Control and prevention of Chagas disease in Europe

Report of a WHO Informal Consultation (jointly organized by WHO headquarters and the WHO Regional Office for Europe)

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Abbreviations

AFSSAPS	Agence française de sécurité sanitaire des produits de Santé
AMC	Academic Medical Centre (Amsterdam)
CNM	National Centre for Microbiology (Madrid)
DPL	diagnostic parasitology laboratory
EIA	enzyme immunoassay
EFS	Etablissement français du Sang
ELISA	enzyme-linked immunosorbent assay
GHPS	Groupe Hospitalier Pitié-Salpêtrière (Paris)
HIV	human immunodeficiency virus
ICT	immunochromatographic test
ID	particle gel immunoassay (PaGIA)
IHA	indirect haemagglutination assay
IFA	indirect immunofluorescence assay
InVS	Institut de veille sanitaire
LSHTM	London School of Hygiene and Tropical Medicine
PAHO	Pan American Health Organization
PCR	polymerase chain reaction
PRL	pathozyme prolactin
RIPA	radioimmunoprecipitation assay
RIVM	National Institute of Public Health and the Environment (Bilthoven)
RNA	ribonucleic acid
T. cruzi	*Trypanosoma cruzi*
SPDL	Scottish Parasite Diagnostic Laboratory (Glasgow)
TESA	trypomastigote excretory–secretory antigen
UK NEQAS	United Kingdom National External Quality Assessment Service
WHO	World Health Organization

Introduction

The World Health Organization (WHO) held an informal consultation on the control and prevention of Chagas disease in Europe at its headquarters in Geneva, Switzerland, on 17–18 December 2009. The meeting was jointly organized by WHO headquarters and the WHO Regional Office for Europe. A total of 31 participants representing nine countries, WHO and the Special Programme for Research and Training in Tropical Diseases attended the meeting (see List of participants, Annex 1).

The two-day meeting was divided into three parts (see Agenda, Annex 2):

(i) presentation of country reports
(ii) thematic working groups
(iii) recommendations and conclusions.

2. Background and rationale

2.1 *Trypanosoma cruzi* infection and Chagas disease

Chagas disease (American trypanosomiasis) results from an infection with the protozoan parasite *Trypanosoma cruzi*. The parasite is mainly transmitted to humans through the infected faeces of triatomine bugs. Other modes of transmission include transfusion of infected blood and congenital infection. More rarely, transmission occurs through oral contamination, organ transplant from an infected donor and laboratory accident. Morbidity and mortality may be important in the acute phase of the disease – especially in children aged <5 years, the elderly, those who are immunosuppressed or in individuals infected with a high number of parasites, as may occur during outbreaks of foodborne disease – and where cardiac and digestive clinical forms are present during the subsequent chronic phase. Nevertheless, the majority of patients show no clinical symptoms and remain in a latent chronic phase carrying a hidden infection that is unknown even to themselves. Such asymptomatic patients may transmit the infection either by the congenital route or by blood or organ donation.

Infected patients are mainly present in the endemic countries of Latin America where infected insects responsible for vectorial transmission are found. These endemic countries have important experience in clinical management of the disease and have developed successful strategies to control the vector and prevent transfusional transmission. Since 1991, the technical secretariat of the Pan American Health Organization (PAHO) has supported the organization of control programmes – primarily against vectorial and blood transmissions – through various intergovernmental initiatives that group endemic countries of the South cone of South America, the Andean region, Central America and the Amazon basin. Control strategies vary according to the country's resources and the specific organization of its health system. Additionally, in the past decade, some countries have also incorporated control of congenital transmission and medical care for the millions of infected people.

2.2 Chagas disease as an emerging global public health challenge

Transmission of Chagas disease in non-endemic countries – that is, transmission in countries outside Latin America with exceptional or no vectorial transmission – has emerged since the beginning of 2000. This phenomenon is mainly linked to population mobility, notably migration (*1*). During the past decades, transmission has occurred in non-endemic countries in North America (Canada and the United States of America), the Western Pacific Region (mainly Australia and Japan) and, more recently, in Europe (*2*).

Sporadic cases of *T. cruzi* infection or Chagas disease have been reported from European countries for >15 years. In 1981, the first probable case of congenital transmission was described in a child born in 1975 in Romania (*3*). In 1982, the first case of probable congenital transmission in an adopted Latin American child by a Swedish family was published (*4*).

In Spain, the first European case linked to a laboratory accident was reported in 1983 (*5*). In 1992, an acute case was reported in a patient who had received blood transfusions during a bone marrow transplant (*6*). In 2001, a congenital case was initially confused with congenital leishmaniasis (*7*).

In 1984, Chagas disease was raised as a possible diagnosis in Denmark (*8*). In 2000, a chronic case was described in a Venezuelan patient who had lived in Denmark for 32 years (*9*).

In 1988, the *Lancet* published the first case of acute disease in a French woman who had travelled to Colombia (*10*). The first European case of Chagasic cardiomyopathy was described in 1996 in a Bolivian patient living in Switzerland (*11*). In 1997, the first case of acute disease in an Italian traveller to an endemic country was published (*12*). In Berlin (Germany), a survey conducted in 1997 among Latin American immigrants showed a prevalence of infection of 2% (*13*).

Since 2000, increasing numbers of cases have been reported in many European countries in the scientific literature (*14*). According to the International Organization for Migration, Latin American migration to Europe has grown rapidly since then. Southern European countries – mainly Spain – have received most of these migrant flows, although other European countries have also seen significant increases. Economic hardship caused by the recession and high poverty levels in Latin America, as well as the tightening of visa regimes in the United States after 2001, are important contributing factors. The close cultural and historic ties of Latin American countries to Europe coupled with many Latin Americans returning to Europe by invoking dual nationality have undoubtedly also facilitated such population movements.

Demographically, the immigrant population mainly comprises young adults with high rates of participation in the labour force and relatively high rates of educational attainment; this population has the capacity to integrate into European societies. Immigration from Latin American countries and the increasing trend towards the feminization of migration is relevant for congenital transmission of *T. cruzi* infection. Illegal immigration is also a challenge given the significant number of undocumented immigrants (*15*).

2.3 Building the non-endemic countries initiative

In 2007, WHO and PAHO convened a meeting[1] of endemic Latin American countries and non-Latin American countries. A major outcome of the meeting was to highlight the presence of *T. cruzi* infection outside Latin America in so-called "non-endemic countries". Recognizing the globalization of Chagas disease, the 28 participating countries called for the establishment of an additional initiative to deal with Chagas disease in the non-endemic countries.

2.4 General objective of the non-endemic countries initiative

The general objective of the new initiative is to control Chagas disease in non-endemic countries and contribute to global efforts to eliminate the disease by (i) diagnosing, managing and treating patients, including infected newborns, from congenital transmission, (ii) preventing transmission of infection by systematically screening blood used for transfusions and organs intended for transplantation, (iii) sharing information about Chagas disease, and training health personnel to facilitate diagnosis and medical care.

The non-endemic countries initiative aims to reach national and regional consensus on strategies to prevent and control Chagas disease in Canada and the United States and in countries of the European and Western Pacific regions where the disease is present.

[1] The meeting – "Revisiting Chagas disease: from a Latin American health perspective to a global health perspective" – was held at WHO headquarters in Geneva (Switzerland) on 5–7 July 2007.

A network of clinicians, biologists, public health specialists, academics and researchers is working together with national health authorities to address this subject under the auspices of WHO.

2.4.1 International meetings

WHO has convened a series of meetings to assess the burden of Chagas disease as a public health problem in non-endemic countries and to formulate an appropriate response.

The first meeting was held at the Etablissement français du sang (EFS) in Paris (France) on 22–23 November 2007. The objectives of the meeting were (i) to define the list of non-endemic countries for Chagas disease, (ii) to identify problems and define priorities and practical actions to be undertaken during the next 1–2 years (with precise milestones), recognizing that some of these problems are specific to non-endemic countries while others should be addressed globally, (iii) to specify the tasks ahead and set up working groups accordingly.

The objectives of second meeting, which was held in Barcelona (Spain) on 5–6 February 2008, were (i) to assess the current situation and update the status of preventive and control measures already implemented in the non-endemic countries, (ii) to discuss the objectives, establishment, structure and functioning of the non-endemic countries initiative, (iii) to implement an information database with the following items: Chagas disease non-endemic countries, reference institutions and human focal points, as well as available epidemiological information and preventive and control measures already implemented.

Participants at the third meeting – held during the 6th European Congress on Tropical Medicine and International Health in Verona (Italy) on 6–10 September 2009) – prepared the first set of recommendations for implementation at the European level. The meeting agreed the urgent need to harmonize policies in European countries and to issue technical and general recommendations to be endorsed by countries.

Non-endemic countries

Non-endemic countries for Chagas disease are defined as those:

- outside Latin America;
- with or without exceptional vectorial transmission to humans;
- where there is population exchange with Latin America.

Countries identified for the initiative	
Europe	Romania
Austria	Sweden
Belgium	Spain
Croatia	Switzerland
Denmark	UK
France	
Germany	**North America**
Greece	Canada
Ireland	USA
Italy	
Luxembourg	**Western Pacific**
Netherlands	Australia
Norway	Japan
Portugal	

The main issues to be addressed in Europe are as follows:

- assessing the epidemiological burden of Chagas disease;
- offering appropriate care to infected people living in European countries;
- implementing early treatment of cases of congenital transmission;
- preventing transmission of infection through blood transfusion or organ transplant;
- reducing the burden of late severe cardiac and digestive manifestations of the disease;
- sharing information with medical communities and policy-makers on the emergence of Chagas disease in Europe.

Complementary informal meetings took place in Jeju Island (Republic of Korea) from 29 September to 3 October 2008 during the XVII International Congress for Tropical Medicine and Malaria and in New Orleans (USA) on 7–11 December 2008 at the 57th Annual Meeting of the American Society of Tropical Medicine and Hygiene.

2.4.2 Surveys and assessments

In order to assess the epidemiological situation, surveys were carried out in Geneva, Switzerland (*16*, *17*) and are planned for other European countries (Belgium and Italy).

In France, a consensus workshop was organized by the Société de pathologie exotique with the support of WHO, in collaboration with the Institut de veille sanitaire, the Etablissement français du sang, departments of infectious diseases in hospitals and universities, and the Académie nationale de médecine (Paris, 27 May 2009 and 26 June 2009) (*18*, *19*).

2.5 Collaboration with other WHO programmes

The WHO Chagas disease control programme collaborates with other key programmes within the Organization. These include the WHO Biological References Programme – through its project on International Biological Reference Preparations for Chagas Disease Diagnostic Tests, implemented by the Blood Products and related Biologicals, Quality and Safety: Medicines Unit of the Essential Medicines and Pharmaceutical Policies Department (Annex 3) – and the WHO Pharmacovigilance Programme – through its project on Pharmacovigilance in Chagas Disease Treatment to improve the reporting of and knowledge about adverse events associated with benznidazol and nifurtimox, also implemented by the Quality and Safety: Medicines Unit of the Essential Medicines and Pharmaceutical Policies Department (Annex 4).

2.6 Legal background

The first official reference to Chagas disease at the European Union level is made in the European Commission's Directive 2004/33/CE (*20*) applying to Directive 2002/98/CE (*21*) of the European Parliament and Council (2003) on quality and safety of blood, which concerns certain technical criteria relating to blood and blood donations. Annex III of the directive defines the admissible criteria for blood donors or blood types and the minimal exclusion criteria for donations from donors who are or were infected with infectious parasitological diseases; the exclusion of Chagas disease carriers is specified. Other European directives, including 2005/62/CE, establish norms to be followed by institutions in carrying out blood transfusions on blood imported from other countries.

In February 2006, the European Parliament published a new directive – 2006/17/CE (*22*) – on the donation and control of human tissues and cells, which referred to Chagas disease. The directive relates to the screening of donors based on their epidemiological history and travels to endemic areas.

The meeting discussed the efficiency of such directives and emphasized the risk of transmission of Chagas disease in France (*23–25*). In November 2006, screening of blood donors at risk of Chagas disease was implemented in France, allowing for the reintegration of blood donors previously excluded for a history of long stays in endemic areas (*26*). In May 2007, screening for *T. cruzi* infection was implemented. Spain implemented a similar measure in 2005 (*27*) in order to be aligned with European Union directives.

3. Aims and objectives of the meeting

The aims of the meeting were to build consensus on the implementation of national measures to prevent and control Chagas disease in Europe and to target the harmonization of national policies at the European level through recommendations to European and national authorities.

General objectives

To build an information and surveillance system at European and country levels.

To provide guidance on preventing transmission (through blood transfusion, organ donation, and tissue and cell transplantation) and reducing the risk of infection among travellers.

To establish an ad hoc integrated system to ensure the early diagnosis and treatment of congenital, acute and reactivation cases.

To propose measures to reduce the risk of developing late chronic manifestations and provide guidance for etiological and non-etiological treatment of the disease.

Specific objectives

assessing the epidemiological information on Chagas disease country by country.
evaluating national policies and progress made against Chagas disease in each country.
obtaining a consensus list of proposals based on previous consensus documents.
establishing technical recommendations.
formulating general recommendations.
preparing a general statement to be submitted to national authorities.

4. Working groups

Participants were assigned to the following four thematic working groups on Chagas disease:

Information and surveillance system – European and country levels.
Prevention and control – prevention of transfusional transmission and transmission through cell, tissue and organ transplantation; early detection and treatment of congenital infection; travel medicine, and appropriate prevention and control measures before and after travel to endemic areas; information, education and communication.
Laboratory screening and diagnosis of *T. cruzi* infection – internal and external quality control.
Medical care – referral systems among blood banks, laboratories and clinical services; drug distribution and pharmacovigilance; associations of patients; protocols and laws.

5. Conclusions and recommendations

5.1 General conclusions

All participants agreed to highlight the following 11 statements:

There is sufficient evidence that Chagas disease is a serious challenge to public health in European countries.
The main affected European countries are evaluating their epidemiological situation and have already identified the critical technical and organizational gaps to be filled.
It is time to take a step forward from technical recommendations to public health decisions.
Decisions about national public health should be made and harmonized at European and international levels with the support of appropriate international institutions.
A European integrated surveillance system should be built to aggregate data and information provided by national authorities.
The risk of transmission of Chagas disease should be prioritized by blood banks and cells, tissue and organ transplant systems.
Access to diagnosis should be ensured for anybody coming from endemic areas for Chagas disease. In particular, appropriate testing of target groups – such as women of childbearing age or patients with cardiac or digestive disorders at risk of having been infected earlier in an endemic country or area – should be implemented.
The capacity of national health systems to correctly diagnose, manage and treat the disease should be ensured.
Diagnostic procedures should be harmonized, validated and disseminated through appropriate guidelines.
Procedures for treatment and clinical management should be harmonized, validated and spread through appropriate guidelines.
National policies should be implemented and then harmonized in European countries, and links established with other parts of the world.

Based on these recommendations, the participants agreed to prepare a general statement to reflect their common vision. [This statement was issued by WHO on 20 January 2010 and is reproduced below.]

Statement – Chagas disease in Europe[1]

20 January 2010 | Geneva

Recommendations of an Informal Consultation meeting on Chagas Disease Control and Prevention in Europe, WHO headquarters, Geneva, Switzerland, 17–18 December 2009.

Chagas disease (American trypanosomiasis) has emerged as an important public health challenge in Europe, where transmission to date has been non-vector-borne. Spread of the disease outside endemic countries in Latin America is mainly due to increased population mobility over the past few decades.

Based on an evaluation of recently compiled epidemiological data by experts in many European countries, WHO convened an informal meeting of Chagas disease experts and European government health officials at which the following recommendations were made to European governments to adapt recent technical recommendations into public health decisions.

Cases of Chagas disease in Europe are known to occur from transfusion of contaminated blood, mother to child (congenital transmission) and during organ transplantation. It is estimated that the number of infected cases in Europe exceeds 80 000, with more than 4 000 laboratory-confirmed cases during the past 10 years in countries: Belgium, France, Italy, Spain, Switzerland and the United Kingdom. Sporadic cases are known to have occurred in other European countries including Austria, Croatia, Denmark, Germany, Luxembourg, the Netherlands, Norway, Portugal, Romania and Sweden.

Representatives of European governments and technical experts at the meeting strongly recommended:

setting up an integrated surveillance system to aggregate data and information about Chagas disease as provided by European national health authorities;
converting previous national technical recommendations into public health decisions;
implementing strict guidelines on control measures for blood banks and organ transplant systems to eliminate the risks of Chagas disease transmission;
testing of target groups such as women of childbearing age and patients with cardiac disorders at risk of having been infected earlier in endemic countries;
putting into practice early detection of cases and treatment of patients with congenital transmission;
providing greater access to diagnosis and medical care for anyone coming from countries/areas where Chagas disease is endemic;
enhancing the capacity of national health systems to correctly diagnose, manage and treat Chagas disease; and
harmonizing and validating diagnostic procedures through appropriate guidelines, with the support of appropriate public health institutions.

An increase in the number of cases in Europe led to the creation in 2007 of an informal network, the "Non-Endemic Countries Initiative" (NECI). This network comprises clinicians, biologists, public health specialists, academic experts, researchers and national health authorities working under the auspices of WHO.

At the meeting of the 6th European Congress of Tropical Medicine and International Health held between 6–10 September 2009 in Verona, Italy, the NECI reached broad consensus on the risks posed by the non-vector borne spread of Chagas disease in Europe and the need to implement measures to prevent its spread further.

Chagas disease was once almost entirely confined to Latin American countries. Patterns of population movement over the past decades show that the disease has spread at first to the United States and Canada and later to European countries. Chagas disease has also been detected in Japan and Australia.

[1] http://www.who.int/neglected_diseases/integrated_media_chagas_statement/en/index.html

5.2 Conclusions and recommendations of the working groups

Participants endorsed the following conclusions and recommendations made by the working groups:

Working group on information and surveillance system

There is enough scientific evidence to consider Chagas disease a public health issue in Europe.
The nature and burden of Chagas disease is not well characterized in Europe.
More epidemiological information is needed to better support prevention and control strategies in non-endemic countries of Europe.

Participants recommended:

- That a surveillance system for Chagas disease be established at both national and European levels.
  - Each country would need to develop its own national surveillance system according to its specific needs.
  - Each national surveillance system would need to provide a common set of data at the European level.
  - Surveillance at the European level would need to be compatible with global surveillance.
- That WHO form a technical working group to promote the design of a common set of data at the European level;
  - these data would be expected to include consideration of surveillance setting (e.g. blood bank/organ donation screening, congenital transmission, clinical case presentation at a multidisciplinary level), and definition of at-risk groups and risk factors.
- That pilot projects be supported to develop surveillance systems for individual countries and at the European level.
- That the results from surveillance of Chagas disease be used at national and European levels to develop prevention and control strategies.
- That more information on Chagas disease be provided to the medical community, public health authorities and at-risk groups originating from endemic countries.

Working group on prevention and control

Prevention

In Europe, prevention of *T. cruzi* infection does not involve measures to control vector transmission because the vectors responsible for transmitting the disease are not present. Rather, prevention measures concern the risk of transmission through blood transfusion and organ, tissue or cell transplantations, acquisition of infection during travel to endemic areas, and congenital transmission.

To prevent vertical transmission, chronically infected non-pregnant women of childbearing age should be treated.

Cases of *T. cruzi* infection caused by blood transfusion have been reported in Europe. To avoid this risk, we recommend that countries develop a strategy to identify and exclude those who may pose a transmission risk and refer them for further management.

Severe or fatal cases of *T. cruzi* infection following organ, tissue and cell transplantations have been reported in Europe, highlighting the need to generalize urgently the above-mentioned recommendations to all European transplantations centres.

Cases of acute Chagas disease have been reported in European citizens returning from Latin American countries. This highlights the need for travel clinics to reinforce counselling to travellers about the risk of vector, oral (foodborne) and blood transfusion transmission of *T. cruzi* infection in endemic Latin American countries.

Severe or fatal reactivations of Chagas disease have been reported in immigrants with chronic *T. cruzi* infection associated with immunosuppression (e.g. HIV/AIDS, drug-induced immunosuppression). For the prevention of such reactivation, it is strongly recommend that such patients are screened and that treatment is considered when appropriate.

Control

Control of *T. cruzi* infections concerns the risk of congenital Chagas disease in chronically infected and pregnant women (confirmed by a laboratory diagnosis test). Since the treatment of pregnant women with benznidazol and nifurtimox is currently contraindicated, we recommend basing the control strategy on the early detection and treatment of congenital infections.

Working group on laboratory screening and diagnosis

The biological diagnosis is not standardized (choice of tests, algorithm) and there is no practical gold standard for diagnosis. There is a need for research, development and improvement in diagnostic tools: serological tests as well as molecular diagnostics.

Commercial (CE marked) tests are recommended to be made available in every country in Europe.

The rule for CE marking of *T. cruzi* infection diagnostics should be changed with additional evaluation of the sensitivity and specificity of marketed products; for now national choices of appropriate acceptance criteria for testing devices must be based on evaluations in the literature.

In-house tests should be validated by reference panels, as available or other scientifically appropriate validation procedures to establish their sensitivity and specificity.

It is recommended to have national or regional reference diagnostic laboratories for evaluation of reagents and new tests. We encourage internal and external regional quality control for laboratory performance.

For screening in blood banks, the use of only one test may be sufficient if it has appropriate sensitivity and specificity. For diagnosis, the current recommendation of WHO to use two different serological tests is still valuable.

There is urgent need for a commercially available confirmatory assay that can be used to supplement the results of screening or diagnostic assays.

It is recommended to train professionals for the execution of parasitological methods which allow the diagnosis of acute cases, included the congenital cases.

It is recommended the urgent development and validation of molecular methods of diagnosis.

Working group on medical care

1. Access to diagnosis and care.
    a. An important number of affected people are being missed by diagnostic and clinical care systems. Important differences exist between and within countries in Europe regarding strategies to provide diagnosis for Chagas disease.
    b. Chagas disease affects mainly vulnerable groups (undocumented immigrants, women and children, including adopted, socially and economically deprived persons).
    c. There is a need to increase opportunities for detection and evaluation of persons at risk, both to reduce harm in affected people and social costs of the disease and to reduce the risk of transmission to the local population (congenital, blood- and organ-borne).
    d. Existing structures (blood and organ banks, primary care facilities, maternities, specialists) should be supported to provide easily accessible diagnostic procedures.
    e. Active case-finding methods should be promoted (outreach programs, others).
    f. Efficient referral of newly diagnosed cases to specialized centres should be implemented.
    g. We recommend the constitution of inter-disciplinary reference centres in each country.

2. Drug distribution and pharmacovigilance
    a. Two medicines (benznidazol and nifurtimox) are recommended for the treatment of specific forms of Chagas disease. Neither is registered in the European Region, and access is not provided by the usual national drug distribution system.
    b. Pharmacovigilance data in Europe are not sufficient.

c. The majority of the >80 000 infected population residing in Europe could benefit from etiological and non-etiological treatment.
d. Governments must commit to:
    i. a proper distribution system within each country;
    ii. official acceptance of drug use within European countries despite lack of proper registration;
    iii. administration under strict control by specialized centres;
    iv. a multi-pronged approach to pharmacovigilance to build minimum capacity in countries with no pharmacovigilance systems (example through spontaneous reporting systems) and to promote active surveillance approaches in advanced settings, for the proactive follow-up of treated patients to characterize the adverse events with these medicines and to use the evidences to optimize treatment policies.
    v. improved initiatives to develop multicentre studies in order to complete scientific evidences on drugs tolerance, pharmacokinetics and efficacy and development of new drugs should be encouraged.

3. Patients associations and communities of individuals at risk
    a. Patients associations and communities play a major role as partners of health structures in accessing to individuals at risk, providing information and improving awareness of Chagas disease.
    b. Cooperation with and involvement of associations and community is strongly encouraged.

4. Protocols and guidelines
    a. Specificities of Chagas disease in Europe may involve modifying existing guidelines.
    b. Based on the generation of new evidences in Europe and on existing national recommendations, we advise the development of shared European recommendations.

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Annex 2. Agenda

Thursday 17 December 2009

08:15–09:00	Registration	
09:00–09:30	Opening Introduction and objectives of the meeting	Dr Lorenzo Savioli, Director of Control of Neglected Tropical Diseases Department, WHO Geneva Dr Roberta Andraghetti Medical Officer, Communicable Diseases Unit, WHO Regional Office for Europe
09:30–10:00	Country presentations: Belgium Presentation and questions	Dr Yves Carlier
10:00–10:30	Country presentations: France Presentation and questions	Dr Pierre Ambroise-Thomas Dr Jean Delmont
10:30–11:00	*Coffee/Tea break*	
11:00–11:30	Country presentations: Germany Presentation and questions	Dr August Sich
11:30–12:00	Country presentations: Italy Presentation and questions	Dr Andrea Angheben
12:00–12:30	Country presentations: the Netherlands Presentation and questions	Dr Tom van Gool Dr Aldert Bart
12:30–14:00	*Lunch*	
14:00–14:30	Country presentations: Portugal Presentation and questions	Dr Jorge Seixas
14:30–15:00	Country presentations: Spain Presentation and questions	Dr Carmen Cañavate
15.00-15.30	Country presentations: Switzerland Presentation and questions	Dr Yves Jackson

15:30–15:45	*Coffee/Tea break*	
15:45–16:15	Country presentations: United Kingdom Presentation and questions	Dr Alan Kitchen Dr Jane Jones
16:15–16:45	Discussion of the epidemiological situation and adopted measures in each country	
16:45–17:00	Presentation on WHO's Chagas disease Programme	Dr Albajar Viñas
17:00–17:20	Information and Surveillance System on Chagas disease in Europe	Dr Josep Ma Jansà
17:20–17:40	Presentation on WHO's Pharmacovigilance Programme	Dr Mitsuko Imai
17:40–18:00	Presentation on WHO's Biological References Programme	Dr Ana Ma Padilla
18:00–19:30	Welcome cocktail	

Friday 18 December 2009

09:00–10:30	Working groups on (i) prevention, (ii) control, (iii) medical care, and (iv) epidemiological information and surveillance system. The groups should work on technical recommendations based on the previous work carried out at the 6th European Congress on Tropical Medicine and International Health (Verona, Italy, 6–10 September 2009) and the congress proceedings currently in the process of being published.	All participants
10:30–11:00	*Coffee/Tea break*	
11:00–12:00	Working groups (continued)	All participants
12:00–13:00	*Lunch*	
13:00–14:00	Presentations by each working group	
14:00–16:00	Review of recommendations, and approval and preparation of general statement	
16:00–16:15	Closure	Dr Jean Jannin Dr Roberta Andraghetti

Annex 3. WHO Biological Reference Standards for Chagas disease diagnostic tests: blood products and related biologicals, essential medicines and pharmaceutical policies

A core function of WHO, set out in its Constitution (Article 2), is to "develop, establish, and promote international standards with respect to food, biological, pharmaceutical and similar products" as well as "to standardize diagnostic procedures as necessary". Under this definition, biological products comprise a class of substances used in medicines that derive from living sources ranging from normal or genetically modified organisms to human tissues for the diagnosis, treatment or prevention of disease. In practice, biological products include vaccines, blood and blood products, biological therapeutics and in vitro biological diagnostic devices.

WHO develops and establishes International Biological Reference Standards and Reference Panels (physical standards). These standards form the basis for comparison of results between different biological assays, facilitate the transfer of laboratory science into worldwide clinical practice, and support the harmonization of international quality and safety regulations. A list of the WHO Biological Reference Standards and Panels is published at: www.who.int/bloodproducts/catalogue.

The work is coordinated by a Secretariat at WHO headquarters and developed through an Expert Committee on Biological Standardization, assisted by the WHO Collaborating Centres for Biological Standards and Standardization. WHO Working Groups and Consultations provide support on specific topics.

During the WHO Consultations on International Biological Reference Preparations for Chagas disease Diagnostic Tests, (held at WHO headquarters in 2007 and 2009), the participants supported the development of a WHO International Biological Reference Panel for Chagas disease diagnostic tests based on the detection of antibodies to *T. cruzi*. Representatives of reference and clinical laboratories, blood establishments, regulatory agencies and manufacturers of diagnostic tests participated in these consultations. The composition, intended use and production of a global reference panel, the design of an international collaborative study to calibrate the proposed reference panel and the tests and technologies to be considered in the WHO collaborative study were discussed.

Two main *T. cruzi* groups have been identified in the endemic regions: *T. cruzi* I and *T. cruz*i II. Some published reports indicate different reactivity of sera from patients living in regions where *T. cruzi* I is prevalent, when measured by tests made from *T. cruzi* II antigens. For this reason, the second WHO Consultation proposed the development of a panel of two positive preparations (defibrinated plasma) representing the *T. cruzi* I and *T. cruzi* II groups, respectively, to facilitate the control of analytical sensitivity of commercial tests in all regions. No borderline positive or negative control sample would be needed. There was also consensus on the use of samples of medium reactivity, in order to distinguish between tests that use poor-quality reagents. It is expected that preparations in the panel should be detected by all the commercially available approved tests.

Confirmation of the *T. cruzi* genotype from infected donors remains difficult for various reasons: (i) serology cannot be used to identify the genotype of the infecting strain; (ii) parasitaemia in blood donors is usually low; (iii) additional ethical approval is required for isolation/detection of the parasite. Nevertheless, a recommendation was made, to make efforts to try to isolate parasites from the donors involved, efforts will be made in this direction and donors will be recalled.

The concentration of antibodies in chronically infected people is usually high and can be demonstrated by conventional tests including the indirect immunofluorescence assay (IFA), the indirect haemagglutination assay (IHA) and the enzyme-linked immunosorbent assay (ELISA). Some of these tests use crude antigen preparations, whereas others use recombinant or synthetic antigens. Other tests that have been recently developed include combinations of recombinant proteins,

synthetic peptides or purified antigens as well as the rapid diagnostic tests. Both screening tests and confirmatory tests will be considered in the collaborative study.

The reactivity of the above-proposed candidate preparations has been assessed in a pilot study using various enzyme immunoassays (EIAs), IFA, HAI and confirmatory tests (radioimmunoprecipitation, immunoblot and TESA-Blot assays). A WHO Collaborative study to evaluate the suitability of these candidate preparations will follow, involving a wide number of tests and 25 laboratories from regulatory agencies, investigative laboratories, blood donor screening laboratories and diagnostic laboratories in the Americas, European and Western Pacific regions.

The WHO project on International Biological Reference Preparations for Chagas Disease Diagnostic Tests is key to implementing access to high-quality diagnosis for Chagas disease worldwide. The availability of internationally agreed reference preparations will contribute to the control of the analytical sensitivity of in-house tests and commercially available kits by test developers, manufacturers, regulators, blood establishments, and reference and diagnostic laboratories. This will contribute to the harmonization of international regulations and facilitate the development of new tests.

Related information:

Recommendations for the preparation, characterization and establishment of international and other biological reference standards (revised 2004). In: *WHO Expert Committee on Biological Standardization. Fifty-fifth report*. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 932); Annex 2:73–131 (available at: http://whqlibdoc.who.int/trs/WHO_TRS_932_eng.pdf).

Report of the WHO Consultation on global measurement standards and their use in the in vitro biological diagnostic field. Geneva, World Health Organization, 2004 (available at: http://www.who.int/bloodproducts/publications/en/Minutes-220804.pdf).

WHO Consultation on international biological reference preparations for Chagas diagnostic tests. Geneva, 2–3 July 2007. Geneva, World Health Organization, 2007 (available at: http://www.who.int/bloodproducts/ref_materials/WHO_Report_1st_Chagas_BRP_consultation_7-2007_final.pdf).

Second WHO Consultation on the development of a WHO reference panel for the control of Chagas diagnostic tests. Geneva, 27–28 January 2009. Geneva, World Health Organization, 2009 (available at: http://www.who.int/bloodproducts/ref_materials/chagas_dev_ref_materials/en/index.html).

Annex 4. WHO pharmacovigilance system

The WHO Programme for International Drug Monitoring provides a forum for WHO Member States to collaborate in monitoring the safety of medicines. The programme, which comprises a network of national drug centres, WHO headquarters and the WHO Collaborating Centre for International Drug Monitoring, is managed by the Quality Assurance and Safety of Medicines Unit of WHO's Department of Essential Medicines and Pharmaceutical Policies. The objectives and policies of the programme are determined by WHO in response to the needs for pharmacovigilance of its Member States. WHO is responsible for developing norms and guidelines and for providing technical support to countries; supporting pharmacovigilance in public health programmes, including control of the neglected tropical diseases; and coordinating exchange of information among Member States on the safety and efficacy of medicines.

National pharmacovigilance centres in Member countries collect individual case reports of suspected adverse drug events and store them in a common database. The database, which now contains about 5 000 000 case reports, is managed by the WHO Collaborating Centre for International Drug Monitoring at the Uppsala Monitoring Centre (Uppsala, Sweden). One of its main functions is to identify previously unknown adverse reactions to medicines based on the regular analysis of information from case reports. Information on these signals is returned to the national centres. Further information about the programme is available at http://www.who.int/medicines.

Pharmacovigilance in public health programmes is an important issue and should be an integral part of all such programmes. Public health programmes and pharmacovigilance have synergistic effects: public health programmes provide an opportunity to implement pharmacovigilance activities and allow a cohort of patients to be monitored for safety under controlled conditions over a period of time; while pharmacovigilance detects, evaluates and prevents adverse events, promotes the rational use of medicines in mass treatment programmes, evaluates the impact of the programmes and improves their acceptability.

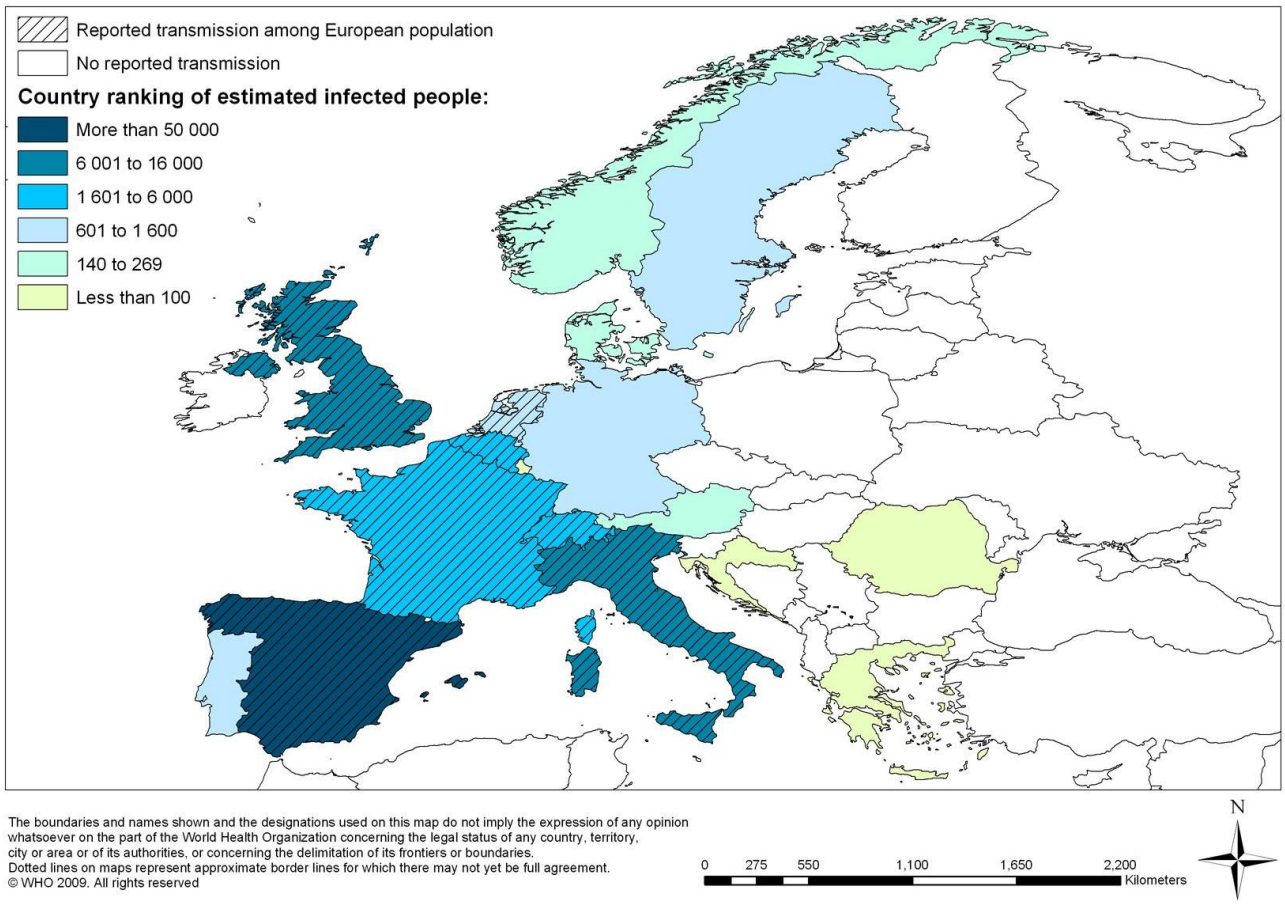
The data stored in the WHO database on adverse events associated with the medicines used to treat *T. cruzi* infection (benznidazol and nifurtimox) are being studied. WHO strongly encourages all national pharmacovigilance centres to collect and contribute case reports concerning these medicines to the WHO Programme for International Drug Monitoring, so that any adverse events can be characterized and subsequently addressed.

Annex 5. Country reports

Countries used different approaches and methodologies to estimate the number of people infected with *T. cruzi*. As a result, the data are not comparable among countries. However, although Chagas disease is under-diagnosed and there remains a lack of information and surveillance systems available at national and European levels, countries calculated their best estimates of the numbers of cases of infection. Since the numbers of officially registered cases and notified cases may be underestimated, these data may contain inadequacies or inconsistencies and should therefore be interpreted with caution.

Before the meeting, WHO circulated a questionnaire to the participants. The results of the questionnaire were analysed and used to generate the country reports (Appendix 1). Map A5 shows the distribution of cases of *T. cruzi* infection by ranking based on the epidemiological information provided by countries.

Map A3. Distribution of cases of *Trypanosoma cruzi* infection in Europe by country, and reported transmission (autochthonous, transfusional or congenital transmission of infection acquired among European travellers to disease-endemic areas) among the European population (data reported to WHO as of December 2009)



AUSTRIA

Epidemiological information

There are an estimated 7 552 Latin American immigrants in Austria, of whom an estimated 140–180 are infected with *T. cruzi*.[2]

In 2008 and 2009, one case each of acute infection was diagnosed and treated. The case in 2008 occurred in an Austrian citizen who had travelled to Latin America; the infection was acquired locally through supposed vector transmission. There is no epidemiological or clinical information about the case in 2009.

Austria has no policy regarding blood screening to prevent infection transmission through transfusion or organ transplantation. There is no policy concerning early diagnosis and treatment of congenital infection.

Number of Latin American immigrants	**7 552**
Estimated number of cases of *T. cruzi* infection	**140–180**
Number of laboratory-confirmed cases	**2**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**ND**
Number of patients treated with benznidazol and nifurtimox	**2**

ND = not determined

Source: WHO data.

BELGIUM

Epidemiological information

In 2006, there were 25 422 Latin Americans officially residing in all regions of Belgium:[3] 4366 from Brazil, 3888 from Chile and 17 668 from other Latin American countries (official information on the national origin of these 17 668 immigrants is not available).

There is no information about the number of illegal immigrants, but this figure can be estimated, as in other European countries, as being 50% of the legally registered immigrants, i.e. 12 711.

Number of Latin American immigrants	**38 133**
Estimated number of cases of *T. cruzi* infection	**1 982**
Number of laboratory-confirmed cases	**19**
Number of pregnant women with *T. cruzi* infection	**16**
Number of cases of congenital transmission	**1**
Number of patients treated with benznidazol and nifurtimox	**3**

Taking into account (i) the estimated number of Latin Americans officially residing in Belgium (25 422); (ii) the national distribution of diagnosed cases among Latin Americans living in Belgium (41.2% from Brazil, 29.4% from the Plurinational State of Bolivia, 17.6% from Ecuador, and 11.8% from other Latin American nationalities; (iii) the prevalence rate of *T. cruzi* infection in Brazil (1.02%) and Ecuador (1.74%),[4] and assuming a rate of 14.8% for the Plurinational State of Bolivia and 1% for the rest of Latin

[2] Guerri-Guttenberg RA et al. Chagas cardiomyopathy: Europe is not spared! *European Heart Journal*, 2008, 29(21):2587–2591.
[3] Registre National - Direction Générale Statistique et Information Economique - RN-DG SIE, Perrin, Dal & Poulain, 2006.
[4] Pan American Health Organization, WHO Department of Control of Neglected Tropical Diseases, 2006. *Estimación cuantitativa de la enfermedad de Chagas en les Américas* [In Spanish]. Montevideo, Uruguay, OPS/HDM/CD/425–06.

American countries (i.e. considering a mean prevalence rate of *T. cruzi* infection of 5.2% among Latin American people living in Belgium), the expected number of infected people in Belgium in 2006 might be 1 321 legal immigrants plus 661 illegal immigrants, or an estimated total of 1 982.

Based on the prevalence of *T. cruzi* infection in diagnosed patients (31.6%), the estimated number of cases of *T. cruzi* among all officially registered Latin American migrants in Belgium in 2006 might be 417 among legal immigrants, plus 209 among illegal immigrants, i.e. an estimated total of 626.

The available data are from the region of Brussels, which registered 301 pregnant Latin American women in 2004, of whom 16 were estimated to be infected with *T. cruzi* (301 x 5.2%). Assuming a maternal–fetal transmission rate of 5%, the estimated number of infected newborns per year is **<1** (0.8%).

Serological diagnosis of *T. cruzi* infection is performed at two centres: the Erasmus Hospital of the Université Libre de Bruxelles and the Institute of Tropical Medicine in Antwerp. From January 1994 to December 2008 (15 years), both hospitals performed serological diagnosis of 2 771 patients, of whom 41 (1.48%) tested positive, or an average of 2–3 patients per year. Of the 41 patients in whom the disease was diagnosed, 19 live in Belgium and 22 in other European countries (France, Italy, Luxembourg, Sweden, the Netherlands and Norway).

Analysis of the individual data of the 19 patients shows that 17 (89.5%) are from Latin American countries and 2 are Belgians who have had multiple stays in various Latin American countries. According to their country of origin, 7/17 (41.2%) are from Brazil, 5/17 (29.4%) from the Plurinational State of Bolivia, 3/17 (17.6%) from Ecuador, 1/17 from Paraguay (5.9%) and 1/17 from Chile (5.9%).

Of the 19 patients, 6 (31.6 %) have a symptomatic chronic form of the disease; 3/6 patients (50%) have cardiac alterations, 1/6 (16.7%) has a digestive alteration (megaesophagus) and 2/6 (33.3%) have a mixed form (cardiac plus digestive alterations).

At least 3 of the 19 patients have been treated with benznidazol: 1 patient (aged 43 years) from the Plurinational State of Bolivia and 2 patients (aged 42 years and 50 years) from Brazil.

Pharmacovigilance

The national pharmacovigilance system has not been used to report adverse events associated with benznidazol or nifurtimox.

Prevention of infection and early detection of congenital cases

There is no national system for systematic detection of congenital infection.

Transfusional and organ, tissue and cell transplantation transmission

EC directives 2004/33 and 2006/17 concerning the exclusion of people at risk of Chagas disease from blood and tissue donations are applied in blood banks as for malaria (that is, based on the results of a questionnaire, which excludes for 6 months donors from Latin American countries but includes them after this period if no symptoms of Chagas disease are recorded).

There is no systematic detection system of organ, tissue and cell transplantation transmission in Belgium.

Travel medicine

Counselling about Chagas disease is done before travel to Latin America. Chagas disease is included in the differential diagnosis of consultations after such trips in most travel clinics.

Laboratory diagnosis

Serological tests and polymerase chain reaction (PCR) are used for the diagnosis of *T. cruzi* infection. These tests are performed in two centres: the Parasitology Laboratory of the Erasmus Hospital (Université Libre de Bruxelles) and the Institute of Tropical Medicine (Antwerp).

Systematic internal quality control is done using positive and negative controls. There is regular global evaluation.

Tests used for serological screening and diagnosis of *T. cruzi* infection in blood banks and health centres

Serological screening and diagnosis have not been implemented in blood banks.

Commercial tests (Biokit ELISA) and in-house tests are used for serological screening and diagnosis. The Université Libre de Bruxelles (Parasitology Laboratory of the Erasmus Hospital) uses IFA and ELISA; the Institute of Tropical Medicine of Antwerp uses ID and ELISA.

A panel of well characterized sera for evaluating the serological tests was been created through contacts with colleagues in reference institutions in Latin America.

Health services

There are no specialized medical centres for Chagas disease, but some Belgian centres of internal medicine are able to provide medical care to patients with the disease.

There is no any referral system between blood banks and laboratory and clinical services.

Other services, protocols and laws, and additional information

There is no drug distribution system for benznidazol and nifurtimox and no system for information and surveillance. Information, education and communication activities have not been implemented. There are no official policies or guidelines for the management of Chagas disease patients. There is no national association of Chagas disease patients.

Sources: Erasmus Hospital of Université Libre de Bruxelles, Brussels, Belgium;
Institute of Tropical Medicine, Antwerp, Belgium.

CROATIA

Epidemiological information

In 2009, a Latin American in whom chronic *T. cruzi* infection had been diagnosed was treated in Croatia with nifurtimox. The infection was suspected to have been acquired through vector transmission in Latin America.

There is no further information about Chagas disease in Croatia.

Number of Latin American immigrants	**ND**
Estimated number of cases of *T. cruzi* infection	**ND**
Number of laboratory-confirmed cases	**1**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**ND**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

Sources: WHO data.

DENMARK

Epidemiological information

In 2000, a case of chronic Chagasic cardiomyopathy was described in a 57-year-old Venezuelan-born woman who showed signs of the disease after having lived in Denmark for 32 years.[5]

There is no further information about Chagas disease in Denmark.

Number of Latin American immigrants	**ND**
Estimated number of cases of *T. cruzi* infection	**ND**
Number of laboratory-confirmed cases	**1**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**ND**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

Sources: Hvidovre Hospital, Hvidovre, Denmark

[5] Enemark H et al. Chronic Chagas disease—an echo from youth. *Ugeskr Laeger*, 2000; 162: 2567–2569.

Epidemiological information

Different groups of people at risk of *T. cruzi* infection have been identified in France (excluding French Guyana). Official data of the main at-risk groups were obtained from The International Adoption Agency and the French ministries of Finances, Foreign Affairs and Migrations (Table 1FRA).

Number of Latin American immigrants and at-risk groups	**208 395**
Estimated number of cases of *T. cruzi* infection	**2 166**
Number of laboratory-confirmed cases	**111**
Number of pregnant women with *T. cruzi* infection	**ND**
Expected number of cases of congenital transmission	**19**
Number of patients treated with benznidazol and nifurtimox	**28**

ND = not determined

Table 1FRA. Groups at risk of *T. cruzi* infection in France

Naturalized and legal migrants	82 396
Population originating from French Guyana	15 585
Adopted children from Latin-American country (1980–2007)	19 389
Children born in France from a Latin American mother (1981–1999)	39 525
Total	156 895

Table 2FRA shows the number of legal Latin American migrants living in France (excluding French Guyana) in 2008 by country of birth, based on official statistics.

Table 2FRA. Number of legal Latin American migrants living in France (excluding French Guyana) in 2008, by country of birth

Country of birth	Number of naturalized persons originated from a Latin American country[a]	Number of legal migrants living in France[b] in 2008 by country	Total
Argentine	3,732	3,560	7,292
Belize	-	20	20
Bolivie	462	958	1,420
Brésil	7,004	14,258	21,262
Chili	5,551	4,773	10,324
Colombie	5,839	10,221	16,060
Costa Rica	140	282	422
Equateur	383	1,983	2,366
Guatemala	832	287	1,119
Guyana	-	385	385
Honduras	152	175	327
Mexique	1,547	5,598	7,145
Nicaragua	186	179	365
Panama	117	124	241
Paraguay	225	318	543
Pérou	2,553	4,840	7,393
El Salvador	479	344	823
Suriname	69	309	378
Uruguay	870	552	1,422
Vénézuela	755	2,334	3,089
Total	30,896	51,500	**82,396**

[a] *1999 census (Insee)*

[b] *France excluding French Guyana.*

Assuming that the number of illegal immigrants is equal to the number of legal migrants (51 500), the total estimated population exposed to *T. cruzi* in France in 2008 was 208 395.

Based on the country prevalence rates of *T. cruzi* infection published by the PAHO in 2006[6] and applied to official data of the at-risk population in France by country of origin, the estimated number of people infected with *T. cruzi* living in France is 1 464 (range, 895–2619) (Table 3FRA).

Table 3FRA. Estimated number of people infected with *T. cruzi* in France (excluding French Guyana), by at-risk groups (data as of June 2009)

At risk Populations	Number of people	Estimated infected persons (Prevalence rates of PAHO, 2006)	Minimal estimated infected persons (Schmunis, 2007 ; Schofield, 2006)	Maximal estimated infected persons ((Schmunis, 2007 ; Schofield, 2006)
Legal Latin-American people				
Naturalized (1999 Census)	30,896	469	260	770
Legal migrants in 2008	51,500	702	424	1,360
Total legal migrants	*82,396*	*1,171*	*684*	*2,130*
Adopted children between 1980-2007	19,389	235	165	384
Children born in France from Latin-American mother (1999 Census)[a]	39,525	19	7	27
French Guyanese living in mainland France	15,585	39	39	78
TOTAL France	**156,895**	**1,464**	**895**	**2,619**
Expatriated (Foreign Ministry)	79,255 (2005)	1 case by year		
Travelers from endemic countries (General Tourism Direction)[b]	16,818 person year (6,138,672 nights)	1 case each 7 years		

[a] For vertical transmission, we used a 5% rate.

[b] For expatriated people and travelers, we used the hypothesis of incidence rates 5 and 10 times lesser than the mean incidence rate of Latin-american people (estimated at 8/100,000 inhabitants by PAHO in 2006)

The calculation does not take into account the number of illegal Latin American immigrants living in France. Assuming there are an equal number of legal and illegal immigrants, the estimated number of cases of *T. cruzi* infection increases by 50%, or 2 166 (range, 1 319–3 979).

Two hospitals in Paris (Groupe Hospitalier Pitié-Salpêtrière and Tenon) provided information on laboratory-confirmed cases, which was supplemented by information found through a literature review.

Since the late 1980s, France has reported 2 cases of acute Chagas disease. The first case, a 65-year-old woman with myocarditis, had made a 12-day trip to Colombia in 1987 (staying at a rural house in Sierra Nevada).[7] The second case was a young woman who was diagnosed in 2004 in Tourcoing (northern France) after travel to French Guyana.[8]

From January 1996 to November 2009, the parasitology laboratory at GHPS confirmed 109 cases, 84 of whom were identified during the screening of 254 people for Chagas disease at the Tenon hospital. Of the 84 laboratory-confirmed cases, 81 cases have a chronic form of the disease and are being followed up for Chagasic myocardiopathy (4 cases); initial cardiac alterations (early conduction abnormalities) (32 cases); mixed (digestive and cardiac) clinical forms (4 cases); asymptomatic (9 cases). A total of 9 patients were lost to follow up. In 23 cases, the clinical form of the disease has not been determined.

From 1988 to 2009, a total of 111 patients were detected in mainland France: 3 were born in Latin America (2 in Argentina and 1 in El Salvador) and were adopted during childhood. The patients were diagnosed in France during adulthood. None of the patients has received organ transplantation or has an immunosuppressive condition.

Benznidazol has been used as a first-line medicine to treat 28 patients in France.

[6] Estimacion cuantitativa de la enfermedad de Chagas en las Americas [Quantitative estimation of Chagas disease in the Americas]. Washington DC, Pan American Health Organization Department of Control of Neglected Tropical Diseases, 2006 (OPS/HDM/CD/425-06.2006).

[7] Brisseau JM et al. Chagas' myocarditis imported into France. *Lancet*, 1988, 1(8593):1046.

[8] Lescure FX et al. Chagas Disease, France. *Emerging Infectious Diseases*, 2008, 14:644–646.

Pharmacovigilance

The national pharmacovigilance system is under the authority of the Agence française de sécurité sanitaire des produits de santé (AFSSAPS). Among the 28 patients treated with benznidazol, 11 patients (40%) had side–effects. Of these 11 patients, 18% had severe side-effects and their treatment was interrupted: 5 patients experienced peripheral neuropathies requiring two treatment interruptions; 2 patients had central nervous system disturbances requiring dose reductions; 2 patients had fever episodes and hypersensitivity rash reactions (1 a drug rash with eosinophilia and systemic symptoms (DRESS) and 1 a Quinck oedema); 2 patients had eruptions without gravity, 1 of whom had a paradoxal reaction with aggravation of heart disease (left ventricular dysfunction with arrhythmia and conduction disturbance) associated with peripheral neuropathy.

Prevention of infection and early detection of congenital cases

There is no systematic detection of congenital infection in France. The number of cases of infection by congenital transmission every year is estimated to be 19 (range, 7–27). This figure does not take into account all children exposed to infection, especially those born in France to Latin American mothers (children who were aged >18 years in 1999 and those born since 1999) and is therefore likely to be underestimated. A pilot study in the maternity hospitals in Paris is under consideration.

The Etablissement français du Sang (EFS) has implemented prevention of transfusional transmission in blood banks. Reference to Chagas disease is made in a questionnaire to donors.[9] Individuals with a history of Chagas disease are permanently deferred. Screening for antibodies to *T. cruzi* is mandatory in at-risk donors (i) originating from an endemic area, (ii) born to a mother originating from an endemic area, and (iii) among travellers and residents.

Potential blood donors are deferred for four months after returning from endemic areas. After the deferral period, they are reinstated if serological tests are negative.

Two ELISA tests are used for donor screening: ELISA using a purified parasite lysate (ELISA CRUZI, bioMérieux Brazil, Jacarepagua – Rio de Janeiro, Brazil) and ELISA with recombinant antigen (BIOELISA CHAGAS, Biokit, Barcelona, Spain). IFA is used as an alternative assay in case of doubt or discrepancy between the results of the two ELISA tests.

Since 2006, France has applied measures to identify and detect at-risk donors for organ, tissue and cell transplantation. The measures used for blood banks have been applied to those for transplantation, taking into account the risk–benefit ratio. The questionnaire for haematopoietic cell donors asks specifically about Chagas disease ("Is there any travel to Latin America within the 21 last days?").

Recommendations on travel medicine are published every year in June in the *Bulletin Epidemiologique hebdomadaire*,[10] but the information about Chagas disease is limited.

Laboratory diagnosis

Direct parasitological diagnosis of *T. cruzi* infection is available in all parasitology laboratories in France. Serological diagnosis is done in Paris (at the GHPS), Montpellier, Cayenne, Tours (National French Blood Bank of EFS) and Lille (only using ELISA Biokit). There is no external quality control system. Molecular biology diagnosis is done in Paris (at the GHPS), Cayenne and Tours (by the national French blood bank of EFS that carries out real-time PCR with parasite quantification).

[9] *Document de préparation à l'entretien médical préalable au don de sang* [Document in preparation for the medical interview before a blood donation]. Paris, Établissement Français du Sang, 2009 (available at:. http://www.dondusang.net/content/medias/media437_vPTxKoouQQFaXvO.pdf).

[10] Recommandations pour les voyageurs : quoi de neuf en 2009 ? [Recommendations for travellers: what's up in 2009? Bulletin épidémiologique hebdomadaire, 2009 23–24.

All French blood banks use commercial serological assays to perform screening. In-house tests are not used. The following kits are used for screening: ELISA CRUZI, bioMérieux Brazil (Jacarepaguá – Rio de Janeiro, Brazil) and BIOELISA CHAGAS, Biokit (Barcelona, Spain). The kits used to confirm diagnosis are: *T. cruzi* ELISA test system, Ortho-Clinical Diagnostics Inc. (Raritan, NJ, USA) and Immunofluor Chagas, Biocientifica SA (Buenos Aires, Argentina).

There is no difference between the commercial tests used for screening and diagnosis in hospitals. The GHPS uses the following commercial tests: IFA slides Immunofluor Chagas, Biocientifica SA (Buenos Aires, Argentina) with conjugate anti IgG, IgM, IgA, BioRad (Marnes la coquette, France) and Chagatest ELISA recombinant v. 3.0, Wiener Laboratory (Rosario, Argentina).

A panel of sera from patients belonging to the Bolivian group from the Tenon hospital is available at the GHPS for evaluation of the serological tests in reference laboratories.

Health services

Health services in France are able to provide medical assessment, clinical diagnosis, etiological and non-etiological treatment and follow-up of asymptomatic and symptomatic patients. Coordination of a group of clinicians is being implemented in Paris[11] in collaboration with the Institut de veille sanitaire (InVS).

There is no formal system of referral between blood banks and laboratories and clinical services, but the EFS refers all positive or suspect patients to the GHPS and to outpatient consultations of the Tenon hospital.

Other services

Drug distribution

Benznidazol and nifurtimox are not registered in France. Distribution of these medicines is ensured through a centralized system managed by the Agence française de sécurité sanitaire de produits de santé (AFSSAPS) through a temporary agreement for delivering non-registered medicines (an "Autorisation temporaire d'utilisation", or ATU).

Information and surveillance system

A system for surveillance of Chagas disease in French Guyana is managed by the parasitology laboratory of the Hospital of Cayenne, the local health authority and InVS. In mainland France, InVS has initiated a collective workshop with laboratories and clinicians to build a surveillance system, which will be fully operational within the next months. InVS has also initiated contacts with AFSSAPS for collaboration in the surveillance system in France.

Information, education and communication

In June 2009, the Société de pathologie exotique and WHO organized a workshop in Paris to establish a consensus in screening, medical care and diagnosis of Chagas disease in France.[12]

Preliminary contacts have been made with associations of obstetricians, neonatalogists, paediatricians, cardiologists to develop IEC activities.

[11] Coordination of a group of clinicians including: Infectious diseases (adults) from H. Tenon and H. Pitié Salpétrière; Cardiology (adults) from H. Tenon; Gastroenterology and visceral surgery from H. Tenon; Neurology from H. Tenon; Paediatrics from H. Robert Debré; Imagery - Radiology from H. Tenon and radiology from H. Bichat Claude Bernard; Laboratories from EFS - IdF; Parasitology from H. Pitié Salpétrière; in collaboration with the InVS.

[12] Atelier de Consensus sur la Maladie de Chagas en Zone Non Endémique. Paris, 26 Juin 2009 [Consensus workshop on Chagas disease in non-endemic areas. Paris, 26 June 2009]. *Bulletin de la Société de Pathologie Exotique*, 2009, 102(5).

Protocols and laws

There are no official policies or clinical guidelines for the management of patients with Chagas disease. For cases of transfusional transmission, there is a national regulation ("Arrêté du 12 janvier 2009 fixant les critères de sélection des donneurs de sang"[13]) for screening of *T. cruzi* infection in at-risk groups in blood banks in France. For transplantation of human tissues and cells, Directive 2006/17/CE of the European Commission of 8 February 2006 on the technical requirements for donating human tissues and cells is partially included in the French legislation but is not fully applied.

Additional information

There are no associations of Chagas disease patients in France, but five Latin American associations have begun collaboration with the Tenon hospital on the topic of Chagas disease.

Sources:	Institut de Veille sanitaire, Saint-Maurice, France; Groupe Hospitalier Pitié-Salpêtrière, Paris, France; Hôpital Tenon, Paris, France; Hôpitaux de Marseille, Marseille, France; Institut de Biologie - Hôtel Dieu, Nantes, France, Etablissement français du Sang, Tours, France, Société de Pathologie exotique, Paris, France.

[13] Arrêté du 12 janvier 2009 fixant les critères de sélection des donneurs de sang [Decree/Order of 12 January 2009 establishing the selection criteria for blood donors]. *Journal Officiel de la République Française*, 2009, 1067:23.

Epidemiological information

Number of Latin American immigrants	**58 000**
Estimated number of cases of *T. cruzi* infection	**935**
Number of laboratory-confirmed cases	**2**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**ND**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

In 1997, a survey of 100 Latin American immigrants living in Berlin[14] investigated the presence of *T. cruzi* infection based on risk factors (rural origin, contact with the Reduviidae bugs) and serological evaluation. Two cases of seroreactivity were detected using IFA and ELISA and 3 sero-reactive cases using IFA alone. The overall seroprevalence according to WHO diagnostic criteria was 2% (2/100).

No detailed information is available on the estimated 58 000 immigrants from Latin America living in Germany because of strict national legislation on data safety. The seroprevalence of 2% found in the 1997 survey is not representative of the whole country. There are an estimated 935 people infected with *T. cruzi*.[15]

There is no information on the number of pregnant women with *T. cruzi* infection or the number of infected newborns.

There is no information available on the number of patients treated at the central level. The Robert-Koch-Institute (the national reference centre in Berlin) does not survey Chagas disease in Germany. Chagas disease is not a notifiable disease in Germany.

Pharmacovigilance

There is a national system to collect information on adverse events (at the Paul-Ehrlich Institute) that could be used to report any adverse Chagas disease events in the future. However, no information on nifurtimox or benznidazol has been collected for the past 10 years.

prevention of infection and early detection of congenital cases

The risk of congenital transmission of *T. cruzi* infection is unknown to virtually all obstetricians in Germany. Therefore, pregnant women and newborns are not tested for it.

Blood transfusion services in Germany are decentralized. Common directives exist[16] and are applied by nearly all services. A pre-donation questionnaire explicitly asks for information on (i) Chagas disease; (ii) travel to endemic countries within the past 6 months; and (iii) the country of origin, which could be a possible endemic zone. Serological screening of potential donors is not done routinely. The same also applies for organ, tissue and cell transplants.

[14] Frank M et al. Prevalence and epidemiological significance of *Trypanosoma cruzi* infection among Latin American immigrants in Berlin, Germany. *Infection*, 1997, 25(6):355–358.

[15] Guerri-Guttenberg RA et al. Chagas cardiomyopathy: Europe is not spared! *European Heart Journal*, 2008, 29:2587–2591.

[16] Paul-Ehrlich-Institut. Bundesamt für Sera und Impfstoffe. Bekanntmachung der Richtlinien zur Gewinnung von Blut und Blutbestandteilen und zur Anwendung von Blutprodukten (Hämotherapie) *gemäß* §§ 12 und 18 Transfusionsgesetzes (TFG) (Änderungen und Ergänzungen 2007) [Publication of the guidelines on the collection of blood and blood components and the use of blood products (haemotherapy) as per §§ 12 and 18 Transfusion Act (Amendments and additions 2007)]. Auszug aus dem Bundesanzeiger - amtlicher Teil 19 May 2007, 92, page 5075.

Pre-travel advice is given on an individual basis. For long-term travellers to Latin America, the risk of Chagas disease is usually mentioned. Occasionally, the possible risk of oral transmission is mentioned to short-term travellers.

Laboratory diagnosis

Diagnostic tests of high quality (different serological tests and PCR) are done by three laboratories:

- Bernhard-Nocht-Institute of Tropical Medicine, Hamburg
- Institute of Tropical Medicine, Munich
- Institute of Tropical Medicine, Berlin.

Various commercial laboratories offer serological screening for *T. cruzi* infection using a single ELISA. Xenodiagnosis used to be performed in Hamburg but was abandoned some 10 years ago.

There is no routine screening in blood banks and no routine screening in health centres or obstetric services.

Health services

There are no specialized centres for Chagas disease in Germany, although reference tropical institutes are usually involved in the management of Chagas disease patients.

Additional information

There is no drug distribution system for benznidazol and nifurtimox and no system for information and surveillance.

There are no information, education and communication activities, no protocols and no local or national laws about Chagas disease in Germany.

There is no association of Chagas disease patients in Germany

Germany is well behind concerning awareness and detection of Chagas disease. However, a new initiative is planed (i) to collect current data on the prevalence of Chagas disease among immigrants in Germany; (ii) to raise awareness among the target community, but also in blood transfusion services and among obstetricians.

Sources: Harvard School of Public Health, Boston, USA; Tropenmedizin Missionsärztliche Klinik, Würzburg, Germany.

Epidemiological information

In 2008–2009, there were an estimated 440 000 Latin American immigrants living in Italy.[17,18] Table 1ITA details their country of origin.

Number of Latin American immigrants	**440 000**
Estimated number of cases of *T. cruzi* infection	**5 520–7 081**
Number of laboratory-confirmed cases	**114**
Number of pregnant women with *T. cruzi* infection	**30**
Number of cases of congenital transmission	**2**
Number of patients treated with benznidazol and nifurtimox	**22**

ND = not determined

Table 1ITA. Estimated number of legal and illegal Latin American immigrants residing in Italy, 2008–2009

Countries	Legal immigrants	Illegal immigrants	Total
Argentina	16 294	ND	ND
Bolivia (Plurinational State of)	6 996	12 000–20 000 (only Lombardia)	18 000–26 000
Brazil	45 196–50 000	around 100 000	around 150 000
Chile	4 372	ND	ND
Colombia	19 832	ND	ND
Costa Rica	446	ND	ND
Cuba	17 638	ND	ND
Dominican republic	21 756	ND	ND
Ecuador	73 235–80 000	ND	ND
El Salvador	6 096	ND	ND
Guatemala	532	ND	ND
Honduras	632	ND	ND
Mexico	5 724	ND	ND
Nicaragua	373	ND	ND
Panama	384	ND	ND
Paraguay	1 246	ND	ND
Peru	76 406–78 000	ND	ND
Uruguay	1 956	ND	ND
Venezuela (Bolivarian Republic of)	6 235	ND	ND
Others	144	ND	ND
TOTAL	**305 493–318 656**	**112 000–120 000**	**Around up to 440 000**

ND = not determined.

Table 2ITA shows the estimated number of immigrants infected with *T. cruzi* according to the estimated prevalence of the infection in Latin American countries.[19]

[17] Guerri-Guttenberg RA et al. Mal di Chagas: un problema emergente di salute pubblica in Italia? [Chagas disease: an emergent public health problem in Italy?] *Le Infezioni in Medicina*, 2009, 17(1):5–13.

[18] Istituto Nazionale di Statistica 2008 http://demo.istat.it/; Dossier statistico immigrazione Caritas/Migrantes, 2009/Migration Regional Agencies).
Schmunis G. Epidemiology of Chagas disease in non-endemic countries: the role of international migration. *Memórias do Instituto Oswaldo Cruz*, 2007; 102:75–85.

Table 2ITA. Estimated number of legal and illegal Latin American immigrants infected with *T. cruzi* residing in Italy, 2008–2009

Countries	Legal and illegal immigrants	Prevalence of *T.cruzi* infection	Estimated number of infected immigrants
Argentina	16 294	4.9%	798
Bolivia (Plurinational State of)	18 000–26 000	14.8%	2 664–3 848
Brazil	150 000	0.8%	1 200
Chile	4 372	1.2%	52
Colombia	19 832	1.2%	238
Costa Rica	446	ND	ND
Cuba	17 638	ND	ND
Dominican republic	21 756	ND	ND
Ecuador	73 235–80 000	0.2%	146–160
El Salvador	6 096	1.5%	91
Guatemala	532	ND	ND
Honduras	632	ND	ND
Mexico	5 724	0.5–6.8%	29–389
Nicaragua	373	ND	ND
Panama	384	ND	ND
Paraguay	1 246	4.5%	56
Peru	76 406–78 000	0.2%	153–156
Uruguay	1 956	0.6%	12
Venezuela (Bolivarian Republic of)	6 235	1.3%	81
Others	144	ND	ND
TOTAL	**417 493–438 656**	**–**	**5 520–7 081**

ND = not determined.

In 2007, there were an estimated 30 infected pregnant women: the rate of infected newborns in the same year was 0.3–2.1.

Of 114 patients in whom *T. cruzi* infection was diagnosed, 76 were from the Plurinational State of Bolivia, 6 from Brazil, 6 from Argentina, 1 each were from Colombia, Ecuador, Mexico and Paraguay, and 20 were from unknown countries of origin. Two Italian travellers to Brazil had acute Chagas disease.

According to the clinical diagnosis, 16 cases show an indeterminate form, 4 cases a cardiac form, 4 a digestive form and 2 a mixed (cardiac plus digestive) form. Two cases had acute Chagas disease, 1 a reactivation of the disease and 85 were not determined. Vector-borne transmission was assumed in the majority of the patients, in one case, transmission was assumed to have been food-borne.

A total of 22 patients have been treated with benznidazol.

Pharmacovigilance

Side-effects are notifiable to the Italian agency of drugs (Agenzia Italiana del Farmaco – AIFA), through an incident report form (available from the Internet). Of the 22 patients, 6 (27%) experienced adverse events during treatment. These adverse events were mainly cutaneous.

Prevention of infection and early detection of congenital cases

There is no systematic detection system at the national level for congenital infection. However, two centres in Italy (Negrar and Florence) have an active system for detecting congenital infection.

There is no transfusional transmission prevention system as such; however, completion of a pre-transfusion questionnaire is required of all potential donors. The questionnaire asks about previous diagnosed tropical diseases and travel to tropical areas. A person in whom Chagas disease has ever been diagnosed is permanently excluded from donating blood. Travellers to tropical areas are temporarily excluded from donating blood for 3 months.

There is no a prevention system to avoid transmission through organ transplantation. Only patients who have already been diagnosed with Chagas disease are excluded from donating organs, tissues and/or cells. A second opinion (by an infectious disease specialist expert in transplant medicine) is sought before organs are used from Latin American donors and patients who are potentially infected with *T. cruzi* or other tropical microbes. There is no mention of which test should be performed.

There is no specific prevention measure related to travel medicine.

Laboratory diagnosis

The following laboratories perform parasitological, molecular and serological diagnosis:

- Centre for Tropical Diseases, Ospedale Sacro Cuore, Negrar, Verona;
- Infectious and Tropical Diseases Unit, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence;
- Istituto Superiore di Sanità, Rome;
- Unitá Operativa Parassitologia, Dipartimento di Scienze di Sanità Pubblica, Policlinico Umberto I, Rome;
- Istituto Nazionale di Malattie Infettive Lazzaro Spallanzani, Rome;
- Policlinico San Matteo, Pavia.

There are no systems for internal and external quality control of laboratories.

There are no routine checks performed in blood banks.

The following tests are used for serological screening and diagnosis in hospitals:

The Centre for Tropical Diseases, Ospedale Sacro Cuore, Negrar, Verona uses two serological tests (commercial kits): a recombinant ELISA (Biokit) and a particle agglutination test (Id-Pagia) (2001–2009) or IFA (2001–2007) or an immune chromatographic test (Chagas ICT Cypress) (2009 to present). Parasitological diagnosis is available through microhaematocrit and a Quantitative Buffy Coat (QBC) test. Molecular diagnosis is available through PCR (U.O. Parassitologia, Dept. Sc. Sanità Pubblica, Rome and CRESIB, Barcelona)

The Infectious and Tropical Diseases Unit, A.O.U Careggi, University of Florence, uses three serological tests (commercial kits): a recombinant ELISA (Biokit), a conventional ELISA (2007–2008 DRG, 2008–2009 Novatec, currently Ortho) and an immune chromatografic test (Chagas ICT Cypress) (2007 up to now). Molecular diagnosis is done through a PCR by external laboratory (U.O. Parassitologia, Dept. Sc. Sanità Pubblica, Policlinico Umberto I, Rome and University of Barcelona).

Other centres use the following tests:

Istituto Superiore di Sanità, Rome: in-house IFA
Policlinico San Matteo, Pavia: recombinant ELISA and ICT
U.O. Parassitologia, Dept. Sc. Sanità Pubblica, Policlinico Umberto I, Rome: Chagas ICT Cypress, PCR in-house
Istituto di Malattie Infettive Lazzaro Spallanzani, Rome: IFA

There is no panel of well characterized sera available to evaluate the serological tests performed by the reference laboratories.

Health services

There are two specific health centres for the medical care of patients:

- Centre for Tropical Diseases, Ospedale Sacro Cuore, Negrar (Verona)
- Infectious and Tropical Diseases Unit, AUO Careggi, University of Florence (Florence).

Other services

There is no drug distribution system, but medicines are available at the Centre for Tropical Diseases, provided by WHO and Infectious and Tropical Disease Unit, AOU Careggi, University of Florence, Florence, through Red de Salud Cordillera, Health Department of Santa Cruz, Plurinational State of Bolivia.

Information and surveillance system

Chagas disease is notifiable as an infectious disease, but notification is not mandatory. Screening of family members of diagnosed patients (for example, the children of seropositive mothers) has not been formalized.

Information, education and communication

In Negrar (Verona), educational activities have been organized with the Bolivian Adoptees Association (in Bergamo) during the last few years. A workshop was organized during the 6th European Congress on Tropical Medicine and International Health (held in Verona on 6–10 September 2009).

In January 2008, an international conference on “Focus sulla Malattia di Chagas: Patologia Emergente di Interesse Multidisciplinare” was held in Florence. A hospital seminar named “Programma per lo screening e il trattamento della Malattia di Chagas” in January 2009.

In September 2008, a seminar on “La Malattia di Chagas: invisibile, emergente, multidisciplinare” was held in Rome at the Policlinico Umberto I Hospital.

Additional information

There is no information about protocols or laws on Chagas disease in Italy.

There is no information about any association of Chagas disease patients in Italy.

Sources: Hospital “Sacro Cuore – Don Calabria”, Negrar, Verona, Italy; Careggi Hospital, University of Florence, Florence, Italy; Centre for Tropical Diseases, Istituto Superiore di Sanità, Rome, Italy; Policlinico “Umberto I”, University "La Sapienza", Rome, Italy; National Institute for Infectious Diseases “Lazzaro Spallanzani”, Rome, Italy; Policlinico S. Matteo, Pavia, Italy.

Epidemiological information

There are 35 211 registered Latin American immigrants in the Netherlands. The total expected infected people is based on local prevalence (Table 1NET). The estimated number of infected pregnant women per year is 18. The estimated number of infected newborns per year is 2.

Number of Latin American immigrants	**35 211**
Estimated number of cases of *T. cruzi* infection	**480**
Number of laboratory-confirmed cases	**7**
Number of pregnant women with *T. cruzi* infection	**18**
Number of cases of congenital transmission	**2**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

Table 1NET. Estimated number of cases of *T. cruzi* infection (data are based on numbers of legal immigrants; they do not include non-legal immigrants or immigrants from the Netherlands Antilles, Suriname and the Guyanas. When estimates of these groups are also included, the range of seropositive cases in the Netherlands ranges from 819 to 1739).

Country	Number of legal immigrants[a]	Local prevalence	Estimated number infected
Argentina	2385	4.13%	99
Belize	18	0.74%	0
Bolivia (Plurinational State of)	598	6.75%	40
Brazil	10074	1.02%	103
Chile	2703	0.99%	27
Colombia	7273	0.96%	70
Costa Rica	474	0.53%	3
Ecuador	1582	1.74%	28
El Salvador	305	3.37%	10
Guatemala	340	1.98%	7
Honduras	271	3.05%	8
Mexico	2514	1.03%	26
Nicaragua	319	1.14%	4
Panama	231	0.01%	0
Paraguay	146	2.54%	4
Peru	2902	0.69%	20
Uruguay	589	0.66%	4
Venezuela (Bolivarian Republic of)	2487	1.16%	29
Total	**35 211**		**480**

[a] Data as of 31 December 2008.

Sources: Centraal Bureau voor de Statistiek, Den Haag/Heerlen, The Netherlands; Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; Harbour Hospital, Rotterdam, The Netherlands; VU University Medical Center, Amsterdam, The Netherlands; National Institute of Public Health and the Environment, Bilthoven, The Netherlands.

All of the 7 cases of Chagas disease diagnosed in the Netherlands have chronic infection: 3 patients were observed at the Academic Medical Centre (AMC – Amsterdam), 1 at the Harbour Hospital (Rotterdam), 1 in the Free University (Amsterdam) and 2 at the National Institute of Public Health and the Environment (RIVM – Bilthoven). Of the 7 cases, 2 were symptomatic cases (1 with cardiomyopathy, the other with megaoesophagus). Of the remaining 5 patients, 2 presented with chest pain and 1 had gastrointestinal complaints. In none of these 3 patients could a causal relationship between symptoms and *T. cruzi* infection be established. No clinical data were available for 2 seropositive patients. All the seropositive patients were assumed to be immunocompetent. In 1 case, congenital infection was suspected; in the other cases, transmission of the infection was assumed to have been vector-borne.[20]

There is no information about the treatment offered to the seropositive cases.

Pharmacovigilance

There is no national pharmacovigilance system or centre in place to report adverse events associated with treatment using nifurtimox and benznidazol. No information is available on adverse events associated with nifurtimox and benznidazol.

Prevention of infection and early detection of congenital cases

There is no systematic detection system of congenital infection.

Only known Chagas disease patients are excluded from donating blood for transfusions or organs, tissues and cells for transplantation.

Travel medicine

Travel clinics offer voluntary counselling to travellers prior to their trips to Latin America. Chagas disease is also included in the differential diagnosis in the consultations given by some specialized travel clinics after these trips.

Laboratory diagnosis

Currently, one centre (the RIVM) offers serodiagnosis of Chagas disease using one serodiagnostic test (details of test not provided).

It is foreseen that in 2010 both molecular diagnosis and the three serodiagnostic tests (Chagas Stat-Pak, Ortho ELISA and TESA Western Blot) will be operational at the Section Clinical Parasitology at the AMC. Microscopic diagnosis is presently already available at the AMC and other laboratories.

There is no internal or external system of laboratory quality control.

Tests used for serological screening and confirmation in blood banks

Blood banks do not screen for Chagas disease at present.

Tests used for serological screening and diagnosis in hospitals (i.e. pregnant women)

No tests are currently in use. Screening and diagnostic facilities are expected to be fully operational in 2010 in the AMC.

[20] Marcu CB, Beek AM, Van Rossum AC. Chagas' heart disease diagnosed on MRI: the importance of patient "geographic" history. *International Journal of Cardiology*, 2007, 117(2):e58–60.

Health services

The AMC provides multidisciplinary care for patients with Chagas disease.

Contacts between the Dutch blood bank (Sanquin) and the AMC enable proper referral.

There is no information on the availability of a panel of well characterized sera in the RIVM.

Other services

Drug distribution

Information on benznidazol and nifurtimox in the Netherlands has not been ascertained.

Information and surveillance system

There is no information and surveillance system for information about diagnosed cases.

Information, education and communication

No information, education and communication activities are carried out specifically for Chagas disease.

Protocols and laws

There are no protocols for Chagas disease in the Netherlands.

Additional information

The AMC has a multidisciplinary team for clinical care of patients with Chagas disease. Expert diagnosis (three serological tests and molecular tests) are expected to be available in 2010.

Epidemiological information

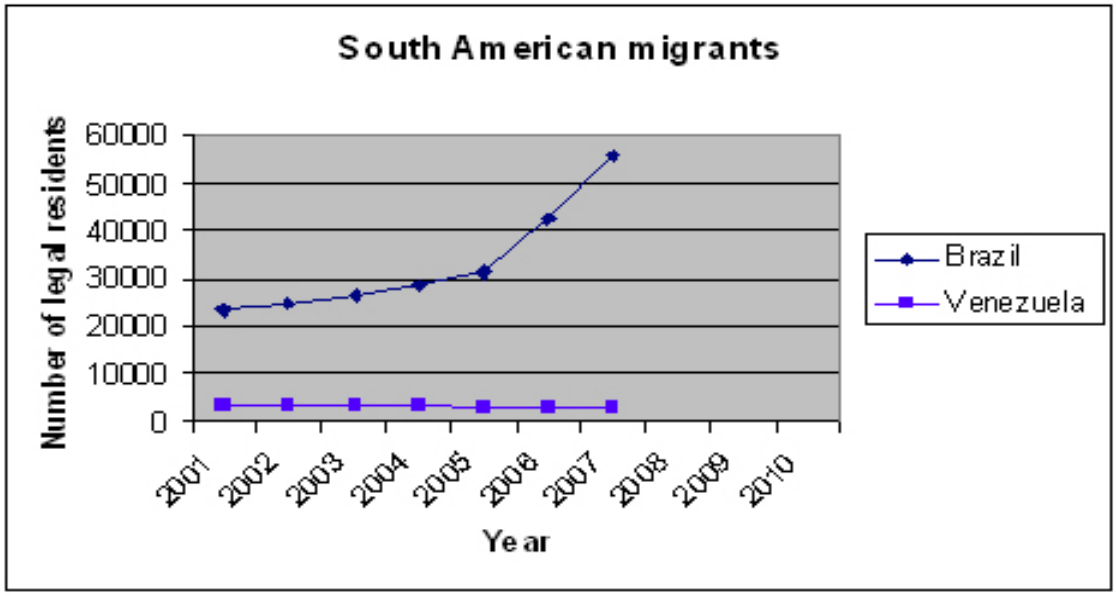
In 2009, there were an estimated 83 000 legal Latin American immigrants living in Portugal: 80 000 from Brazil and 3000 from the Bolivarian Republic of Venezuela. In 2007, there were 55 665 and in 2008 there were 3 177. The number of Venezuelan immigrants has remained stable from 2001 to 2008, while the number of Brazilian migrants has increased, especially since 2005[21] (Table 1POR).

There is no information about the number of illegal Latin American immigrants.

Number of Latin American immigrants	**83 000**
Estimated number of cases of *T. cruzi* infection	**850**
Number of laboratory-confirmed cases	**8**
Number of pregnant women with *T. cruzi* infection	**50**
Number of cases of congenital transmission	**2**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

Table 1POR. Number of legal migrants in Portugal of Brazilian and Venezuelan origin, 2001–2007



According to estimates published by PAHO in 2006[22] of the estimated prevalence rate of *T. cruzi* infection in Brazil (1.02%) and the Bolivarian Republic of Venezuela (1.16%), there were 850 infected people living in Portugal in 2009: 816 from Brazil and 34 from the Bolivarian Republic of Venezuela.

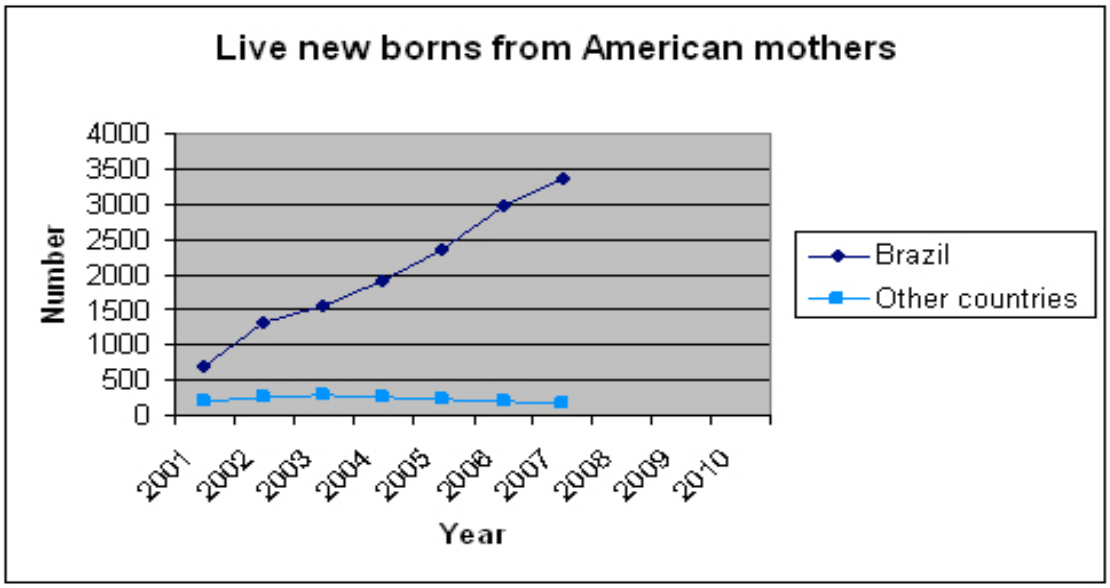
In 2007, there were 3 355 live newborns born to Brazilian women living in Portugal.[1] The estimation for 2009 is 3 750. Based on the PAHO estimates of *T. cruzi* infection in Brazil (1.02%) in 2005, the number of infected pregnant Brazilian women in 2009 is 38.25. In 2007, the reported number of live newborns from other Latin American countries was 191. The estimate for 2009 is 200. Based on the estimated prevalence of *T. cruzi* infection in the Bolivarian Republic of Venezuela (1.16%) in 2005, the number of infected pregnant Venezuelan women in 2009 is 2.32. The total number of estimated pregnant women infected with *T. cruzi* in Portugal in 2009 is 40.57.

[21] Carrilho MJ, Patricio L. A Situação Demográfica Recente em Portugal [Recent demographical situation in Portugal]. *Revista de Estudos Demográficos* 2008, 44:35–80.

[22] Pan American Health Organization, WHO Department of Control of Neglected Tropical Diseases. 2006. *Estimación cuantitativa de la enfermedad de Chagas en les Américas* [in Spanish]. Montevideo, Uruguay, OPS/HDM/CD/425-06.

Following the evolution of the number of Latin American migrants in Portugal, the number of live newborns from Brazilian mothers has increased constantly in 2001–2008, while the number of live newborns from other Latin American countries has remained stable (Table 2POR).

Table 2POR. Number of live newborns born to Latin American mothers living in Portugal, 2001–2007



Assuming an average rate of congenital transmission of 5% among the total number of estimated pregnant women infected with *T. cruzi* (40.57) in Portugal, there were an estimated 2 cases of congenital transmission in Portugal in 2009.

In the past 15 years, 3 patients have received medical care for *T. cruzi* infection at the Institute of Hygiene and Tropical Medicine (IHTM) in Lisbon. All 3 patients were Brazilian, aware of their infection and presented with an indeterminate form of the chronic phase. Follow-up was not possible for logistic reasons. Vector transmission was the probable route of infection in all 3 cases. No additional cases from Lisbon are known, but not all infectious disease services had been contacted by the time this report was written.

Information about cases of *T. cruzi* infection was collected from infectiologists in the cities of Coimbra, Porto and Faro. In Porto, Chagas disease was diagnosed in 2 patients: 1 patient had severe Chagasic cardiomyopathy and was scheduled for heart transplantation but died before undergoing surgery; the characteristics and outcome of the other patient are unknown. In Coimbra, 3 cases were diagnosed: 2 cases presented an indeterminate form of chronic infection; the other had severe Chagasic cardiomyopathy and died. All 3 patients were Brazilians who knew their Chagas disease diagnosis. No cases have been reported so far from other Portuguese cities. Consequently, the total number of Chagas disease laboratory-confirmed cases in Portugal is 8.

There are not reports of patients receiving treatment with nifurtimox or benznidazol.

Pharmacovigilance

Since benznidazol and nifurtimox have not yet been used to treat any Chagas disease patients, there is no information about pharmacovigilance.

Prevention of infection and early detection of congenital cases

There is no systematic detection of congenital infection in Portugal.

Although epidemiological screening through a pre-donation questionnaire is recommended in Portugal, there are no standardized specific questions about Chagas disease and they are not universally used. No systematic blood screening of donors is performed.

The Histocompatibility Centre in Lisbon is aware of the Chagas disease problem and sends blood samples from donors and donation recipients suspected of having *T.cruzi* infection for screening to the IHTM. No information is available from other histocompatibility centres in Portugal.
Most pre-travel medicine advisers mention the risk of *T. cruzi* infection and Chagas disease. There is increasing awareness among health workers of Chagas disease in the differential diagnosis of returning travellers since participating in the course on travel medicine held at the IHTM.

Laboratory diagnosis

The IHTM laboratory performs a commercial recombinant ELISA test, a commercial indirect immunofluorescence assay and an in-house qualitative PCR.

There are no routine checks performed in blood banks.

There is no systematic external laboratory quality control and no panel of well characterized sera available for the evaluation of serological tests.

Health services

Usually, patients with Chagas disease are referred for hospital consultation by their general practitioners and are attended to by specialists with or without the collaboration of the referring general practitioner.

There is no general referral system between blood banks and laboratory and clinical services in Portugal, but a specific agreement is in place between the Lisbon Regional Centre of Blood of the Portuguese Institute of Blood and the Infectious Disease Service at the University Hospital of Santa Maria.

Other services

There is no national drug distribution system in Portugal. Etiological drugs have to be obtained through a hospital pharmacy for each specific patient with a temporary drug use licence.

There is no Chagas disease information and surveillance system and no information, education and communication activities are carried out in Portugal.
There is no information and surveillance system.

Protocols and laws

There is no information about protocols for Chagas disease in Portugal.

The Decreto-Lei n.º 267/2007[23] transcribes the European Union 2004/33/CE directive into the Portuguese law for blood donations. There are not national or local directives for control activities or patient management.

Additional information

There is no information about any association of Chagas disease patients in Portugal.

Sources: Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Lisbon, Portugal; Hospital Egas Moniz, Lisbon, Portugal; Hospitais Universitários de Coimbra, Coimbra, Portugal; Hospital de Faro, Faro, Portugal; Hospital de São João, Porto, Portugal.

[23] Decreto-Lei, Numéro: Decreto-Lei n.º 267/2007; Journal officiel: Diaro da Republica, Numéro: D.R. n.º 141, Date de publication: 24/07/2007, Page: 04696-04717; Référence: (MNE(2007)55697).

A case of asymptomatic Chagas disease in a 5-year-old child, probably caused by congenital transmission, was published in 1981. The child was born in Romania in 1975 and had never visited an area endemic for Chagas disease.[24]

Number of Latin American immigrants	**ND**
Estimated number of cases of *T. cruzi* infection	**ND**
Number of laboratory-confirmed cases	**1**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**ND**
Number of patients treated with benznidazol and nifurtimox	**ND**

ND = not determined

[24] Pehrson PO, Wahlgren M, Bengtsson E. Asymptomatic congenital Chagas' disease in a 5-year-old child. *Scandinavian Journal of Infectious Diseases*, 1981, 13(4):307–308.

Epidemiological information

According to the Municipal Register, the values of which are higher than the official numbers of legal immigrants, the estimated number of Latin American immigrants was 1 445 571 as of September 2009[25] (Table 1SPA).

An estimated 39 985-65 258 Latin American immigrants were infected with *T. cruzi* (Table 2SPA).

Number of Latin American immigrants	**1 445 751**
Estimated number of cases of *T. cruzi* infection	**39 985–65 258**
Number of laboratory-confirmed cases	**3 617**
Number of pregnant women with *T. cruzi* infection	**914–1 656**
Number of cases of congenital transmission	**41–121**
Number of patients treated with benznidazol and nifurtimox	**195**

ND = not determined

Table 1SPA. Estimated number of Latin American immigrants in Spain by country of origin in 2009

Country of origin	Immigrants up to January 2009[a]	Legal immigrants up to September 2009[b]
Argentina	193 746	102 715
Bolivia (Plurinational State of)	220 150	111 638
Brazil	127 847	54 365
Chile	48 896	29 615
Colombia	292 748	288 255
Ecuador	402 088	441 455
Paraguay	79 470	27 602
Peru	138 555	143 405
Uruguay	61 769	34 254
Venezuela (Bolivarian Republic of)	64 242	39 808
Costa Rica	1 888	909
Cuba	56 264	51 414
Dominica	520	362
El Salvador	5 595	2 853
Guatemala	4 007	1 631
Honduras	24 260	9 312
Nicaragua	10 625	3 270
Panama	2 350	1 203
Dominican Republic	85 650	86 007
Mexico	25 398	15 269
Rest of Latin America	1 103	409
Total	**1 847 171**	**1 445 751**

[a] www.ine.es (Statistical use of the Municipal Register), http://www.ine.es/en/prensa/np551_en.pdf
[b] http://extranjeros.mtas.es/es/InformacionEstadistica/

[25] See press release issued by the Instituto Nacional de Estadística [National Statistics Institute] dated 3 June 2009 (available at http://www.ine.es/en/prensa/np551_en.pdf; accessed May 2010).

The number of births to mothers from endemic areas was assumed to be the same as the number of pregnant women.[26] The number of infected pregnant women was estimated according to previously reported prevalence rates (Table 3SPA). The estimated number of infected newborns is 41–121. (Table 4SPA).

Table 2 SPA. Estimated number of infected people by country of origin

Origin	Immigrants	Prevalence[a]	Estimates of infected immigrants
Argentina	193 746	4.13	8 002
Bolivia (Plurinational State of)	220 150	6.75–18.2[b]	14 860–40 133
Brazil	127 847	1.02	1 304
Chile	48 896	0.99	484
Colombia	292 748	0.96	2 810
Costa Rica	1 888	0.53	10
Ecuador	402 088	1.74	6 996
El Salvador	5 595	3.37	189
Guatemala	4 007	1.98	79
Honduras	24 260	3.05	740
Mexico	25 398	1.03	262
Nicaragua	10 625	1.14	121
Panama	2 350	0,01	0
Paraguay	79 470	2.54	2 019
Peru	138 555	0.69	956
Uruguay	61 769	0.66	408
Venezuela (Bolivarian Republic of)	64 242	1.16	745
Total			**39 985–65 258**

[a] Pan American Health Organization, WHO Department of Control of Neglected Tropical Diseases. 2006. *Estimación cuantitativa de la enfermedad de Chagas en les Américas* [In Spanish]. Montevideo, Uruguay, OPS/HDM/CD/425-06.
[b] Prevalence in Bolivian blood donors in Spain 2002–2006, National Centre for Microbiology (CNM).

[26] www.ine.es (vital statistics).

Table 3SPA. Estimated number of pregnant women and infected pregnant women in 2005, 2006, 2007 and 2008 in Spain

Country	2005		2006		2007		2008	
	Pregnant women	Infected pregnant women	Pregnant women	Infected pregnant women	Pregnant women	Infected pregnant women	Pregnant women	Infected pregnant women
Argentina	2 341	97	2 451	101	2 553	105	2 507	104
Bolivia (Plurinational State of)	2 995	202–545	4 207	284–766	6 476	437–1 179	6 478	437–1 179
Brazil	1 454	15	1 956	20	2 634	27	3 188	33
Chile	503	5	597	6	627	6	699	7
Colombia	5 006	48	4 770	46	5 115	49	5 314	51
Ecuador	9 950	173	9 088	158	9 348	163	9 503	165
Honduras	178	5	251	8	429	13	664	20
Mexico	381	4	427	4	486	5	537	6
Paraguay	493	13	843	21	1 538	39	2 197	56
Peru	1 526	11	1 886	13	2 061	14	2 440	17
Uruguay	686	5	741	5	756	5	807	5
Venezuela (Bolivarian Republic of)	795	9	955	11	1 090	13	1 191	14
Total	**26 308**	**586–929**	**28 172**	**677–1159**	**33 113**	**876–1618**	**35 525**	**914–1 656**

Table 4SPA. Estimated number of newborns infected with *T. cruzi* in 2005, 2006, 2007 and 2008 in Spain

Year	Estimated number of newborns born to infected pregnant women	Expected number of infected newborns[a]	
		4.5%	7.3%
2005	586–929	26–42	43–68
2006	677–1159	30–52	49–85
2007	876–1618	39–73	64–118
2008	914–1656	41–75	67–121

[a] Rates of congenital transmission according to CNM data and Muñoz et al. (2009) *Clinical Infectious Diseases*, 48:1736–1740.

Autochthonous cases

Congenital cases

2005–2009 Catalonia: 5 cases (4 acute cases and 1 chronic case)[27,28,29]

2004–2009 CNM: 18 cases (Valencia, Murcia, Madrid, Malaga, Zaragoza, Basque Country)

Transfusional cases

6 cases (3 acute cases and 3 chronic cases): Cordoba (1), Madrid (1), Galicia (1), Malaga (2), Basque Country (1)).

(Source: *Chagas disease and blood donation*. Secretariat General for Health; available at http://www.msps.es/profesionales/saludPublica/medicinaTransfusional/publicaciones/docs/InformeChagasInglesJul09.pdf; accessed May 2010).

[27] Riera C et al. Congenital transmission of *Trypanosoma cruzi* in Europe (Spain): a case report. *American Journal of Tropical Medicine and Hygiene*, 2006, 75:1078–1081.

[28] Muñoz J et al. Congenital *Trypanosoma cruzi* infection in a non-endemic area. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2007, 101:1161–1162.

[29] Muñoz J et al. Prevalence and vertical transmission of *Trypanosoma cruzi* infection among pregnant Latin American women attending 2 maternity clinics in Barcelona, Spain**.** *Clinical Infectious Diseases*, 2009 June 15, 48(12): 1736–1740.

Imported cases

Catalonia

480 cases followed at the Hospital Clinic in Barcelona[30,31]

202 laboratory-confirmed cases (2004–2007)

asymptomatic (72%)

cardiac disease (19%)

digestive disease (9%)

46 other cases[3]

405 cases at Unitat de Medicina Tropical i Salut International Drassanes

441 cases from other Catalonian hospitals (data collected by Direcció General de Salut Pública and Agència de Salut Pública de Barcelona).

Murcia

The first 418 diagnosed cases[32] presented with the following clinical forms:

asymptomatic (57.3%)

cardiac disease (14.6%)

cardiac and digestive disease (12.5%)

digestive disease (15%)

To date, more than 700 cases have been diagnosed.

Rest of Spain

1 693 cases (CNM data as of August 2009). This figure may be overestimated because:

(i) immigrants move around Spain,

(ii) CNM is a reference centre and confirms cases from different hospitals including some Catalonian and Murcian hospitals.

Of 357 patients who were diagnosed at the Hospital Ramón y Cajal, Madrid, clinical data were available for 252 (71%).[33]

43 out of 252 had (17.1%) cardiac disease

4 out of 252 (1.6%) had cardiac and digestive disease

9 out of 252 (3.5%) digestive disease

4 out of 252 (1.6%) asymptomatic patients (coinfected with HIV)

3 out of 252 (1.2%) patients coinfected with HIV (one case was a reactivation with *T. cruzi* infection of the central nervous system).[34]

Most confirmed cases of *T. cruzi* infection are being treated and followed up. Of 195 patients who received treatment with benznidazol, 189 (97%) were Bolivians in their 40s (median age, 36 years; interquartile range, 16–69), 137 (70%) were women, 152 (78%) were from rural areas where 126

[30] Muñoz J et al. Clinical profile of *Trypanosoma cruzi* infection in a non-endemic setting: immigration and Chagas disease in Barcelona (Spain). *Acta Tropica*, 2009, 111(1):51–55.

[31] Soriano Arandes A. et al. Prevalence of Chagas disease in the Latin American immigrant population in a primary health centre in Barcelona (Spain). *Acta Tropica*, 2009 November; 112(2):228–230.

[32] Las enfermedades olvidadas se hacen visibles en el Primer Mundo, donde afectan ya a 50 millones de personas [The neglected diseases become visible in the First World, where there are already 50 million people affected]. *Boletín Fundación BBVA*, 2010, No. 21.

[33] Perez de Ayala et al. Chagasic cardiomyopathy in immigrants from Latin America to Spain. *Emerging Infectious Diseases*, 2009, 15(4):607–608.

[34] Rodríguez-Guardado A et al. Cribado de enfermedad de Chagas en pacientes inmigrantes VIH positivos procedentes de zonas endémicas [Screening for Chagas disease in immigrant patients with HIVcoming from endemic areas]. *Enfermedades Emergentes*, 2009, 11(1):16–17; Torrus D et al. Afectación cerebral por Trypanosoma cruzi en paciente con SIDA. [Cerebral involvement by *Trypanosoma cruzi* in a patient with HIV]. *Enfermedades Emergentes*, 200911(1):51.

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(83%) had seen the vector and 90 (59%) had other infected relatives. There have been no cases of reactivation due to immunosuppression.

Pharmacovigilance

The pharmacovigilence system is not used for benznidazol or nifurtimox.

Adverse reactions to benznidazol have been documented in a series of observations (Table 5SPA).

Table 5SPA. Adverse events reported in Chagas disease patients treated with benznidazol

Reference	No. of patients treated	Patients with adverse events	Type of adverse event
Ramos JM et al. (2009) TM&IH 14 (Suppl. 2): 240	35	14 (7 interrupted)	Cutaneous rash, 8 (23%) Gastrointestinal symptoms, 3 (8.6%) Polyneuropathy 2 (5.7%) Hepatitis 1 (2.8%)
Soriano A et al. (2009) Acta Trop. 112:228-230	5		Headache, urticariform rash, anorexia
Pérez de Ayala A et al. (2009) MSPS pp. 1-84	90	35 (18 interrupted)	Cutaneous rash, 28 (31.1%) Gastrointestinal symptoms, 9 (10%) Polyneuropathy, 2 (2.2%) Transitory leukopenia, 1 (1.1%)

Among 195 patients treated with benznidazol at Hospital Ramón y Cajal, 154 (79%) were evaluable (completed therapy or discontinuation for adverse reactions): 83 (53.9%) presented an adverse reaction graded according to the National Cancer Institute, Cancer Therapy Evaluation Program, Common Toxicity Criteria Ver. 2.0:

Grade 1: 38 patients (45.8%)
Grade 2: 37 patients (44.6%)
Grade 3: 7 patients (8.4%)
Grade 4: 1 patient (1.2%)

Altogether, 42 out of 154 patients (27.3%) discontinued benznidazol and 3 patients (1.9%) received second-line treatment with nifurtimox, which was well tolerated in all cases.

Prevention of infection and early detection of congenital cases

There is no systematic detection of congenital infection at the national level. Only the Valencian Community has introduced a regulation for the serological screening of pregnant women from endemic areas (since October 2007).[35] The regulation attempts the early detection of congenital *T. cruzi* infection.

In Catalonia, systematic detection of congenital infection is due to be implemented in February 2010:[36]

systematic detection of infected pregnant women in at-risk populations.
screening of all newborns from infected pregnant women.
screening of the other children of infected pregnant women.

In the rest of Spain, the detection of congenital cases of Chagas disease relies on the initiative of health professionals in the national health system. In Madrid, detection is carried out according to a

[35] http://www.sp.san.gva.es/DgspPortal/docs/CIRCULAR_3_2007.pdf
[36] (http://www.gencat.cat/salut/depsalut/html/ca/dir2384/protchagas2010.pdf)

consensus document elaborated by the Working Group on Chagas Disease of the Madrid Autonomous Community.[37]

Transfusional transmission

Mandatory screening of blood donors at risk for *T. cruzi* infection has been implemented since October 2005 for:[38]

donors born in endemic areas
donors born to mothers born in endemic areas
recipients of blood transfusions in endemic areas.

Although not included in the Royal Decree, blood banks also screen individuals who have resided in, but were not necessarily born in, endemic areas.

Transmission via organs, tissue and cell transplantation

A Spanish law regulates the activity of tissue banks.[39] The Royal Decree demands that Chagas disease screening must be performed in some risk situations, without specifying these situations.

In addition, recipients of organs from infected donors receive specific prophylactic treatment to prevent *T. cruzi* infection. Alternatively, recipients are followed up for early detection of infection and further treatment as appropriate.

Under the National Plan for Cord Blood Donations,[40] screening for Chagas disease is mandatory for:

donors born in endemic areas
donors born to mothers born in endemic areas
recipients of blood transfusions in endemic areas.

Screening for *T. cruzi* infection is mandatory in suspected donors in accordance with the Consensus Document on Organ Donors' Infections.[41]

Travel medicine

The Centres of International Vaccination provide the necessary advice to the travellers. The Units of Tropical Medicine from the main hospitals of the national health system also provide counselling before the trip and differential diagnosis and specific care after the trips, when they are needed.

Laboratory diagnosis

The Parasitology Department of the National Centre for Microbiology (ISCIII) serves as the national reference laboratory for serological, parasitological and molecular diagnosis of *T. cruzi* infection.

Reference laboratories for serological and parasitological diagnosis are available in the autonomous communities of Asturias, Basque Country, Catalonia, Murcia and Valencia.

In Catalonia and Murcia, molecular diagnosis is also available.

[37] http://www.se-neonatal.es/upload/files/Documento_Consenso_Chagas_2008.pdf
[38] Ministerio de Sanidad y Consumo – Real Decreto 1088/2005, de 16 de septiembre, por el que se establecen los requisitos técnicos y condiciones mínimas de la hemodonación y de los centros y servicios de transfusión [Royal Decree 1088/2005 of 16 September establishing the minimum technical requisites and conditions for blood donation and for blood transfusion centres and services]. *Boletín Oficial del Estado*, 2005, 225, 31288–31304.
[39] http://www.ont.es/legislacion/ficherosPDF/RD1301.pdf
[40] http://www.ont.es/infesp/Paginas/PlanNacionalSCU.aspx
[41] http://www.ont.es/consenso/ficheros/dc1.pdf.

Serological screening in hospitals is performed by rapid tests as the first choice and/or commercial ELISA or IFA.

In Catalonia, suspected cases are confirmed using western blot with parasite total antigen. In other parts of Spain, such cases are periodically followed up using two serological tests and PCR for at least two years.

There are systems of internal quality control, but there are no external systems.

Tests used for serological screening and confirmation in blood banks

Table 6SPA summarizes the serological tests used in blood banks; Table 7SPA details the tests used in screening and confirmation. Most blood banks use commercial tests. Those blood banks with a low number of Latin American donors send the samples to the Centro Nacional de Microbiología (CNM).

Table 6SPA. Serological tests used in blood banks

Blood Banks CCAA[a]	Test
Andalucía	Certest ELISA, TEST ELISA PARA CHAGAS III (BiosChile) Abbott
Aragón	Simple Chagas WB, Operon S.A.
Asturias	Ortho® *T. cruzi* ELISA test system
Baleares	DiaMed-ID PaGIA[b]
Canarias	Novagnost™ Chagas IgG (NovaTec Immundiagnostica GmbH)
Cantabria	DiaMed-ID PaGIA[b]
Castilla y León	ELISA + IFA CNM
Castilla La Mancha	Donor deferral. No testing
Cataluña	bioelisa Chagas (biokit)
Comunidad Valenciana	Novagnost™ Chagas IgG (NovaTec Immundiagnostica GmbH)+ Inmunofluor Chagas (Biocientífica)
Extremadura	Donor deferral. No testing
Galicia	Ortho® *T. cruzi* ELISA test system
Madrid (CT-CRE)	bioelisa Chagas (biokit) + Certest ELISA, TEST ELISA PARA CHAGAS III (BiosChile) Abbott
Madrid (CTCM)	ABBOTT PRISM Chagas
Murcia	Ortho® *T. cruzi* ELISA test system
Navarra	ELISA + IFA (CNM)
País Vasco	bioelisa Chagas (biokit)+ Certest ELISA, TEST ELISA PARA CHAGAS III (BiosChile)-Abbott
Rioja	ELISA + IFA (CNM)

[a] CCAA, Autonomous Community
[b] DiaMed-ID PaGIA is not manufactured any more. Former users of this test are changing to different ELISA kits.

Tests used for serological screening and diagnosis in hospitals

Many hospitals of the national health system send samples from patients to reference laboratories for diagnosis and confirmation of *T. cruzi* infection. Table 7SPA summarizes the serological tests used in hospitals.

Table 7SPA Serological tests used in blood banks and hospitals for screening and confirmation of *T. cruzi* infection

Test name	Company/laboratory	Blood banks	Hospitals	Screening	Confirmation
IFA Tc in-house	CNM, ISCIII, Madrid			Yes[a]	Yes[a]
ELISA Tc in-house	CNM, ISCIII, Madrid/Fac. Farmacia, Barcelona			Yes[a]	Yes[a]
Western blot in-house	Fac. Farmacia, Barcelona				Yes[a]
Inmunofluor Chagas (Biocientífica)	Inverness Medical	Yes	Yes		Yes
Chagas ELISA (Vircell)	Inverness Medical		Yes	Yes	
Ortho® *T. cruzi* ELISA test system	Johnson & Johnson	Yes	Yes	Yes	Yes
Certest ELISA, TEST ELISA PARA CHAGAS III (BiosChile)	Abbott Laboratories	Yes	Yes	Yes	Yes
ABBOTT PRISM Chagas	Abbott Laboratories	Yes		Yes	
bioelisa Chagas (biokit)	Izasa	Yes	Yes	Yes	
Novagnost™ Chagas IgG (NovaTec Immundiagnostica GmbH)	Diasorin/Radim Ibérica/Siemens Healthcare Diagnostics	Yes	Yes	Yes	
Chagatest ELISA recombinante v.3.0.	Wiener Lab		Yes	Yes	
Simple Stick Chagas	Operon S.A.		Yes	Yes	
Simple Chagas WB	Operon S.A.	Yes	Yes	Yes	
OnSite Chagas Ab Combo Rapid Test (CTK Biotech)	Lab. Leti/Inverness Medical		Yes	Yes	

[a] In-house tests are used in some reference laboratories.

A panel of well characterized sera is available at CNM: Qpanel Brasil and CNM.

Health services

Primary health-care centres, hospitals, units of tropical medicine and international health units and centres (specialized in immigrants' health care). For example:

Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Hospital Clinic.
Unitat de Medicina Tropical I Salut International Drassanes, Barcelona.
Unidad de Medicina Tropical, Hospital Carlos III, Madrid.
Unidad de Medicina Tropical y Parasitología Clínica, Hospital Ramón y Cajal, Madrid.
Unidad Regional de Medicina Tropical, Hospital Universitario de la Arrixaca, Murcia.
Consulta de Salud Internacional, Hospital Virgen de Rocío, Sevilla.
Consulta de Enfermedades Importadas y Parasitología Clínica, Hospital General Universitario de Valencia, Valencia.
Consulta de Enfermedades Importadas y Parasitología Clínica, Hospital General Universitario de Alicante, Alicante.
Others.

Blood banks send positive serum samples to reference laboratories for confirmation. All seropositive donors are referred to the units of tropical medicine or to their reference hospital for confirmation of diagnosis and medical care if it is needed.

Other services

Drug distribution

Benznidazol is provided by the Ministry of Health and Social Affairs (Foreign Drugs Service).

Information and surveillance system

In Catalonia, an information and surveillance system to collect information on diagnosed cases is due to be implemented in February 2010 (http://www.gencat.cat/salut/depsalut/html/ca/dir2384/protchagas2010.pdf).

Information, education and communication

Public health programmes tailored to immigrants from Latin America are run by the tropical medicine units of Hospital Ramón y Cajal (Madrid), Hospital Virgen de la Arrixaca (Murcia) and Drassanes (Barcelona).

Training of health personnel is carried out during annual workshops on different aspects of Chagas disease organized in Barcelona by CRESIB, Hospital Clinic; specialized courses on parasitological and molecular diagnosis are offered by the National Centre of Tropical Medicine together with the National Centre for Microbiology (ISCIII).

Protocols and laws

Institutional, municipal, state/departmental/autonomic, national protocols

Consensus document on laboratory diagnosis
Gascon et al. (2005) Med. Clin. (Barc.) 125(6):230–235

Consensus document on management of chronic heart Chagas disease
Gascon et al. (2007) Rev. Esp. Cardiol. 60(3):285–293

Consensus document on management of gastroenterological Chagas disease
Pinazo et al. (2009) Gastroenterol Hepatol. Oct 17 [Epub ahead of print]

Consensus document on early detection of congenital cases:
http://www.se-neonatal.es/upload/files/Documento_Consenso_Chagas_2008.pdf

Management protocol of imported Chagas disease in the Valencian Community
http://www.matronas-cv.org/categorias-principales/documentos/profesionales/i/475/65/enfermedad-de-chagas-importada-protocolo-de-actuacion-en-la-comunitat-valenciana

National Plan of Cord Blood, National Transplant Organization
http://www.ont.es/noticiasHome/ficherosPDF/PNSCU.pdf

Consensus Document on Organ Donors' Infections
http://www.ont.es/consenso/ficheros/dc1.pdf

Review on Chagas disease and blood donation.
http://www.msps.es/profesionales/saludPublica/medicinaTransfusional/publicaciones/docs/InformeChagasInglesJul09.pdf

Guide for infectious diseases in immigrants.
http://www.msc.es/profesionales/saludPublica//prevPromocion/promocion/migracion/docs/estudioInmigracion.pdf

Local or national laws about Chagas disease

ROYAL DECREE 1088/2005, 16th September, establishing the technical requirements and minimum conditions of hemodonation, and transfusion Centres and services
http://www.msc.es/profesionales/saludPublica/medicinaTransfusional/legislacion/docs/RD_1088-2005.pdf

ROYAL DECREE 1031/2006, 10th November, regulating tissue bank activity.
http://www.ont.es/legislacion/ficherosPDF/RD1301.pdf

Control of congenital and perinatal infections in Valencian Community.
http://www.sp.san.gva.es/DgspPortal/docs/CIRCULAR_3_2007.pdf

Additional information

There are four associations of Chagas disease patients in the cities of Barcelona, Valencia, Murcia and Madrid. Asociación de Amigos de Personas con Enfermedad de Chagas (ASAPECHA).[42]

Sources: Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain; Hospital Universitario Ramón y Cajal, Madrid, Spain; Hospital Clínica Puerta de Hierro, Madrid, Spain; Hospital 12 de Octubre, Madrid, Spain; Hospital Carlos III, Madrid, Spain; Centro de Transfusión, Cruz Roja Española de Madrid, Spain; Hospital General Universitario de Alicante, Alicante, Spain; Hospital Clínic de Barcelona, Barcelona, Spain; Unitat de Medicina Tropical i Salut International Drassanes, Institut Català de la Salut, Barcelona, Spain; Consorci d'Atenció Primària de Salut de l'Eixample, Barcelona, Spain; Hospital Universitario Vall d'Hebron, Barcelona, Spain; Hospital Sant Joan de Déu, Barcelona, Spain; Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Hospital de Bellvitge, Barcelona, Spain; Facultat de Farmacia, Universitat de Barcelona, Barcelona, Spain; Unidad de Salud Internacional del Barcelonés Nord i Maresme (Santa Coloma de Gramenet), Barcelona, Spain; Hospital Universitario Reina Sofía, Córdoba, Spain; Hospital Virgen de la Luz, Cuenca, Spain; Hospital General de Elche, Elche, Spain; Hospital Santa Caterina, Girona, Spain; Hospital Regional Universitario Carlos Haya, Málaga, Spain; Hospital Universitario Virgen de la Arrixaca, Murcia, Spain; Hospital Universitario Central de Asturias, Oviedo, Spain; Hospital Universitario Virgen del Rocío, Sevilla, Spain; Consorcio Hospital General Universitario, Valencia, Spain; Complexo Hospitalario Universitario de Vigo, Vigo, Spain.

[42] http://www.asapecha-valencia.com/home, http://www.asapecha.entitatsbcn.net

SWEDEN

A case of congenital Chagas disease was published in 1982.[43] Intracranial calcifications were observed on examination at the age of 5 months.

It is estimated that there are approximately 58 196 Latin American immigrants in Sweden, of whom around 1 118 may be infected with *T. cruzi*.[44]

Number of Latin American immigrants	**58 196**
Estimated number of cases of *T. cruzi* infection	**1118**
Number of laboratory-confirmed cases	**1**
Number of pregnant women with *T. cruzi* infection	**ND**
Number of cases of congenital transmission	**1**
Number of patients treated with benznidazol and nifurtimox	**1**

ND = not determined

Sources: Karolinska Institute, Roslagstull Hospital, Stockholm, Sweden.

[43] Pehrson PO, Wahlgren M, Bengtsson E. Intracranial calcifications probably due to congenital Chagas' disease. *American Journal of Tropical Medicine and Hygiene*, 1982, 31(3):449–451.

[44] Guerri-Guttenberg RA et al. Chagas cardiomyopathy: Europe is not spared! *European Heart Journal*, 2008, 29:2587–2591.

SWITZERLAND

Epidemiological information

Number of Latin American immigrants	**35 000**
Estimated number of cases of *T. cruzi* infection	**3 000**
Number of laboratory-confirmed cases	**180**
Number of pregnant women with *T. cruzi* infection	**30**
Number of cases of congenital transmission	**5**
Number of patients treated with benznidazol and nifurtimox	**99**

ND = not determined

There are 35 000 registered Latin American immigrants in Switzerland and 30–60 000 undocumented Latin American immigrants, 6000–10 000 of whom are Bolivians. The expected number of infected people is approximately 2000–3000 (most Bolivians are undocumented, thus not precisely counted).

The first case of Chagas disease in Switzerland was diagnosed in Geneva in 1996.[45] Since then, 180 cases have been diagnosed as follows:

- 172 Bolivians, 4 Argentinians and 4 Brazilians
- 5 congenital cases,
- 175 chronic cases (35 of whom have cardiopathy and 2 have digestive involvement),
- 1 death following reactivation secondary to cardiac transplant and immunosuppressive treatment.

There has been no identified transmission by blood transfusion or organ transplant.

The estimated number of infected pregnant women per year is 25–50.
The estimated number of infected newborns per year is 0–5.

Altogether, 99 patients have received treatment (87 patients with nifurtimox and 12 with benznidazol): 5 acute cases occurred in children or neonates, 1 case reactivated following a cardiac transplant and 93 were adults in the chronic phase. All patients were Bolivians, except 2 Argentinians and 1 Brazilian.

* Sources: Hôpital cantonal universitaire de Genève, Geneva, Switzerland; l'Office fédéral de la statistique, Bern, Switzerland.

Jackson Y et al. Congenital transmission of Chagas disease in Latin American immigrants in Switzerland. *Emerging Infectious Diseases*, 2009, 15(4):601–603.

Martinez de Tejada B et al. Congenital Chagas disease in Geneva: diagnostic and clinical aspects. *Revue Medicale Suisse*, 2009, 5(222):2091–2096.

Jackson Y et al. Prevalence, Clinical staging and risk for blood-borne transmission of Chagas disease among Latin American migrants in Geneva, Switzerland. *PLoS Neglected Tropical Diseases*, 2010, 4(2):e592.

Pharmacovigilance

Swissmedics system has been informed of serious adverse effects in 3 cases (DRESS syndrome with nifurtimox)
1 myocarditis (nifurtimox)
1 anaphylaxis (nifurtimox)

Prevention of infection and early detection of congenital cases

[45] Sztajzel et al. Chagas' disease may also be encountered in Europe. *European Heart Journal*, 1996, 17:1289–1291.

Congenital cases

Systematic detection of congenital infection is carried out only at the maternity unit of the Geneva University Hospitals: serologies in pregnant mothers, chord blood parasitological detection and PCR if negative, newborn's serology at 9 months.[46]

Transfusional transmission

A questionnaire is used to screen potential donors for *T. cruzi* infection. If the answer to the question: "are you suffering from Chagas disease?" is positive, then the donation is rejected.

Organ, tissue and cell transplantation transmission

At present, there are no measures taken for infection prevention for organ, tissue and cell transplantation transmission.

Travel medicine

There is no standardized counselling for preventing the acquisition of Chagas disease in travellers.

Laboratory diagnosis

Diagnostic tests of high quality are done by two laboratories:
- Geneva University Hospitals: 2 serologies with Biokit ELISA Chagas, Chagas Stat pak rapid test, microscopic examination).
- Swiss Tropical Institute, Basel: Biokit ELISA Chagas, in-house IFA, PCR, microscopical examination)

Systematic laboratory quality control systems (internal and external) are in place in Geneva (external control is done by Professor Luquetti in Brazil). Internal quality control is performed in Basel.

Tests used for serological screening and confirmation in blood banks

At present, no tests are used for serological screening and confirmation in blood banks.

Tests used for serological screening and diagnosis in hospitals (i.e. pregnant women)

Screening:
Commercial kits: Chagas Stat-Pak, Chembio, USA
No in-house tests.

Diagnosis:
Commercial kits – Biokit ELISA, Biokit, Spain and in-house tests – IFA from killed epimastigotes (Swiss Tropical institute Basel) for discordant results.
Despite the availability of in-house tests, there is no panel of well characterized sera for the evaluation of such tests.

Health services

Several health centres in Switzerland provide medical care for Chagas disease patients, but specialist care is only available at the Geneva University Hospital's Department of Community Medicine and Primary Care.

[46] Jackson Y et al. Congenital transmission of Chagas disease in Latin American immigrants in Switzerland. *Emerging Infectious Diseases*, 2009, 15(4):601–603.

At present, there is no referral system between blood banks and laboratory and clinical services.

Other services

Drug distribution

There is no etiological drug distribution system in place in Switzerland and neither benznidazol nor nifurtimox are registered. Therefore, the availability of these two drugs depends on WHO (nifurtimox) or direct importation by local institutions (benznidazol). The drugs used require a special acceptance form from the national drugs administration (Swissmedics).

Information and surveillance system

There is no formal information and surveillance system in Switzerland; however, local monitoring is carried out in Geneva (by Dr Yves Jackson).

Information, education and communication

Information and education of laboratory technicians, medical students and residents is done at Geneva University Hospitals. Specialist information is disseminated during meetings and congresses.

Protocols and laws

A protocol for screening for congenital transmission is applied only at Geneva University Hospitals.

There are no laws concerning Chagas disease in Switzerland

Additional information

There is no association of Chagas disease patients in Switzerland, but a project is due to be implemented in Geneva.

UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN

Epidemiological information

Number of Latin American immigrants	**400 000**
Estimated number of cases of *T. cruzi* infection	**14 000**
Number of laboratory-confirmed cases	**28**
Number of pregnant women with *T. cruzi* infection	**50**
Number of cases of congenital transmission	**5**
Number of patients treated with benznidazol and nifurtimox	**0**

In 2007, a strategy paper on Latin America published by the Foreign and Commonwealth Office estimated that there were 700 000–1 000 000 Latin Americans visiting or living in the UK, including 200 000 Brazilians, 140 000 Colombians, 70–90 000 Ecuadorians and 10 000–15 000 Peruvians. These figures include visitors; estimates of those resident in the UK may be nearer 300 000–500 000. The majority of this population resides in London. A separate study has suggested that there may be around 20 000 Bolivians living in the UK. There are no data available on undocumented migrants, but official estimates should be taken to be underestimates of likely total numbers of Latin American residents in the UK.

Assuming an average *T. cruzi* seroprevalence rate of 1–5% among Latin American migrants, there are an estimated 3 000–25 000 with *T. cruzi* infection living in the UK. The seroprevalence rate may be higher among immigrants from highly endemic countries such as the Plurinational State of Bolivia.

Assuming that:

- 50% of the Latin American population in the UK is female;
- 75% of the population is aged 16–65 years, of whom 50% are of childbearing age;
- a crude birth rate of 20/1000 per year (in Latin America).

The crudely estimated number of infected women delivering babies each year ranges from approximately 10–100.

Using an estimated rate of vertical transmission of 0% to 10%, the crude estimates of infected newborns each year varies from 0 to 10. This number would vary with country of origin of the mother reflecting different seroprevalence rates.
Since 1987, there have been 28 diagnosed cases.

Table 1UK. Number of diagnosed cases of *T. cruzi* infection in the UK (data as of 21 December 2009)

	Total No.	Age range	No. males	Age range	No. females	Age range	No data
Argentina	2	39–54	0	X	2	39–54	
Bolivia (Plurinational State of)	13	28–64	8	28–64	5	40–45	
Brazil	2	57	2	57	0	X	
Chile	1	47	0	X	1	47	
Colombia	1	42	0	X	1	42	
Ecuador	1	46	1	46	0	X	
Uruguay	1	54	0	X	1	54	
Venezuela (Bolivarian Republic of)	1	54	0	X	1	54	
No data	6	45–58	4	45–58	1	53	1
TOTALS	28	28–64	15	28–64	12	39–54	1

Table 2UK. Cardiac status by Kuschnir classification	
ICD grade O	13
CCD grade I	4
CCD grade II	0
CCD grade III	3
No data	6
To be evaluated	1
Yet to present	1

The cardiac status of the 28 patients is summarized in Table 2UK.

Of the 28 cases, 3 were detected via national blood service screening; the rest were identified through clinical suspicion. All cases were imported and infection was presumed to have been vector borne. No patients have been treated so far. Treatment of one chronic case is scheduled for January 2010.

Sources: Health Protection Agency, London, UK; Hospital for Tropical Diseases, London, UK; National Health Service Blood and Transplant, London, UK

Pharmacovigilance

Since benznidazol and nifurtimox have not been used to treat any Chagas disease patients, there is no information on pharmacovigilance.

Prevention of infection and early detection of congenital cases

Congenital cases

There is no detection system at present, but advocacy is carried out for antenatal screening of at-risk mothers.

Transfusional transmission

The procedure for prevention of infection in the UK is the same as that for blood transfusions and tissue and cell transplantations. Pre-donation screening has been in place since 1999. All donors are questioned about all relevant risks at every donation. Those who are at risk of *T. cruzi* infection are dealt with according to the guidelines. If they have returned from a risk area <6 months ago, the donation is deferred. If they have returned >6 months ago, a donation is collected and screened prior to release (Table 3UK).

Table 3UK. Questionnaire about blood or cell donations

Obligatory – a donor must not donate if: Born in South America or Central America (including Southern Mexico, but not the Caribbean islands). Mother was born in South America or Central America (including Southern Mexico, but not the Caribbean islands). Has had a blood transfusion in South America or Central America (including Southern Mexico, but not the Caribbean islands). Has lived and/or worked in rural subsistence farming communities in these countries for a continuous period of 4 weeks or more.
Discretionary – a donor may donate and the donation may be used if: At least 6 months have elapsed following the date of the last exposure and a validated test for *T. cruzi* antibody is negative.

Organ, tissue and cell transplantation transmission

Only the known Chagas disease patients are excluded from donating blood for transfusions or from donating organs, tissue and cells for transplantation.

Travel medicine

There is no systematic counselling at the national level before travel, although individual travel clinics may include information on Chagas disease.

Chagas disease might be considered in the differential diagnosis of illness in returning travellers, depending on local expertise in infectious diseases.

Laboratory diagnosis

In London, Liverpool and Glasgow, the diagnostic methods used are IFA, ELISA, PCR, xenodiagnosis and culture.

Internal quality control is carried out in all laboratories performing screening for *T. cruzi* infection and/or diagnosis. The United Kingdom National External Quality Assessment Service (UK NEQAS) is commencing a scheme in May 2010, which will be available in Europe on request.

Tests used for serological screening and confirmation in blood banks

Lab21 T.cruzi EIA is used for screening. This is a commercial OEM assay originating in Spain. Confirmatory tests are Ortho T.cruzi EIA and DiaPro Chagas Ab EIA, both standard commercial assays. The in-house IFA using lyophilized Ag from BioLabs in Argentina is also used.

Tests used for serological screening and diagnosis in hospitals (i.e. pregnant women)

At present, no antenatal screening is carried out.

Diagnosis:

Commercial kits:
PRL - Pathozyme Chagas (ELISA, Omega Diagnostics)
SPDL - CELISA (Cellabs Pty)
DPL (LSHTM) – CELISA (Cellabs Pty)

In-house kits:
PRL - IFA (*T. cruzi* antigen supplied by Professor Miles at the London School of Hygiene and Tropical Medicine, LSHTM)
DPL (LSHTM) – IFA (*T. cruzi* antigen supplied by Professor Miles, LSHTM)
DPL (LSHTM) – IFA (no other details known)
SPDL – IFA (no other details known)

Health services

The Hospital for Tropical Diseases in London provides medical care to Chagas disease patients in England and Wales. Patients in Northern Ireland and Scotland are seen in Edinburgh.

There is a referral system between blood banks and laboratory and clinical services; positive cases are referred to the Hospital for Tropical Diseases. Scotland does not screen but permanently defers at-risk donors.

Other services

Drug distribution

Nifurtimox and benznidazol can be obtained from WHO.

Information and surveillance system

Information on diagnosed cases is collated at the London School of Hygiene and Tropical Medicine and Hospital for Tropical Diseases London, the Health Protection Agency and Health Protection Scotland. Enhanced surveillance is planned to be developed.

Information, education and communication

Advocacy for antenatal screening is being pursued. There are no systematic programmes with at-risk communities or health-care professionals, although links have been developed with Médecins Sans Frontières to reach at-risk communities. Information on Chagas disease is due to be included in a country-specific resource to assist health-care practitioners in managing the health needs of their immigrant patients.

Protocols and laws

WHO guidelines are followed, but no other formal protocols are available locally or nationally.

The disease is not notifiable legally, but laws governing blood and tissue donation are compatible with European legislation.

Additional information

There is no association of Chagas disease patients in the UK.

Appendix 1. Questionnaire

Epidemiological information

1) Estimated number of Latin American immigrants

Note: It is important to consider both legal and illegal immigrants, taking this information from your National Institutes of Statistics/Migration… If possible, classified according to their country of origin.

2) Expected number of infected people

Note: Taking into account known European percentages of infection prevalence among Latin American communities, by country of origin, and applying these percentages to the estimated number of immigrants from each nationality in your country, it is possible to calculate the expected number of infected people. For instance, the prevalence found among Bolivian communities in Europe is between 15% and 20%, and much lower for other nationalities.

3) Estimated number of infected pregnant women

4) Estimated number of infected newborns

5) Number of already diagnosed cases

Note: With key information about them: autochthonous/imported case, acute/chronic infection phase, clinical form (asymptomatic, cardiac, digestive, neurological, mixed forms), possible transmission route, immunocompetent/immunosuppressed patient, among others.

6) Number of patients already treated

Note: With key information about them: age, supposed transmission route, supposed place of infection, place of birth, acute/chronic phase or reactivation due to immunosuppression.

Pharmacovigilance

7) Use of the national pharmacovigilance system/centre to report adverse events with nifurtimox and benznidazol treatments (No/Yes. If yes, please specify which)

8) In case of the existence of adverse events reports with nifurtimox and benznidazol, please indicate the number of those reports and the type of these adverse events.

Prevention of infection and early detection of congenital cases

9) Existence of a systematic detection system for congenital infection (No/Yes. If yes, please specify which)

Note: Screening and laboratory diagnosis confirmation of infected pregnant women and systematic detection (parasitological diagnosis at birth and serological diagnosis after eight month of age) of newborns at risk.

10) Existence of blood bank infection prevention for transfusional transmission (No/Yes. If yes, please specify which).

Note: Prevention through a pre-donation questionnaire and screening tests.

11) Existence of infection prevention for organ, tissue and cell transplantation transmission (No/Yes. If yes, please specify which)

Note: Prevention through a pre-donation questionnaire and screening tests.

12) Existence of any implemented prevention tool in travel medicine (No/Yes. If yes, please specify which)

Note: Counselling prior to the trips to Latin America and inclusion of Chagas disease in the differential diagnosis in the consultations after these trips.

Laboratory diagnosis

13) Existence of laboratories for parasitological, molecular and serological diagnosis (No/Yes. If yes, please specify which)

Note: With at least three different serological tests for confirming doubtful cases.

14) Existence of systematic laboratory internal and external quality control systems (No/Yes. If yes, please specify which)

Note: Applied to all laboratories performing the *T. cruzi* infection screening and diagnosis.

15) Tests used for serological screening and confirmation in blood banks

Commercial kits: Yes / No (Please, specify name, methodology and manufacturer)
In-house tests: Yes / No (Please, specify methodology)

16) Tests used for serological screening and diagnosis in hospitals (i.e. pregnant women)

Commercial kits: Yes / No (Please, specify name, methodology and manufacturer)
In-house tests: Yes / No (Please, specify methodology)

17) Existence of a panel of well characterized sera available for evaluation of the serological tests in the reference laboratories

Yes / No (If yes, please, specify source and performance of the tests).

Health services

18) Existence of health centres for patient medical care
(No/Yes. If yes, please specify which)

Note: For medical assessment, clinical diagnosis and etiological and non-etiological treatment of asymptomatic and symptomatic (cardiac, digestive, neurological, mixed forms…) cases.

19) Existence of a referral system between blood banks and laboratory and clinical services (No/Yes)

Note: For diagnosis confirmation of all screened patients with positive results.

Other services

20) Existence of an etiological drug distribution system (No/Yes. If yes, please specify which)

Note: For benznidazol and nifurtimox.

21) Existence of an information and surveillance system (No/Yes. If yes, please specify which)

Note: For information collection of diagnosed cases.

22) Existence of any information, education and communication activity (No/Yes. If yes, please specify which)

Note: Including health personnel training.

Protocols and laws

23) Existence of institutional, municipal, state/departmental/autonomic, national protocols (No/Yes. If yes, please specify which)

Note: For transmission prevention and screening, diagnosis, treatment of patients.

24) Existence of local or national laws about Chagas disease (No/Yes. If yes, please specify which)

Note: About prevention (transfusional and organ, tissue and cell transplantation), control (secondary prevention with the early diagnosis of all cases) and medical care of patients (including cardiologic, digestive, neurological, psychological, social, work aspects, among others).

Additional information

25) Existence of any association of Chagas disease patients
(No/Yes. If yes, please specify which)

26) Additional/optional information

- History information (first diagnosed cases…), others.
- Short, medium and long term perspectives at political, scientific, other levels.
- Others