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Chagas disease in Italy: breaking an epidemiological silence

A Angheben (andrea.angheben@sacrocuore.it)^{1,2}, M Anselmi^{1,2}, F Gobbi^{1,2}, S Marocco¹, G Monteiro¹, D Buonfrate^{1,2}, S Tais³, M Talamo⁴, G Zavarise⁵, M Strohmeyer^{6,2}, F Bartalesi⁶, A Mantella⁶, M Di Tommaso⁷, K H Aiello⁷, G Veneruso⁸, G Graziani⁹, M M Ferrari¹⁰, I Spreafico¹⁰, E Bonifacio¹¹, G Gaiera¹², M Lanzafame¹³, M Mascarello¹³, G Cancrini¹⁴, P Albajar-Viñas¹⁵, Z Bisoffi^{1,2}, A Bartoloni^{6,2}

1. Centre for Tropical Diseases, Sacro Cuore – Don Calabria Hospital, Negrar, Italy
2. COHEMI project (COordinating resources to assess and improve HHealth status of MIgrants from Latin America)
3. Service of Epidemiology and Laboratory for Tropical Diseases, Sacro Cuore – Don Calabria Hospital, Negrar, Italy
4. Infectious Disease Unit, G. Rummo Hospital, Benevento, Italy
5. Paediatric Division, Sacro Cuore – Don Calabria Hospital, Negrar, Italy
6. Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy
7. Obstetric and Gynaecologic Department, Careggi University Hospital, Florence, Italy
8. Infectious Diseases Unit, Anna Meyer Children's University Hospital, Florence, Italy
9. Immunohaematology and Transfusion Unit, Careggi University Hospital, Florence, Italy
10. Obstetrics and Gynaecology Clinic, L. Mangiagalli Hospital, Milan, Italy
11. Obstetrics and Gynaecology Division, Sacro Cuore – Don Calabria Hospital, Negrar, Italy
12. Infectious Diseases Division, San Raffaele Hospital, Milan, Italy
13. Infectious Diseases Division, G.B. Rossi University Hospital, Verona, Italy
14. Public Health Sciences Department, La Sapienza University, Rome, Italy
15. WHO Programme on Control of Chagas disease, Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

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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 transfusions, 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	<i>T. cruzi</i> infection rate in countries of origin Seroprevalences according to Schmunis et al [2]; PAHO [6]	Estimated number of <i>T. cruzi</i> 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/ μ l.

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).

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].

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%)

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

Y Jackson (yves.jackson@hcuge.ch)¹, F Chappuis²

1. Division of primary care medicine, Department of community medicine, primary care and emergency medicine, Geneva University Hospitals and University of Geneva, Switzerland
2. Division of humanitarian and international medicine, Department of community medicine, primary care and emergency medicine, Geneva University Hospitals and University of Geneva, Switzerland

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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 nucleic 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 nifurtimox). 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

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

L Basile¹, J M Jansà², Y Carlier³, D D Salamanca⁴, A Angheben⁵, A Bartoloni⁶, J Seixas⁷, T Van Gool⁸, C Cañavate⁹, M Flores-Chávez⁹, Y Jackson¹⁰, P L Chiodini¹¹, P Albajar-Viñas (albajarvinasp@who.int)¹², Working Group on Chagas Disease¹³

1. Department of Health, Generalitat of Catalonia, Barcelona, Spain
2. Directorate General of Public Health and Foreign Healthcare, Ministry of Health, Social Affairs and Equality, Madrid, Spain
3. Faculty of Medicine, Free University of Bruxelles, Brussels, Belgium
4. French Institute for Public Health Surveillance (Institut de Veille Sanitaire, InVS), Saint Maurice, France
5. Centre for Tropical Diseases, COHEMI network, Hospital S. Cuore, Don Calabria, Negrar, Verona, Italy
6. University Hospital Centre Careggi, COHEMI network, Firenze, Italy
7. Clinical unit of Tropical Diseases, Institute of Hygiene and Tropical Medicine, New University of Lisbon, Lisbon, Portugal
8. Department of Medical Microbiology, University of Amsterdam, Amsterdam, the Netherlands
9. National Centre of Microbiology, Instituto de Salud Carlos III, Madrid, Spain
10. Division of primary care medicine, Geneva University Hospitals and University of Geneva, Geneva, Switzerland
11. Hospital for Tropical Diseases, London, United Kingdom
12. World Health Organization (WHO) Programme on Control of Chagas disease, Department of Control of Neglected Tropical Diseases, WHO, Geneva, Switzerland
13. The members of this group are listed at the end of the article

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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 assess 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 Brazilians, 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 health-care 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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Members of the Working Group on Chagas Disease in Europe:

Apart from the authors of this article, the present working group is composed of:

Dr. Mariella Anselmi (Centro per le Malattie Tropicali, Ospedale S. Cuore, Don Calabria, Negrar, Verona, Italy. COHEMI network), Dr. Luigi Gradoni (Dipartimento di Malattie Infettive, Parassitarie e Immunomediate, Istituto Superiore di Sanità, Roma, Italy), Dr. José Antonio Pérez Molina (Hospital Ramon y Cajal, Madrid, Spain), Dr. Joaquim Gascón (Hospital Clínic, Barcelona, Spain. COHEMI network), Dr. Jordi Gomez i Prat (Centre de Salut Internacional i Medicina Tropical Drassanes, Barcelona, Spain), Dr. Luisa Sánchez Serrano (Instituto de Salud Carlos III, Madrid, Spain), Dr. Magdalena García (Consortio Hospital General Universitario de Valencia, Valencia, Spain), Dr. Bartolomé Carrilero Fernández (Hospital Universitario Virgen de la Arrixaca, Murcia, Spain), Dr. Jane Jones (Health Protection Agency, London, UK), Dr. Emmanuel Bottieau (Institute of Tropical Medicine, Antwerp, Belgium), Dr. Xavier Lescure (Hôpital Tenon, Paris, France), Dr. Pierre Ambroise-Thomas (Académie nationale de Médecine, Meylan, France), Dr. Jean Delmont (Centre de formation et recherche en médecine et sante tropicales, Marseille, France), Dr. Guillaume Le Loup (Service de Maladies infectieuses tropicales, Hôpital Tenon, Paris, France), Dr. Luc Paris (Service de Parasitologie-Mycologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, France), Dr. Françoise Gay-Andrieu (Laboratoire de Parasitologie-Mycologie, Institut de Biologie - Hôtel Dieu, Nantes, France), Dr. Aldert Bart (Parasitology Section, Dept Med Microbiol, Academic Medical Center, Amsterdam, the Netherlands), Dr. August Stich (Tropenmedizin Missionsärztliche Klinik, Würzburg, Germany), Dr. Israel Molina (Hospital Vall d'Hebron, Barcelona, Spain), Dr. Carmen Muñoz (Hospital Sant Pau, Barcelona, Spain), Dr. Carmen Cabellos (Hospital de Bellvitge, Barcelona, Spain), Dr. Lluís Valerio (Unitat de Salut Internacional Metropolitana Nord, Barcelona, Spain), Dr. Angel Lluís Ballesteros (Hospital de Badalona, Barcelona, Spain), Dr. Cristina Soler (Hospital de Santa Caterina, Girona, Spain), Dr. Toni Soriano (Hospital Joan XXIII, Tarragona, Spain) and Dr. Jean Jannin (Innovative and Intensified Disease Management Unit, Department of Control of Neglected Tropical Diseases, WHO, Geneva, Switzerland)

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

J A Perez-Molina (jose.perezmolina@gmail.com)¹, A Perez-Ayala¹, P Parola², Y Jackson³, S Odolini⁴, R Lopez-Velez¹, for the EuroTravNet Network⁵

1. Tropical Medicine, Infectious Diseases Service, Hospital Ramón y Cajal, Instituto Ramon Y Cajal De Investigación Sanitaria, Madrid, Spain
2. Department of Infectious and Tropical Diseases, Hôpital Nord, Marseille, France
3. Division of Primary Care Medicine, Department of Community Medicine And Primary Care, University Hospitals of Geneva and Geneva University, Geneva, Switzerland
4. Institute for Infectious and Tropical Disease, University of Brescia, Brescia, Italy
5. <http://www.istm.org/eurotravnet/main.html>

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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-Q₃: 26-55). The median age of the patients was 35 years (Q₁-Q₃: 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 EuroTravNet 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)
	Ophthalmological 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

C Di Girolamo (chiara.digirolamo@unibo.it)¹, C Bodini¹, B L Marta¹, A Ciannamè², F Cacciatore¹

1. Centre for International Health, Department of Medicine and Public Health, Alma Mater Studiorum University of Bologna, Bologna, Italy
2. The International Centre for the History of Universities and Science (CIS), Department of Philosophy, Alma Mater Studiorum University of Bologna, Bologna, Italy

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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 ten-fold 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 stigmas 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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EUVAC-Net - the surveillance network for vaccine-preventable diseases is now hosted by ECDC

T Derrough (tarik.derrough@ecdc.europa.eu)¹, A Navarro Torné¹

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

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As of 15 September 2011, the European Centre for Disease Prevention and Control (ECDC) will be coordinating the former EUVAC.NET network: a surveillance network for measles, mumps, rubella, congenital rubella, pertussis and varicella in the 27 Member States of the European Union (EU) and in the three countries of the European Economic Area (EEA) [1]. Data will be hosted by the European Surveillance System (TESSy) at ECDC.

EUVAC.NET was established at Statens Serum Institute (SSI, Denmark) in 1999 following an agreement with the European Commission's Directorate General for Health and Consumer Policy (DG SANCO). Since December 2008, EUVAC.NET has been co-funded by SSI and ECDC.

For more than ten years, this well established and recognised surveillance network has provided prominent information on the epidemiology of vaccine-preventable diseases (VPD) in 32 European countries (27 EU Member States together with Croatia, Iceland, Norway, Switzerland and Turkey). It was instrumental in supporting the World Health Organization European Office (WHO-EURO) goal of eliminating measles and rubella in the European Region and will serve as the basis for the continued effort in reaching this target. It has also helped develop the surveillance activities of mumps, pertussis and varicella as well as coordinate efforts for measles, rubella and pertussis laboratory activities. The number of publications and visits to the EUVAC.NET website is a testimony of the success and contribution that this network has had to public health.

ECDC has worked closely with SSI during the transition period to ensure that the high quality and timeliness of data collection are maintained in the new framework of surveillance. ECDC will publish regular comprehensive reports on the epidemiology of the VPD covered by the former EUVAC.NET in order to help guide the prevention and the control in the EU and EEA countries. The widely-used EUVAC.NET website will cease to be active and dedicated webpages will be available on the ECDC website displaying updated surveillance data [1].

A particular feature that was initiated by SSI and will continue is the display of vaccination schedules across the EU. Strengthening and harmonising laboratory activities for pertussis will be part of the new activities ECDC takes on board as well as supporting the development of the WHO-EURO measles and rubella laboratory network.

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New WHO Europe Action Plan to fight MDR-TB

Eurosurveillance editorial team (eurosurveillance@ecdc.europa.eu)¹

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

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As the multidrug- and extensively drug-resistant tuberculosis (M/XDR-TB) is spreading at alarming rates in the World Health Organization (WHO) European Region – about 81,000 (18.4%) of the estimated 440,000 patients worldwide with MDR-TB are considered to live in this region – the WHO Regional Office for Europe has launched an action plan to contain the spread of drug-resistant TB in the region by the end of 2015 [1,2]. This action plan was endorsed on 15 September 2011 by all 53 countries of the WHO European Region [3].

The plan has been prepared in consultation with representatives of the 53 countries of the WHO European Region, experts, patients and communities affected by the disease. The plan takes into account new diagnostic techniques, patient-centred models of care and services tailored to special populations. It includes six strategic directions, such as collaboration on more effective drugs, vaccines and testing, and seven areas of intervention, such as improving access to testing and treatment.

The areas of intervention of this new action plan are aligned with and have the same aim as the Global Plan to Stop TB 2011–2015 [4] and the World Health Assembly resolution [5] on prevention and control of M/XDR-TB: universal access to diagnosis and treatment of M/XDR-TB.

The targets set by the new action plan, to be achieved by the end of 2015, are:

- to decrease by 20% the proportion of MDR-TB cases among previously treated patients,
- to diagnose at least 85% of estimated MDR-TB cases,
- to treat successfully at least 75% of patients notified as having MDR-TB.

If fully implemented, the plan is expected, by 2015, to diagnose 225,000 MDR-TB patients within three days of presenting to a healthcare service with TB symptoms, to successfully treat 127,000 MDR-TB patients, and to prevent the emergence of 250,000 new MDR-TB and 13,000 new XDR-TB cases. According to WHO Regional Office for Europe, this would interrupt the transmission of MDR-TB and save 120,000 lives.

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