
Chronic – indeterminate	178 (69)
Chronic with cardiac involvement	51 (19.8)
Chronic with digestive tract involvement	3 (1.2)
Chronic with cardiac and digestive tract involvement	1 (0.4)
Information not available	15 (5.6)

diagnosed by positive results in at least one, mostly two, serological assays (immunofluorescence, ELISA or immunochromatography) with the strategies or combinations varying depending on the diagnosing centre. One newborn was diagnosed by positive *T. cruzi* nucleic acid test of umbilical cord blood. Two other newborns were diagnosed by detection of amastigote forms of *T. cruzi* in the placenta with confirmation by positive serology and nucleic acid assay. The patient with *T. cruzi* reactivation was diagnosed by identifying amastigote forms in the skin and in a bone marrow biopsy, and by a positive peripheral blood buffy coat.

Treatment

Criteria for treatment initiation were based on recommendations from the World Health Organization and on guidelines from the United States [11,12]. Until 2009, nifurtimox was used for availability reasons. Since then, benznidazole has been more easily available and has become the first-line treatment. Anti-parasitic treatment was initiated in 129 patients (50%). Ninety-three patients received nifurtimox (10 mg/kg/day) and 36 received benznidazole (5 mg/kg/day; max:300 mg/day). Overall, adverse events caused premature treatment termination (less than 60 days) in 41 patients (31.8%; nine with benznidazole and 32 with nifutimox). A full description on tolerance of nifurtimox in patients treated in Switzerland has been published [13].

Discussion

To our knowledge, 258 cases of Chagas disease were diagnosed and recorded in Switzerland between 1979 and 2011. Considering the limited number of medical centres and laboratories working on parasitic diseases in Switzerland, this figure probably reflects the actual situation correctly. Almost all cases were diagnosed in Geneva, which has several reasons: (i) a large community of Bolivian migrants live in Geneva, (ii) local policies allow access to primary healthcare for uninsured individuals, (iii) repeated epidemiological investigations on Chagas disease and information sessions with the community have created confidence and reinforced the cooperation between migrants and the Geneva University Hospitals (HUG), (iv) screening programmes have been implemented in the Canton of Geneva. Such programmes have so far not been put in place in blood banks, maternity wards and health institutions of other Swiss cantons, with the exception of Lausanne in the Canton of Vaud. The implementation of screening in Geneva is the main explanation for the shift from a low number of detected cases with a high proportion of symptomatic individuals (until 2007) to a higher number of cases with a high proportion of asymptomatic individuals (since 2008). Previous studies in Geneva showed 25% prevalence within the Bolivian community, mostly in women of child-bearing age who had a positive attitude towards blood donation in Geneva, which highlighted the risk of blood-borne and congenital transmission [5,14].

Chagas disease represents an emerging and complex health issue in Switzerland considering (i) the presence of a significant number of infected persons, (ii) their social situation with poor access to healthcare and very low socioeconomic status, (iii) the active vertical transmission and the potential for transmission through blood and organ donations, and (iv) the low awareness and consideration by public health authorities and health professionals [15]. The situation of Chagas disease in Switzerland is emblematic of the European context, as until now only Spain and France have adopted public health policies to control the spread of this emerging infection [16]. National recommendations or programmes of case detection and management or prevention of local transmission do not currently exist in Switzerland. Specific tests to diagnose chronic Chagas disease are available in a limited number of laboratories. Neither of the two drugs active against *T. cruzi*, benznidazole and nifurtimox, are registered by the Federal Pharmaceutical Office and thus require specific agreement for each treatment, nor are they easily available.

Since 2008, some progress has been made regarding the management of Chagas disease in Switzerland. Serologies are now available in two laboratories (HUG and the Swiss Tropical and Public Health Institute in Basel). A rapid diagnostic test has been validated and is being used in HUG and the University Hospital of Lausanne [17]. Systematic screening of Latin American pregnant women was first implemented at HUG in 2008, followed in 2010 by a wider strategy of screening all persons at risk, i.e. Latin American immigrants, persons who received blood transfusion in Latin America or persons born to a Latin American mother. In 2011, the University Hospital of Lausanne is expected to adopt similar protocols. Systematic screening of blood donors at risk is under discussion at local (Geneva, Lausanne) and national levels. Ties with Latin American communities have been strengthened through information exchange and awareness campaigns. Education of medical students and health professionals through clinical meetings, presentations in congresses and publications in national medical journals has been initiated.

Considering the number of Latin American immigrants living in Switzerland and the proportion of *T. cruzi* infections in this community, up to 3,000 cases could be present in the country. The main challenges for the control of this emerging health threat are: (i) raising awareness both in communities at risk of infection and in health professionals, e.g. primary care physicians, gynaecologists/obstetricians, paediatricians, cardiologists, gastroenterologists, and radiologists, (ii) developing national protocols for screening and treatment, targeting high-risk groups such as pregnant woman, newborns, Bolivian citizens, immunosuppressed migrants, (iii) preventing blood- and organ-borne transmission by appropriate screening strategies, (iv) taking into account the social vulnerability of individuals at

risk in the design of programmes and their implementation, and (v) facilitating contacts with the communities at risk through outreach programmes, for example in churches and cultural groups.

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Chagas disease in European countries: the challenge of a surveillance system

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A study of aggregate data collected from the literature and official sources was undertaken to estimate expected and observed prevalence of *Trypanosoma cruzi* infection, annual incidence of congenital transmission and rate of underdiagnosis of Chagas disease among Latin American migrants in the nine European countries with the highest prevalence of Chagas disease. Formal and informal data sources were used to estimate the population from endemic countries resident in Europe in 2009, diagnosed cases of Chagas disease and births from mothers originating from endemic countries. By 2009, 4,290 cases had been diagnosed in Europe, compared with an estimated 68,000 to 122,000 expected cases. The expected prevalence was very high in undocumented migrants (on average 45% of total expected cases) while the observed prevalence rate was 1.3 cases per 1,000 resident migrants from endemic countries. An estimated 20 to 183 babies with congenital Chagas disease are born annually in the study countries. The annual incidence rate of congenital transmission per 1,000 pregnancies in women from endemic countries was between none and three cases. The index of underdiagnosis of *T. cruzi* infection was between 94% and 96%. Chagas disease is a public health challenge in the studied European countries. Urgent measures need to be taken to detect new cases of congenital transmission and take care of the existing cases with a focus on migrants without legal residency permit and potential difficulty accessing care.

Introduction

Chagas disease is caused by the parasite *Trypanosoma cruzi* and is considered endemic in 21 Latin American countries. It currently affects around 10 million people in Latin America, and 10 to 30 per cent of cases have developed or will develop cardiac, digestive or nervous system disorders [1]. In the last two decades many efforts have been made to reduce the incidence of Chagas disease in endemic countries [2], but exchange of population between Latin America and Europe, the United States, Australia and Japan has resulted in increased detection of *T. cruzi* in these countries [3]. In non-endemic regions, the parasite can be transmitted vertically (congenital transmission from mother to fetus), and by infected blood and organ donors [4].

In 2008, more than 38 million migrants were living in Europe, of whom 11% came from Latin America [5]. This figure did not include migrants without valid residency permit (irregular, undocumented migrants) [6], people born outside Europe who have acquired citizenship of a European country, or children from foreign countries adopted by European families. Official figures thus clearly underestimate the number of migrants from endemic areas, and therefore also the number of *T. cruzi*-infected people.

Currently, only a small number of persons infected with *T. cruzi* have been detected in Europe [4]. Several reasons account for this fact:

- Most European health professionals have little or no experience with the detection and management of Chagas disease [7].
- Access to screening programmes for the communities at risk is very limited as only a few institutions offer screening, mostly in major urban areas.
- The diagnosis of the chronic phase is usually delayed as most patients remain asymptomatic for many years [8].

There is no common European legislation to prevent the transmission of *T. cruzi* by blood donation, although in Spain and France screening of Latin American donors is mandatory, while in countries like Italy or the United Kingdom (UK) blood donation by migrants from endemic Latin American countries is prohibited and their country of origin is recorded by questionnaire [4].

Only some autonomous communities of Spain, such as Valencia [9] and Catalonia [10], have protocols for screening of pregnant women from Latin America to prevent congenital transmission. The rest of Spain and other European countries, except for some focal institutional experiences [11], have not adopted any governmental preventive measures yet.

Very few studies have estimated the prevalence of Chagas disease in European countries [12-15]. In Spain, it was estimated that between 40,000 and 65,000 residents were infected with *T. cruzi* in 2009 [4], while in other European countries the estimate range was between 12,000 and 15,000 [16].

The lack of an information system to report Chagas disease cases and transmission in all European countries makes it difficult to provide an overall figure of all diagnosed cases in Europe so far, and therefore no exact overview of the burden and public health impact of Chagas disease in Europe can be made.

For this reason, the World Health Organization (WHO) set up in 2009 a working group of experts on Chagas disease from those European countries where *T. cruzi*-positive cases had been detected (Austria, Belgium, Croatia, Denmark, France, Germany, Italy, the Netherlands, Portugal, Romania, Spain, Sweden, Switzerland and United Kingdom). The aim was to collect and asses the available information, create a network of experts to exchange information and experience between countries and define a common strategy for the epidemiological surveillance of Chagas disease [17].

This paper presents the efforts of this group of experts to provide a preliminary view of the situation in Europe, using a consensual, homogeneous methodology. The objectives of this study were to estimate the expected and observed prevalence of cases of *T. cruzi*-infected people from endemic countries of origin, the annual incidence of congenital transmission and the estimated rate of underdiagnosis among cases of *T. cruzi* infection in 2009 in the participating countries.

Methods

Study design and population

An epidemiological study was designed to analyse aggregate measures of the prevalence of *T. cruzi* infection and the incidence of congenital transmission of Chagas disease in 2009. The units of observation were the European countries that according to the WHO estimate, had more than 400 cases of Chagas disease [4], i.e. Belgium, France, Germany, Italy, the Netherlands, Portugal, Spain, Switzerland and the UK.

Case definition

For the purposes of this study, according to the WHO case definition [18], a case of Chagas disease was considered as any individual who, as a result of a screening programme or of testing as a possible case, was positive for antibodies against *T. cruzi* in two serological (ELISA) assays.

Inclusion and exclusion criteria

The target population included three categories:

- Subjects of any age born in countries endemic for Chagas disease who were regular residents of the above-mentioned European countries in the year 2009 or the latest year for which this information was available.
- The undocumented migrants from disease endemic countries resident in the above-mentioned European countries.
- Children born in countries endemic for Chagas disease and adopted by families from the above-mentioned European countries.

Latin Americans not born in countries endemic for Chagas disease (e.g. the Caribbean islands) were excluded.

European travellers to endemic countries and cases of Chagas disease diagnosed in European travellers presumably infected in endemic countries were excluded due to the small expected number of cases and the difficulty in obtaining information about them.

Information sources

The study population was quantified using official published data obtained from national institutions in the included European countries, Eurostat and data collected by the working group and collaborators of the project. All these sources are listed in Table 1 and the corresponding data are shown in Table 2.

The numbers of diagnosed cases of Chagas disease in each European country was provided by members of the national reference institutions and members of the WHO working group.

The infection rates used to calculate the expected prevalence rate among the estimated resident population of Latin Americans in European countries (Table 3) were those published by the WHO in 2006 [19]. The rates for Bolivia were calculated according to available data on the Bolivian population living in Europe [20,21]. The rates for French Guyana and Surinam were provided respectively by the Institute of Health Surveillance (Institut de Veille Sanitaire, France) and by the Department of Medical Microbiology of the University of Amsterdam (the Netherlands) and rely on estimations on immigrants from these countries living in Europe.

Table 1

Information sources for estimates of migrant residents (legal and undocumented), adoptions and annual births in nine studied European countries

Country	Category	Institution and reference year
Belgium	Legal immigration	National register, Directorate of Statistics and Economic Information (DGSIE), 2006
	Estimated undocumented immigration	Faculty of Medicine, Free University of Bruxelles, Brussels, Belgium 2006
	Adoptions	Adoption in French and Dutch-speaking Belgium, Belgian Directorate of adoption, 2001–2009
	Annual births	National register, Directorate of Statistics and Economic Information (DGSIE), 2006
France	Legal immigration	Institute of Health Surveillance (INVS), 2008
	Estimated undocumented immigration	Institute of Health Surveillance (INVS), 2008
	Adoptions	Institute of Health Surveillance (INVS), 1980–2007
	Annual births	Institute of Health Surveillance (INVS), 2008
Germany	Legal immigration	Eurostat, 2008
Italy	Legal immigration	Italian National Institute of Statistics (ISTAT), 2009
	Estimated undocumented immigration	Centre for Tropical Diseases, Hospital Ospedale Sacro Cuore Don Calabria, Verona, Italy, 2009
	Adoptions	Commission for international adoptions, Presidency of the Council of Ministers, 2000–2009
	Annual births	ISTAT, 2008
the Netherlands	Legal immigration	Statistics Netherlands, 2008
	Estimated undocumented immigration	Central government (Rijksoverheid), 2005
Portugal	Legal immigration	Statistics Portugal (INE), 2009
	Estimated undocumented immigration	Institute of Hygiene and Tropical Medicine, New University of Lisbon, Lisbon, Portugal
	Annual births	INE Portugal, 2009
Spain	Legal immigration	Statistics Spain (INE), 2009
	Estimated undocumented immigration	Statistics Spain (INE), 2009
	Adoptions	Statistics Spain (INE), 2000–2007
	Annual births	Statistics Spain (INE), 2008
Switzerland	Legal immigration	Federal departement of justice and police, 2009
	Estimated undocumented immigration	Division of primary care medicine, Geneva University Hospitals and University of Geneva, Geneva, Switzerland , 2009
	Adoptions	Federal office of statistics, Section demography and migration, 1979–2008
	Annual births	Demographic portrait of Switzerland, 2008
United Kingdom	Legal immigration	Office for National Statistics, Social Surveys Dataservice, 2009
	Estimated undocumented immigration	1. Sveinsson, Kjartan Páll. Bolivians In London - Challenges and Achievements of a London Community, Runnymede Community Studies, Runnymede Trust. 2007 2. Buchuck S. Crossing borders: Latin American exiles in London. Untold London, 2010 3. Bérubé M. Colombia: In the crossfire. Migration Information Source. Migration Policy Institute. 2005 4. James M. Ecuadorian identity, community and multi-cultural integration. Runnymede Trust. 2005
	Annual births	Office for National Statistics, Vital Statistics Outputs Branch, 2009

The applied rates of congenital transmission (1.4% and 7.3%) came from cohorts of migrant pregnant women living in Europe [11,22].

Data collection and analysis

To estimate the expected prevalence of *T. cruzi*-infected people in the studied countries, we first calculated the number of regular residents originating from endemic countries, according to the data published by the national statistical institutes in each country. When there were no published data, these were obtained from governmental sources or from members of the working group (Table 1).

To calculate the undocumented migrant population, we used estimates from governmental sources, national referral centres and indexed and non-indexed publications (Table 1). In the case of Spain, the official number of regular residents was subtracted from the number of migrants included in the municipal census.

In the case of children born in endemic countries and adopted by European families, we sought official data sources on adoption by country of birth (Table 1). The inclusion of this population in the study depended on the availability of data on adoptions, and finally data from five countries (Belgium, France, Italy, Spain, and Switzerland) were included.

To obtain the expected absolute number of cases of *T. cruzi* infection, the number of regular and undocumented migrants from Latin America and the number of adopted children, stratified by country of origin, was multiplied by the corresponding national infection rates in the countries of origin. A two-sided confidence intervals method with continuity correction for the single proportion [23] was applied to calculate the expected number of cases in migrants for every endemic country of origin. The expected number of cases obtained was divided by the corresponding reference population to obtain the expected prevalence rate (shown as percentage). In the case of minimum and maximum values for reference population, an average value was applied to calculate the expected prevalence.

To calculate the observed prevalence of *T. cruzi*-infected people, the members of the working group were asked to actively search for cases diagnosed in their country up to the year 2009, dividing this amount by the total reference population to obtain the observed prevalence rate, shown as percentage.

To estimate the expected annual incidence of congenital transmission, national data on annual births of children of women from endemic areas stratified by country of birth or nationality of the mother as registered in 2009 or the latest year available was collected (Table 1). These figures were multiplied by the respective rates of infection in endemic countries, which provided an estimate of the absolute number of mothers infected with *T. cruzi* who gave birth in one year. Applying the range of congenital transmission rates (1.4% to 7.3%) to this result gave an estimate of the number of *T. cruzi*-infected children born in each participating European country. The annual incidence rate of congenital transmission in the population at risk was obtained by dividing the number of children infected in one year by the number of pregnancies in that year.

To estimate the index of underdiagnosis we calculated the rate ratio between the observed and expected prevalence rates. The result represents the proportion of diagnosed cases divided by the total estimated cases. The index is presented as a percentage obtained from the following formula: *1-rate ratio*.

Table 2

Estimates of migrants resident in nine studied European countries, legal and undocumented, originating from countries endemic for Chagas disease, and births to mothers from endemic countries, 2009

Country	Resident immigrants								Annual births	
	Regular population		Estimated undocumented (min–max)		Adoptions		Total (min–max)			
	Nb	%	Nb	%[a]	Nb	%	Nb	%[a]	Nb	%
Belgium	28,880	1	14,440	1	490	1	43,810	1	722	1
France	97,981	4	51,500	5	19,389	51	168,870	5	5,545	10
Germany	85,313	4	Not reported	-	Not reported	-	85,313	3	Not reported	-
Italy	260,864	12	112,000–120,000	11	6,784	18	379,648–387,648	12	3,351	6
The Netherlands	220,172	10	17,400	2	Not reported	-	237,572	7	Not reported	-
Portugal	110,113	5	11,011	1	Not reported	-	121,124	4	3,950	7
Spain	1,263,342	56	484,509	47	6,354	17	1,754,205	53	35,525	67
Switzerland	35,761	2	38,000–42,000	4	4,994	13	78,755–82,755	2	375	1
United Kingdom	162,517	7	250,000–335,000	28	Not reported	-	412,517–497,517	14	3,433	6
Total	**2,264,943**	**101[b]**	**978,860–1,075,860**	**99[b]**	**38,011**	**100**	**3.281,814–3,378,814**	**101[b]**	**52,901**	**98[b]**

[a] In the case of minimum and maximum values, the percentage refers to the average value.

[b] The deviation is due to rounding.

Results

More than three million migrants from endemic countries (MEC) were estimated to live in the nine European countries included in the study, representing 1% of the total population living in Europe. Due to immigration from Brazil, Portugal was the country with the highest percentage of migrants coming from endemic areas. Among the countries where no Romance language is spoken, the Netherlands had the highest percentage of migrants coming from endemic countries, mainly from Surinam (84% of MEC in the Netherlands), a former Dutch colony and an endemic country for Chagas disease with a low infection rate.

Prevalence in migrants and adoptees

For details about MEC living in Europe, multiple sources of information were used (Tables 1 and 2). However, it was not possible to identify all people at risk due to the lack of data stratified by endemic country. Between 40,227 and 62,724 people infected with *T. cruzi* resided regularly in the included countries, accounting for between 1.8% and 2.8% of all regular MEC (Table 4). The highest prevalence estimation for regular MEC was seen in Spain, where between 2.3% and 3.8% of them were infected with *T. cruzi*.

The estimated numbers of undocumented MEC infected by *T. cruzi* were very high: prevalence estimations were substantially higher than for regular MEC, with the

Table 3

Distribution of the migrant population from countries endemic for Chagas disease resident in nine studied European countries, and estimated number of people infected, 2009

Endemic country		Infection rate	Total regular and undocumented immigrant population[a]		Estimated number of infected people[b]		
		%	Nb	%[c]	Nb	95% confidence interval	%[c]
Argentina		4.13	237,678	7.1	9,815	9,626–10,006	10.4
Belize		0.74	2,464	0.1	18	11–29	0
Bolivia	min	10	268,926	8.4	26,893	26,597–27,188	56.4
	max	27.5	290,926		80,014	79,539–80,470	
Brazil		1.02	670,299	20.1	6,837	6,703–6,971	7.2
Chile		0.99	99,483	3.0	985	925–1,045	1.0
Colombia	min	0.96	476,244	15.4	4,496	4,334–4,620	5.1
	max		546,244		5,168	5,025–5,353	
Costa Rica		0.53	4,808	0.1	25	16–37	0
Ecuador		1.74	612,809	18.4	10,662	10,479–10,847	11.2
El Salvador		3.37	15,389	0.5	519	476–565	0.5
Guatemala		1.98	9,183	0.3	182	157–210	0.2
Guyana		1.29	23,555	0.7	13	7–24	0
French Guyana	min	0.25	18,987	0.6	47	36–63	0.1
	max	0.5			94	78–116	
Honduras		3.05	27,121	0.8	827	773–884	0.9
Mexico		1.03	74,346	2.2	766	714–825	0.8
Nicaragua		1.14	13,317	0.4	152	129–178	0.2
Panama		0.01	4,555	0.1	0	0–5	0
Paraguay		2.54	87,550	2.6	2,224	2,136–2,320	2.3
Peru	min	0.69	268,957	8.2	1,856	1,775–1,936	2.0
	max		273,957		1,890	1,808–1,972	
Surinam	min	0.15	183,216	5.5	287	257–330	0.7
	max	0.5			954	898–1,008	
Uruguay		0.66	69,702	2.1	460	418–502	0.5
Venezuela		1,16	93,836	2.8	1,089	1,023–1,154	1.1
Undetermined[d]			19,389	0.6	165 384		0.3
Total			**3,281,814–3,378,814**	**100**	**68,318–123,078**		**100**

[a] The total immigrant population from Bolivia, Colombia and Peru is a range of values due to estimations of undocumented population.

[b] Estimates based on infection rate of the country of origin.

[c] In the case of minimum and maximum values, the percentage refers to the average value.

[d] This number refers to adoption in France, for which no data is available stratified by endemic country, and the estimate of people infected was calculated by the Institut de Veille Sanitaire, France.

highest estimated prevalence in Spain (between 3.9% and 7.8% of undocumented MEC), and Switzerland (between 2.5% and 7.8% of undocumented MEC).

France had the highest number of positive cases among children adopted from endemic countries, although these were from countries with low infection rates. Cases represented between 0.8% and 2% of French adoptions from endemic countries. The overall expected prevalence in the participating countries ranged from 1.2% to 2.4% of total adoptions of children from endemic settings.

Congenital transmission

In the studied countries almost 53,000 children were born in 2009 from mothers originating from endemic countries. Of these, between 1,347 and 2,521 were born from mothers infected with *T. cruzi*, and there was congenital transmission in between 20 and 184 cases. This corresponds to between none and three infected children per 1,000 births to mothers at risk (Table 5). With 67% of births from mothers originating from endemic countries occurring in Spain, almost 90% all of cases of congenital transmission occurred in that country. In other countries, there were between none and six cases of congenital transmission per year.

Underdiagnosis

By 2009, 4,290 cases of infection with *T. cruzi* were diagnosed in the study countries (Table 6), and 89% of all cases were detected in Spain. The total observed prevalence rate was 0.13% of the total MEC. The lowest observed rates occurred in Germany (0.002%) and the Netherlands (0.003%) and the highest in Switzerland (0.223%).

The index of underdiagnosis shows that, in general, between 94% and 96% of expected cases were not diagnosed (Table 6). The index of underdiagnosis was lowest in Switzerland, where between 89% and 95% of expected cases were not detected, while in Germany, the Netherlands, Portugal and the UK, more than 99% of expected cases in migrants were not diagnosed.

Overall, the Latin American nationalities with the greatest presence in Europe were Brazilans, Colombians and Ecuadorians, although most expected cases of Chagas were attributed to Bolivian migrants (Table 3).

Discussion

The Control of Chagas disease is a recent public health challenge in many countries in Europe. The reason is that it is an imported disease mainly affecting the migrated poor population from different Latin American countries who often have limited access to diagnosis and treatment of this disease. This also makes it difficult to quantify the disease impact in terms of expected cases. However, it is a challenge that requires urgent action due to the risks involved in the context of blood, organ and tissue donation, and the risk of congenital transmission to infants of infected mothers. In addition, the presence of potentially infected population groups who may present with heart, digestive tract and general disorders in the medium and long term, needs to be considered also with a view to the individual patient and the impact on clinical costs.

To quantify the European expected prevalence the authors decided to use initially the WHO official infection rates for every disease endemic country [18]. On the other hand, it was observed that all prevalence studies on Latin American immigrants living in Europe showed rates in the Bolivian community higher than the 6,75% WHO official estimated rate [20,21,24,25]. For this reason we preferred to use a more realistic range for Bolivian migrants (minimum 10.0%, maximum 27.5%) that was based on the known epidemiological situation in Europe. This choice could have introduced some bias at the methodological level by elevating the results in only one community. Nevertheless, the authors believe that this decision was necessary because the final results were closer to the reality that

Table 4

Estimated numbers of migrants from Chagas disease-endemic countries infected with *Trypanosoma cruzi* and expected prevalence in the nine studied European countries in 2009

Country	Legal (min-max)		Estimated undocumented (min-max)		Adoptions (min-max)		Total (min-max)	
		Prevalence		Prevalence		Prevalence		Prevalence
Belgium	451-601	1.6-2.1	226-301	1.6-2.1	6-19	1.2-3.9	683-921	1,6-2.1
France	1,253-1,542	1.3-1.6	730-897	1.4-1.7	165-384	0.8-2	2,148-2,823	1.3-1.7
Germany	1,123-1,481	1.3-1.7	Not reported	-	Not reported	-	1,123-1,481	1.3-1.7
Italy	4,133-5,322	1.6-2	2,220-6,520	1.9-5.6	111-194	1.6-2.9	6,464-12,036	1.7-3.1
Netherlands	776-1,528	0.3-0.7	191-245	1.1-1.4	Not reported	-	967-1773	0.4-0.7
Portugal	1,141	1	114	1	Not reported	-	1,255	1
Spain	28,974-48,510	2.3-3.8	18,884-37,874	3.9-7.8	126-234	2-3.7	47,984-86,618	2.7-4.9
Switzerland	535-750	1.5-2.1	982-3,132	2.5-7.8	66-88	1.3-1.8	1,584-3971	2-4.8
United Kingdom	1,841-1,849	1.1	4,270-10,352	1.5-3.5	-	-	6,111-12,201	1.3-2.4
Total	**40,227-62,724**	**1.8-2.8**	**27,617-59,435**	**2.7-5.8**	**474-919**	**1.2-2.4**	**68,318-123,078**	**2-3.6**

professionals involved in the detection of cases see every day in health systems.

Another relevant point is that other applied national infection rates, based on the population in disease-endemic countries, do not take into account the effects of heterogeneity of the immigrant population living in Europe (i.e. age groups, socio-economic differences, rural-urban origin, etc.) and these differences are not reflected in the results.

The results of this study highlight the difficulty in obtaining accurate data on the population at risk and specific information on diagnosed cases, the lack of official national data, the underestimation of migrants in the official figures, and the lack of a system for reporting detected cases in non-endemic countries.

According to the estimations of expected cases in the different non-endemic countries, and to offer a better view of the situation, we classified the countries in three groups. The first category includes only Spain, which accounts for almost 75% of expected cases. The second group is represented by France, Italy and the UK, while the third group is represented by the other non-endemic countries (Belgium, Germany, the Netherlands, Portugal and Switzerland). The key role played by Spain in the prevention and control of Chagas disease in Europe is not only due to the high expected prevalence of *T. cruzi* infection, but also relates to its pivotal position in the migrant flow to Europe and the cultural and linguistic proximity to Latin American countries. France has played a key role in the development of recent studies and specific interventions and regulations for Chagas disease [26], although the country had a low expected number of cases. This and the existence of French national territory in the endemic region of Latin America (French Guyana) places France in a distinctive position in the prevention and control plans for Chagas disease in non-endemic European countries.

Table 5

Estimated congenital transmission and prevalence rate per 1,000 pregnancies in women from Chagas disease-endemic areas, residing in nine studied European countries, 2009

Country	Annual births	Infected pregnant women (min–max)		Infected infants (min–max)	
		Number of cases	Cases per 1,000 pregnancies	Number of cases	Cases per 1,000 pregnancies
Belgium	722	10–13	14–18	0–1	<1
France	5,545	53–74	10–13	1–5	<1
Germany	Not reported	Not applicable	-	Not applicable	-
Italy	3,351	55–76	16–23	1–6	1
The Netherlands	Not reported	Not applicable	-	Not applicable	-
Portugal	3,950	40	10	1–3	<1
Spain	35,525	1,125–2,226	32–63	16–162	0-5
Switzerland	375	6–8	16–21	0–1	1
United Kingdom	3,433	58–84	17–24	1–6	1
Total	**52,901**	**1,347–2,521**	**25–48**	**20–184**	**0–3**

Table 6

Diagnosed cases, observed and expected prevalence rates and percentage of underdiagnosis of Chagas disease in migrants from endemic areas residing in nine studied European countries, up to 2009

Country	Cases diagnosed	Observed prevalence rate (%)	Expected prevalence rate (min–max, %)	Index of underdiagnosis (min–max, %)
Belgium	19	0.043	1,6-2.1	97.2–97.9
France	111	0.066	1.3-1.7	94.8–96.1
Germany	2	0.002	1.3-1.7	99.8–99.9
Italy	114	0.03	1.7-3.1	98.3–99.0
The Netherlands	7	0.003	0.4-0.7	99.3–99.6
Portugal	8	0.007	1	99.4
Spain	3,821	0.218	2.7-4.9	92.0–95.6
Switzerland	180	0.223	2-4.8	89.2–95.2
United Kingdom	28	0.006	1.3-2.4	99.6–99.7
Total	**4,290**	**0.13**	**2-3.6**	**93.9–96.4**

The observed prevalence was extremely low, compared with the expected rates, in Belgium, the Netherlands, Portugal and the UK, suggesting a lack of awareness and interventions (protocols, studies, etc) against Chagas disease in those countries. The UK, especially London where most Latin American immigrants to the UK reside [27], ranks second in Europe in terms of residents estimated to be infected with *T. cruzi* and cases of congenital transmission, with numbers nearly identical to those of Italy. These results are entirely novel and in contrast to UK estimates published in previous studies [16]. This discrepancy could be due to potential underestimation in official statistics of the Latin American population actually resident in the UK.

The study highlights the presence of positive cases in undocumented migrants, especially in Spain, Italy and Switzerland. These countries have large Bolivian communities not represented in official statistics [24,28] that makes it even harder for the national authorities to identify the population at risk. On the other hand these results can offer only an incomplete picture of the reality due to the limitations of estimating the reference population. Nevertheless the present study offers new information not included in previous studies that only included documented migrants [3,15]. The fact that being an undocumented migrant could be associated with originating from poor endemic areas with higher prevalence rates highlights the value of developing demographic studies that can contribute to providing more reliable estimates of this population.

The estimated results on underdiagnosis are a good indicator of the limited epidemiological impact of Chagas disease in the context of European health and surveillance systems. Epidemiological silence, understood as the lack of detected cases, which is common in some European countries, shows the need for greater involvement of European health authorities in controlling neglected tropical diseases, among others Chagas disease. The priority could be the implementation of screening programmes of target populations and the training of professionals in the detection of possible cases. The legislation or protocols already implemented in countries such as Spain or France would be very useful to reduce the differences in preparedness and available programmes between European countries. Such collaboration would be of help in developing a European surveillance system, which is essential for further progress in controlling Chagas disease.

The control of congenital transmission is undoubtedly one of the most important measures for the prevention and control of Chagas disease that should be addressed by surveillance systems because of the effectiveness of treatment in infants. Likewise, the establishment of regulations for blood and organ donation is essential to limit the impact of Chagas disease in countries where there is no vector transmission. Systematic screening of the risk population, at present only carried out in some regions of France, Spain and Switzerland, should also be introduced after carrying out cost-effectiveness analyses to decide which measures could be most appropriate.

In terms of public health, the authors believe that the main proposals and challenges for European countries where cases have already been identified or that have residents from endemic areas are:

- To create an international information and surveillance system for the reporting of cases, control of transmission, exchange of information between European countries, and training of primary healthcare workers.
- To carry out studies to define the risk of congenital transmission in pregnant women from Latin America and to evaluate the impact of potential screening protocols for the control of congenital transmission according to the results obtained.
- To carry out epidemiological studies allowing for reliable estimation of true prevalence rates among immigrants resident in Europe.
- To consider systematic screening (by questionnaire or serological tests) blood, organ and tissue donors from endemic Latin American regions.
- To publish official statistics of migrants from Chagas-endemic countries in each European country containing data by regular and irregular status according to their country of origin.
- To facilitate access to diagnosis and treatment to groups of migrants at risk of being excluded from the national health systems such as undocumented immigrants.
- To reinforce the teaching on international health and tropical diseases in the curricula of health sciences in European Universities.

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Surveillance of Chagas disease in pregnant women in Madrid, Spain, from 2008 to 2010

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One of the most important modes of transmission of *Trypanosoma cruzi* infection in areas where it is not endemic is vertical transmission: from mother to child. The objective of this report is to assess the efficacy of different programmes of serological screening to monitor infection with *T. cruzi* in pregnant Latin American women living in Madrid (Spain). To achieve this, a retrospective study was undertaken from January 2008 to December 2010 in seven hospitals in the Autonomous Community of Madrid. Serological screening programmes were classified in two main strategies: a selective one (pregnant women from Bolivia) and a universal one (pregnant women from Latin America). A total of 3,839 pregnant women were tested and the overall prevalence was 3.96%. The rate of congenital transmission was 2.6%. The current monitoring programmes have variable coverage ranging between 26% (selective screening) and 100% (universal screening). Monitoring of pregnant women from Latin America only reaches full coverage if universal screening of pregnant women is carried out at any moment of pregnancy, including at delivery. A common national regulation is necessary in order to ensure homogenous implementation of screening.

Introduction

In the last ten years, due to the increase in the immigrant population from Latin America, *Trypanosoma cruzi* infection has become one of the most common imported parasitoses in Spain. By the end of 2009, around 3,600 cases had been confirmed, although estimates that take into account the prevalence of *T. cruzi* infection in Latin America suggest that between 40,000 and 65,000 affected people currently reside in Spain [1].

Taking into account the data provided by the Spanish Statistical Institute (INE) in January 2010, 25.7% (429,826 of 1,670,196) of the immigrant population from *T. cruzi*-endemic areas were residing in the Autonomous Community of Madrid (Figure). Of this population, 39.1% (167,917 of 429,826) were women aged between 15 and 44 years [2].

The three main transmission routes of *T. cruzi* in non-endemic regions are: transfusion of blood products, vertical transmission and organ transplantation [1]. That is why, between March 2002 and December 2004, the Madrid branch of the Spanish Red Cross carried out the first serological screening of candidates for blood donation from areas where Chagas disease is endemic, to establish their suitability as donors. The potential donors, who were not born in Spain, were interviewed and 44% of them were identified as coming from endemic areas. The prevalence of *T. cruzi* antibodies in the donors coming from endemic areas was 0.8% and 75% of those who tested positive were from Bolivia [3].

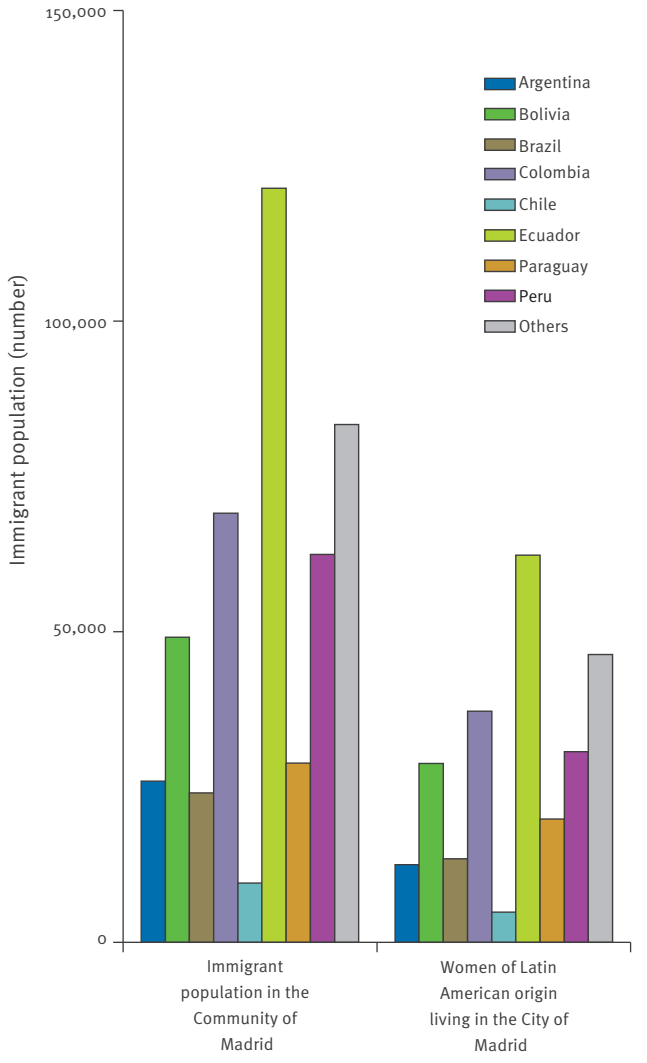
Since September 2005, in accordance with the Royal Decree RD1088/2005 [4], all blood transfusion centres in Spain have been obliged to carry out serological screening of the population considered to be at risk [4]. This means that they systematically exclude from donation individuals (i) who come from areas where Chagas disease is endemic, (ii) who were born to mothers from such areas, and (iii) who have received transfusions or have spent prolonged periods of time in such areas (one month or longer in mainly rural areas) [5,6]. In the past 22 years, there have been at least six cases of transfusional Chagas disease in Spain: one of them was reported in Madrid and proved fatal [7,8].

Another important mode of infection is vertical transmission from a seropositive mother to her child during pregnancy or delivery. At present, there is no national Spanish policy that establishes monitoring of Chagas disease in pregnant women and their newborns. Only the Autonomous Communities of Valencia and Catalonia have regulations in place and have systematically performed screening since November 2007 and February 2009, respectively [9,10]. Nevertheless, it is important to mention that there are different initiatives in other Communities. To date, cases of congenital infection have been reported in Valencia, Catalonia, Murcia, Aragon, the Basque Country and Andalusia [1].

In Madrid, as in other areas of Spain, the birth rate has increased among the migrant population in the last five years. In 2009, of the 35,038 deliveries registered in Spain to mothers from Latin America, 9,171 (26.2%) were to mothers resident in Madrid. The most common countries of origin of these mothers were: Ecuador, Colombia, Bolivia and Peru (27.9%; 12.9%; 12.7% and 11.7%) [2].

Figure

Immigrant population and women born in Latin America and registered in the Municipal Register of Madrid, Spain, January 2010



Source: Spanish Statistical Institute (www.ine.es).

Currently, the only way to control Chagas disease in pregnant women is determining the presence of *T. cruzi* antibodies in those who come from areas where the infection is endemic, thus facilitating early diagnosis and treatment of congenital infection and also allowing postnatal treatment of the mother to reduce the risk of transmission in future pregnancies. Therefore, the main objective of this report is to describe and assess different programmes to monitor pregnant women coming from different areas in Latin America, because treatment of children leads to a cure rate next to 100% whereas it is much lower in adults [11].

Material and methods

The serological screening of pregnant women at risk of *T. cruzi* infection was implemented within the framework of the Working Group on Chagas Disease of the Madrid Autonomous Community. This study assesses observationally and retrospectively the general coverage of the screening programme, the prevalence of infection and the rate of congenital transmission. The study included seven hospitals serving 48.5% (3,131,315 of 6,458,684) of the population of the Autonomous Community of Madrid, according to INE data in January 2010.

The programme included meetings to inform healthcare personnel and managers in the public hospitals involved and to draw attention to the need to incorporate a test to detect *T. cruzi* antibodies as an additional routine test performed on pregnant women from areas where Chagas disease is endemic.

Since there is no standard reference test, each hospital chose a serological test in accordance with its infrastructure. This determined the type of screening, which was either universal (applied to all pregnant women from countries where the disease is endemic - option 1; or to all pregnant women from Latin America - option 2) or selective (applied only to pregnant Bolivian women - option 1; or to pregnant Bolivian women plus pregnant women born in both low-risk and high-risk areas according to maps indicating distribution in particular countries or other risk indicators - option 2). For this last option, all pregnant Bolivian women were considered to be from a high-risk area, and the rest of Latin American pregnant women were considered to come from low-risk areas. The serological screening for Chagas of low-risk pregnant women was carried out taking into account the recommendations and maps for the selection of blood donors [5,6,12] and their clinical epidemiological background.

On the other hand, depending on the specific organisation of each hospital and the attendance of pregnant women at their prenatal sessions, serological screening was systematically performed only in the first or

second trimester, or at any moment of the pregnancy including delivery (Table 1).

For the detection of cases of congenital infection, an agreed follow-up protocol was used which involved monitoring children born to seropositive mothers during the first nine months of life [13]. Tests were performed at delivery, after one month, and at nine months of age, while the option of performing more tests during the first nine months was not ruled out. The parasite detection was carried out by direct microscopic observation, microhaematocrit test [15] and PCR [8].

Data were collected via a form designed for the analysis of aggregate data. The coverage of each screening programme was calculated as the proportion of pregnant women tested of the total number of pregnant women attending the seven hospitals from areas where the disease is endemic, from January 2008 to December 2010. The overall prevalence was calculated as the proportion of pregnant women confirmed as positive of the total number of pregnant women tested. Any pregnant woman born in Cuba, the Dominican Republic or any other country where Chagas disease is not endemic, was excluded from the analysis. The prevalence by country of origin was defined as the proportion of pregnant women confirmed as positive from each country of the total number of pregnant women tested from that country. For this last calculation, the data used were those from hospitals that recorded the country of origin of the entire population of pregnant women included in the programme (five of the seven hospitals).

The rate of congenital transmission was calculated as the proportion of children infected of the total number of pregnant women confirmed as positive.

Results

The characteristics of the hospitals, number of deliveries, start date of screening, type of screening, and

Table 1

Characteristics of hospitals and screening programmes for *Trypanosoma cruzi* infections in pregnant women, Madrid, Spain, January 2008–December 2010

Hospital	Number of beds	Attending population	Number of deliveries (2010)		Start date of screening	Type of screening	Screening tests	Confirmation / Complementary tests[a]
			Total	Endemic zone / Bolivia				
1	1,750	750,000	7,513	1,826 / 443	Jul 2008	Selective[b] (pregnancy or delivery)	ICT[c]	ELISA + IFI / PCR
2	1,328	787,000	6,599	1,359 / 191	Dec 2007	Selective[d] (pregnancy or delivery)	ICT[e]	ELISA + IFI / PCR
3	616	397,083	3,193	272 / 15	Nov 2008	Universal[f] (first trimester)	ICT[c] (Nov 2008-Feb 2010); ELISA[a] +IFI[a] (Feb-Dec 2010)	ELISA + IFI / PCR
4	630	213,654	2,010	81 / 2	Oct 2008	Universal[g] (2008-2009 first trimester; 2010 second trimester)	ELISA[a]+IFI[a]	ELISA + IFI
5	362	264,691	2,288	115 / 3	Jan 2008	Universal[f] (first trimester)	ELISA[a]+IFI[a]	ELISA + IFI / PCR
6	447	189,359	1,647	123 / 6	Feb 2008	Universal[g] (pregnancy or delivery)	ELISA[h]/ ICT[c]	ELISA + IFI / PCR
7	1,136	529,528	2,700	361 / 77[i]	Mar 2008	Universal[g] (pregnancy or delivery)	ICT[g] + ELISA[j]	ELISA + IFI

ELISA: Enzyme-linked immunosorbent assay; ICT: Immunochromatographic test; IFI: Indirect immunofluorescence; PCR: Polymerase chain reaction.

[a] In-house tests at the National Microbiology Centre, Instituto de Salud Carlos III [14].

[b] Pregnant women from Bolivia or risk areas according to maps indicating distribution in particular countries, and pregnant women with any other previous clinical or epidemiological risk.

[c] Simple Stick Chagas (Operon S.A., Zaragoza, Spain).

[d] Only Bolivian pregnant women.

[e] Ab Combo Rapid Test (CTK Biotech. Inc., San Diego, USA).

[f] Pregnant women from Latin America except Cuba and the Dominican Republic.

[g] Latin American women without exceptions.

[h] Bioelisa Chagas (Biokit, Lliça d'Amunt, Spain).

[i] Initially monitored in Hospital 7, delivery in Hospital 1.

[j] Chagas ELISA (Vircell S.L., Granada, Spain).

both screening and confirmation tests are described in Table 1. Two hospitals carried out the selective serological screening and the rest adopted a universal screening. The proportion of deliveries to women from areas where the disease is endemic over the total number of deliveries attended in 2010 for each hospital, ranged from 4% (81/2,010) in Hospital 4 to 24.3% (1,826/7,513) in Hospital 1 (Table 1). The coverage of monitoring only reached 100% in the hospitals that adopted a universal serological screening programme (all pregnant women from Latin America, without excluding those who came from countries where the disease is not endemic) at any moment during the pregnancy as well as at delivery (Hospital 6 and 7). The hospitals that adopted a universal screening programme systematically applied in the first or second trimester of pregnancy, did not cover pregnant women who were only attended at the time of delivery, Hospitals 3, 4 and 5 (Table 2).

A total of 3,839 pregnant women were tested, and the overall prevalence was 3.96% (152/3,839). The hospitals that adopted a universal screening programme found a prevalence between 0.5% (Hospital 5) and 4.2% (Hospital 7). In contrast, the hospitals that selectively screened only pregnant Bolivian women (Hospital 2) or pregnant Bolivian women plus pregnant women from other countries with clinical and epidemiological background (Hospital 1) registered a prevalence of 10% and 6.2%, respectively (Table 2). The data from Hospitals 1, 2, 3, 4 and 6 which had recorded the country of origin of the pregnant women included in the study identified a prevalence of 11.4% in Bolivian women. Data from hospitals which had not recorded the country of origin indicated a 3.1% prevalence in all the Latin American pregnant women. The prevalence in pregnant women from other countries was not calculated, as the data regarding distribution by country of origin were incomplete (Table 3). The rest of seropositive women were from Argentina, Colombia, Paraguay and Peru. Detectable parasitaemia was present in 44% (27/62) of all the pregnant seropositive women who were tested by PCR (Table 2).

Four infected children were detected and they were all born to Bolivian mothers. Given that 95.4% (145/152) of seropositive mothers were from Bolivia, the overall rate (2.6%) of congenital transmission was similar to that for Bolivians (2.8%). Three of the four children were born asymptomatic and two of them received specific treatment with benznidazole in the hospitals where they were diagnosed. The first child was monitored during 15 months. The parasitological tests were negative after treatment (two months). Serological tests returned a negative result three months after treatment and they remained negative for the whole monitoring period (15 months). The other child was diagnosed in December 2010, parasite clearance was obtained one month after treatment and in March 2011 serology was still positive. This child is currently under serological monitoring. The mother of the third asymptomatic child moved to another region where the treatment and follow-up were completed. The fourth child was born with Down's syndrome and congenital cardiopathy. It was treated first with benznidazole, and then with nifurtimox. After recovering from *T. cruzi* infection, it died suddenly at the age of nine months.

Table 2

Distribution of the pregnant women included in the study and cases of congenital transmission of *Trypanosoma cruzi* infections by hospital, Madrid, Spain, January 2008–December 2010 (n=3,839)

Hospital	Number of pregnant women						Congenital cases (%)	
	Tested before December 2010	Coverage %	Positive screening test	Confirmed positive[a]	Prevalence[b] %	Positive PCR		
1	257	31[c]/26[d]	30	16 / 18	6.2	7 / 15	2[e]	(12.5)
2	521	100[c]/38[d]	53	52 / 53	10	15 / 40	1[f]	(1.9)
3	292	452	4	4 / 4	1.4	1 / 2	0	(0.0)
4	209	NC	7	2 / 4	1	ND	0	(0.0)
5	219	NC	3	1/ 3	0.5	1 / 1	0	(0.0)
6	639	100[d]	13	6 / 9	0.9	3 / 4	1[g]	(16.7)
7	1,702	100[d]	71	71 / 71	4.2	ND	0	(0.0)
Total	**3,839**		**181**	**152 / 165**	**4**	**27 / 62**	**4**	**(2.6)**

NC: not calculated; ND: not determined.

[a] Number of women confirmed as positive compared to those pregnant women with a positive result in the screening.

[b] Calculated from the number of pregnant women confirmed as positive out of the total number of pregnant women tested.

[c] Based on the number of pregnant women tested out of the total number of deliveries to Bolivian women (selective screening).

[d] With respect to the total number of pregnant women from areas where infection is endemic (universal screening).

[e] Diagnosed using PCR and direct observation.

[f] Diagnosed using microhaematocrite and PCR.

[g] Diagnosed using PCR in two independent samples.

Discussion

According to estimates from the Pan American Health Organization (PAHO), the number of people infected with *T. cruzi* in Latin America has come down from the 20 million that they estimated in the 1980s to 8 million in 2005 [16]. This reduction is believed to have been achieved due to the different control initiatives that have been set up (Southern Cone Initiative to Control/ Eliminate Chagas Disease - INCOSUR, Initiative of the Andean Countries to Control Vectoral and Transfusional Transmission of Chagas Disease - IPA, Andean´s Countries Initiative for controlling Chagas disease - ICA and Initiative of the Amazon Countries for Surveillance and Control of Chagas Disease - AMCHA) and the commitment of the governing authorities in each of the countries involved.

In the past, Spain has registered cases associated with the three main modes of infection in non-endemic regions: transfusion of blood products [7,8], organ transplantation [17] and vertical transmission [18-20] At present, according to the Royal Decree 1088/2005 [4], blood donations from donors who come from areas considered to be at high risk, or with a history of being exposed to high risk, must be tested in order to avoid the use of contaminated blood. The same measures were adopted by the Spanish National Transplant Organization [21,22]. However, there are no national regulations in Spain for the monitoring of pregnant women from areas where the disease is endemic.

This paper shows that, given the absence of regulations, each hospital adopted a screening programme that fitted its own organisation and facilities, and this means that the current monitoring programmes have variable coverage.

Despite the lack of homogeneity, according to the data collected, the observed overall prevalence of seropositive pregnant women coming from endemic areas for Chagas disease of 3.9% (152/3,839) was similar to that described in hospitals in Catalonia and Valencia: 3.4% (46/1,350) and 4.7% (29/624), respectively. However, the prevalence reported here among pregnant Bolivian women in Madrid (11.4%) was lower than that reported in other studies carried out in Catalonia and Valencia, 22% (42/46) and 17.5% (24/29), respectively [18,23]. As in those studies, the pregnant women who tested positive generally came from Cochabamba and Santa Cruz, regions in Bolivia where the disease is hyperendemic. Since data were not collected on pregnant Bolivian women who tested negative, it is probable that the difference in prevalence between regions in Spain reflects the origin of the Bolivians living in those regions and the prevalence in those areas of origin [24]. On the other hand, the overall rate (2.6%) of congenital transmission found in Madrid was lower than that reported in Catalonia (7.3%) [18], although the proportion of pregnant women with detectable parasitaemia was similar (27/62 in Madrid compared with 18/35 in Catalonia). Taking our data into account, it can be concluded that there are two possible screening options: (i) screen only pregnant Bolivian women (the high-risk population), or (ii) screen all pregnant women from areas where the disease is endemic. In 2008 when the programme began, there were insufficient automatic high-throughput serological tools, but this situation has changed in the recent years. At present, testing pregnant women for *T. cruzi* antibodies when they first come into contact with the healthcare system, would represent a cost of approximately EUR 2 each, if this test is added to the tests for ToRCHeS syndrome (Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex, syphilis, HIV). Taking into account the data in Table 3, the screening of the 798 Bolivian women would have costed EUR 1,596 for the three years. This means that the detection of one congenital case would cost on average EUR 399. If universal screening was carried out, the detection of one congenital case would cost EUR 1,920 (3,839 x EUR 2 / 4 congenital cases). Thus, selective screening of pregnant Bolivian women is more cost-effective than screening all pregnant women from areas where the disease is endemic. However, it is important to highlight that cases of congenital infection were also reported in children born to Argentinean mothers [19,20]. If screening is not carried out under either of these protocols, the question would remain on the cost to be incurred by the healthcare system

Table 3

Distribution and prevalence of *Trypanosoma cruzi* infection in pregnant women by country of origin, Madrid, Spain, January 2008–December 2010 (n=3,839)

Country of origin	Number (%)	Number of confirmed positive cases	Prevalence %
Colombia	239 (13.3)	0	0
Ecuador	379 (21.1)	0	0
Peru	192 (10.7)	0	0
Venezuela	18 (1)	0	0
Brazil	39 (2.2)	0	0
Bolivia	798 (44.4)	91	11.4
Chile	15 (0.8)	0	0
Paraguay	60 (3.3)	0	0
Argentina	17 (0.9)	0	0
Nicaragua	4 (0.2)	0	0
Other	38 (2.1)	0	0
Total pregnant women from countries where the disease is endemic	1,799 (100)	91	5.1
Total pregnant women from countries where the disease is not endemic	59 (100)	0	0
Data not available[a]	1,981 (100)	61[b]	3.1
Total	**3,839 (100)**	**152**	**4**

[a] Hospitals that did not collect information on the country of origin.

[b] Includes pregnant women from: Bolivia (n=54); Argentina (n= 1); Paraguay (n=1); Colombia (n=2); Peru (n=2) and of unknown origin (n=1).

for the treatment of 30% to 50% of these children who would develop severe forms of Chagas disease in the future.

Furthermore, the monitoring of pregnant women also offers the possibility of detecting other adult family members for the first time, together with the detection of children whose condition was previously overlooked. According to data from one of the hospitals included in this study, between three and five affected family members can be detected together with every pregnant infected woman identified (E Vilalta, personal communication, February 2011). As the immigrant population is predominantly composed of young adults [18,23] monitoring pregnant women would facilitate not only the treatment of infected children, but also the passive detection of the relatives and the other infected immigrants who could be treated. Thus, universal serological screening is an important ethical requirement and would still prove to be cost-effective by reducing the risk of developing severe illness that may result from infection.

Conclusion

Monitoring of pregnant women only reaches full coverage if universal screening of pregnant women from Latin America is carried out at any moment of pregnancy, including the delivery. A common national regulation is necessary in order to ensure homogenous implementation of screening. Thus, newborns can be cured if they are treated at an early stage of the disease.

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Clinical, electrocardiographic and echocardiographic abnormalities in Latin American migrants with newly diagnosed Chagas disease 2005-2009, Barcelona, Spain

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Following Latin American migration, Chagas disease has inevitably appeared in non-endemic countries in Europe and elsewhere. New policies are necessary to prevent transmission in those countries but the long, often undetected chronic period of the early stages of the disease also renders epidemiological studies important. The main objective of our study was to determine the presence of clinical, electrocardiogram (ECG) and echocardiographic abnormalities in a population of Latin American migrants infected with *Trypanosoma cruzi* at the moment of diagnosis. We performed a hospital-based observational study of 100 adult patients with newly diagnosed Chagas infection between January 2005 and December 2009. Thirty-seven patients were classified within the Brazilian Consensus on Chagas cardiomyopathy early cardiac stages (A or B1) and 49 presented pathological findings (stage B2) according to the Panamerican Health Organization Classification. Overall, 49 patients showed ECG and/or echocardiographic alterations. The presence of ECG and ecocardiographic alterations were significantly associated (p=0.038). The most frequent ECG and echocardiographic findings were right bundle branch block (12 cases) and impaired left ventricular wall relaxation (24 cases), respectively. In conclusion, ECG and echocardiographic alterations coherent with Chagas cardiomyopathy were found in a large proportion of newly diagnosed Latin American migrants infected with *T. cruzi*. In the mid-term, Chagas disease might become an important cause of chronic cadiomyopathy in our attendance area.

Introduction

Chagas disease is a zoonosis caused by the parasite *Trypanosoma cruzi*, a flagellated protozoa mainly transmitted to humans by the faeces of blood-sucking triatomine bugs (*Triatoma infestans* and others). A hundred years from its description, Chagas disease remains a neglected tropical disease and is as such recognised by the World Health Organization [1]. Until the late twentieth century, Chagas had a geographical distribution that was confined to that of its vector, namely in Central and South America. Today, the disease is no longer confined to Central and South America. Non-endemic countries in Europe and elsewhere have seen the emergence of Chagas disease following migration of chronically infected individuals from endemic areas. In Europe, for example, there are an estimated 2,300,000 Latin American migrants, both documented or undocumented [2,3] and non-endemic countries need to consider implementing preventive policies concerning blood transfusion, organ transplantation and vertical transmission [4,5].

Acute Chagas disease manifests clinically with fever and lyphadenopathy, unspecific general malaise and is self-limiting. It is followed by a long asymptomatic period of latency (or chronic disease) characterised by the presence of antibodies against *Trypanosoma cruzi*. In this stage, clinical examination of the chest, oesophagus and colon may be normal, the 12-lead electrocardiogram (ECG) can show no irregularities or minor alterations. After decades of undetected, asymptomatic disease, over 40% of infected individuals develop clinical symptoms reflecting the tissue damage. They usually involve the heart or digestive tract. The clinical outcome of the chronic phase of Chagas disease ranges from the absence of sings and symptoms to sudden premature deaths due to silent severe cardiomyopathy. Classically it is considered that up to a 30% of those infected will develop cardiac symptoms or ECG alterations within 10-30 years after the initial infection [6].

Although the pathogenesis of Chagas is not completely understood, a growing consensus points to a combination of direct tissue effects of the parasite with an immunologic response that may paradoxically increase

the tissue inflammation and thus over time lead to fibrosis [7]. Such low-intensity inflammation causes the specific Chagas cardiomyopathy and sooner or later affects the conduction system. This affection is reason for the often pathological ECG findings in Chagas patients [8].
Chagas cardiomyopathy marks the prognosis of the disease. It results in impairment of contractile function and final dilation of all four heart chambers. Eventually, ventricular tachycardia or refractory congestive heart failure threaten the lives of those affected [9].

Spain has become the main European destination of Latin migration in recent decades [10]. We undertook a hospital-based descriptive study to determine the presence of cardiac (clinical, ECG and echocardiographic) alterations in of a population of infected Latin American migrants at the moment of the diagnosis as well as to estimate their clinical and functional cardiac staging.

Methods

Between January 2005 and December 2009, we studied all consecutive adult patients newly diagnosed with Chagas infection at the Unitat de Salut Internacional Metropolitana Nord. The Unitat de Salut is a referral unit shared by the Primary Care Service and the tertiary care Hospital Universitari Germans Trias i Pujol. Both are located in the Barcelona Metropolitan Area, Spain; they serve a population of over two million people of which approximately 6% are Latin American migrants. The unit belongs to the Institut Català de la Salut, the main public health provider in Catalonia and, therefore, the medical visits were free of charge. The majority of patients were referred by family practitioners as foreseen in the protocol of the Chagas screening program for populations at risk (i.e. Latin American pregnant women, Bolivian natives, other Latin American migrants with any risk factor for Chagas disease) at primary care level in Catalonia [11].

Exclusion criteria for the study were: (i) documented previous diagnose of Chagas infection or antichagasic treatment, (ii) age less than 15 years, (iii) presence of hypertension, diabetes, coronary artery disease or other concurrent diseases associated with cardiomyopathy and, (iv) pregnancy.

Individuals were considered as Chagas cases when two commercialised enzyme-linked immuno sorbent assay (ELISA)-based serological tests against crude and recombinant *T. cruzi* antigens, were positive. In case of discrepant results, a third test, based on indirect immunoflourescence (IIF) was performed.

All newly-diagnosed Chagas patients underwent a clinical evaluation, including full medical history, physical examination, ECG with 30 seconds DII strip and a two-dimensional and Doppler echocardiography.

The following variables were assessed: age, sex, country of origin and having lived in rural environment (yes/no), previous adobe housing (yes/no) self-reported family history of Chagas infection (yes/no), mother with Chagas infection (yes/no), cardiac symptoms, ECG alterations, echocardiographic abnormalities, debut as acute cardiac event (i.e. tachyarrythmia, cardiac syncope, pulmonary or systemic tromboembolism and acute heart failure) and Chagas cardiomyopathy staging.

The variable "cardiac symptoms", assessed as a dichotomy variable (yes/no) included at least one of the following features: antecedents of chest pain, palpitations, syncope, pulmonary thromboembolism, stroke and symptoms of heart failure such as oedema of the lower legs or dyspnoea on exertion.

The ECG alterations assessed were: sinus bradycardia, right bundle branch block, left anterior fascicular block, left bundle branch block, posterior fascicular block, atrial fibrillation, any degree of atrioventricular block, ventricular extrasystoles and Q wave or diffuse ST-T changes presence.

Figure 1

Classification schemes to grade Chagas cardiomyopathy

Brazilian Consensus Classification [12]
A: Abnormal ECG findings. Normal echocardiogram. No signs of CHF.
B1: Abnormal ECG findings. Abnormal echocardiogram with LVEF› 45%. No signs of CHF.
B2: Abnormal ECG findings. Abnormal echocardiogram with LVEF‹ 45%. No signs of CHF.
C: Abnormal ECG findings. Abnormal echocardiogram. Compensated CHF.
D: Abnormal ECG findings. Abnormal echocardiogram. Refractory CHF.

Panamerican Health Organization Consensus [13]
A. Acute Chagas disease
A.1. Symptomatic disease
A.2. Asymptomatic disease
B. Chronic Chagas disease
B.1. Absence of pathological findings
B.2. Presence of pathological findings

CHF: congestive heart failure; ECG: electrocardiogram; LVEF: left ventricular ejection fraction.

The echocardiographic alterations assessed were: left ventricular wall dysfunction, ventricular aneurysm (apical or other), low ejection fraction (if ‹50%) and valve disease attributable to Chagas endocardial fibrosis.

For the Chagas cardiomyopathy staging we used the Brazilian Consensus [12] and the recent Panamerican Health Organization Classification of Chagas cardiomyopathy [13] (Figure 1). The Brazilian Consensus classification categorises "left ventricular low ejection fraction" according to data based on echocardiographic outcomes (Figure 1).

The relative frequency of the variables and their association with socio-demographic (age, sex, family history and mother with Chagas infection) or setting characteristics (having lived in rural environment, previous adobe housing) were analysed using SPSS 12.0 software (SPSS Inc, Chicago, IL). The chi-square test was applied to compare qualitative variables.

We performed a multivariate logistic regression. Depending variables were to have cardiac symptoms, and to present ECG or echocardiographic alterations; independent variables were age, sex, previous adobe housing and reported family or mother with *T. cruzi* infection.

Results were presented in terms of crude and adjusted (by age, sex and rural environment) odds ratios (OR) and 95% confidence intervals (95% CI). A tendency test compared ECG or echocardiographic alterations' presence with the Brazilian Consensus staging of cardiomyopathy. The p value was set at 0.05 for statistical significance.

Results

During the study period, 116 Latin American immigrants were newly-diagnosed with *T. cruzi* infection. Patients were excluded because of previous diagnosis or treatment of Chagas infection (8), age under 15 years (2), concurrent cardiovascular diseases (2), pregnancy (4). One hundred patients remained in the study. The median age of the patients was 38.2 (SD= 10.2) years, 65 were female and the vast majority were from Bolivia. Socio-demographic and clinical characteristics are shown in Table 1.

Overall, 41 patients had some ECG alteration at the moment of the diagnosis. The most common alteration was a single right bundle branch block (12 cases) which, combined with any other alteration, accounted for 18 of 41 abnormal ECG findings. Echocardiographic changes were seen in 31 patients, and allowed the diagnosis of Chagas cardiomyopathy in eight individuals with a normal ECG (Table 2). The presence of ECG and echocardiogram alterations showed a significant association (p= 0.038).

Table 1

Socio-demographic and clinical characteristics of newly diagnosed Chagas disease patients, hospital-based study Barcelona, Spain 2005-2009 (n= 100)

Variable	N (%)
Mean Age	38.2 (10.2)
Sex	
Male	35 (35)
Female	65 (65)
Country of origin	
Bolivia	95 (95)
Other Southern American countries[1]	5 (5)
Rural environment	93 (93)
Adobe house	91 (91)
Reported family history of *T. cruzi* infection[2]	66 (67%)
Reported mother with *T. cruzi* infection[3]	19 (20%)
Single ECG alterations	
Sinus bradycardia	7 (7)
Right bundle branch block	12 (12)
Left anterior fascicular block	6 (6)
Left bundle branch block	0
Posterior fascicular block	1 (1)
Atrial fibrillation	1 (1)
Atrioventricular block	3 (3)
Ventricular extrasystoles	0
Q wave/ST-T changes	1 (1)
2 alterations	9 (9)
3 alterations	1 (1)
Total ECG alterations	**41 (41)**
Abnormal echocardiographic alterations	
Left ventricular wall dysfunction	24 (24)
Ventricular aneurysm (apical or other)	2 (2)
Low ejection fraction (‹50%)	4 (4)
Valve disease i.e Mitral regurgitation|	1 (1)
Total echocardiographic alterations	**31 (31)**
Total ECG and/or echocardiogram alteration	**49 (49)**
Debut as cardiac event	3 (3)[4]
Cardiac symptoms	31 (31)

ECG: Electrocardiogram.

[1] Ecuador (2), Brasil (1), Uruguay (1), Venezuela (1).

[2] Information available for n= 98 patients.

[3] Information available for n= 95 patients.

[4] Pulmonary tromboembolism (1), rapid atrial fibrillation (1), syncope (1).

Table 2

Electrocardiogram and echocardiographic findings in newly diagnosed Chagas disease patients, hospital-based study Barcelona, Spain 2005-2009 (n= 100)

ECG		Echocardiogram		Total
		Normal	Abnormal	
	Normal	51	8	**59**
	Abnormal	18	23	**41**
Total		**69**	**31**	**100**

p=0.038

No statistically significant relations were found between cardiac symptoms, ECG or echocardiographic alterations and age or sex (Table 3).

According to the Panamerican Health Organization Classification, none of the patients was classified as stage A, 100 were in stage B and of those 51 in stage B1, and 49 in stage B2. According to the Brazilian Consensus, 25 patients were in stage A and 14 in stage B, of those 12 in stage B1 and two in stage B2, none were in stage C. Overall, 37 patients were in an early stage of Chagas cardiomyopathy (stage A and B1).
The tendency test comparing the Brazilian Consensus classification and the presence of ECG and echocardiographic alterations was performed. For both variables, test results were complementary. They showed a statistically significant association between higher grade in the Brazilian Consensus classification and ECG or echocardiographic alterations respectively; for ECG alterations the p value was <0.001, the OR 11.03 (95% CI: 6.7-18.1) and for echocardiographic alterations p<0.001 and OR 3.4, (95% CI: 1.6-7.1).

Discussion and conclusion

In our study of newly diagnosed Chagas disease patients, previous adobe housing was associated with presence of ECG alterations. This may be explained by the high probability of repetitive exposure of those living in adobe houses to triatomine bites with subsequent reinfections that can trigger autoimmune reaction and greater tissue damage [14]. In contrast with the majority of Chagas epidemiological studies, the presence of reported infection in the family and mother were associated with a decreased risk of ECG abnormalities. Several articles published, although not in a conclusive way, suggest the opposite. A familial aggregation could exist among Chagas cardiomyopathy cases due to a higher number of mother-to-child transmissions by highly infectious *T. cruzi* strains or due to a longer infection period [15,16]. This fact could be explained by taking into account that the infected individual, usually asymptomatic and mainly with normal cardiac tests, was considered as "reference case" and a *T. cruzi* active research was done among close asymptomatic relatives. Of course, it was also carried out among patients with a beginning cardiac complication but, on the whole, family clustering tends to occur in chronic asymptomatic cases and overestimates their relationship with the asymptomatic stages of the disease. In our study, the presence of family and maternal history of Chagas infection relied on reported information from the patients; as relatives could not be serologically tested, this result should be interpreted cautiously. Overall, it likely represents a bias exemplifying the inherent shortcomings in studying a disease outside its own bio-geographic, endemic framework.

Factors consistently related in the literature to poor prognosis, such as age, male sex and multiple ECG alterations were not confirmed in our analysis. However, age is a risk factor for Chagas cardiomyopathy beyond any doubt [17,18], and it should be taken into account that in our small study group only 11 individuals were over 50 years old.

Table 3

Cardiac symptoms, electrocardiographic and echocardiographic alterations in newly diagnosed Chagas disease patients by age, sex, housing and infections in the family, hospital-based study Barcelona, Spain 2005-2009 (n= 100)

	Univariate analysis		Multivariate analysis	
Cardiac Symptoms	OR (95% CI)	p	OR (95% CI)	p
Age	1.01 (0.9-1.1)	0.7	1.01 (0.9-1.0)	0.8
Sex	2.34 (0.9-6.3)	0.08	2.45 (0.8-7.5)	0.1
Adobe housing	0.39 (0.1-1.4)	0.1	0.29 (0.1-1.3)	0.1
Reported family history of *T. cruzi* infection	0.83 (0.3-2.1)	0.7	0.79 (0.3-2.3)	0.7
Reported mother with *T. cruzi* infection	0.34 (0.1-1.3)	0.1	0.28 (0.1-1.2)	0.09
ECG alterations				
Age	0.98 (0.9-1.0)	0.3	0.98(0.9-1.0)	0.3
Sex	0.78 (0.3-1.8)	0.6	1.42 (0.5-4.0)	0.5
Adobe housing	5.87 (1.1-31.6)	0.02	11.52 (1.8-75.9)	0.01
Reported family history of *T. cruzi* infection	0.23 (0.1-0.7)	0.003	0.12 (0.04-0.4)	0.001
Reported mother with *T. cruzi* infection	0.30 (0.1-0.9)	0.02	0.23 (0.1-0.7)	0.01
Echocardiographic alterations				
Age	1.05 (0.9-1.1)	0.2	1.07 (0.9-1.2)	0.2
Sex	0.38 (0.1-1.8)	0.2	0.21 (0.02-1.7)	0.1
Adobe housing	0.61 (0.1-4.5)	0.5	0.66 (0.04-9.8)	0.8
Reported family history of *T. cruzi* infection	0.53 (0.1-3.1)	0.5	0.65 (0.1-7.3)	0.7
Reported mother with *T. cruzi* infection	0.56 (0.1-2.8)	0.5	0.68 (0.1-5.2)	0.7

CI: confidence interval; T: Trypanosoma.

Fourty-one of our patients showed some of ECG alterations, a far higher prevalence compared with that obtained in recent studies in other European countries such as Switzerland (11.3% [19], France (23.6% [20] or even Barcelona urban area (19%) [21]. In contrast, it seems to follow a pattern similar to that described in studies carried out in endemic areas in South America: Northern Argentina (37.5%) [22] and Bolivia (50.8%) [23]. This may be explained by the origin of our study population. Nearly all patients came from rural high-prevalence Bolivian environments, especially from Santa Cruz and Cochabamba Departments.

The prognosis of our patients is cause for concern. In one study carried out in rural Brazil, mortality over a six-year period was approximately 20% among infected persons with right bundle branch block [24]. Right bundle branch block was by far the most common ECG alteration in our sample (12 cases). Considering that the treatment given to patients, a 60-day course of benznidazol, could at best retard the progression of cardiac disease [25], close clinical follow up and early identification of complications are crucial. They are the only realistic options with benefit for patients. However, close follow up remains a challenge due to the often great instability of migrant populations in terms of employment and housing.

The predominant echocardiographic abnormalities were alterations in left ventricular wall relaxation, usually to a moderate degree, as a likely reflection of the underlying fibrosis [26]. Unlike the ECG, echocardiography is a dynamic test that requires experience. Even in specialised centres, major disparities between echocardiographic features and post-mortem lesions have been described in Chagas disease patients [27]. However, we were able to identify with echocardiography eight of cardiac abnormalities that would not have been picked up through ECG results alone. This could be due to presence of very early fibroid lesions without ECG changes in a study population that was mainly in the early stages of heart disease.

Coherently with the outcomes of other studies [28, 29], it may be reasoned that ECG and echocardiogram evaluate different aspects i.e. conduction system and structural-functional situation of the left ventricle, respectively of a specific cardiomyopathy in which left ventricular relaxation can be often identified as the earliest alteration [30]. Hence, both tests should be routinely carried out at the moment of diagnosis [31].

The Brazilian Consensus classification of Chagas cardiomyopathy proved useful in categorising the cardiac function based on ECG or echocardiogram abnormalities. As in a recent Swiss study, it was considered as a suitable tool to staging Chagas cardiomyopathy in Europe [19]. The PAHO classification, however, may give a better idea of the Chagas disease burden at public health level as it clearly divides the infected population into those with and without pathological (clinical, ECG or echocardiographic) findings.

The central limitation of our study was the lack of patients in advanced stages of Chagas cardiomyopathy. Therefore, it was not possible to estimate the association between the severity of heart disease and the presence of concrete ECG or echocardiographic findings. Besides, the absence of a Latin American-migrant control group without Chagas disease makes it impossible to determine to what extent the described cardiac alterations are attributable to Chagas disease in Latin Americans. Moreover, the study population may not be fully representative of all Latin American migrants in the European Union or other non-endemic countries due to a possible under-representation of non-Bolivian or middle class patients. Patients assessed had been "filtered" by their family doctors and, therefore, they probably do not reflect exactly the clinical situation of Latin American patients in the community.

Our study results show that clinical, ECG and echocardiographic alterations coherent with Chagas cardiomyopathy were found in a large proportion of Latin American migrants with chronic Chagas disease. The majority were in early asymptomatic stages of the disease. Given these findings and the high number of migrants from endemic areas in our attendance area, Chagas disease might become an important cause of chronic cadiomyopathy in the mid-term in our attendance area. It should be considered in every Latin American patient with unexplained ECG abnormalities, cardiac symptoms or acute cardiovascular events. Chagas disease should no longer be perceived as an exotic disease. Due to its multiorgan, particularly cardiac manifestation, we recommend to involve a multidisciplinary collaborative patient management, including primary care physicians, cardiologists and tropical-medicine experts. Every effort directed towards identifying asymptomatic infected Latin American migrants should be encouraged st

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Targeted screening and health education for Chagas disease tailored to at-risk migrants in Spain, 2007 to 2010

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Chagas disease is endemic in Latin America, but migration has expanded the disease's geographical limits. Spain is the most affected country in Europe. From 2007, a specific Chagas disease programme aimed at at-risk migrants was developed in three Spanish cities (Madrid, Jerez de la Frontera and Alicante). The objectives of the programme were to increase participants' knowledge and decrease their fears about the disease and to encourage them to undergo screening for *Trypanosoma cruzi* infection. The programme was specially focused on migrants from Bolivia and Latin American women of childbearing age. Culturally tailored interventions were carried out in non-clinical settings. A total of 276 migrants were screened using a rapid immunochromatographic test following talks on the disease: the results were then later confirmed by standard serological tests. Of those tested, 44 (15.9%) were confirmed cases of Chagas disease. All of them came from Bolivia and a quarter were pregnant women. Of the 44 cases, 31 were later followed up at a specialised Chagas disease clinic. We consider that the adaptation of the programme to the target population's needs and collaboration with non-governmental organisations and migrants' associations contributed to the acceptance of the programme and the increasing number of patients seen at a specialised clinic

Background

Chagas disease, caused by the parasite *Trypanosoma cruzi*, is naturally transmitted in endemic areas by triatomine vectors. Between 8 and 10 million people are estimated to be infected worldwide [1]. In Latin America, where it is endemic, it is the leading cause of cardiomyopathy [1]. After the 1990s, migration from Latin America resulted in an expansion of the disease's geographical limits, to include non-endemic regions, where other modes of transmission (blood and organ donation and mother-to-child transmission) may spread the infection [2].

Among European countries, Spain has the largest number of migrants from Latin America, globally ranking second to the United States [3]. There is evidence that Chagas disease is a serious challenge to public health in European countries, with being Spain the most affected country: in 2009, it was estimated that between 39,985 and 65,258 migrants were infected in Spain, mostly people from Bolivia [4]. After the first cases of the disease due to blood transfusion were diagnosed [5,6], the Spanish Government implemented in 2005 a law regulating the screening of blood donors from endemic areas [7]. To tackle health issues related to *T. cruzi*-infection of migrants, in 2007 the Tropical Medicine Unit at the Ramón y Cajal Hospital in Madrid developed a holistic approach to the management of Chagas disease.

All clinical and non-clinical activities described in this analysis were provided free of charge for every patient. The study was approved by the Ramón y Cajal Hospital's ethics committee.

Chagas disease clinic, Ramón y Cajal Hospital

The Tropical Medicine Unit at the Ramón y Cajal Hospital is a referral centre for tropical diseases and parasitology within the national health system. In addition to providing assistance to migrants [8], a specialised clinic was set up four years ago for the diagnosis, evaluation, follow-up and treatment of patients with Chagas disease, according to a specific protocol [9]. There is also a telephone consultation service, to facilitate patients' access to the doctors even if they cannot attend the clinic. This clinic offers the patients free access to healthcare (without the need for prior referral by a physician) and free-of-charge assistance, including antiparasitic treatment with benznidazole, even if they are not legal residents.

Building up a Chagas disease programme

'*New citizens, new patients*', a culturally tailored community-based health education programme for migrants settled in Spain, was set up in 2007. The programme is run by a multidisciplinary team of physicians, intercultural mediators and a psychologist. A Chagas disease-specific programme was developed, focused primarily on migrants from Bolivia and Latin American women of childbearing age. Its objectives were to improve migrants' knowledge and decrease their fears regarding the disease and to encourage them to undergo screening for *T. cruzi* infection, particularly Latin American women of childbearing age. Staff of non-governmental organisations (NGOs) and migrants' associations promoted talks on the disease to migrants using their services and used a variety of approaches to encourage them to participate, such as placing advertisements on the walls of their premises and talking to people in person or by telephone.

In an initial phase, we obtained background information on migrants' knowledge and beliefs about Chagas disease in order to tailor our planned activities to the target population. First, from May to July 2007, we carried out qualitative research consisting of nine in-depth interviews with migrants in Madrid (seven women and two men) from different areas of Bolivia (Cochabamba, Santa Cruz, Potosí, Oruro and La Paz) [10]. This research revealed a general lack of knowledge about the disease, as well as many fears and false beliefs. In addition, the questionnaires demonstrated a lack of knowledge regarding vertical transmission and symptoms of the disease [10].

Second, in June to November 2007, the data obtained through the qualitiative research were used to design a questionnaire and to tailor educational material to the target population. The questionnaire comprised two sets of questions: one regarding social and demographic characteristics and the other on knowledge and beliefs about the disease.

Delivering information about Chagas disease

Development of a leaflet about Chagas disease

A culturally tailored leaflet about the disease was designed following the qualitative research. Healthcare staff and intercultural mediators participated in its design. It was fully illustrated in order to make it understandable, regardless of the reader's educational level. It was used to illustrate talks that were given and was also distributed during social events. The material is freely available on the Internet, from the Tropical Medicine Unit, Ramón y Cajal Hospital [11]: information about Chagas disease and specialised centres is provided in Spanish, English and French, so that patients, professionals in both health and social fields and the general population may benefit from it.

Talks to groups of migrants in non-clinical settings

From December 2007 to July 2010, we organised talks on Chagas disease to groups of migrants in Madrid, Jerez de la Frontera (Cádiz) and Alicante. These cities were chosen because of the proportion of resident at-risk migrants, the absence of any similar ongoing public health activities related to the disease and the availability of specific consultations for Chagas disease in the cities. A total of 487 migrants from Latin America were informed about Chagas disease through 44 talks, organised in collaboration with five NGOs and migrants' associations in Madrid (42 talks), Jerez de la Frontera, Cádiz (one talk) and Alicante (one talk). Of the participants, 350 (72%) were from Bolivia and 299 (61%) were women) (Table 1). The above-mentioned questionnaire was filled out by participants just before the talks took place. On the basis of the completed questionnaires, the speakers were able to adapt their talk accordingly. The speakers were experienced healthcare workers, who were assisted by a Latin American intercultural mediator (specifically trained for this purpose). The NGOs and migrants' associations involved have considerable influence over Bolivians living in Madrid, Cádiz and Alicante. Another organisation is focused on pregnant women and young mothers at risk of social exclusion. Staff of the organisations encouraged migrants to attend the talks and informed them when they would be held.

Spreading information through the media and social events

General information about Chagas disease and information regarding the ongoing programme was also spread through media (press and radio) targeting migrants and social events for people from Latin

Table 1

Characteristics of participants attending talks on Chagas disease, Spain, December 2007–July 2010 (n=487)

Item	Number (%)[a]
Talks	44
Participants	
Total	**487**
Mean per talk	11
Median age in years (range)	32 (1–68)
Sex	
Female	299 (61.4)
Male	188 (38.6)
Women of childbearing age[b]	257 (52.8)
Country of origin	
Bolivia	350 (71.9)
Ecuador	60 (12.3)
Peru	31 (6.4)
Other	46 (9.4)

[a] Unless otherwise indicated.

[b] 15–45 years.

America, such as the Bolivian National Day celebrations in Madrid in 2008 and 2009. The leaflet was also distributed at such social events. Participants were encouraged to share the information they had received in this kind of event (as well as in the talks) with their friends and relatives.

Targeted screening for *T. cruzi* infection

During 2008 and 2009, a rapid immunochromatographic test (ICT) (Simple Chagas WB, Operon) was offered to participants after the talks. A finger-prick blood sample was also collected on filter paper and sent to the reference laboratory (the National Microbiology Centre) for confirmation, using both indirect fluorescent antibody technique and enzyme-linked immunosorbent assay.

Each screened participant (or parent, if a young child was tested) was informed of the result immediately after the ICT (confidentiality was maintained). Pre- and post-test counselling were provided for all who participated. Once the results of the serological tests from blood samples on filter paper had been obtained, every patient was informed by telephone. Those found to be positive for *T. cruzi* were given an appointment at the specialised clinic. Psychological support was provided if requested.

From May 2008 to December 2009, 276 (78.4%) of participants attending the talks were screened (Table 2). Among the 76 who chose not to be tested, 15 had been previously screened: 13 in Spain and two in Argentina (six were *T. cruzi* positive and nine were negative).

Table 2

Targeted screening for *Trypanosoma cruzi* infection: results and characteristics of participants, Spain, May 2008–December 2009 (n=276)

Item	Number/total (%)[a]
Participants in talks	352
Participants who were tested by rapid immunochromatographic test	276/352 (78.4)
Country of origin of tested participants	
Bolivia	211/276 (76.4)
Ecuador	29/276 (10.5)
Peru	16/276 (5.8)
Other	20/276 (7.2)
Sex of tested participants	
Female	179/276 (64.9)
Male	97 /276 (35.1)
Confirmed positive cases	
Total	**44/276 (15.9)**
From Bolivia	44/44
Pregnant women	11/44
Confirmed *T. cruzi*-positive patients who later attended the Chagas disease clinic	31/44

[a] Where appropriate.

The ICT yielded six false-negative (2.2%) and 13 false-positive (4.7%) results, giving a sensitivity of 86.3%. A total of 44 (15.9%) participants were confirmed cases of Chagas disease. All of them came from Bolivia and 33 were from the regions of Cochabamba and Santa Cruz. The seroprevalence rate in the Bolivians who were screened was 20.9% (44/211). Of the 44 infected with *T. cruzi*, 30 were women of childbearing age. Of these 30 women, 11 were pregnant.

Despite our efforts to contact all infected patients, 13 of the 44 confirmed cases did not attend the Chagas disease clinic. Eight of these patients were contacted by telephone after they failed to attend their scheduled appointment: five of them stated they did not attend because they had been working and the other three had moved to other cities. All eight indicated that they had intended to request an alternative appointment. It was impossible to reach the five remaining patients who did not attend their appointment.

Consultations for Chagas disease

We have seen an increasing number of consultations for Chagas disease since 2003. The most remarkable increase took place between 2007 and 2008, after the Chagas disease programme has been established: twice as many patients were seen in 2008 compared with 2007 (394 versus 191) [10].

Discussion and conclusion

The establishment of Chagas disease – a neglected tropical disease – in countries of the European Union (EU) – represents a challenge for public health. The strength of the Chagas disease-specific programme described here was that it was accessible and tailored to at-risk migrants. This was mainly thanks to the cultural adaptation of all the activities and the adaptation of the team according to the migrants' circumstances and needs. The programme consisted of practical interventions, such as talks, delivering of information and targeted screening, to detect infected people in order to offer them clinical follow-up and treatment. It could also help to avoid new infections. Its weakness is that it relies on the need for financial support and an enthusiastic and dynamic group willing to adapt to the target population's needs. This is especially hard in the current economic crisis. A clinical centre for referral is also necessary.

Our background qualitative research showed a lack of knowledge about vertical transmission of the parasite [10]. Congenital transmission rates up to 7% have been documented in Spain [12]: it is important to note that 30 of the 44 confirmed cases of Chagas described in this study were women of childbearing age.

Migrants from Latin America are often not aware of Chagas disease. Particularly if they are asymptomatic, they may be less likely to access healthcare facilities to request screening [10]. In addition, it may be difficult for them to attend for screening, due to their working

hours. Collaboration with NGOs and migrants' associations enabled us to bring the programme closer to these groups. We also adapted our working hours to meet the needs of the target population.

Probably due to this flexibility, there was a good uptake of the rapid test: more than 78% of participants at the talks were screened. Unfortunately, the ICT used did not prove to be sufficiently sensitive to allow its use as a screening tool without performing an additional test to confirm all results. Consequently, since January 2010 it has no longer been used. However, if a highly sensitive rapid test using peripheral blood samples were available, it would be an ideal method for screening at-risk populations in the EU.

The prevalence of the disease may vary according to the screened population and the recruitment scenario. It is expected that the prevalence among those recruited in primary healthcare or in non-clinical settings will be lower than that found in referral clinical settings [9,13]. Among those screened in our study, the prevalence was 15.9%. This figure is greater than the 12.8% recently found in a Swiss cohort [14], but less than the 23.6% found in another similar study in France following a public information campaign [15]. The mean prevalence of these three series combined was 15.2% (234/1,542), rising to 24.6% (226/918; range: 20.9–26.2%) among participants who were from Bolivia.

According to studies performed in specialised centres, many patients with Chagas disease in Spain are female Bolivian migrants aged 30–40 years who may transmit the parasite vertically or horizontally through blood or organ donation [9]. Although screening for *T. cruzi* is currently performed for at-risk blood and solid organ donors in Spain, there are no official national guidelines for screening pregnant women in the country. In our study, 11 infected pregnant women were detected: all the mothers and their babies were followed up in the clinic. No newborns were infected in this cohort.

Not all patients with confirmed infection later attended the Chagas disease clinic. Their failure to attend may have been due to work-related problems or because they were no longer in Spain (more than 22,000 Bolivians in Spain migrated to another country during 2009) [16]. This highlights the need to increase efforts to adapt the intervention programme to the target population.

As migrants usually do not know about the existence of specialised centres for tropical diseases in the host country, we consider it crucial to provide information about where people should go for diagnosis, follow-up and treatment of Chagas disease. We included this information in the talks, which may have contributed to the high percentage of *T. cruzi*-positive participants who later attended the Chagas disease clinic.

An increasing number of consultations for Chagas disease was observed, which may be a result of the programme. Information on the disease was also delivered through media specifically targeting migrant groups. This initiative had a great impact: for example, a 50% increase in the number of patients attending the Chagas disease clinic was seen (unpublished data) after an article on healthcare resources for the disease in Spain was published in 2008 in a newspaper aimed at people from Latin America [17].

In conclusion, the holistic approach described in this article can help to reduce the public health problem of Chagas disease in non-endemic countries. Moreover, referral of *T. cruzi*-infected people to a specialised clinic with free access, follow-up and treatment should also contribute to it success. Early diagnosis can also lead to an improvement in the quality of life and prognosis of patients with the infection.

Our programme is currently ongoing, delivering information in non-clinical settings and offering management of patients with the disease at a specialised unit. As Spain is the country in Europe most affected by the disease, our programme may not be directly relevant to some European countries. Nevertheless, we believe this programme could help to guide the implementation of prevention and control strategies in other countries in Europe affected by the disease.

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The current screening programme for congenital transmission of Chagas disease in Catalonia, Spain

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Due to considerable numbers of migrants from Chagas disease-endemic countries living in Catalonia, the Catalonian Health Department has recently implemented a screening programme for preventing congenital transmission, targeting Latin American pregnant women who attend antenatal consultations. Diagnosis of *Trypanosoma cruzi* infection in women is based on two positive serological tests. Screening of newborns from mothers with positive serology is based on a parasitological test during the first 48 hours of life and/or conventional serological analysis at the age of nine months. If either of these tests is positive, treatment with benznidazole is started following the World Health Organization's recommendations. The epidemiological surveillance of the programme is based on the Microbiological Reporting System of Catalonia, a well established network of laboratories. Once a positive case is reported, the responsible physician is asked to complete a structured epidemiological questionnaire. Clinical and demographic data are registered in the Voluntary Case Registry of Chagas Disease, a database administered by the Catalonian Health Department. It is expected that this programme will improve the understanding of the real burden of Chagas disease in the region. Furthermore, this initiative could encourage the implementation of similar programmes in other regions of Spain and even in other European countries.

Introduction

Due to migration flows the traditional epidemiological pattern of Chagas disease has dramatically changed during the past decades [1]. Previously defined as a mainly rural vector-borne disease confined to South America [2], Chagas disease is nowadays diagnosed all over the world wherever there are Latin American migrants [3]. With a view to eliminating the transmission of Chagas disease in non-endemic countries, the World Health Organization (WHO) recommends strengthening national and regional capacities in order to prevent and control congenital transmission, and improving case management of congenital and non-congenital infections, including strategies for case finding, diagnosis and treatment at different health-care levels [4,5].

Unlike vector and oral transmission of the causative pathogen *Trypanosoma cruzi*, which is only possible in endemic areas, infection through blood and organ transplantation or vertical transmission of the parasite can occur in any country [6]. During the past decade some non-endemic countries, among others France, Spain and the United Kingdom, have established legal requirements to ensure the safety of blood supply and organ transplantation by monitoring them for Chagas disease [7,8]. However, systematic screening for *T. cruzi* among pregnant Latin American women in non-endemic countries is still uncommon.

To date only a few cases of congenital transmission in non-endemic countries have been published, the majority, seven of ten, from Spain [9]. The remaining three cases were reported in Switzerland (two cases) [10] and in Sweden (one case) [11]. These few documented cases do probably not reflect the true situation but rather reflect a lack of screening programmes and surveillance systems following *T. cruzi*-positive pregnant women and their children.

The clinical characteristics of congenital *T. cruzi* infection are heterogeneous, ranging from asymptomatic (60-90% of infected newborns) [12-14] or oligosymptomatic infants to severe cases with meningoencephalitis, myocarditis or respiratory distress syndrome (RDS) [13,15]. Whilst effectiveness of Chagas disease treatment in women of reproductive age, aimed to prevent or reduce the likelihood of vertical transmission, remains controversial [16], treatment of infected children during the first year of life ensures therapeutic success in almost 100% of cases [17]. This highlights the importance of routinely testing newborns from *T. cruzi*-infected women.

The need for early detection and treatment of congenitally transmitted cases prompted the Catalonian Health Department to implement a systematic screening programme for Chagas disease among Latin American pregnant women and their children [18]. In this paper we describe this screening programme that was developed thanks to the collaboration between different Catalonian experts on Chagas disease and the WHO Department of Control of Neglected Tropical Diseases. It was implemented in Catalonia from January 2010.

The programme encompasses serological screening of Latin American pregnant women attending antenatal consultation, screening and treatment of their newborns, and an epidemiological surveillance system.

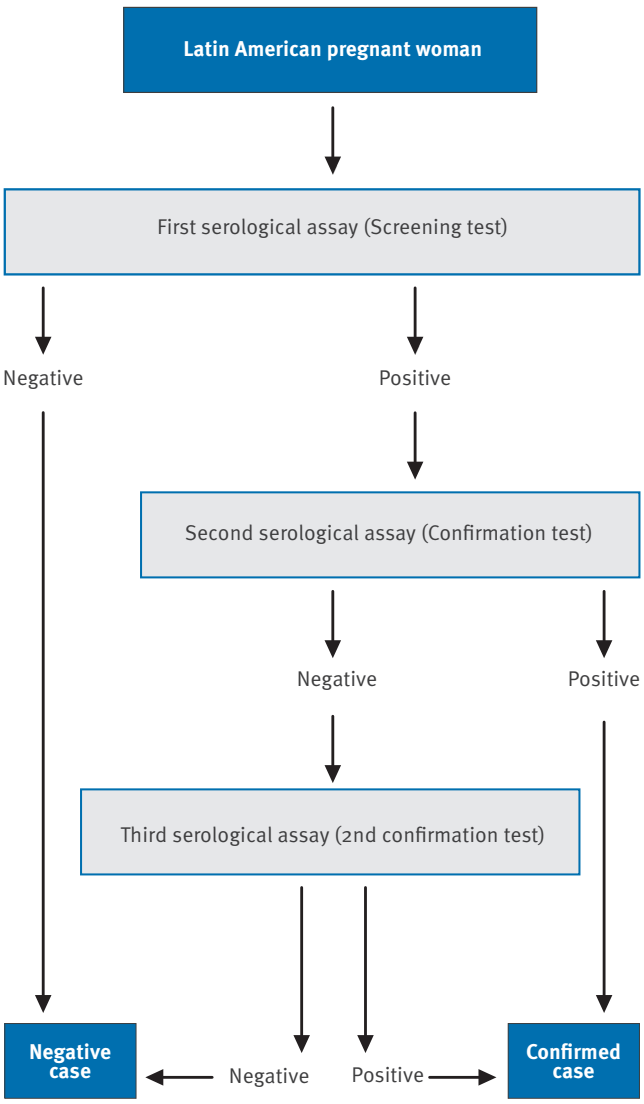
Screening strategy

Screening of pregnant women

The main target population of the programme is Latin American pregnant women attending antenatal consultation in Catalonia. The health system in Spain is universal and free of charge, thus it is unlikely that pregnant migrants, even if undocumented, will not attend the antenatal consultations. Screening for Chagas disease is offered during the first trimester of pregnancy (or whenever the women sought healthcare in the case of uncontrolled pregnancies) to all Latin American women from endemic countries (Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, French Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Surinam, Uruguay, Venezuela), Spanish women born to Latin American mothers (second generation) and Spanish female travellers who have been living in endemic areas for more than one month [18].

Figure 1

Serological screening of pregnant Latin American women for Chagas disease, Catalonia



The laboratory diagnosis during the chronic phase of Chagas disease is based on two serological tests. Commercially available assays use either lysates of the epimastigote form of the parasite grown in liquid culture or recombinant antigens [19]. Given the lack of a widely accepted standard for serological diagnosis of chronic *T. cruzi* infected patients, the Pan American Health Organization (PAHO) recommends to perform the diagnosis with two serological assays performed in parallel [20]. Within these limits, the 40 laboratories participating in the programme use their own testing algorithm for the screening pregnant women (Figure 1). The different serological assays used in the region are summarised in the Table. If the two chosen serological techniques give conflicting results, one additional test is performed in a reference laboratory [18].

When the diagnosis of *T. cruzi* infection is established, the women are referred to medical consultation. Specific treatment for Chagas disease in these women is only offered once they have stopped breast-feeding.

Table

Assays available in Catalonian laboratories for the diagnosis of chronic Chagas disease

Enzyme-linked immunosorbent assays (ELISA)
Bioelisa Chagas (Biokit, Lliça d'Amunt, Barcelona, Spain)
ELISA cruzi Chagas disease (BioMerieux, Marcy-L'Etoile, France)
Whole Cell Lysate Antigen ORTHO Trypanosoma cruzi ELISA Test System (Johnson and Johnson, HighWycombe, United Kingdom)
Chagas IFA IgG + IgM (Vircell, Granada, Spain)
Architect Chagas (Abbott, Spain)
Indirect immunofluorescence (IF)
Chagas IFA IgG + Ig M (Vircell, Granada, Spain)
Inmunofluor Chagas (Biocientifica S.A., Buenos Aires, Argentina)
IFI Mardx Diagnostics inc. (Trinity Biotech, Ireland)
Rapid tests
OnSite Chagas AB (CTK, Biotech, Inc., San Diego, United States)
Simple Stick Chagas (Operon S.A., Zaragoza, Spain)
Others assays
In house Western blot (WB)

Screening of newborns and their siblings

Diagnostic screening is provided for newborns born from serological positive mothers. Direct microscopic examination of the buffy coat of blood from heparinised microhaematocrit tubes or using the Strout technique were the standard parasitological tests used for diagnosis of congenital transmission in the Catalonian programme [18]. The screening for *T. cruzi* infection is preferably carried out within the first 48 hours of the newborn's life whether it has symptoms or not. If the microhaematocrit is positive, the newborn is considered infected and specific treatment is started. When screening is not performed early in life or if the parasitological test is negative in the first hours, the children continue normal follow-up until they are nine months old. At that age the children are tested with a conventional serological analysis to detect specific immunoglobulin G (IgG) (Figure 2). IgG maternal antibodies against *T. cruzi* disappear in non-infected infants older than eight months [21]. In the case of a positive parasitological test at birth or a positive serological result at nine months, treatment is carried out according to WHO recommendations [5]. The most widely used drug for treating congenital Chagas disease in Spain is benznidazole, although nifurtimox has a similar efficacy profile [22]. Screening and, if necessary, treatment for Chagas disease are also extended to the other children of *T. cruzi*-positive mothers.

Although some studies have suggested that PCR can be more sensitive than parasitological techniques for early detection of congenital infections [23], the PCR was not included in the programme [18] following WHO recommendations [5]. It seems reasonable to assume that standardisation of PCR techniques will lead to the inclusion of this tool in the future.

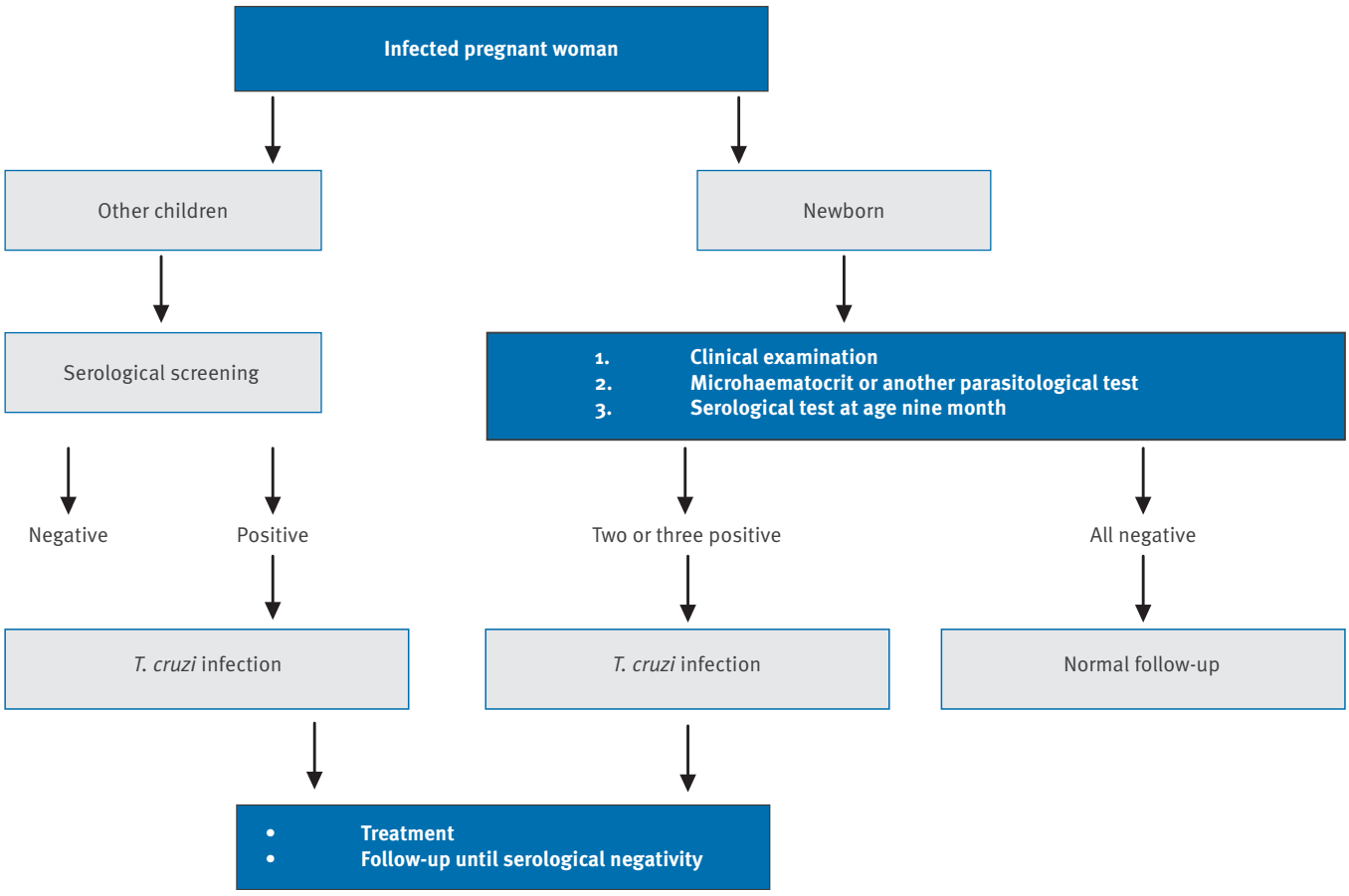
Epidemiological surveillance system

The epidemiological surveillance of Chagas disease for the screening programme is based on the Microbiological Reporting System of Catalonia (MRSC). This is a collaborative network of Catalonian laboratories that has been collecting information from different pathogens of public health importance since 1993. A total of 40 microbiology laboratories encompassing 47 hospitals and health centres throughout Catalonia participate in this system. These centres include the largest hospitals and represent more than 80% of hospital beds in the region (a list of the laboratories is available at: http://www.gencat.cat/salut/depsalut/html/ca/dir2088/labs_notif_microb.pdf).

When a positive case of *T. cruzi* infection among pregnant women or their children are reported by laboratories to the MRSC, the Catalonian Health Department contacts the physician in charge of the patient and a structured epidemiological questionnaire is completed.

Figure 2

Serological screening for Chagas disease of Latin American newborns and their siblings, Catalonia



Clinical and demographic collected data is registered in the Voluntary Case Registry of Chagas Disease, a database administered by the Catalonian Health Department (Figure 3).

The main goals of this surveillance system are to assess the implementation of the protocol in the region and to periodically report the results to health providers and public health authorities.

Discussion

Different factors contributed to the decision of the implementation of this screening programme in Catalonia [18]. Firstly, due to migration flows, the Latin American migrant population in Spain has increased dramatically in the last 10 years, reaching just under two million migrants in 2010 [24]. Ecuador, Argentina and Bolivia were the predominant countries of origin, and represented almost 50% of all Latin American migrants living in the country [24]. Consequently, the estimated number of patients infected with Chagas disease was also high in Spain and vertical transmission of this disease a potential risk [25]. Applying the seroprevalence estimates published by the PAHO in 2006 it was estimated that between 39,985 and 65,258 *T. cruzi*-infected individuals were living in Spain in 2008 [5]. Taking into account that 35,525 children were born to Latin American women during that year, it was estimated that between 914 and 1,656 of these mothers were infected with *T. cruzi*. Assuming a transmission rate between 4.5% and 7.3%, the expected number of infected newborns would range between 41 and 121 [5].

For Catalonia, it was estimated that between 10,000 and 20,000 *T. cruzi*-infected migrants were living in this region in 2010 [26]. The number of pregnancies in women from endemic countries during that year was of 6,795. Considering that between 203 and 387 women could be infected, the expected number of *T. cruzi* infected newborns within this region for 2010 could range between seven and 16 (personal communication: Maternal and Child Health Programme, Directorate of Public Health, Generalitat of Catalonia, September 2011).

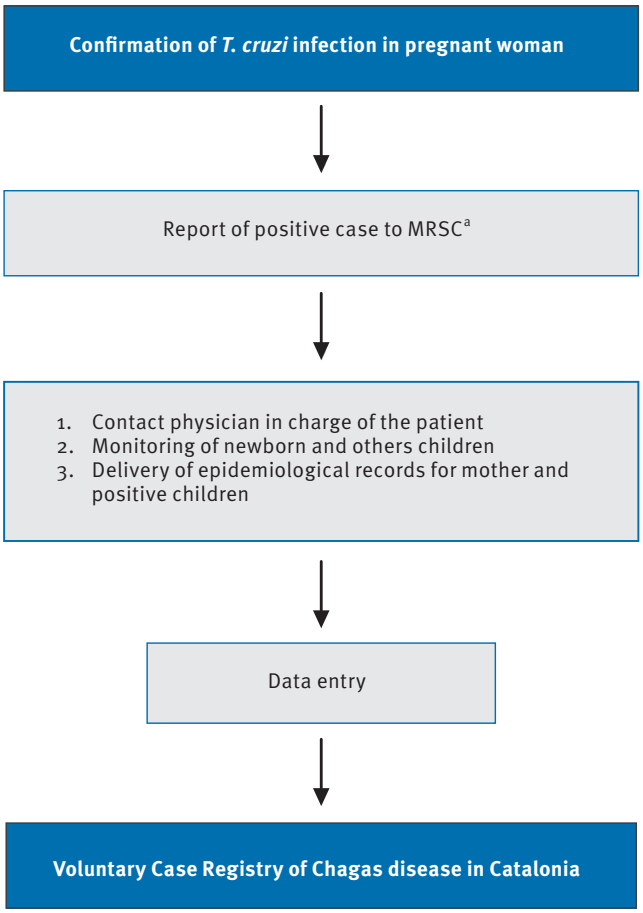
Secondly, a study carried out in the main maternity wards in Barcelona between 2005 and 2007 documented that the potential risk for vertical transmission of Chagas disease in Catalonia was already a reality [27]. During these years 1,350 Latin American pregnant women from endemic countries were tested, and 46 were found to be positive for *T. cruzi*, with a general seroprevalence of Chagas disease of 3.4% (27,5% among Bolivian women). Three of the 41 children with follow-up in that survey were infected, giving a vertical transmission rate of 7.3% [27]. Two further cases of vertical transmission, not related to the above study, were also reported in the region in 2004 [28] and in 2006 [29].

Finally, a study assessing the economic impact of Chagas disease screening programmes among pregnant women in a non-endemic area such as Spain was carried out in Barcelona in 2009 [30]. Two decision models were evaluated; the option of screening the newborn and the mother versus not screening either of them [30]. In this study the screening of Latin American pregnant women and their infants was the more cost-effective strategy compared with the option not to screen [30].While the therapeutic success in chronic infected adults with Chagas disease is poor, between 8% and 25% [31], treatment of infected children during the first year of life ensures therapeutic success in almost 100% of cases [17] and avoids all medical costs relative to a delayed symptomatic manifestation of the disease.

Currently, recognition of Chagas disease in Europe is low and there are no programmes for the prevention of vertical transmission implemented at national level in any European country. In Spain, a similar regional initiative has been implemented in the Valencian Community in 2009, although with the difference that an epidemiological surveillance system linked to the programme was not established [32].

Figure 3

Surveillance system for the Chagas disease screening programme, Catalonia



[a] Microbiological Reporting System of Catalonia

During the implementation of the Catalonian screening programme, we noticed that the knowledge of healthcare providers about Chagas disease was limited, a situation that is similar in other non-endemic countries [33]. To solve this inadequacy, continued training and information brochures has been offered to all personnel involved in the diagnosis and care of patients with Chagas disease.

The main challenge in the implementation of this protocol has been the coordination between the different levels of the health system. It is essential to increase networking between primary healthcare providers and hospitals and to reinforce the communication with public health authorities. To achieve the goal of the elimination of Chagas disease transmission, the WHO aims to reinforce regional and national capacities and strengthen worldwide epidemiological surveillance systems [4]. In this sense, one of the strengths of this programme is the source of data. The MRSC is an already well established network for public health surveillance that encompasses the majority of diagnostic laboratories in Catalonia. This system provides robust and reliable information, decreasing the risk of information bias.

The main limitation of this surveillance system is that the MRSC does not cover all the laboratories within the region. To solve this problem, hospitals and laboratories not covered by the MRSC network are asked monthly to report *T. cruzi*-infected patients. Moreover, in the surveillance system only positive cases are collected, so for now it is difficult to calculate the programme coverage without the information on all screened cases. Regard this problem; other solutions are currently being explored.

Conclusions

Non-endemic countries should consider congenital *T. cruzi* infection as a public health problem. Estimation of the burden of Chagas disease among migrants from endemic countries is essential to develop preventive measures and the right tools for the management of this disease in destination countries.

A screening program for *T. cruzi* in Latin American pregnant women, such as the one currently in place in Catalonia, would improve the knowledge about the real burden of Chagas disease in a non-endemic setting. This protocol is only a small step towards the goal of controlling Chagas disease worldwide, but we hope it may encourage the implementation of similar programmes in other regions of Spain and even in other European countries.

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EuroTravNet: imported Chagas disease in nine European countries, 2008 to 2009

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In recent years, Chagas disease has emerged as a disease of importance outside of endemic areas, largely as a result of migration. In Europe, clinicians may have to treat infected migrants from endemic areas as well as people with acute infections transmitted congenitally, through organ donation or blood transfusion. We describe here the characteristics of patients diagnosed with chronic Chagas disease at the core clinical sites of the EuroTravNet network during 2008 and 2009. Of the 13,349 people who attended the sites, 124 had chronic Chagas disease. Most (96%) were born in Bolivia and the median number of months in the country of residence before visiting a EuroTravNet core site was 38 months (quartile $(Q)_1$–Q_3: 26–55). The median age of the patients was 35 years (Q_1–Q_3: 29–45) and 65% were female. All but one were seen as outpatients and the most frequent reason for consultation was routine screening. Considering that Chagas disease can be transmitted outside endemic regions and that there is effective treatment for some stages of the infection, all migrants from Latin America (excluding the Caribbean) should be questioned about past exposure to the parasite and should undergo serological testing if infection is suspected.

Background

Chagas disease is a zoonosis caused by the parasite *Trypanosoma cruzi*. It is endemic in the American continent, particularly Latin America, being present from the southern United States to Chile and Argentina [1,2]. Although the burden of the disease has decreased in the last 20 years in endemic areas due to various control measures, thousands of new cases are diagnosed there each year [1-3] and 28 million people are estimated to be at risk of contracting the disease [1,2]. In the American continent, the incidence of chronic *T. cruzi* infection in 2005 was 8 per 100,000 population for vectorial cases (n=41,200) and 130 per 100,000 births for congenital cases (n=14,385), prevalence was 1.44% (n=8–10 million) and the mortality rate was 0.0023% (there were 12,500 deaths) [1]. After acute infection, people remain infected for life if not treated and 20–30% of chronically infected people will develop organ involvement, predominantly cardiac disease, after 10 to 30 years [2]. In endemic areas of Latin America, Chagas disease is the leading cause of cardiomyopathy and is the main cause of death due to cardiovascular disease in patients aged 30–50 years [4].

In endemic areas, *T. cruzi* is transmitted to humans by triatomids (known as kissing bugs). However, Chagas disease has emerged outside these areas as a result of travel and migration. As a consequence, imported Chagas disease has been recognised as an emerging public health problem in North America, Western Pacific countries (mainly Australia and Japan) and Europe [5].

Sporadic cases have been described in Europe in the last 20 years arising from acute infection after travel to an endemic area [6], blood transfusion [7], laboratory accident [8], and, most recently, as a result of reactivation in an HIV-coinfected patient [9]. Indeed, in non-endemic countries, blood transfusion is one of the main modes of acquiring the infection, making implementation of screening programmes in at-risk donors advisable in all European blood banks [10].

Since 2000, increasing numbers of cases have been reported in many European countries [11-15]. It has been estimated that during 1999 to 2009 the number of people infected with *T. cruzi* in Europe has exceeded 80,000, of which more than 4,000 were laboratory confirmed [16]. The most affected countries were Spain, with an estimated 40,000 to 65,000 cases (3,617 laboratory-confirmed cases), United Kingdom 14,000 (28 laboratory confirmed), Italy 5,500 to 7,000 (114 laboratory confirmed), Switzerland 3,000 (180 laboratory

confirmed), France 2,166 (111 laboratory confirmed), Belgium 1,982 (19 laboratory confirmed), Sweden 1,118 (1 laboratory confirmed), Germany 935 (2 laboratory confirmed), Portugal 850 (8 laboratory confirmed), and the Netherlands 480 (7 laboratory confirmed) [16].

Migrants from Latin America accounted for 15% of all migrants in countries of the European Union in 2008; most of them came from Ecuador, Brazil, Colombia and Bolivia [17]. In many European countries, screening for Chagas disease has now become a frequent reason for consultation, especially at units specialising in tropical medicine or imported infections [11-13,18,19], whereas previously the disease had been practically unknown in these countries. There is a lack of awareness of the disease, which may lead to misdiagnosis. The potential severity of the disease, even if those infected are asymptomatic, should not be underestimated.

This article describes the characteristics of patients diagnosed with Chagas disease during 2008 and 2009 at the core clinical sites of the European Travel Medicine Network (EuroTravNet), a network of clinical specialists in tropical and travel medicine.

EuroTravNet

This network was founded in 2008 by the International Society of Travel Medicine to assist the European Centre for Disease Prevention and Control (ECDC) in the detection, verification assessment and communication of communicable diseases that can be associated with travel, with a particular emphasis on tropical diseases. It was created by grouping the European sites of Geosentinel, the Global Surveillance Network of the International Society of Travel Medicine and the United States Centres for Disease Prevention and Control.

EuroTravNet has 15 core clinical sites – institutes from nine European countries (France, Germany, Italy, Netherlands, Norway, Spain, Sweden, Switzerland and United Kingdom) – which participate in surveillance of travel-related diseases by collecting epidemiological data of ill travellers or migrants. Data were collected using the surveillance platform and database of the Global Surveillance Network of the International Society of Travel Medicine (GeoSentinel), to which the sites contribute [12,13].

People who presented at a EuroTravNet core site from 1 January 2008 to 31 December 2009 after international travel or migration to Europe were tested. For the purposes of this analysis, we included all those in whom we detected IgG antibodies against *T. cruzi* antigens using at least two different serological methods (usually enzyme-linked immunosorbent assay, indirect immunofluorescence or indirect haemagglutination) and identified them as confirmed chronic Chagas cases. To identify acute cases, a direct method to detect the parasite was used (microhaematocrit, Strout test or Giemsa staining) [20,21].

As for other EuroTravNet analyses [22,23], data that could not be linked to an individual patient were collected using a standardised, anonymised questionnaire and entered by all EuroTravNet core sites into the GeoSentinel database.

We defined a migrant as a person born in a country different from their country of residence and a VFR (visiting friends and relatives) traveller as a person whose primary purpose of travel was to visit friends or relatives and for whom there was a gradient of epidemiological risk between their home and travel destination, regardless of race, ethnicity or administrative/legal status [24].

EuroTravNet data

A total of 6,957 and 6,392 people who presented with health complaints or for health screening associated with travel or migration were seen at the participating sites in 2008 and 2009, respectively. These 13,349 patients included 1,631 VFR travellers and 1,145 migrants.

Of the 13,349 patients, 124 were infected with *T. cruzi*: 121 in Spain and three in Switzerland. There were no additional cases reported in the other EuroTrovNet countries during the study period (Germany, France, Italy, Netherlands, Norway, Sweden and United Kingdom). All the patients came from endemic areas and had developed the chronic form of the illness. Most of them had arrived in their country of destination in Europe between 2001 and 2007 and the median time from arrival to their first visit at a EuroTravNet core site was 38 months. Only one patient presented after travel from their country of residence: a Bolivian in their early 30s who had travelled for three weeks to Bolivia in 2008, attended the EuroTravNet site just after their return, and had no evidence of newly acquired acute disease. We consequently consider this as chronic infection of a migrant: there were therefore no cases of Chagas disease associated with travel from a European country.

Demographic data and characteristics of the 124 patients are presented in the Table. Almost all patients (96%) were born in Bolivia, which was the most probable country of exposure in these cases (determined by physicians on the basis of past epidemiological risk factors). The median age of the patients was 35 years and women accounted for 65% of all cases.

All patients but one were seen as outpatients, mainly at the Madrid site of EuroTravNet. The most frequent reason for consultation was routine screening (these asymptomatic patients attended for a general health examination) and, for some patients (n=9), Chagas disease was diagnosed after consultation for other related or non-related medical problems such as eosinophilia, constipation, anterior uveitis or musculoskeletal complaints.

Implications of the EuroTravNet findings

Some one hundred years after its discovery, it is clear that Chagas disease still affects millions in Latin America and is no longer restricted to endemic areas. The majority of *T. cruzi* infected people outside Latin America are actively working, asymptomatic migrant adults, 18–49 years, with chronic infection [13,14,25]. Most will have been infected during childhood and therefore, based on the natural course of the disease, these migrants would now be at an age when the first manifestations of visceral involvement may be expected to appear. Furthermore, the high number of women among Latin American migrants means that congenital transmission of *T. cruzi* may be a cause for concern [26]. It has been estimated that the rate of mother-to-child transmission of *T. cruzi* in this population is about 7% [25]. Physicians in non-endemic countries should therefore be aware during their routine clinical practice of the existence or even the potential transmission of this disease.

A limitation of our analysis is that most data come from one site (Madrid) and that not all European countries are represented in the network. Additionally, only core sites from EuroTravNet contributed to this study. However, the characteristics of the patients in this report are quite similar to those of Chagas patients in Europe [11-14], probably because Spain is by far the most affected European country [16]. The patients were migrants who attended as outpatients, mainly for screening while asymptomatic (93%), were predominantly female (65%), with a median age of 35 years and of Bolivian origin (96%). In fact, Bolivia is the country with the highest prevalence of Chagas disease in Latin America [1,2].

Table

Demographic data and characteristics of *Trypanosoma cruzi*-infected patients detected through EuroTravNet, 2008–2009 (n=124)

Item	Data	Number of patients (%)[a]
EuroTravNet core site visited (also the place of diagnosis)	Madrid, Spain	121 (97.6)
	Geneva, Switzerland	3 (2.4)
Sex	Female	81 (65.3)
	Male	43 (34.7)
Median age in years (Q1–Q3)	35 (29–45)	124
Median number of months of residence[b] (Q1–Q3)	38 (26–55)	123[c]
Country of birth (also the probable country of exposure)	Bolivia	119 (96.0)
	Argentina	2 (1.6)
	Paraguay	2 (1.6)
	Ecuador	1 (0.8)
Probable area of exposure (all in Bolivia, where known)	Cochabamba	40 (32.3)
	Santa Cruz	37 (29.8)
	Sucre	5 (4.0)
	Tarija	4 (3.2)
	Guayaquil	1 (0.8)
	Santa Fe	1 (0.8)
	Not reported	36 (29.0)
Clinical setting	Migrant healthcare	123 (99.2)
	Seen after travel	1 (0.8)
Patient type	Outpatient	123 (99.2)
	Inpatient	1 (0.8)
Diagnosis	Chronic Chagas disease	124 (100.0)
Reason for presentation	Screening (while asymptomatic)	115 (92.7)
	Abnormal laboratory test[d] and screening (while asymptomatic)	3 (2.4)
	Musculoskeletal symptoms	2 (1.6)
	Abnormal laboratory test[d] and gastrointestinal symptoms	1 (0.8)
	Gastrointestinal symptoms	1 (0.8)
	Opthamological symptoms	1 (0.8)

Q: quartile.

[a] Where appropriate.

[b] Number of months in the country of residence before diagnosis of Chagas disease.

[c] Data unavailable for one patient.

[d] Tests detecting, for example, eosinophilia and anaemia, and elevated liver function tests.

It is noteworthy that the median time between their arrival in their country of residence and the date they first visited the EuroNetTrav site was 38 months. This delay could hinder the early detection and treatment of visceral complications and perinatal infection, and the prevention of congenital transmission

Anti-trypanosomal drug treatment is strongly recommended for all cases of acute, congenital or reactivated infection, and for patients up to 18 years of age with chronic disease [1,27,28]. The efficacy of treatment in late chronic infection is doubtful, but treatment should generally be offered to adults aged 19–50 years without advanced heart disease [1,27,28]. It is optional for those older than 50 years because benefit of treatment has not been proved in this population [27-29]. Treatment of infected women of childbearing age could also have an additional benefit by decreasing or preventing congenital transmission [30].

Considering that Chagas disease can be transmitted outside endemic regions and that there is effective treatment for some stages of the infection, all migrants from Latin America (excluding the Caribbean) should be questioned about past potential exposure to the parasite and undergo serological testing if infection is suspected. Serological testing is especially indicated for children (as they have a better response to treatment), women of childbearing age and pregnant women (for prevention of mother-to-child transmission), HIV-infected patients or other immunocompromised people (due to potential reactivation of latent infection), and blood or organ donors (because of the risk of acute infection in the recipient). Surveillance networks such as EuroTravNet can play a central role in case detection and, as sentinels, may contribute to the description of trends in imported infections of medical importance

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Chagas disease at the crossroad of international migration and public health policies: why a national screening might not be enough

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Since the year 2000, Chagas disease, traditionally known as a rural Latin American affliction, has been rising in the ranking of international health priorities due to the growing migration flows from endemic areas to non-endemic ones. Using the example of Italy and reporting preliminary results of a study carried out in the district of Bologna, the paper will argue that a disease-centred public health approach might be inadequate when dealing with complex and uncertain situations, in which complete statistical data are not available or not reliable, and in which the involved actors, health professionals on the one side, migrants on the other, appear to be unaware of the issue, or might even be denying it. In such a context, an effective public health approach should be capable of crossing disciplinary boundaries and bridging the gap between health services and communities, as well as between health and social issues.

Chagas disease: still a silent affliction?

Traditionally known as a rural Latin American affliction, Chagas disease is still, more than 100 years after its discovery, affecting between 8 and 10 million people worldwide, with an incidence of more than 40,000 new cases per year [1].

This parasitic illness caused by *Trypanosoma cruzi*, transmitted by a vector in endemic areas and through non-vectorial transmission routes in non-endemic countries, is listed by the World Health Organization (WHO) among the so-called 'neglected tropical diseases'. Such conditions, close companions of poverty, are tightly linked to marginalisation and social disadvantage. Nationally as well as internationally, they are of low public health priority, they do not raise much scientific interest nor do they attract research investments. Suffice it to say that the only two current treatment options for Chagas disease, which are poorly effective in the chronic phase and have significant toxic side effects, were developed in the 1960s, and that since then, in over 35 years, not a single new drug has been approved [2].

Since the year 2000, due to the growing migration flows from endemic areas in Latin America, the scientific literature has increasingly reported imported as well as autochthonous cases of Chagas disease in many European countries [3]. Significantly, since it began to be perceived as a potential threat for most developed countries, the condition has been rising in the ranking of international health priorities. Articles are being published by the most influential medical journals; initiatives from non-governmental organisations and public–private partnerships are thriving [4]; Chagas disease has been addressed, during the 63rd World Health Assembly, in a resolution concerning control and elimination in endemic and non-endemic countries [5]. Although the recent WHO initiative for non-endemic countries calls for a broad approach and for the foundation of inter-disciplinary reference centres in all non-endemic countries [6], the strategies adopted until now to address the new potential public health challenge have missed to acknowledge the complexity of the relations between a long-forgotten disease, international migration and public health legislation and policies.

Using the example of Italy, this paper will argue that a disease-centred public health approach might be inadequate when dealing with complex and uncertain situations, in which complete statistical data are not available (i.e. for undocumented migrants) or not reliable (i.e. estimates of infection prevalence in non-endemic areas), and in which the involved actors, health professionals on the one side, migrants on the other, appear to be unaware of the issue, or might even be denying it. The considerations we raise here for public discussion are based on a review of the literature and on the preliminary results of a study that is being carried out by the authors in the district of

Bologna (Emilia-Romagna region) in collaboration with S.Orsola-Malpighi Teaching Hospital.

The research, aimed at evaluating the presence and impact of Chagas disease among Latin American migrants living in the area, adopts a multidisciplinary, multi-method and participative action research approach and promotes the active engagement of all involved stakeholders. Medical doctors work in close collaboration with anthropologists, and the data collection and analysis combine epidemiological tools with qualitative research methodologies (i.e. ethnography, in-depth interviews and focus groups).

Chagas disease in Italy: a complex emerging public health challenge

Since the late 1990s, after migration flows between Europe and Latin America reversed their former westbound direction, the number of Latin American migrants living in Europe has more than doubled. In 2005, nearly 2 million people born in Latin America were living in western European countries, mostly in Spain, Italy and Portugal. In the period from 2004 to 2009, in Italy, the number of Latin American migrants has doubled from 169,000 to 343,000; estimates say the figure in 2010 could be close to 600,000 when including undocumented migrants [7]. Worried about the increase in imported cases of Chagas disease, and fearing a domestic spread of the infection through blood transfusions and organ transplantation, Spain, France and the United Kingdom have implemented control or exclusion measures to address what was perceived as an emerging public health threat [6,8]. Italy has yet to adopt specific health policies and the related scientific debate is still nascent [9]. Several reasons might lie behind this difference, as illustrated in the following paragraphs.

A first consideration relates to the fact that, compared to other European countries, Italy is a relatively new migration country, in which migratory processes have greatly changed over a short period of time and migrants come from a wide variety of nations. Notably, Italy started registering positive net migration balances in the mid 1970s, but has since 1990 seen a tenfold increase in its migrant population. Today, almost 5 million foreign nationals live in Italy, originating from 190 countries and representing 7% of the whole population. The majority of them traditionally come from eastern Europe and northern Africa, while migrants from Latin America, who arrived mainly in the past decade from Peru, Ecuador and Brazil, account today for less than 10% of the total migrant population [7], representing a new and relatively small community. Preliminary results from our research conducted in the district of Bologna show that compared with migrants originating from other areas, such as North Africa or eastern Europe, Latin American migrants tend to be perceived as more similar to the local population and less associated with the stigma of poverty, ignorance and criminality. Overall, there is little awareness of their presence, despite the fact that, at the regional level, their number in Emilia-Romagna has increased by 34% from 2005 to 2008 [10].

A second challenge that might have delayed addressing the issue of Chagas disease is the difficulty in estimating the epidemiological burden of the condition. Part of the reason is that the prevalence rates for *T. cruzi* infection in the countries of origin, commonly used to calculate the expected prevalence in migration countries, are estimates resulting from different and heterogeneous data sources and also differ within those countries, being much higher in rural areas [8,11]. Moreover, such uncertainty is associated with the difficulty in collecting data about migrant populations, particularly undocumented residents. In this respect, current legislation in Italy requires migrants to be employed in order to be eligible for a residence permit. Therefore, due to the instability of occupational conditions worsened by the economic crisis [12], more and more people periodically drop from the status of legal to that of illegal migrant and become invisible for official statistics [7]. In our study, in order to trace the presence of this hidden population, we retrospectively analysed the registers of two out-patient clinics run by non-profit organisations that, in agreement with the regional health system, offer primary care to undocumented migrants. Both clinics had undocumented Latin American migrants among their patients [10].

A third characteristic of the Italian context is that, compared to other European countries and possibly related to its weaker colonial history, there has never been a strong tradition of tropical medicine [13]. To date, only a few referral centres, dedicated to tropical infectious disease and travel medicine, are equipped to routinely diagnose and treat Chagas disease, and there are no standardised protocols to be followed [14,15]. Since the majority of Italian health personnel is not trained to suspect the condition and search for it among the resident population (of both Italian and foreign origin), and diagnostic and therapeutic tools are de facto not available or not promptly accessible, underdiagnosis is likely to occur.

Finally, the complex socio-political and cultural implications of Chagas disease, which impact on its distribution in endemic countries, and on the access to healthcare in endemic as well as non-endemic ones, need to be mentioned. As previous research, conducted by the authors in endemic areas (Buenos Aires and Chaco region, Argentina) showed [16], and as reported in the international literature, Chagas disease is a complex phenomenon whose roots lie in historical, socio-political and economic processes that strongly link endemic with non-endemic countries [17]. In most endemic countries the disease has not been considered for decades as a public health priority, with the effect of substantially excluding from information and diagnosis the majority of the people, particularly those living in remote rural areas. As a consequence, many

migrants travel without being aware of their serological status. Furthermore, in endemic countries Chagas disease is a stigmatised condition that can lead to the exclusion from the labour market, stereotypically associated with rural poverty, ignorance and marginalisation [18]. The ethnographic research conducted in the district of Bologna confirmed these perceptions and revealed that also among Latin American migrants, mentioning Chagas disease often evokes a denial reaction related to those stigmata which may hamper access to further information and service [10].

Why, in Italy, national screening might not be enough

In the absence of regulated interventions and official guidelines, the few referral centres in Italy that are presently equipped to diagnose and treat Chagas disease have taken laudable initiatives to set up screening services and programmes targeted to Latin American migrants [14.15]. Even if these initiatives, often based on the good will and voluntary action of committed professionals, are to be welcomed also for their coordination effort, they are geographically limited to a few areas of the country and cannot reach the whole target population. Since they are hospital-based interventions, they concentrate on the serological and clinical aspects of the disease, often overlooking the broader determinants mentioned above. The gap between implemented practices and needed national plans could become a fruitful space for discussion in order to draw on the experience already gained and to develop comprehensive, harmonised and effective public health policies at the country level.

Indeed, acknowledging the complexity of the Italian scenario, a biomedical, disease-centred rather than people-centred approach could be ineffective in protecting individuals' and community health, and might even become harmful if used as a control measure rather than as a health promotion strategy. This is not meant to disregard the importance of effective biomedical tools in managing the disease, which remain crucial in several aspects, but rather to raise awareness about the risk in relying exclusively on them.

Communicable diseases have, at different times in history, given rise to responses such as the forced expulsion of suspected carriers, quarantine and, in the contemporary setting, health screening [19,20]. Chagas disease is therefore but a recent case in a long tradition of real and perceived public health threats linked to the movement of people. However, with the globalisation of communication, commerce and travel, and migration being a structural and growing component of such processes, prevention and containment policies which rely mainly on control measures are likely to become increasingly costly and ultimately ineffective [21,22].

Furthermore, public health approaches targeted to a specific condition tend to hinder the development of more comprehensive strategies [23]. Failing to acknowledge and address the wider determinants of health and disease, and to take into account and respond to people's perceived needs, these approaches are likely to be unsuccessful when facing conditions which are multi-causal and have many interdependencies on the socioeconomic, cultural and political side, such as Chagas disease has proved to have.

Moving from these broad considerations to analysing the practical implementation of measures such as a screening protocol for at-risk populations, a crucial issue to be addressed is the different pattern of accessibility and utilisation of health services by foreign communities and individuals. An abundant literature examines the barriers which impair migrants' access to health services, particularly to prevention programmes, compared to national populations, considering factors such as linguistic difficulties, lack of information, time and job constraints, or fear [24]. A low social status is in itself a determinant of poor interaction with the healthcare system, in quantity and quality. This is not an issue specific for migrants, rather a general disadvantage of lower socioeconomic groups, in which however migrants are over-represented [25]. In this context, screening protocols built on existing services might be unable to reach at-risk populations and therefore ineffective as a control or prevention measure. This is particularly relevant considering that Chagas disease is predominantly an asymptomatic condition and many infected individuals will not seek healthcare.

Further issues need to be raised when analysing the distinctive features of the current Italian socioeconomic and political context, in which the described access barriers for migrants appear increasingly difficult to overcome [26]. The immigration law approved in 2002 strictly bound the legal status of migrants to the needs of the labour market and made irregular immigration an endemic feature in Italy [27], which is worsening in the current context of economic distress. Further legal developments, adopted in 2009 under the name of 'security package' [28], introduced, among other norms, the criminalisation of irregular entry and stay in Italy. After the adoption of the law, non-profit organisations that run clinics for undocumented migrants reported a decrease of up to 50% in patients' access. Even though it was soon after clarified that access to health facilities could not lead to any kind of alert or registration (except in those cases where a report is mandatory by law, on an equal footing with Italian citizens), these legal developments still spark fear and confusion among migrants [29].

Our preliminary results confirm that significant barriers to health services exist also for Latin American migrants living in the district of Bologna. These barriers relate mainly to a lack of information on migrants' rights and available services, as well as to language difficulties. Financial barriers were mentioned as a factor delaying care for the unemployed and those who rely on temporary jobs and below-standard incomes.

Geographical accessibility was cited as particularly relevant for migrants living outside the city, while fear and insecurity in using public services were pointed out as the main existing barriers specifically for undocumented migrants [10]. Moreover, the local representatives of the main Latin American nationalities, whom we reached through qualitative interviews, have remarked that people could distance themselves from interventions explicitly targeted to Chagas disease, in order to avoid the prejudices that accompany the condition in their countries of origin (rural poverty and ignorance). Some of them also objected to the public disclosure of a direct link between their origin as migrants and the disease, fearing the possibility of a political use of such information to promote anti-immigration policies (unpublished results).

A possible way forward: crossing boundaries and bridging gaps

An effective public health approach should start by acknowledging that assessing merely the quantitative side of the problem is not enough. This is due to extrinsic limitations (unavailability and/or unreliability of data) as well as to the intrinsic biomedical bias which still affects mainstream epidemiology [30]. As recently recommended by, among others, the WHO Commission on Social Determinants of Health, a rich and diverse evidence base should be developed in order to adequately address the bio-psycho-social dimensions of public health challenges, and to evaluate interventions, including evidence from multiple disciplines and methodological traditions as well as knowledge and experience from key stakeholders [31]. In this respect, social and human sciences, particularly sociology, political science and anthropology, can provide theoretical insights and methodological tools which can be applied in public health to help translating research into effective policy and practice [32]. In fact, qualitative data, on which these disciplines greatly rely, are crucial in order to explain the subjective experience of a problem or its impact on people's lives, as well as to understand the ways in which context affects an intervention and its potential for success or failure.

The issue of Chagas disease in Italy should therefore be assessed, and addressed, by multidisciplinary teams in which public health professionals, clinicians and social and human sciences professionals work together in close collaboration, adopting quantitative as well as qualitative research methods. In our experience, this approach has greatly helped in identifying aspects of the issue that would have remained obscure to conventional epidemiology, such as the perceived needs and priorities of Latin American migrants, their problems and fears in accessing the health services, as well as the perceptions of health professionals towards their presence in our country.

The results of such analysis should be used to inform a national plan aimed at expanding the availability of diagnostic and therapeutic tools for Chagas disease within the health services according to the assessed needs, and at setting standardised protocols for screening and treatment. They should further be used to remove the identified access barriers to services in order to reduce inequalities in the utilisation of health services which can impair the effectiveness of any intervention. Finally, they should inform adequate training programmes for health personnel to increase their capacity to deal with the biological as well as psycho-social and cultural aspects of the new condition. Physicians should be able to consider and collect in a medical history all those factors that affect the health status and play a major role in the development of the disease.

A further step would be to complement the disease-centred with a multi-method approach and participatory, community-based action research programmes aimed at a broad promotion of the right to health. Evidence from the literature shows that working in partnership with relevant stakeholders and involving the community are effective practices for successful health interventions [33]. Such practices can also trigger participation and empowerment of community members, particularly those in marginalised groups, allowing them to take part in decisions related to the improvement of the conditions that affect their well-being. Moreover, the action research strategy allows to progressively tailor the interventions to the local context, a good example of proactive medicine that can improve the responsiveness of health services to population needs.

Working together with Latin American migrants living in the district of Bologna has allowed us to understand that, in order to effectively act on Chagas disease, the issue has to be framed within a broader action aimed at making health and social services more open, integrated and equity-oriented, and more broadly at promoting the right to health and healthcare through the promotion of all related human rights. This applies to endemic as well as to non-endemic countries.

Dealing with Chagas disease therefore offers a strategic opportunity for experimenting with innovative public health approaches, capable of crossing disciplinary boundaries and bridging the gap between health services and communities, as well as between health and social issues.

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