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Screening strategy for Chagas disease in a non-endemic country (Switzerland): a prospective evaluation

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Summary

The WHO recommends screening of Latin American migrants for Chagas disease to reduce morbidity and mortality and increase the likelihood of eradicating the disease. The objective was to assess the feasibility and acceptability of a screening strategy in one Swiss canton. From February 2011 to September 2012, people attending six healthcare centres of different types were offered a rapid diagnostic test if they or their mother were of Latin American origin (or, at the blood donation centre, if they had travelled for ≥ 1 year in Latin America). In addition, testing was offered during events where Latin Americans gathered. In total, 1,010 people were tested, mainly originating from Brazil (24%), Ecuador (13%) and Chile (10%). 54% were born in Latin America, 15% had a Latin American mother, and 29% were travellers. The prevalence of Chagas disease was 2.3% among migrants (15.5% in the community testing) and 0% among travellers. The prevalence was 18.0%, 0.8%, 0.5% and 0% among Bolivians, Ecuadorians, Brazilians and other countries respectively. Predictors for Chagas disease were: born in Latin America (OR = infinite, $p < 0.001$), Bolivian origin (OR = 95, 95% CI: 19–482, $p < 0.001$), being tested in the community (OR = 56, 95% CI: 14–218, $p < 0.001$), and age > 35 years OR = 3.4, 95% CI: 1.1–10.5, $p = 0.03$). The prevalence of Chagas disease was much higher in people attending social events than healthcare centres, suggesting that observations based only on health facility data underestimate the real prevalence of Chagas disease. Screening in the community was well accepted and should be promoted to reach the population at highest risk.

Keywords: Chagas disease, migrants, screening, non-endemic country, rapid diagnostic test, blood donors, primary care, community

Introduction

Chagas disease is caused by *Trypanosoma cruzi*, a tropical protozoan parasite transmitted by the blood-sucking bug

Triatoma. It affects around 8 million people worldwide and is no longer restricted to Latin America. Migration and travel have caused the disease to spread out of the continent and reach most countries in the world. This phenomenon has been observed particularly in populations able to transmit the disease in the absence of the vector, such as in pregnant women through vertical transmission [1–4] and blood and organ donors [5–10]. This situation has led the World Health Organization (WHO) to recommend screening migrants of Latin American origin living in non-endemic countries for Chagas disease [11, 12], both to reduce morbidity and mortality, and to work towards eradicating the disease globally. Providing treatment to patients with Chagas disease would not only reduce their risk of developing potentially severe cardiac or intestinal impairments, but would also help to stop transmission in women of childbearing age and through blood transfusions or organ transplants. However, the best screening strategy is not yet known and might not be the same for all settings. Testing of sick patients attending primary healthcare centres has existed for many years in some non-endemic countries, but the systematic screening of asymptomatic people has been introduced more recently. The latter now exists in several cities in Spain, such as Barcelona [13–15], Asturias [16], Elche [17] and Madrid [18], as well as in Italy [19], France [20] and Canada [21]. These studies have enabled us to know the true prevalence of the disease among Latin American migrants, which is essential in order to design an efficient screening strategy. In Geneva, Switzerland, people attending a primary healthcare facility specifically for migrants have been screened [4], revealing that 12.8% of people tested were positive. This high prevalence and the large Latin American population living in Switzerland (estimated to be around 80,000 people [22–24]), highlight the importance of investigating the situation in the nearby canton of Vaud, where testing for Chagas disease had never been offered and the prevalence is thus totally unknown.

In addition to the prevalence of the disease, knowledge of the positive predictors for Chagas disease is important to

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better target screening for the highest risk population. The few studies which have investigated predictors in asymptomatic migrants have found that Bolivian origin [4], having heard about the disease, knowing someone with Chagas disease, and having lived in adobe houses and rural areas [13] are significantly associated with having the disease.

Another important element in the design of an effective screening strategy is the type of diagnostic test to be used. Rapid diagnostic tests with excellent performance [25, 26] are available for Chagas and are ideal in the context of a mobile population because they allow immediate results. It is also essential to understand the acceptability of and barriers to screening in the migrant Latin American population to have a feasible and durable strategy.

This study aims to assess the feasibility and acceptability of a systematic screening strategy for Chagas disease in the canton of Vaud. It also aims to estimate the number of people needed to test, according to demographic and clinical characteristics, for screening to focus on the population most at risk in the future.

Materials and methods

Population and setting

The study took place in six healthcare centres located in Lausanne and the surrounding area. The inclusion criteria were being born (or having spent a considerable part of infancy) in Latin America or having a mother who was born in Latin America (excluding the Caribbean). At the Department of Ambulatory Care and Community Medicine (DACCM), which serves as an outpatient clinic for the University Hospital of Lausanne, the clinician in charge offered a rapid diagnostic test for 20 Swiss francs (22 USD) during routine emergency consultations. At the Point d'Eau (PDE), an urban, low-level healthcare centre attended mainly by undocumented immigrants, the three nurse practitioners offered a rapid test during the usual consultation for 3 Swiss francs. At the maternity hospital, Latin American women attending the obstetric clinic were offered the diagnostic test for 60 Swiss Francs (66 USD). The test was also offered during consultations at two family planning centres (FPC), which provide sexual counselling and related activities, for the price of 22 Swiss francs (24 USD). Systematic screening was implemented at the blood donation centre (BDC), where an additional inclusion criterion was used: having travelled in Latin America for more than one year. Finally, screening was offered free of charge during events (such as cultural celebrations) where people of Latin American origin, Bolivians in particular, gathered (see [fig. 1](#) below).

Study design

From February 2011 to September 2012, Latin Americans attending the six healthcare centres mentioned above were offered screening for Chagas disease. Screening was first offered to patients attending the DACCM and the PDE. The screening was extended to the two FPC in November 2011 and to pregnant women attending the maternity hospital in January 2012. At the blood donation centre, people were tested from the beginning of the study. In May 2012, screening in the community was proposed by a team com-

posed of a Bolivian pharmacist working as cultural mediator, a medical doctor specialising in tropical diseases, a Bolivian medical doctor and a master's student in medicine working on the topic. Latin American associative organisations were contacted to assist in choosing events which attracted sufficient numbers of people and to help disseminate the information. A leaflet and poster explaining the transmission, symptoms, clinical course, screening and treatment of Chagas disease in French, Spanish and Portuguese, were developed based on a Spanish leaflet from the "Hospital Universitario Ramón y Cajal" of Madrid. These educational materials helped to spread information about the availability of screening at the different healthcare centres, as well as the management and treatment of positive cases.

A rapid diagnostic test (Chagas Stat-Pak, Chembio, USA) was used in all settings except at the blood donation centre, where a serology test was used. At the maternity hospital, the rapid test was performed at the central laboratory at the same time as the other screening tests required during pregnancy. An internal quality control test was performed on each new batch of rapid diagnostic tests. When the test was positive, patients were offered an appointment at the Tropical Diseases Unit of the DACCM for confirmation of the diagnosis by conventional serology (BioElisa Chagas, Biokit®), and management and treatment of Chagas disease.

Data collection and analysis

Age, sex, country of origin or travel, eligibility criteria and test results (the main outcome measure) were collected prospectively. At the DACCM, the PDE and the maternity hospital, nine symptoms and signs (dyspnoea, palpitations, chest pain, dysphagia, odynophagia, constipation, signs or symptoms of cardiac insufficiency, abnormal cardiac sounds and intestinal obstruction) known to be predictive of symptomatic Chagas disease [27] were assessed by the clinician in charge. Data were collected prospectively and anonymously, and entered into an Excel database which was then analysed in Stata version 10.1. Simple proportions and crude odds ratios (a simple stratification was used to adjust for Bolivian origin) were calculated, as were 95% confidence intervals (95% CI) using the exact test and p-values (two-sided) using Pearson χ^2 statistics.

Ethical considerations

The study, including the use of verbal consent, was approved by the 'Commission cantonale d'éthique de la recherche sur l'être humain', Lausanne, Switzerland. Verbal consent testified by the written signature of the health worker in charge of the diagnostic testing was obtained for each participant prospectively. Written consent could not be obtained because most of the participants had an illegal status in Switzerland and were afraid that writing their name could lead to denunciation.

Results

Population tested

In total, 1010 adults were tested for Chagas disease: 107 (11%) at the DACCM, 83 (8%) at the PDE, 32 (3%) at the two FPC, 11 (1%) at the maternity hospital, 693 (69%) at the BDC and 84 (8%) in the community. 593 (59%)

were women (0.2% unknown). The median age was 34 years (IQR 25–46, range 7–76). The most frequent countries of origin (or travel) were: 238 (24%) Brazil, 133 (13%) Ecuador, 100 (10%) Chile, 90 (9%) Colombia, 89 (9%) Peru and 78 (8%) Bolivia. **Table 1** details the distribution of country of origin for each testing centre. 546 (54%) were born in Latin America, 152 (15%) had a Latin American mother and 291 (29%) were travellers (2% unknown). The travellers had a mean duration of stay in Latin America of four years (IQR 1.2–10.0, range 0.25–34). Sex, median age, screening criteria and positive results are presented by country in **table 2** and **figure 1**. Among the 231 patients who were asked about symptoms and signs predictive of Chagas disease, 28 (12%) presented with one or more symptoms/signs, the most frequent being dyspnoea and precordialgia, which were found in eight participants each, and constipation, found in five people.

Positive cases for Chagas disease

The overall prevalence was 1.6% (16/1010, 95% CI: 0.9–2.6%) and therefore the number needed to test was 63. Among migrants (excluding travellers), the prevalence was 2.3% (16/698, 95% CI: 1.3–3.7%). None of the travellers who presented at the BDC were affected. The prevalence in the community was 15.5% (13/84, 95% CI: 8.5–25.0%), at the DACCM it was 2.8% (3/107, 95% CI: 0.6–8.0%), and at the other testing sites it was 0% (**fig. 2**). The prevalence was 18.0% (14/78, 95% CI: 10.2–28.3%) among Bolivians, 0.4% (1/238, 95% CI: 0–2.3%) among Brazilians, 0.8% (1/133, 95% CI: 0–4.1%) among Ecuadorans and 0% among persons originating from other countries. The me-

dian age of the 16 positive Chagas cases was 45 years (IQR 36–52, range 30–56), compared to a median age of 34 years for negative persons ($p = 0.03$). Interestingly, only 1 of the 42 (2%) Bolivians tested at the healthcare clinics was positive, while 13 of the 36 (36%) Bolivians tested in the community were positive (**table 2**). All positive cases were born in Latin America. The three positive cases who were asked about the symptoms and signs predictive of Chagas disease all had at least one of them.

Figure 1: Screening places for Chagas disease. The Department of Ambulatory Care and Community Medicine (DACCM) serves as an outpatient clinic for the University Hospital of Lausanne; the Point d'Eau (PDE) is an urban, low-level healthcare centre attended mainly by undocumented immigrants; the family planning centres (FPC) provide sexual counselling and related activities.

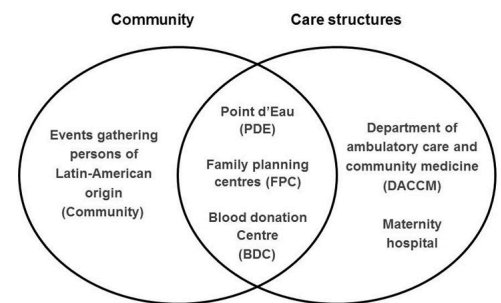
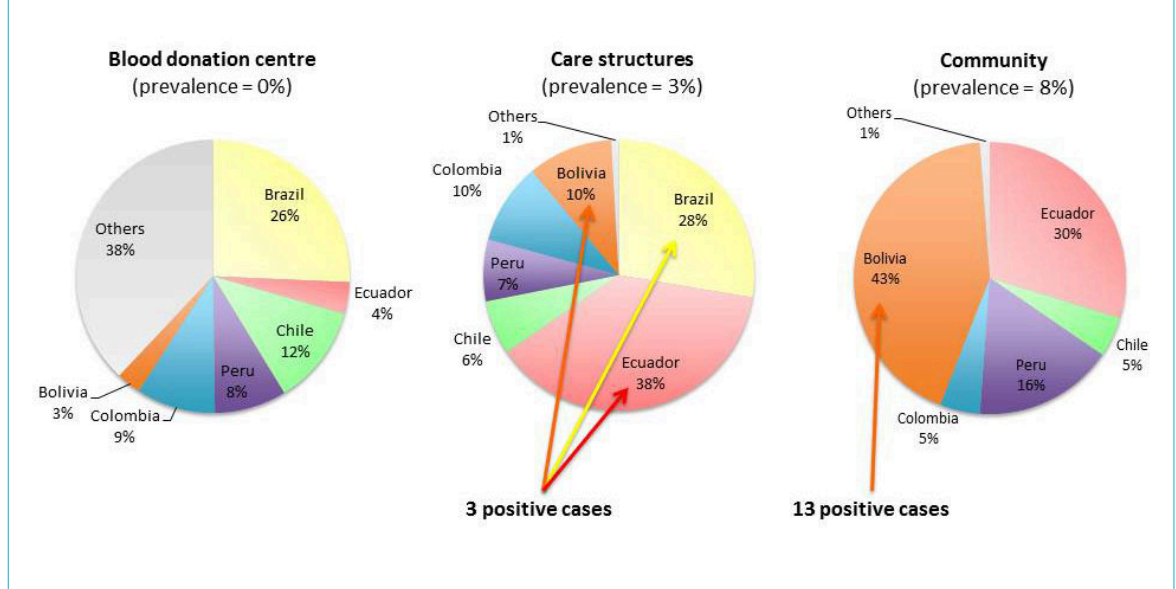


Table 1: Number and characteristics of persons tested by country and by screening location.

	Screening location	Total	Care structures				
	Community		Blood donation centre	Maternity hospital	Department of ambulatory care and community medicine	Point d'Eau	Family planning centres
Female (n, %)	60 (71%)	352 (51%)	11 (100%)	69 (64%)	71 (86%)	30 (94%)	593 (59%)
Age in years (median, IQR)	41 (32–49)	33 (24–46)	31 (26–35)	33 (25–41)	42 (32–51)	31 (28–39)	34 (25–46)
Country				n			n (%)
Brazil	0	178	3	32 (1 pos)	19	6	238 (24%)
Ecuador	25	26	3	34 (1 pos)	30	15	133 (13%)
Chile	4	82	2	7	5	0	100 (10%)
Colombia	4	65	0	12	3	6	90 (9%)
Peru	14	59	2	6	8	6	89 (9%)
Bolivia	36 (13 pos)	20	1	10 (1 pos)	7	4	78 (8%)
Mexico	0	49	0	1	0	1	51 (5%)
Argentina	0	44	0	2	0	0	46 (5%)
Venezuela	1	38	0	2	1	0	42 (4%)
Uruguay	0	16	0	0	1	0	17 (2%)
Guyana	0	12	0	0	0	0	12 (1%)
Guatemala	0	10	0	0	2	0	12 (1%)
Nicaragua	0	9	0	0	0	0	9 (1%)
Costa Rica	0	8	0	0	0	0	8 (1%)
Paraguay	0	1	0	0	7	0	8 (1%)
El Salvador	0	8	0	0	0	0	8 (1%)
Honduras	0	6	0	0	0	0	6 (1%)
Panama	0	4	0	0	0	0	4 (0%)
Not recorded	0	58	0	1	0	0	59 (6%)
Total n (%)	84 (8%) (15% pos)	693 (69%)	11 (1%)	107 (11%) (3% pos)	83 (8%)	32 (3%)	1010 (100%) (1.6% pos)

IQR = interquartile range Positive (pos) Chagas cases are shown in italics.

Figure 2: Number of persons tested for Chagas disease by country and by screening place. Groups with positive cases are pointed with arrows. Care structures include the Department of Ambulatory Care and Community Medicine (DACCM), the Point d'Eau (PDE), the family planning centres (FPC) and the maternity hospital.



Predictors for positivity

Regarding the predictors of positivity (table 3), being born in Latin America (n = 546) was the strongest factor (OR = infinite, p <0.001), followed by Bolivian origin (n = 78, OR = 95, 95% CI: 19-484, p <0.001) and being tested in the community (n = 84, OR = 56, 95% CI: 14-219, p <0.001). The latter factor remained significant even after adjusting for Bolivian origin (OR = 23, 95% CI: 2-243, p <0.001). Symptoms of Chagas disease were significantly associated with positivity, although the number of people for whom the information was very small. Finally, age >35 years (n = 478, OR = 3.4, 95% CI: 1.1-10.5, p = 0.03) was predictive of Chagas disease, while sex was not significant (p = 0.76).

Discussion

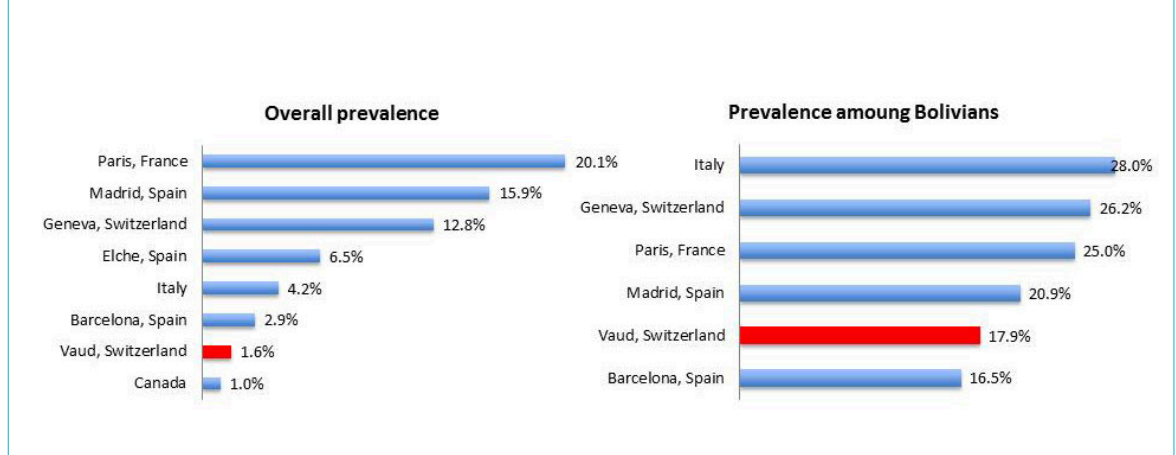
A prevalence of 2.3% was found for Chagas disease in Latin American migrants living in the canton of Vaud, Switzerland. This rate is similar to that found in migrants attending a healthcare centre in Barcelona over the past 14 years (2.9%) [13]. It is, however, lower than the rates found in other European cities such as Elche (6.5%) [17], Madrid (15.9%) [18] and Paris (20.1%) [20]. In Italy, systematic screening found an overall prevalence (including travellers, expatriates, adopted children, blood donors and HIV positive patients) of 4.2% [19], and a prevalence of

Table 2: Number of persons tested, proportion of women, distribution of screening criteria, median age and number of positive cases, by country.

Country	Number of persons tested n (%)	Proportion of women %	Screening criteria B/M/T, %*	Age in years median (IQR)	Number of positive cases n (%)
Brazil	238 (24%)	59%	56/17/26	35 (25-47)	1 (0.4%)
Ecuador	133 (13%)	63%	89/4/7	35 (29-42)	1 (0.8%)
Chile	100 (10%)	56%	53/23/22	32 (24-49)	0
Colombia	90 (9%)	66%	59/11/29	32 (24-44)	0
Peru	89 (9%)	58%	53/20/25	35 (24-48)	0
Bolivia	78 (8%)	69%	78/5/17	36 (29-48)	14 (17.9%)
Mexico	51 (5%)	61%	24/14/63	27 (22-47)	0
Argentina	46 (5%)	46%	41/24/33	32 (22-47)	0
Venezuela	42 (4%)	38%	43/10/48	44 (33-52)	0
Uruguay	17 (2%)	47%	35/35/29	33 (27-48)	0
Guatemala	12 (1%)	58%	33/8/58	33 (28-40)	0
Guyana	12 (1%)	67%	8/25/67	32 (20-55)	0
Nicaragua	9 (1%)	33%	22/0/78	37 (33-53)	0
Costa Rica	8 (1%)	63%	25/25/50	28 (26-36)	0
Paraguay	8 (1%)	88%	88/0/13	35 (26-41)	0
El Salvador	8 (1%)	63%	38/50/13	22 (20-24)	0
Honduras	6 (1%)	50%	17/33/50	33 (21-46)	0
Panama	4 (0.4%)	75%	25/25/50	45 (32-56)	0
Not recorded	59 (6%)	53%	8/19/56	37 (26-52)	0
Total n (%)	1,010 (100%)	59%	54/15/29	34 (25-46)	16 (1.6%)

IQR = interquartile range B: born in Latin America; M: born to a Latin American mother; T: travel in Latin America * The sum of the three percentages does not always reach 100% due to missing data.

Figure 3: Prevalence of Chagas disease found in several studies in non-endemic countries. Studies from Paris, France (21), Madrid, Spain (19), Geneva, Switzerland (10), Italy (20), Elche, Spain (18), Barcelona, Spain (14-16) and Canada (22). Migrants include people born in Latin America or born from a Latin American mother.



11.3% among migrants. Only Canada found a lower prevalence (1.0%) among refugees [21] (fig. 3). The prevalence of Chagas disease in our study was much higher in people attending social events than healthcare centres. This suggests that observations based mainly or exclusively on healthcare facility data tend to underestimate the true prevalence of Chagas disease. This testing at social events could be performed using rapid, point-of-care diagnostic tests, as few people would be missed due to the high sensitivity of the test (in our study only 0.5 people would have been falsely negative if the test had 96% sensitivity).

Prevalence according to country of origin

In Geneva, the canton to the east of Vaud, 12.8% of the 1,012 Latin American migrants screened were positive for Chagas disease [7]. This high prevalence compared to our study can probably be explained mainly by the high proportion of Bolivians: 48% in Geneva compared to 8% in Vaud. In support of previous studies, we found that the majority of affected people originated from Bolivia. The 17.9% prevalence among Bolivians (or 21.5% if we exclude blood donors) is close to that documented in other studies: Barcelona (16.5%), Madrid (20.9%), Paris (25.0%) and Geneva (26.2%). Excluding the BDC, where testing is compulsory, the number needed to test was low for Bolivians - only four people need to be tested to find a positive case - but high for migrants originating from other countries (130). Special attention should therefore be paid to Bolivians when designing a strategy.

Prevalence according to place of screening

In addition to the country of origin, the high variation in prevalence between studies can be explained by the different populations screened and the different screening locations. In our study, the prevalence was much higher in people tested in the community than at the healthcare clinics, regardless of their country of origin. A possible explanation is that people tested in the community were of lower social status and thus originating from the rural regions harbouring the highest levels of endemicity of Chagas disease. Indeed, people without a resident permit tend to avoid contact with the health system as much as possible, even though the low-level health facility in Lausanne targets precisely this population, and even though there is a system in place in the other healthcare facilities for migrants to improve their attendance.

Prevalence in specific populations

None of the 11 pregnant women (of whom only one originated from Bolivia) screened at the maternity hospital were positive. In other studies, the prevalence among pregnant women was 1.3% in Elche [1], 1.4% in Italy [19], 9.7% in Geneva [4], 3.4% in Barcelona [2] and 4.7% in Valencia [3]. In this study, only a very small proportion (11%) of the pregnant Latin American women attending the maternity hospital were tested, and none were positive. Since the end of the study, the testing rate has improved, however, and several pregnant women have tested positive in Vaud. There were also no positive cases detected at the BDC. In the literature, the prevalence at BDCs varies between 0% in Porto and Italy [10, 19], 0.003% in France [6], 0.007% in United States [8] and 0.6% in Catalonia [5]. In

Table 3: Predictors of being positive for Chagas disease.

Predictor	Total cases n/N (%)	Positive cases n/N (%)	Negative cases n/N (%)	Crude OR (95% CI)	p-value
Born in Latin America	546/992 (55%)	16/16 (100%)	530/976 (54%)	∞	<0.001
Symptoms of Chagas disease	28/233 (12%)	3/3 (100%)	25/230 (11%)	∞	<0.001
Bolivian origin	78/951 (8%)	14/16 (88%)	64/935 (7%)	95 (19-484)	<0.001
Tested in the community	84/1010 (8%)	13/16 (81%)	71/994 (7%)	56 (14-219)	<0.001
Tested in the community (when being Bolivian)	36/78 (46%)	13/14 (93%)	23/64 (36%)	23 (2-243)	<0.001
Age >35 years	478/1006 (48%)	12/16 (75%)	466/990 (47%)	3.4 (1.1-10.5)	0.03
Female sex	593/1008 (59%)	10/16 (63%)	583/992 (59%)	1.2 (0.4 -3.2)	0.76

Catalonia, donors who have stayed in an endemic country for more than one month are screened, while in France and the United States, travellers with a stay of any duration are screened.

Clinical predictors

Although clinical features could only be evaluated in the context of medical consultations (and not in counselling sessions), having symptoms or signs predictive of chronic Chagas disease was frequent among positive cases (this evaluation was performed by the physician prior to knowing the test result). This might be because transmission of Chagas has decreased substantially during the past 20 years, meaning that most cases were infected a long time ago and are therefore more likely to be at the symptomatic stage of the disease. This hypothesis is corroborated by the fact that older age was a predictor of positivity in our study, as well as in a study in Geneva [7]. These symptoms and signs were not the reason for the consultation and would not necessarily have been assessed by the clinician in charge if not required by the study. Theoretically, to decrease the overall number of people needed to test, the presence of one of these clinical features could be used as a screening criterion in populations with a very low pre-test probability, such as non-Bolivian Latin Americans. However, a screening strategy also aims to detect people during the asymptomatic phase, when treatment has the highest potential impact. Moreover, a medical examination is not pragmatic outside of formal healthcare facilities.

Screening at community level

When the difficulty of reaching those at risk through a healthcare facility became apparent, direct screening in the community was offered, targeting particularly people of Bolivian origin. However, attendance at Latin American social events requires strong commitment from health workers, as these often take place outside of normal working hours. Moreover, it was not always possible to offer screening for Chagas disease during such events, as organisers were sometimes afraid that this activity could impact on the celebration. In contrast, we observed that even when organisers were sceptical, participants at the celebration were pleased to have the opportunity to become more informed and, in particular, to be directly screened. The cultural mediator was a key person in the process of approaching and convincing the community leaders of the importance of testing for Chagas disease. We reached the conclusion that due to the availability of rapid diagnostic tests for Chagas disease, testing at a community level is feasible, effective and well accepted by the community.

Feasibility of the screening strategy

The proportion of participants who consented to be tested was high in all places, except at the maternity hospital. At the latter, nurses highlighted that patients were declining the test because of the high price of the test. Indeed, Chagas is not currently part of the screening tests recommended by the Swiss Society of Gynaecology and Obstetrics and thus is not reimbursed by healthcare insurance. At the other facilities, where the price of the test was much lower, the uptake on the screening strategy depended mainly on the method used by the facility to identify Latin Americans. At the outpatient clinic, for example, the reception-

ist added a reminder for clinicians on the patient's medical file if they originated from Latin America, encouraging a high uptake. In health facilities where the clinician in charge had to remember to offer the test, the uptake was much lower, especially when the reason for attendance had nothing to do with Chagas disease. An unexpected difficulty encountered was convincing people who had tested positive to seek treatment. They reported a number of fears, including i) being denounced to legal authorities (as the vast majority of positive cases were undocumented migrants) despite the assurance of total separation between health and security services in Switzerland, ii) losing their jobs due to non-attendance relating to the numerous medical consultations, iii) earning less money (as their salary is often hour-based), and iv) experiencing adverse drug reactions (ADRs) from the medication used to treat Chagas disease. In 2008 in Geneva, nifurtimox was used to treat Chagas disease, and rumours about serious ADRs spread in the community. These fears highlight the importance of an active presence in the community. Providing information through leaflets and posters, as we did, is important but evidently not sufficient to tackle these specific problems. Possible options to improve confidence in healthcare could be to create an association of people affected by Chagas disease or to form an expert patient group.

Conclusion

As migration from Latin America to Switzerland is increasing, it is time an efficient strategy for the systematic screening and treatment of Chagas disease was set up to stop transmission in non-endemic countries and to decrease morbidity. According to our findings, which are supported by those of other studies, the Bolivian population in particular should be targeted. For people originating from other Latin American countries, where the prevalence is much lower, adding criteria that are predictive of Chagas disease could be a good method to reduce the number who need testing. Further research on the most efficient combination of criteria for screening is needed, with the consideration that the profile of the migrant population may change rapidly, and screening strategies will have to be adapted accordingly. Screening for Chagas disease directly in the community, where the positivity rate is much higher, rather than only at healthcare facilities, is essential, and allows problems arising from misinformation and (sometimes justified) fears to be tackled. The warm welcome from the Latin American community when screening was offered to them in a more convenient way, and their realisation that this neglected and serious disease could be appropriately managed, should strengthen the willingness of non-endemic countries to continue to work actively to achieve the WHO goal of eradicating Chagas disease globally.

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Potential competing interests

The authors have no conflicts of interest to declare.

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