BREAKING THE SILENCE

An Opportunity for Patients with Chagas Disease

CHAGAS COALITION

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Letter from the Global Chagas Disease Coalition

Dear Reader,

Not long ago, on the occasion of the 100th anniversary of the discovery of Chagas disease, several campaigns denounced the scant progress made over that century in the care of those affected. Since then, some progress has been made in different spheres—medical, scientific and political—but major challenges still remain. This is an appropriate time to celebrate what has been achieved and to take the next step.

In endemic countries, good results have been achieved with vector control and several areas have received certification of interruption of vectoral transmission. Almost 100% of the blood in blood banks is now being screened. These advances have reduced the number of new cases. The next decisive step is to achieve **the same support for the diagnosis and treatment of patients with the disease**.

The importance of achieving this goal is underscored by the current global development agenda, and various advances have made that more feasible today than ever before: the first-line treatment benznidazole is now being manufactured by two companies and a paediatric formula of the drug is available; new scientific evidence supporting the importance and usefulness of treatment has emerged; and proposals have been made on ways to simplify diagnosis in rural areas. Although more research into new diagnostic tools and drugs is needed, **Chagas disease can be treated today**.

However, a great deal remains to be done before treatment will be available to all those who need it. At present, less than 1% of people with Chagas disease receive treatment, and it would take 300 years to treat all those affected at the current rate. To change this situation, we have decided to give an account of the current situation, describe the challenges that must be overcome and share, by way of case studies, the actual experience of programmes that have succeeded in increasing the number of people receiving treatment.

We invite you to join us in this effort to improve access to the diagnosis and treatment of Chagas disease. Our vision is “a world where Chagas disease is controlled and universal access to treatment is a reality”. Children are our first priority, followed by pregnant women, so as to prevent congenital transmission of Chagas disease to the child. At the same time, it is essential to accelerate efforts to stimulate innovation in diagnostic techniques and new treatments. If we are to achieve these goals, we all need to work together.

Thank you.

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SUMMARY

"We have always lived with vinchucas since we were children living in an adobe house. ... I am studying biochemistry and I heard about the disease and the vinchucas in the faculty. Remembering my childhood, I realised that I should get tested. And I tested positive. (...) more people need to be made aware of the danger. The topic should be on the news to encourage more people to come for testing. So many people must have [the disease] and in the long term they run serious risks. But they simply don't know."

César Jhonny Hidalgo (27), patient of the ISGlobal-CEADES Platform in Cochabamba, Bolivia.

Few diseases better fit the description of being "neglected" than Chagas disease. According to the World Health Organisation (WHO), between **6 and 7 million people worldwide** have this infectious disease and at least 7,000 of them die as a result every year. The cost of Chagas disease in direct health care and lost productivity amounts to billions and the burden it imposes undermines the effectiveness of health systems in vulnerable areas on both sides of the line separating poor countries from developed countries.

At the same time, patients with Chagas disease get sick and die under a veil of silence. Not even one person out of every 100 of those infected receives the treatment that could control or even cure their condition, and patients and their families are faced with a bewildering array of medical, institutional and social obstacles that make it impossible for them to find an adequate response or solution. Compared to other diseases that particularly target the world's poorest communities, the silence—both political and in the media—surrounding Chagas disease is striking and has delayed the implementation of the solutions that are available to those in a position to apply them.

Not even one person out of every 100 of those infected receives the treatment

This report identifies some areas in which **decisive action on the part of public authorities and donors could make a real difference** for an at-risk population of nearly 25 million people:

- **Including comprehensive care** for Chagas disease in the health care system, with particular focus on the detection, diagnosis and treatment of the disease; and ensuring the referral of all those who test positive for the infection during blood donor screening.
- Ensuring that **healthcare personnel receive appropriate training** because they are not always aware of the current consensus in the medical community on the usefulness of treating patients with Chagas disease and they very often lack the resources necessary to deal with the disease.
- Ensuring the quality of **health information systems**, which play a crucial role in identifying the extent of the problem, determining drug needs, and managing pharmaceutical supplies.
- **Guaranteeing funding and public leadership**, which determine the resources allocated to the fight against the disease and the political will to implement the most effective strategies.

In this context, **special mention should be made of access to diagnosis and medicines**. Despite the efficacy, albeit with certain limitations, of the current treatments, the availability of these drugs is very far from desirable levels. Treatment is hampered not only by the difficulty of ensuring a quality supply of these drugs at accessible prices but also by practical obstacles because it involves several visits to a physician and is not always free of cost.

The treatment of affected patients should not be a matter of debate

There are practical as well as ethical reasons for breaking the veil of silence that surrounds Chagas disease. First, since effective therapies exist and are available, the treatment of affected patients should not be a matter of debate. There is no excuse for inaction, which would be contrary to the mandate of the Sustainable Development Goals.

Controlling Chagas disease is also an issue of **public responsibility** in that the elimination of the parasite from even one individual reduces the probability of that person developing symptoms and also contributes to interrupting the chain of transmission, one of the biggest challenges faced by both professionals and institutions. Treatment is also an effective form of prevention in a context where there are an estimated 35,800 new cases every year caused by vector-borne and congenital transmission (between 2% and 7% of mothers who test positive transmit the disease to their child).

The **economic argument** for combatting Chagas disease is irrefutable. It has been estimated that the mean annual health care cost per individual treated is $474 and that the annual cost per case in terms of lost productivity is more than $4,600. The total annual financial burden of Chagas disease worldwide is estimated to be around $7.2 billion, an amount equivalent to all the aid allocated by the five largest European donors to the health sector.

None of these human, institutional or economic costs are inevitable. As shown by the case studies undertaken for this report in three very different countries (Bolivia, Argentina and the USA), a coordinated effort involving public and private actors offers hope in the fight against Chagas. The programmes implemented in those three countries combine strong leadership, economic resources and creativity, all placed at the service of vulnerable populations. The possibility of reproducing these experiences in all the affected regions is one of the aspirations of the global roadmap for the fight agains Chagas disease defined by the WHO and the Pan American Health Organisation (PAHO).

Our target is to increase the number of those receiving treatment—currently less than 1% of infected patients—to 100% in the case of newborn infants and patients aged under 18 years and to achieve a tenfold increase in the number of adults treated by 2020. To achieve these targets, this report makes several proposals:

We ask the governments of affected countries:

1. Political commitment to implementing a global strategy to fight Chagas disease, with special emphasis on Latin America

- To sign a regional policy resolution to improve access to the diagnosis and treatment of Chagas disease in line with the WHO/PAHO recommendations

2. Implementation of programmes aimed at speeding up access to diagnosis and treatment

- To allocate sufficient resources to Chagas programmes to ensure a mean annual increase of 45% in the number of patients treated up to 2020
- To ensure the availability of diagnostic and pharmaceutical supplies in all health centres where they are needed
- To invest in training healthcare personnel in the detection, diagnosis and treatment of Chagas disease
- To include adults with chronic Chagas disease in comprehensive treatment programmes
- To encourage the population to get tested through information campaigns, educational programmes, and other awareness raising activities

3. Control of transmission

- To implement universal **screening of at-risk women** of childbearing age to prevent the transmission of the infection from mothers to their children. To treat all women diagnosed with T. cruzi infection and all newborns who test positive for the infection, in both endemic and non-endemic countries.
- To continue ongoing vector control activities and ensure systematic screening for *T. cruzi* infection by blood banks and organ donation programmes in Latin America and in non-endemic countries.

We ask public and private actors:

4. That all those working with Chagas disease should adhere to the "roadmap" for improving access to diagnosis and treatment in the following ways:

- Supporting the efforts of national programmes
- Channelling efforts towards the priorities specified in the roadmap.
- Spreading the message about the importance of improving access to diagnosis and treatment


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An Opportunity to Combat Chagas Disease, the Silent Killer

AN OPPORTUNITY TO COMBAT CHAGAS DISEASE, THE SILENT KILLER

Chagas Disease:

Cause: the parasite *Trypanosoma cruzi.*

Routes of transmission: vector-borne (via the triatomine or kissing bug, an insect known in the various endemic areas as the *vinchuca, chinche besucona, barbeiro, chipo, pito*); congenital (from a mother to her child); and via blood transfusion or organ transplant. Oral transmission through contaminated food has also been recently documented[2,3].

Effects: 30% of patients with chronic infection develop irreversible cardiac complications, 10% develop intestinal disease, and in a smaller percentage the nervous system is affected[4].

Around 60% of patients never develop symptoms; however, since it is impossible to know which patients will be affected, **all patients diagnosed with *T. cruzi* infection must be treated**.

The WHO has designated Chagas disease as one of the planet's 17 **neglected diseases** on the planet. It affects **over 6 million** people and endangers a further **25** million who are at risk of contracting the infection[1]. Every year, there are about 35,800 new cases and the disease **kills over 7,000 people** (Infographic 1)[2,3]. The disease generates **an annual cost of $7.2** billion, an economic burden borne by national health systems and affected families,[4] which is similar to that of other much better known infectious and chronic diseases, such as certain cancers, and an amount equivalent to all the aid allocated by the top five European donors to the health sector.

It is estimated that 90% of people with Chagas disease are unaware that they are infected and that less than 1% of them receive treatment

Despite this high global burden, **Chagas disease is still neglected** in the countries where it is endemic and in those where it is an emerging disease. It is estimated that 90% of people with Chagas disease are unaware that they are infected and that less **than 1% of them receive treatment** despite the existence of treatments recommended by the WHO and PAHO. As a result, for hundreds of thousands of people, Chagas disease **is a silent killer**. It is the parasitic disease responsible for the highest number of deaths in the Americas and particularly affects the poorest and most vulnerable sectors of the population, often those **who lack the political influence** to demand care[5].

Estimates of the numbers affected vary according to the source, and even the WHO and PAHO have acknowledged that there is a complete lack of reliable epidemiological data. **It is now accepted that the disease is not confined to rural areas, but is also found in urban areas and in non-endemic countries.** Chagas disease has become a major international public health problem and a coordinated effort is needed to ensure that the people affected are diagnosed and treated.

As a result of migratory flows, Chagas disease is no longer solely a Latin American problem and is now found in non-endemic areas, including Europe, the USA, Japan, and Australia[6,7]. In the USA alone, there are an estimated 300,000 people infected with the parasite[6], and in Europe estimates range from 123,000 to 170,000, depending on the source[7,8].

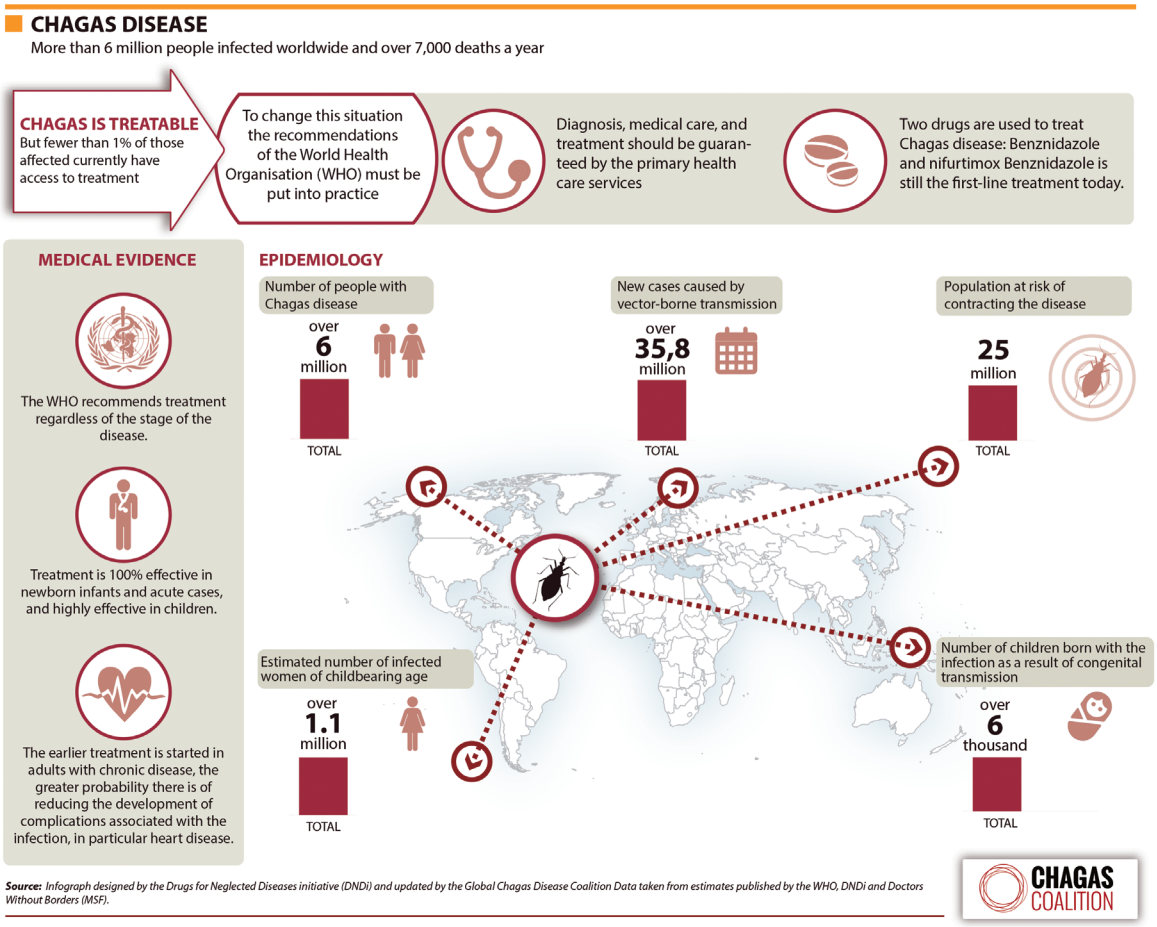
Box 1. Available Diagnostic Methods and Treatments Do Not Reach Patients

There are solutions for this disease. In **2010**, the World Health Assembly's Resolution 63.20 recommended **that countries should include the care of patients with Chagas** disease in their primary health services and strengthen regional mechanisms for improving access to and the distribution of aetiological treatments for the disease. In the same year, the PAHO published its ***Strategy and Plan of Action for the Prevention and Care of Chagas Disease***. One of the priorities specified by that document was reducing the morbidity and mortality related to Chagas disease by scaling up the coverage of diagnostic services, improving access to quality health care for people infected with *T. cruzi*, and ensuring timely treatment[9].

In **2012**, the WHO launched **a 2010-2020 roadmap** for the control of neglected diseases, which includes Chagas disease. And in **2014**, the PAHO published a list of so called "ten commandments" of managing Chagas disease in the primary care setting, which specified that all patients diagnosed with the infection should have the benefit of receiving aetiological treatment (trypanocidal)[10].

Despite all of these recommendations, only 20,000 patients worldwide were treated for Chagas disease in **2013**,[11] less than 1% of the estimated number of those affected. Screening and diagnostic programmes either do not exist or are ineffectual. Progress will require greater political commitment and the allocation of the financial and human resources needed to introduce the routine diagnosis and treatment of these patients into public health systems. The key components of a strategy designed to achieve this goal will be discussed later in this report.

Infographic 1.



Source: *Infograph designed by the Drugs for Neglected Diseases initiative (DNDi) and updated by the Global Chagas Disease Coalition Data taken from estimates published by the WHO, DNDi and Doctors Without Borders (MSF).*

Infographic 2. **Estimated Number of People With Chagas Disease in the World**

Source: Compiled by the authors based on data from the WHO and other sources.

Chagas Disease in the Global Health Agenda

In addition to the WHO resolutions, the fight against Chagas disease also appeared on the policy agenda in 2012 thanks to another initiative: ***Uniting to Combat Neglected Tropical Diseases (NTDs) — the London Declaration***. The London Declaration brought together various stakeholders (pharmaceutical companies, donors, health agencies and national programmes) in collaboration with the World Bank and the WHO with the aim of eliminating 10 of the 17 neglected diseases on the planet. To achieve this goal, the signatories of the declaration made a commitment to driving progress towards achieving the goals for NTD defined by the WHO roadmap. During the meeting, the pharmaceutical company Bayer pledged to donate nifurtimox, the second-line treatment for Chagas disease, to national control programmes until 2020. Abbott, AstraZeneca, Eisai, Novartis, Pfizer and GlaxoSmithKline joined the DNDi initiative to give that organisation access to the compound libraries and to develop new drugs. The Mundo Sano Foundation, the only original Latin American signatory, committed to continuing its projects relating to Chagas disease and pledged to invest no less than $5 million before 2020. The Bill & Melinda Gates Foundation announced a five-year, $363-million commitment to combat NTDs, but none of this contribution has specifically targeted Chagas disease as yet.

The Health Ministers of Ibero-American countries unanimously endorsed the Declaration of Veracruz in 2014, pledging to assess the extent of the problems caused by vector-borne diseases and to take the necessary steps to deal with them. The recently launched **Sustainable Development Goals (SDG)** may help to honour these commitments by directly supporting the people affected by Chagas disease and by obliging the governments of affected countries to give an account of their progress towards the control of neglected diseases.

A great deal remains to be done before Chagas

Together, these milestones afford an unprecedented opportunity for progress, but **a great deal remains to be done before Chagas disease is accorded its rightful place on the policy agenda** and solutions are provided for patients still waiting for treatment. Despite increased investment, there is still much less R&D related to the development of new treatments for Chagas disease than for other neglected diseases. R&D investment for Chagas between 2003 and 2013 was **$161.5 million, insufficient to cover the needs**. The amount earmarked for Chagas disease represents only 1% of the total amount invested in neglected diseases.

This report explains why it is essential to diagnose and treat people infected with *T. cruzi* infection (Chagas disease). It analyses the conditions required to achieve this goal and presents three case studies in different settings to illustrate the possibilities of an effective strategy for overcoming the barriers to access.

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Ethical and Practical Arguments in Favour of Access to Treatment

ETHICAL AND PRACTICAL ARGUMENTS IN FAVOUR OF ACCESS TO TREATMENT

Access to diagnosis and treatment for patients with Chagas disease should be a priority in all affected countries. There are many arguments to support this assertion, including the impact of the disease on patients, the magnitude of the problem, and an elementary cost-benefit analysis. The most important, however, must be the **right of every person to a healthy life**.

Access to diagnosis and treatment for patients with Chagas disease should be a priority

The WHO Constitution states that the highest attainable standard of health is a fundamental right of every human being: "The right to health includes **access to timely**, acceptable, and affordable health care of appropriate quality." The right to health is also guaranteed by international and regional human rights treaties and the constitutions of countries throughout the world[12]. There is no reason why people with Chagas disease should be an exception, and access to diagnosis and treatment is, therefore, their right.

The **indefensible inequality of the current situation is demonstrated clearly by** the fact that *T. cruzi* infection is the leading cause of heart disease in Latin America and that less than 1% of the infected population is receiving treatment. Approximately one-third of the 6 to 7 million people infected with *T. cruzi* will develop cardiovascular and gastrointestinal complications[3]. Without guaranteed access to diagnosis and treatment, most of these patients, who come mainly from poor and vulnerable communities, are deprived of their right to timely medical care. According to some estimates, **this situation currently leads to 7,000 deaths every year**[3].

The Benefits of Available Therapies

All patients diagosed with Chagas disease *"at any phase of the disease should receive the full cycle of medical care in accordance with the current recommendations, which includes the benefit of receiving aetiological treatment (trypanocidal) correctly indicated, monitored and assessed"*[13].

There are currently two trypanocidal drugs used to treat Chagas disease: benznidazole, recommended as a first-line treatment by the WHO; and nifurtimox, the second-line treatment. Both drugs are almost 100% effective in newborns and highly effective in the treatment of patients in the acute phase of the disease. However, the longer the person has been infected the more the effectiveness of treatment diminishes and the risk of adverse events increases. For this reason, treatment is **absolutely indicated** for patients in the acute phase and during the early chronic phase, in children and young patients, and in chronic cases when infection has been reactivated due to immunosuppression[13].

The WHO/PAHO clearly recommends treatment for patients with long-term chronic disease but specifies that the decision in such cases should be taken on a case-by-case basis and **subject to the judgement of the prescribing physician**.

Table 1 lists evidence-based treatment recommendations for each phase of Chagas disease. The results relating to the efficacy of treatment are classified according to the strength of the supporting evidence (ranked from highest to lowest depending on the type of study)[14]. The evidence of effectiveness is stronger in the acute and early chronic phases of the disease.

Table 1. Evidence-Based Recommendations and Efficacy of Treatment[15,14,16,17,18,19,20,21]

Patient Groups by Disease Phase, Age and Presence and Severity of Complications		Aetiological Treatment*	Efficacy Based on Eventual Seronegative Conversion
Acute phase	Recent infection via vectorial transmission	Always	65% to 100%
	Congenital infection		
	Oral transmission		
	Acute disease due to reactivation (by immunosuppression)		
Early chronic phase	Infected children (paediatric age group)	Always	
Chronic phase	Women of child-bearing age	Should be offered	50% to 75 %
	Adults aged 18-50 indeterminate phase		
	Adults aged 18-50 with no symptoms or moderate lesions		
	Imminent immunosuppression (eg, transplant candidates)		
	Adults aged over 50 years without advanced heart disease	Optional	30%
	Patients with advanced Chagasic heart disease and congestive heart failure	Not usually offered	Contraindicated
	Patients with megaoesophagus		
Otros casos	During pregnancy	Never	
	Patients with liver or kidney failure		

(*) Based on current evidence.

There is evidence of moderate efficacy for all the groups of patients who should be offered treatment. While the evidence of efficacy in the chronic phase is not so strong, neither is there any evidence that treatment is not beneficial to such patients. Treatment is contraindicated during pregnancy and in patients with liver or kidney failure[15,22].

Until recently, adults infected with *T. cruzi* were not treated because the disease was considered to be in the chronic phase. From the 1970s until the 1990s, the prevailing theory was that the damage to cardiovascular and digestive tissues was not caused by the parasite but rather by an inflammatory autoimmune reaction. Given this hypothesis, it was not considered necessary to eliminate the parasite. However, there is now more evidence that it is actually the presence of the parasite that causes and maintains a specific hypersensitivity immune response, formerly called an autoimmune inflammatory process. **This new understanding has given rise to a new paradigm that recognises the importance of antiparasitic therapy**, which can prevent the disease and its complications[23]. Treatment should therefore be offered to adults infected with *T. cruzi*, particularly if they are asymptomatic. It has also been shown that treating women of childbearing age with trypanocidal agents can prevent subsequent congenital transmission of *T. cruzi*[24]. Antiparasitic treatment is, however, absolutely contraindicated during pregnancy.

Finally, it is important to remember that, regardless of whether patients with chronic disease receive aetiological treatment, they may also require treatment of cardiac or digestive symptoms.

To conclude, in light of the new paradigm and the evidence on the benefits of therapy with the existing antiparasitic agents—benznidazole and nifurtimox—there is no justification for not treating these patients. There is undoubtedly a need for further studies to improve our understanding of the disease, for research directed towards developing new and better treatments and a test that can measure the efficacy of treatment by confirming the absence or reduced presence of parasites in the blood. Nevertheless, considerable advances can be made with the current information and tools.

Box 2. After the BENEFIT Study: What Next?

BENEFIT (Benznidazole Evaluation for Interrupting Trypanosomiasis)—an international, multicentre, double-blind and placebo-controlled trial—was started over ten years ago to determine whether the estimated 1.2 million people living with heart disease caused by chronic Chagas disease could benefit from a 60-day course of treatment with benznidazole. The study did not show incremental benefits in cardiac outcomes, underlining the need to revisit the current strategies for antiparasitic chemotherapy in patients with heart disease secondary to infection with *T. Cruzi*[25]. However, it did demonstrate that the treatment had a trypanocidal effect.

The BENEFIT trial is a wake-up call for the need to step up efforts in the diagnosis and treatment of Chagas disease and in research. These results, which essentially do not change the current recommendations, underscore the **need to start treatment during the early phases of the disease**. They also highlight the urgent need to develop new drugs and gain a better understanding of the key components of the disease to facilitate progress towards innovative solutions.

A Public Health Responsibility

Aetiological treatment (parasiticidal) of Chagas disease is also a public health strategy because eliminating the parasite from an infected individual reduces the likelihood that the disease will develop and interrupts the chain of transmission[14]. Reducing the number of infected people reduces the risk of transmission.

Over 35,800 new cases occur every year

Despite advances in vector control and blood donor screening, transmission of *T. cruzi* is not fully controlled and an estimated 25 million people are still at risk of infection[1]. Over 35,800 new cases occur every year[2]. Several challenges must be overcome, including the existence of vectors with multi-resistance to insecticides[26] and the impact on the vector cycle of changes in the environment, agriculture and urbanisation. Another important development in recent years has been the increase in the number of reported cases attributed to contaminated food or drink.

Without vector control disease management is not permitted. In endemic areas, effective vector control is fundamental to the successful treatment of patients because of the risk of reinfection. An essential criteria for treatment is that the patient lives in a home free of the vector that transmits the parasite.

It is also essential to ensure that 100% of blood transfusions are safe and to establish regulations governing the screening of organ transplants

The risk of congenital transmission must also be addressed. In 2% to 7.3% of positive mothers, the disease is transmitted to the child during pregnancy or delivery[27,28]. Unfortunately, programmes that screen women during pregnancy to prevent congenital transmission are not being implemented systematically, and where they do exist these programmes are finding it difficult to detect cases where transmission has occurred and ensure that the newborn child receives treatment. We now have evidence that **treating women of childbearing age before they become pregnant can prevent transmission** of the parasite to their children. That finding underscores once again the importance of treatment as a strategy for controlling disease transmission.

El tratamiento de mujeres en edad fértil interrumpiría la transmisión

With 25 million people at risk for infection[3], it is not only imperative to sustain ongoing efforts but also to innovate with up-to-date control strategies designed to overcome the challenges identified **and to recognise that treatment must be a key component of any prevention strategy**. Treating patients with Chagas disease benefits the individual and also helps to **break the cycle of disease transmission**, another important reason why improving access to diagnosis and treatment should be a priority[28].

Finally, in addition to being a public health responsibility, ensuring that all those affected by Chagas disease receive the full cycle of care is also a **social responsibility** because of the impact of the disease on the patients' health.

A Profitable Investment

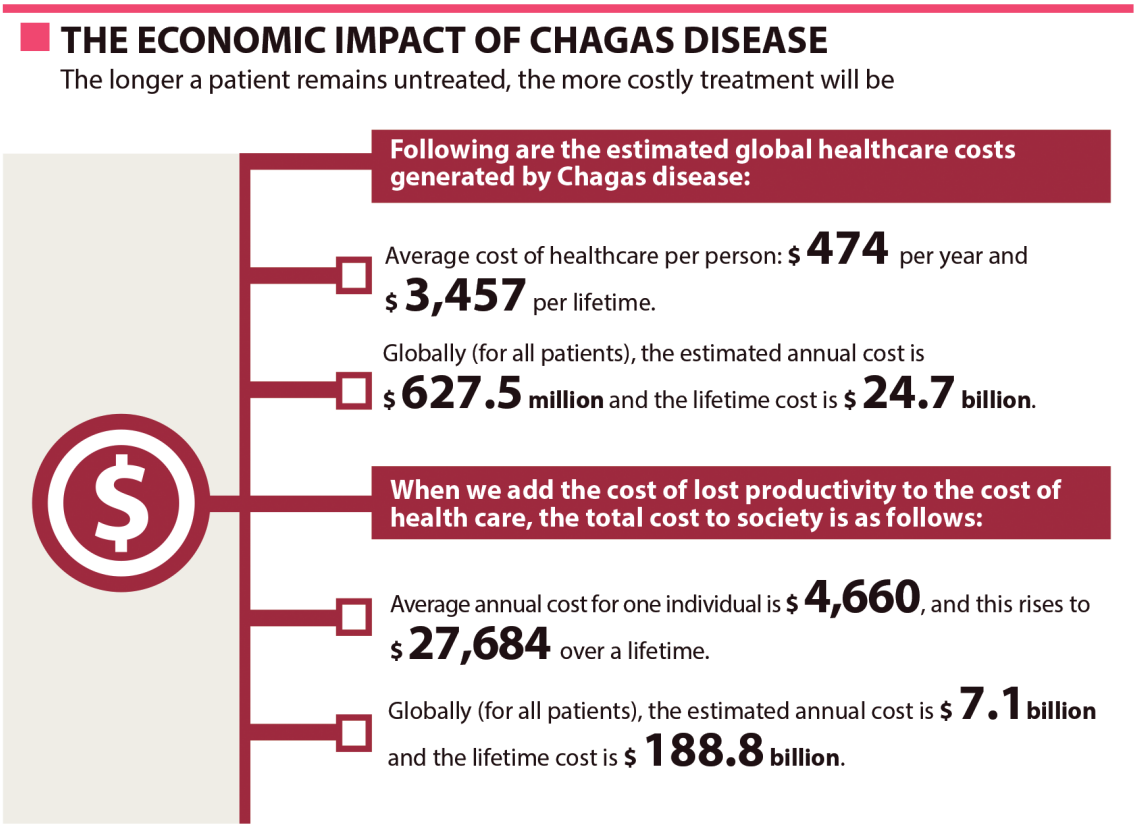
Given the high prevalance of Chagas disease and the economic burden it imposes on health care systems, we must consider the significant economic implications of ensuring that these patients are diagnosed and receive treatment in addition to the ethical and medical arguments[4].

Chagas disease is the parasitic disease responsible for most deaths in Latin America. In terms of disability-adjusted life years (DALYs *), it is the leading tropical disease and the fourth infectious disease[29]. Moreover, its impact has now spread outside of the endemic region: an estimated 500,000 people infected with *T. cruzi* live in other parts of the world, including the USA, Europe, Australia and Japan[6].

* **DALY** A unit of health status where life expectancy according to age is adjusted by the loss of health and years of life due to disability from disease or injury. This measurement is often used to assess the overall burden of disease. It is used as a measure of utility in cost-effectiveness analysis. (http://htaglossary.net/)

According to a study published in 2013,[4] the total annual cost to society in terms of public health worldwide (calculated on the basis of the estimated number of people affected) was nearly $6.3 billion. To this we must add the human loss of 806,170 DALYs. To understand the magnitude of the problem, we must translate these DALYs into costs, primarily in terms of lost productivity. When we do this, the estimated **worldwide annual cost** of the disease is $7.2 billion.

Infographic 3.



$ = US dollars - *Source:* *Infograph designed by the Drugs for Neglected Diseases initiative (DNDi) and updated by the Global Chagas Disease Coalition Data taken from studies by Lee,BY, Bacon KM, Bottazzi ME and Hotez PJ. Global economic burden of Chagas disease: a computational simulation model, Lancet Infectious Diseases.*

The economic burden of Chagas disease is similar to or exceeds that of prominent diseases such as rotavirus and cervical cancer[30]. The total accumulated cost (health spending plus DALYs) amounts to $188.796 billion per lifetime. What is more, a large part of the burden of this disease will emerge in the future[4].

Disease control and access to treatment are not only desirable from the perspective of public health and the patient's right to health care, there is also a strong economic argument because of the substantial costs incurred worldwide. **The few cost-effectiveness studies that have been carried out have shown screening of pregnant women and their families and the treatment of infected women to be efficient and effective measures**[31,29].

The few cost-effectiveness studies that have been carried out have shown screening of pregnant women and their families and the treatment of infected women to be efficient and effective measures

Box 3. The Sustainable Development Goals' mandate regarding Chagas Disease

In 2015, the international community agreed on the 17 **SDGs**, many of which will have an impact on people living with Chagas disease or at risk of being infected. Many aspects of this new global development agenda are highly relevant to Chagas disease, including the fight against climate change, poverty reduction, and access to decent housing and education. Goal 3 is a commitment to "ensuring healthy lives and promoting the well-being for all at all ages" and one of its targets is to end the epidemics of AIDS, tuberculosis, malaria and **Neglected Tropical Diseases (NTDs) by 2030**. Goal 3 also includes two other key commitments: to achieve universal health coverage and to achieve access to essential medicines for all.

Another remarkable achievement of the SDG agreement is that it obliges countries **to monitor and give an account of progress indicators**. By 2030 we should see a substantial increase in the number of patients diagnosed and treated for Chagas disease, if not universal coverage, and definitive control of congenital transmission.

Table 2[9, 32] lists the indicators agreed on by the WHO and PAHO in recent years. The seven milestones and targets for controlling Chagas disease by 2020 include the interruption of intradomiciliary vectorial transmission, oral transmission, transmission through blood and organ transplantation, and congenital transmission, as well as the care of the infected patients[33].

In this section we have reviewed the ethical and practical arguments for making access to diagnosis and treatment of Chagas disease a priority in all the affected countries. The next section will discuss the main components of a recipe that could ensure that such access is achieved.

Table 2

2013	**WHO Milestones 2020 (based on the London Declaration)**	
Indicators	100% of countries with access to antiparasitic medication 100% of countries with definitive control of congenital transmission 100% of infected persons/patients with the disease receiving medical care	
2010	**The PAHO approves the STRATEGY AND PLAN OF ACTION FOR CHAGAS DISEASE PREVENTION, CONTROL, AND CARE**	
GOAL 2: To reduce morbidity and mortality by improving access to health services for affected persons, both symptomatic and asymptomatic, as well as increasing coverage of testing, quality medical care, and timely treatment of cases.		
Objectives	**Indicators**	**Specific Objectives**
2.1. To ensure the diagnosis, care and treatment of people infected with *T. cruzi*	• 100% coverage for the diagnosis, care and treatment of children identified with *T. cruzi* infection in seroprevalence studies. • 100% coverage with respect to diagnosis and timely, adequate treatment of adults with a confirmed diagnosis of Chagas' infection or disease, in keeping with national treatment standards.	• Include diagnosis of Chagas disease in the primary health care system to ensure timely medical attention and treatment for all patients infected with *T. cruzi*, without distinction of gender or ethnicity. • Strengthen the countries' treatment supply chains to increase access to treatment. • Establish referral and counter-referral mechanisms to manage each case according to its clinical complexity.
2.2. To implement secondary prevention of congenital Chagas disease.	• Number of countries with functioning programmes for the prevention and control of congenital Chagas disease. • Increasing annual coverage of *T. cruzi* screening in pregnant women and at-risk populations. • 100% coverage for testing of pregnant women with *T.Cruzi* infection and treatment of infected newborns.	• Diagnosis of mothers with *T. cruzi* infection and follow-up of their children up to 12 months of age, with treatment of mothers during the post-partum and post-lactation period, on medical prescription, following individual assessment. • Procure evidence that all infants testing positive during the postnatal period receive medical care and treatment and are cured.
2.3. To perform technology research and innovation, with special emphasis on developing new and better diagnostic tools, as well as drugs for treatment of the disease.	• Number of countries with access to the drugs. • Number of research and development projects supported.	• Promote research, development and technological innovation to create new and better drugs and diagnostic tools for all stages of the disease, based on regional priorities. • Development and production of drugs for paediatric use. • Improvements in distribution and access processes.
2009	**The PAHO approves resolution CD49.R19 ELIMINATION OF NEGLECTED DISEASES AND OTHER POVERTY-RELATED INFECTIONS**	
GROUP 1: Diseases that have a greater potential for being eliminated (with available cost-effective interventions)		
Indicators	• To integrate the diagnosis of Chagas disease into the primary health care system so as to provide treatment and health care to all patients for both the acute and chronic phases and to reinforce the supply chain of the existing medicines within countries to scale up access. • To prevent the development of cardiomyopathies and intestinal problems related to Chagas disease by offering appropriate medical attention to those affected by the disease in its various stages. • Screening of pregnant women and treatment of newborns. • Aetiologic treatment of children	

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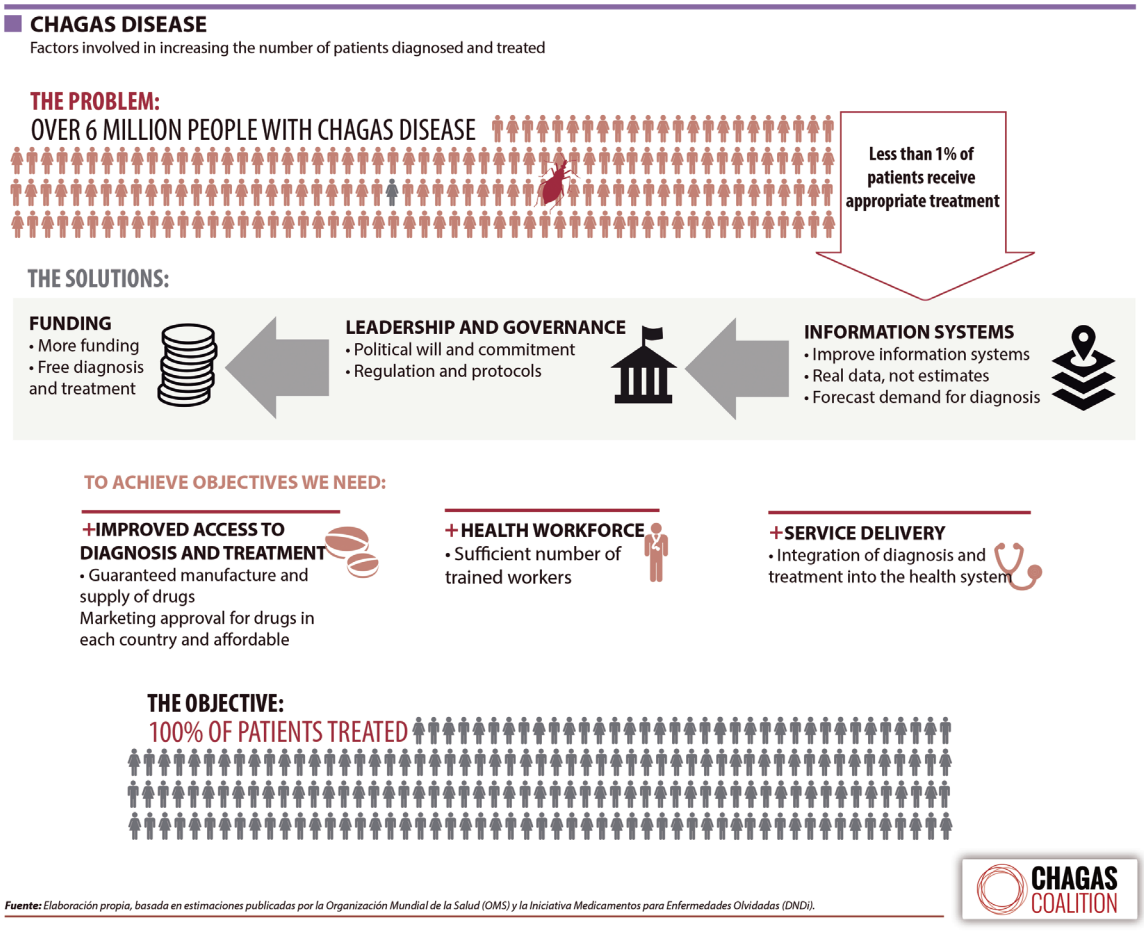
A Recipe for Success

A RECIPE FOR SUCCESS

Despite the good reasons for making medical care widely available to people with Chagas disease, less than 1% of those affected currently receive treatment. Overcoming the bewildering array of obstacles that impede access to care will require **more robust health systems and greater commitment on the part of all the key actors**: government, health professionals and patients.

In this chapter, we describe the essential ingredients for a health system that can guarantee that patients with Chagas disease receive the **full cycle of care**. To do this, we have used the WHO model, which describes the six building blocks[36] that enable health systems to overcome barriers and increase access to safe, high-quality services. The proposals set out in this chapter would decrease the morbidity and mortality associated with Chagas disease, equip health systems to respond more effectively to people's needs, and protect the population from financial and social risks. **Infographic 4** shows the factors involved in increasing the number of patients diagnosed and treated.

Infographic 4.



Fuente: *Elaboración propia, basada en estimaciones publicadas por la Organización Mundial de la Salud (OMS) y la Iniciativa Medicamentos para Enfermedades Olvidadas (DNDi).*

The Provision of Services

Three key components are required to ensure that a health system is capable of properly identifying and treating people infected with *T. cruzi*:

(1) ***Integration of the diagnosis and treatment*** of Chagas disease into the health system

(2) Screening of ***pregnant and at-risk women*** and follow-up care of newborn infants with *T. cruzi* infection

(3) ***Referral for treatment of all positive cases detected at blood banks***

The main challenge facing health systems in the poor countries most affected by Chagas disease is providing effective access to care. The reality in endemic countries is that most people with Chagas disease live in remote rural areas with few resources, far from any laboratory capable of analysing blood samples and at distances that make post-treatment follow-up very difficult. Programmes aimed at combatting Chagas disease need to provide more support for these populations by introducing systematic measures within the health system to ensure that those affected in the target population are diagnosed and have access to treatment. To achieve this goal, the PAHO recommends ***the incorporation of the diagnosis and treatment of Chagas disease into the primary health care system***[32] to ensure that infected individuals are identified and have access to treatment. The authorities in non-endemic countries—where the prevalence of Chagas disease is much lower—will have to decide whether this recommendation applies to their particular situation.

The PAHO recommends the incorporation of the diagnosis and treatment of Chagas disease into the primary health care system

Identifying at-risk individuals is the second major challenge. It is important to take advantage of every opportunity to diagnose potential patients by routinely offering diagnostic tests during pregnancy, by screening children in school programmes when they are being vaccinated, and by offering diagnostic tests to relatives of people who test positive during blood donor screening. In summary, the steps that **must be incorporated into existing programmes** and interventions undertaken to control Chagas disease are t**he detection of at-risk individuals**, followed by diagnosis and treatment when required (or referral for treatment).

The need for **universal screening of pregnant women** in endemic areas—and of women belonging to risk groups in non-endemic areas—should be beyond all doubt. The PAHO recommendations indicate that "congenital Chagas disease can be controlled by diagnosing and treating the newborn children of mothers with *T. cruzi* infection"[13].

In 2% to 7% of pregnant women who test positive for *T. cruzi*, the infection is transmitted to the newborn and diagnosed after delivery[27,28]. However, this initial diagnosis is inconclusive and in children who test positive for the infection at birth the result must be confirmed by an additional test nine months later. If the second test result is positive, the infant receives treatment. This nine-month interval is a risk factor that leads to fewer infants receiving treatment and there is a need for tests that can provide a definitive diagnosis immediately after birth.

The risk of congenital transmission from mother to infant is 21 times higher in untreated women than in women who receive aetiological treatment before they become pregnant[24]. Universal screening of pregnant women in endemic countries should therefore be extended to all women of childbearing age.

The third challenge has to do with the referral of positive cases detected at **blood banks**. When a blood donor tests positive for *T. cruzi*, there is no guarantee that he or she will automatically receive treatment. All those testing positive should be referred to a health centre for complete assessment and appropriate treatment.

In short, it is the duty of everyone involved to ensure that all patients diagnosed in the course of screening are offered treatment.

Box 4. A Psychosocial Perspective

The six-building-block framework used in this chapter does not take into account the role of the patient or of the general population. However, in this analysis we must take these aspects into account because a **lack of information, education and communication** is known to be a barrier to treatment. It is important to study the at-risk population's knowledge of Chagas disease as well as the culturally specific factors (practices and conceptions) that influence their attitudes to health care and may have an impact on the demand for care.

People who might be affected by Chagas disease **tend not to seek out information or medical care** because they do not understand the benefits of doing so. Chagas disease has its origins in extremely poor and socially marginalised rural and periurban areas where the fear of stigma and of the disease itself prevents people from seeking help.

The concept of **comprehensive care** implies a psychosocial approach in which the delivery of health care services is complemented by effective information, education and awareness campaigns designed to stimulate the demand for care in the population.

Health Care Workforce: Training and Resources

Health professionals working with people who may have *T. cruzi* infection do not necessarily consider the possibility that their patients may have Chagas disease. Moreover, if they do consider the possibility, their response may be conditioned by the financial resources and supplies at their disposal, by the policies of their health services, and by the attitudes of the patients themselves.

At every level of care, it is essential to **train health care personnel** and ensure that processes are put in place to ensure that patients have access to diagnosis and treatment. Health care systems must invest in programmes to raise awareness among staff of the importance of detecting, diagnosing and treating Chagas disease and educate them about the paradigm shift[23] in our understanding of the disease and the benefits of treatment. This must be complemented by the training they require to integrate these new approaches into their work.

At every level of care, it is essential to train health care personnel and ensure that processes are put in place to ensure that patients have access to diagnosis and treatment

Including the diagnosis and treatment of Chagas disease in the curricula of courses for health professionals would help to solve the problem at its root.

Despite the recent shift in the clinical management of Chagas disease towards the use of antiparasitic therapy, health workers who trained when such treatment was not recommended can be resistant to the new paradigm. It is, therefore, crucial to **spread the word about the current medical consensus beyond the domain of Chagas experts** and specialists and to ensure that it reaches other scientific and professional associations, especially those of family doctors, paediatricians, obstetricians, infectious disease specialists, nurses and laboratory technicians.

Chagas is not a disease that has to be treated exclusively by specialists: it can and should be treated at the primary care level.

Many health professionals work long hours in overstretched medical facilities. As a result, efforts to assign them the additional responsibility of diagnosing and treating Chagas disease have sometimes been met with resistance. To facilitate the integration of such care, health workers must receive quality training, be confident of the availability of the necessary supplies, and have access to specialists who can be consulted about technical questions.

Quality of Health Information Systems

Information systems capable of ensuring systematic and standardised collection and storage of data—including data related to diagnosis and treatment—are another key element in the battle against Chagas disease. Such systems make it possible to assess the extent of the problem, to define policies and actions at the local, national and regional level, and to predict the demand for diagnostic supplies and drugs. These data must be analysed and taken into account in decisions regarding disease control if we are to make progress in the fight against Chagas disease.

These data must be analysed and taken into account in decisions regarding disease control if we are to make progress in the fight against Chagas disease

To rescue Chagas disease from the current situation of neglect, greater efforts are needed to assess the extent of the problem and the impact of the disease, including more reliable prevalence studies, systems for reporting cases and detecting outbreaks, and reports to inform decision-making. Only some of the countries affected keep complete and systematic records of the cases of Chagas disease diagnosed. Moreover, even if cases are reported and registered, the data will still be incomplete if there is no effective system to detect and diagnose affected individuals in the community. At the very least, endemic countries must ensure that all cases of Chagas disease—acute and chronic—are reported and recorded by the system. Argentina, where *T. cruzi* infection is a mandatory reportable disease, provides a positive example.

It is also difficult to **forecast the global demand for diagnostic and pharmaceutical supplies** without reliable epidemiological data and information about the policy in each country regarding the integration of Chagas treatment into the health system. The current lack of data makes it difficult to forecast needs and budgets at the local and national levels and also complicates the production process for the pharmaceutical companies that produce the drugs.

The DNDi, in coordination with the PAHO and the WHO (and national programmes in endemic countries), have created a tool for calculating demand, which has been used by the directors of national programmes. In some cases, the tool overestimated the amount of benznidazole required because it failed to take into account the country's low capacity for distributing the supplies and treating patients. Although the tool needs to be further refined to take into account each country's capacities, mechanisms for predicting demand will continue to play an important role in ensuring that supply-chain problems do not impede access to drugs.

Access to Diagnosis and Medicines

Health services can only diagnose and treat patients if they have access to diagnostic tools and treatments. The **production and accessibility** of such resources are therefore **fundamental**. In this section, we highlight three factors that are essential to access to diagnostic tools and treatments:

(1) Production, pricing and approval of drugs.

(2) The importance of R&D in ensuring access to diagnosis and treatment.

(3) Supply-chain management.

With respect to the first factor, the usefulness of the two treatments that have demonstrated efficacy—benznidazole and nifurtimox—has been questioned because of the adverse effects and prolonged duration of treatment as well as the unsatisfactory evidence of efficacy in chronic cases

Although further research is needed to develop better treatments, the benefits of the **existing drugs have been sufficiently demonstrated to justify their use**, and their shortcomings should not be used as an excuse to deny treatment to patients. **A guaranteed and uninterrupted supply of drugs at affordable prices** is essential to ensure that countries can place advance orders for the drugs needed to treat patients once they have been diagnosed.

Existing drugs have been sufficiently demonstrated to justify their use, and their shortcomings should not be used as an excuse to deny treatment to patients

Box 5. The Cases of Benznidazole and Nifurtimox

Benznidazol, the first-line antiparasitic treatment for Chagas disease recommended by the WHO, is classified as an essential medicine. The original manufacturer was Roche, but the technology used in its production was subsequently transferred to **LAFEPE**, a state facility in Brazil. Unfortunately, LAFEPE's production and distribution of the drug has not met expectations. Even before that, LAFEPE's willingness and capacity to meet international demand for benznidazole had been called into question after a shortage affecting several countries in 2011.

As a result of that shortage, the Argentine government set up a public-private consortium led by the Mundo Sano Foundation and the Ministry of Health, which contracted production of the active ingredient to a local company called Maprimed and the development and production of the drug (Abarax) to ELEA, an Argentine pharmaceutical company. The first batch of drugs produced by the consortium was donated in early 2012. Since then, **ELEA has been manufacturing generic benznidazole** in 50 mg and 100 mg formats at a cost of $45 and $60 per 100-tablet bottle, respectively.

When the drug received marketing approval in Argentina, it was added to the WHO essential medicines list. Benznidazole is currently authorised for sale in Bolivia, Paraguay, Chile, Honduras and Guatemala and is awaiting approval in several other countries. However, there are still a few countries where the drug has not yet been submitted for approval. Although **benznidazole is available** through ELEA and the laboratory has the necessary Good Manufacturing Practice (GMP) certification, their product is **more expensive** than the one provided by LAFEPE. The price of the drug is sensitive to changes in the price of the active ingredient, which can increase the cost of producing the drug by up to 40%. Moreover, the final price varies by country because of costs associated with distribution and importation.

At the meetings of the PAHO subregional Chagas initiatives in 2015, the Mundo Sano Foundation—with the collaboration of ELEA—offered to donate a two-year supply of benznidazole for the treatment of congenital Chagas disease.

Nifurtimox—the second-line treatment, produced in 120 mg and 250 mg tablets—is donated by Bayer and distributed through the PAHO Strategic Fund. It is unknown whether Bayer will maintain this commitment if the demand for treatment should increase.

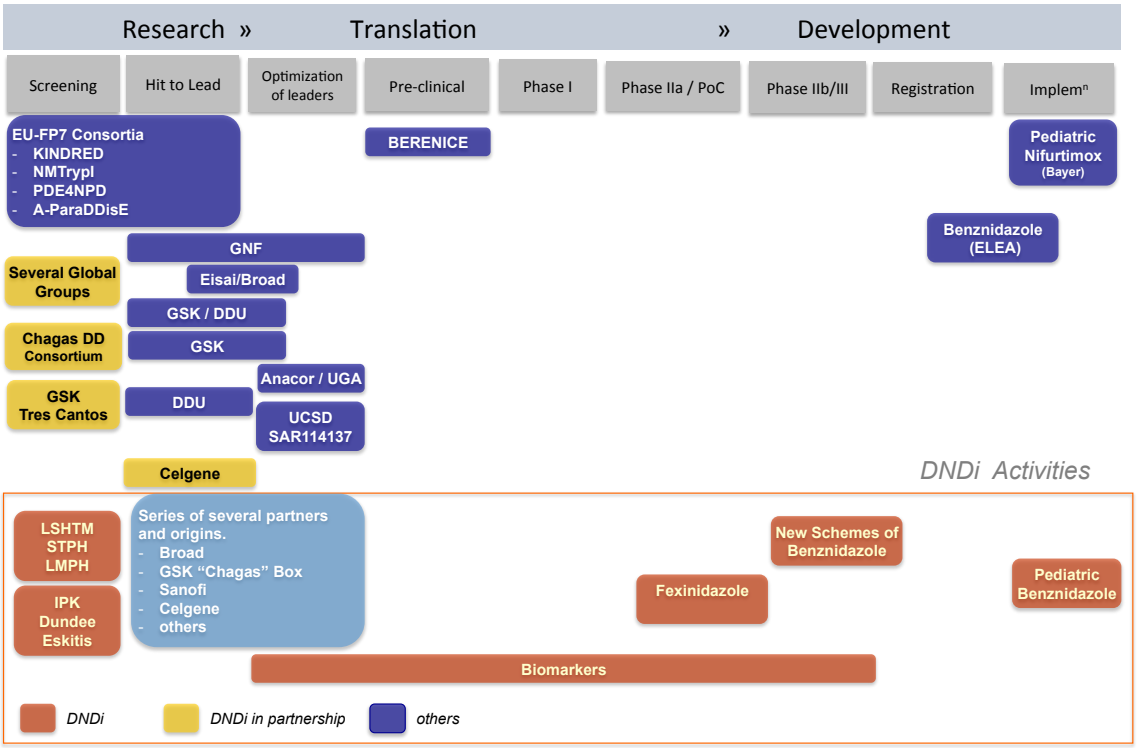
Using current techniques, at least two tests are needed to confirm a diagnosis of Chagas disease, **making it important to promote research** aimed at developing simpler and better diagnostic tools that offer greater precision (sensitivity and specificity) and efficiency. Infants diagnosed during the neonatal period by means other than a parasitologic test must undergo a serologic test at nine months of age to confirm the diagnosis. This delay increases the risk that the family may not bring the infant back for definitive diagnosis and treatment. In fact, all the diagnostic techniques except rapid tests[37]—a convenient option that provides patients with a speedy diagnosis—are quite complicated. Simpler diagnostic algorithms need to be established by incorporating new diagnostic techniques appropriate to the different care settings (primary, secondary and tertiary facilities).

Further research is also needed to develop new drugs for the treatment of Chagas disease, especially for patients with chronic disease. Experts generally agree on the need for treatments that are at least as effective as those currently in use but have better tolerability and safety profiles, do not require regular clinical examinations or laboratory tests, and—ideally—involve a shorter duration of treatment. Evaluating new treatment regimens with benznidazole and nifutrimox—at lower doses or with shorter durations of treatment, either as monotherapy or in combination with other drugs—is one of the top priorities. The evaluation of new molecules for the treatment of Chagas disease is part of the longer-term strategy.

Further research is also needed to develop new drugs for the treatment of Chagas disease

The current situation with respect to the development of new treatments suggests that some progress is being made on the global R&D portfolio for Chagas disease.

Infographic 5. **Global Outlook for Chagas R&D in 2016**



The **development of biomarkers** to improve and expedite the measurement of treatment efficacy is also crucial. With the tools currently available, it is impossible to know for certain whether a patient has been cured until many years or even decades later. Tools that can confirm a cure, identify signs of disease progression, or identify patients at greater risk of developing complications are urgently needed.

Box 6. R&D Incentives in Neglected Diseases: Benefits, Abuses and Impact on Access

To encourage R&D for **neglected diseases, incentives must be offered** to attract the interest of pharmaceutical companies, which view diseases that mainly affect less developed countries as lacking in market potential. However, it is important to ensure that these incentives are accompanied by mechanisms designed to **safeguard the future accessibility and affordability of the resulting products**.

The controversy surrounding such incentive programmes is focused on two issues. First, the incentives do not always reward the development of drugs that are truly new. Second, there is no guarantee that the benefits of these incentives will have a positive impact on the affected populations. Solutions to this problem could include the addition of a **novelty requirement** and/or the introduction of formulas that ensure that pharmaceutical companies will commit to making the drugs available to affected populations at reasonable prices (for example, requiring prior approval in endemic countries or formal agreements to facilitate access).

The recent case of benznidazole in the United States is an example of what can happen if measures to ensure access are not included in the design of these incentives. In 2007, the US Congress passed legislation that introduced priority review vouchers (PRVs) as a means of encouraging the development of drugs for NTDs. This incentive gives pharmaceutical companies access to an expedited Food and Drug Administration (FDA) review process. With a PRV, approval takes 6 months instead of the usual 12 months, and the cost of bringing the product to market decreases accordingly. However, companies are not required to use a PRV for the drug for which the voucher was originally issued. The voucher can instead be used for another product or even be sold. Another mechanism available in the United States is orphan drug status. This designation identifies a drug as a potential recipient of various incentives, including tax credits for clinical testing and support in the sales and marketing process.

On 3 December 2015, KaloBios announced that it had bought the worldwide rights to a version of benznidazole from a company called Savant Neglected. According to a presentation given by then-CEO Martin Shkreli, KaloBios intended to obtain orphan drug status and a PRV and subsequently increase the price of benznidazole to levels similar to those of hepatitis C drugs (between $70,000 and $90,000 per treatment). Although the outcome remains uncertain, the public was understandably alarmed by Shkreli's plan. Outraged observers demanded to know what impact the transaction would have on patients in the United States and the rest of the world.

These are just two examples of incentives, but there are others. The important point is that **any incentive must include a coherent and robust strategy for guaranteeing access to the drugs.**

Drugs for the treatment of Chagas disease are distributed in Latin America through the PAHO Strategic Fund, a useful mechanism for negotiating prices and donations and for guaranteeing that the drugs can be used in countries where they are not approved for sale. But this arrangement also has disadvantages: the countries of the region are dependent on a system for which few alternatives are available in the event of a shortage. Outside of Latin America, each country has its peculiarities. In the United States, benznidazole is supplied by the Centers for Disease Control (CDC) through clinical trial protocols. In other countries, it is supplied through the WHO.

Expediting the necessary approval and certification in such cases could improve access

In many cases, the product lacks the necessary certification that it meets national standards. Dealing with this anomalous situation increases the cost of treatment and is a barrier to access for both doctors and patients. ***Expediting the necessary approval and certification in such cases could improve access***, especially in the countries where a large number of people are affected by Chagas disease.

Finally, investment in **improving national distribution systems** in terms of both capacity and management is essential. There have been cases in which treatment was available at a central location but not at local medical facilities.

Funding

Only scant funding has been allocated to patient care because programmes have traditionally been more focused on prevention and control. In order to ensure access to care for all patients with Chagas disease, it is essential to prioritise programmes and ensure that interventions involving diagnosis and treatment have the resources they need. To make this possible, budgets must be increased to cover the cost of medical services, human resources and information systems, and access to diagnostic supplies and treatments must be guaranteed.

In order to ensure access to care for all patients with Chagas disease, it is essential to prioritise programmes and ensure that interventions involving diagnosis and treatment have the resources they need

Irrespective of the funding mechanisms used, diagnosis and treatment of Chagas disease should be free for patients in order to guarantee **universal access for all those affected**. The current situation is that full coverage is not guaranteed in all countries. Finally, mechanisms should be put in place to prevent the most vulnerable patients and their families from incurring catastrophic expenses and loss of income if they have to travel long distances or miss work in order to receive care.

Leadership and Governance

Health programmes should be underpinned by **clear legal frameworks** regulating rights and obligations. No uniform regulations for Chagas disease currently exist: screening systems at blood banks, measures undertaken to prevent congenital transmission and indications for treatment vary from country to country. The clinical protocols used by affected countries should be updated and a greater level of consensus is needed. Clarification of treatment-related regulations would simplify the work of medical professionals and reduce their resistance to the diagnosis and treatment of patients with Chagas.

WHO/PAHO recommendations should be applied at the national level

In this context, it is important to reiterate the recommendation of the WHO and the PAHO—that the full cycle of care for Chagas disease should be offered at the primary health level—and to highlight the latter organisation's recent list of ten recommendations for the care of patients with Chagas disease. These **recommendations should be applied at the national level** and incorporated into each country's laws and regulations. Protocols and guidelines should also be adapted to make them more patient-oriented and more applicable to primary care facilities. Finally, it would be useful if the WHO/PAHO could incorporate the latest advances in diagnosis and treatment into the existing management guidelines and strongly encourage countries to make further progress in this area.

If we are to win the battle against Chagas disease, the governments of affected countries, apart from ensuring the necessary changes in the regulatory framework, must also **make a political commitment** to the implementation of a global strategy with a particular focus on Latin America. All stakeholders—academia, civil society, non-governmental organisations and the private sector—must work with the authorities on a single agenda to address Chagas disease. **This is why it is essential to have a global roadmap** for stakeholders that promotes comprehensive Chagas programmes and R&D aimed at the development of new medicines and tools to improve the treatment of the disease.

In the previous chapter, Table 2 presented the goals set by international bodies between 2009 and 2013 for the fight against Chagas disease. The most recent objectives—the milestones for 2020 included in the London Declaration—were criticised by some observers, who considered that they were difficult to assess and lacked clear recommendations on the need for diagnosis and treatment.

Since then, progress has been made. The third WHO progress report highlighted the importance of promoting active strategies for diagnosis, treatment and interruption of transmission. The PAHO published its ten treatment recommendations and has encouraged the adoption of more goals and progress indicators related to diagnosis and treatment as well as disease control. However, **in order for significant progress to be made in these areas, the goals and indicators specified by the roadmap need to be further expanded**. Such a move would serve to reinforce the message about the need to scale up access to treatment and improve the indicators by making them more specific and easier to assess.

Finally, there can be no progress if we only advance on at the global level. Change is also needed at both the regional level—through the Chagas initiatives—and the national level—through **local roadmaps**—under the leadership of governments and health ministries.

@Juan Millás

Recommendations: A Strategy for Increasing Access to Diagnosis and Treatment for Patients with Chagas Disease

RECOMMENDATIONS: A STRATEGY FOR INCREASING ACCESS TO DIAGNOSIS AND TREATMENT FOR PATIENTS WITH CHAGAS DISEASE

"In my opinion, the experience of La Plata has shown that most patients can be treated in a primary care setting. [...] and that public-private partnerships are not only possible, but in fact very fruitful for both parties."

Dr Ana Pereiro, Project Coordinator, Mundo Sano Foundation

Like many other infectious diseases, Chagas disease is controlled through **comprehensive programmes** comprising a broad range of interventions. In addition to case management (diagnosis and treatment), these include information and education activities, screening and surveillance, transmission control efforts, and training of health care personnel.

This report focuses on the **urgent need to increase the number of patients** being diagnosed and treated for Chagas disease. **Access to diagnosis and treatment** must be a priority in all of the countries where these patients live. The good news is that we have the tools we need to improve diagnosis and treatment if the political will and commitment is there. Success stories have clearly demonstrated that good results can be achieved with the strategy proposed in Box 7.

Box 7. Lessons Relating to the Diagnosis and Treatment of Chagas Disease Learned from Three Success Stories

Three case studies that illustrate the strategy proposed in this report are included in the appendices. We present these cases in order to share the key recommendations that have emerged from the positive experiences of programmes based on a comprehensive approach to the problem of Chagas disease in three very different countries. Each one of these examples shows what can be achieved with this approach.

Diagnosis and treatment in a non-endemic area: the case of the city of La Plata in Argentina

The city of La Plata is located in a region where the insect vector that transmits Chagas disease is not present. However, in 2010 the prevalence of *T. cruzi* infection among pregnant women in the city was 1.75% due to the presence of a migrant population originally from areas where the prevalence of the disease is high. The Mundo Sano Foundation, working with the city's Department of Health and Public Medicine, set up an early detection and treatment programme, providing medical care in 46 healthcare facilities throughout the city and screening students in all public schools for the infection. As of November 2015, this innovative programme had **tested 11,922 individuals, diagnosed 976 with *T. cruzi* infection, and treated 802 patients**.

Bolivia: A platform for the comprehensive care of Chagas disease and expansion of the network to include the National Health Service

Bolivia, where Chagas disease is endemic in 60% of the territory, is the country in the Americas with the largest number of new vector-borne cases. Estimated national prevalence is 6.1% and this figure varies considerably across different areas of the country. In 2009, **ISGlobal and the CEADES Foundation** created the Bolivian Platform for the Integral Care of

Patients With Chagas Disease, an organisation with the following objectives: ensuring diagnosis and treatment for adults with Chagas disease, providing training in the clinical management of the disease, and undertaking research and development projects. Today, the Bolivian Platform has six health care centres in three of the country's departments (Cochabamba, Chuquisaca and Tarija). A model based on care protocols and consolidated in these three areas over an initial four-year period is now being introduced countrywide into Bolivia's **National Health Service** centres. As of December 2015, the Platform **had tested 24,700 patients, of whom 21,387 have been diagnosed with *T. cruzi* infection. In total, 10,454 patients have begun treatment** and over 80% of them have completed the full course.

Chagas in the USA: the Chagas Disease Centre of Excellence at Olive View-UCLA Medical Center

Some **300,000 people** living in the USA, a non-endemic country, have Chagas disease. Although triatomine bugs are found in some areas of the USA, vectorial transmission is rare and most of the cases reported involve immigrants from countries where the disease is endemic or children born to women from those countries. When the Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center opened a clinic in Los Angeles county (southern California) for the diagnosis and treatment of the disease in 2007, it was the first specialised centre for Chagas disease in the USA. Since then, through the clinic and community outreach activities, **7,357 people have been tested**. Of these, **200 tested positive** for *T. cruzi* infection and **162 have received treatment**. The centre has also conducted several studies on the disease in the USA.

An analysis of these three, very different, cases provides us with key pointers for success. These conclusions should help other projects to more quickly scale up access to diagnosis and treatment of Chagas disease.

- **Leadership** on the part of the **competent authorities** is a key factor.
- **Partnerships** and agreements should be established between all the actors involved.
- **Collaboration between the different actors is essential. And coordination** with primary care networks and Chagas programmes at both local (the department) and national level (in the case of Bolivia and Argentina) is crucial.
- Experience highlights the need for systems regulating the i**nformation flow** between different levels of coordination to ensure adequate prioritisation, epidemiological surveillance and accurate forecasting of the demand for drugs.
- Strategies that are embedded in the **national health system** and require no external resources facilitate implementation and are more likely to improve access.

- **The financial and operational capacity of the health system** and the available human resources should be assessed in order to **adapt the programme to each setting**.
- **Personnel motivation** has been a distinguishing factor directly related to the results achieved in all three cases.
- **Access to the necessary medicines is essential** and testing should not start until the supply of drugs is guaranteed

Drawing on experience and scientific evidence, we have drawn up a preliminary proposal for an ideal framework, which defines the goals that should be achieved, the actions needed to achieve them, and indicators that should be used to monitor results (**Box 8**).

From now on we must work continuously with all the stakeholders to develop the best strategies and tools for scaling up the diagnosis and treatment of this disease and to one day achieve our goal: ***"a world where Chagas disease is controlled and universal access to treatment is a reality"***. If we are to achieve this goal, all the stakeholders must be mobilised and take action, and to this end we make the following recommendations:

We ask the governments of affected countries:

1. To make a political commitment to implementing a global strategy to combat Chagas disease, with special emphasis on Latin America.

- To sign a regional resolution to scale up access to the diagnosis and treatment of Chagas disease in line with WHO/PAHO recommendations.

2. To implement programmes aimed at accelerating access to diagnosis and treatment:

- Increase the resources allocated to the Chagas programmes to facilitate an average increase of 45% a year in the number of patients treated up to 2020 (mean annual growth over the period).
- Ensure the availability of the drugs and the supplies needed for diagnostic procedures in national health service facilities.
- Invest in training health care personnel in the detection, diagnosis and treatment of Chagas disease.
- Include adults with chronic Chagas disease in comprehensive care programmes.
- Implement information, education and communication activities to encourage people to be tested.

3. To control transmission:

- Implement universal screening of at-risk women of childbearing age in order to prevent mother-to-child transmission. To treat women with *T. cruzi* infection and positive children at birth, in endemic and affected countries.
- Continue vector control efforts and ensure systematic screening in blood banks and organ donation programmes in Latin America and in non-endemic countries (including developed countries).

We ask public and private actors:

4. That everyone working with Chagas disease adhere to the "roadmap" and work towards increasing access to diagnosis and treatment:

- By supporting the work of the national programmes undertaken to achieve this goal in affected countries.
- By channelling efforts towards furthering the priority goals established by the roadmap.
- By spreading the word about the importance of increasing access to diagnosis and treatment.

The Chagas Coalition's next undertaking will be to convene a group of experts to draw up practical guidelines and recommendations on how to increase the number of cases diagnosed at community, city, provincial, country, and regional level. Our aim is to go from the 1% of affected patients receiving treatment today to a situation in which 100% of newborn infants will be diagnosed and treated and 100% of children under 18 years will be treated. In the case of adults, the objective is to treat eight times more adults in 2020 than are treated today.

Box 8. **How to Achieve Universal Access to Diagnosis and Treat**

Blocks	Actions
Provision of services	- Integrate diagnostic testing and treatment into the health system - Screen women of childbearing age and pregnant women. Follow up for infected newborns - Sceen all donors at blood banks - Sustain vector control measures
Health care personnel	- Train educators, biochemists, nurses and doctors
Information systems	- Include epidemiological data on Chagas disease in medical information systems - Analyse the extent of the problem and forecast the demand for care and treatment
Financing	- Production of quality drugs at an affordable price with approval in every country - Efficient management of the supply chain - R&D to develop simplified diagnostic methods, new drugs, and techniques for assessing cure - Encourage patients to come forward for treatment (stimulate demand)
Access to diagnosis and medicines	- Allocate more financial resources to comprehensive programmes and increase funding for diagnosis and treatment - Guarantee free diagnosis and treatment and protect vulnerable patients from catastrophic expense (cost of transport, absence from work) - Allocate resources to R&D
Leadership and governance	- High level political commitment resulting in agreements and goals in line with the WHO/PAHO recommendations and the SDGs - Clear national policy reflecting commitments made - Update legislation and protocols, including those relating to control of transmission (blood banks, organ transplantation, congenital disease, etc) and guidelines for diagnosis and treatment - Commitment of local, municipal, provincial and national actors - Close collaboration with WHO/PAHO

Coverage of Access to Testing and Treatment

- 100% of children
- 100% of pregnant women and newborns
- 100% of women of childbearing age
- 100% of health centres providing diagnosis and treatment for other patients

Quality and Safety

- 0% reinfections
- Diagnostic tests with 100% sensitivity and specificity
- Increase the efficacy of therapy
- Reduce adverse effects of therapy
- Existence of alternative therapies
- 0% serious safety incidents
- Effective methods for assessing response to treatment

Optimum Scenario

GOALS	Overall Results
Improve health	- Reduced morbidity - Prevalence and incidence - Reduced mortality
Guarantee response capacity	- Reduced disease burden - 100% of epidemics detected and controlled
Financial and social protection	- 100% of at-risk people tested and diagnosed - Free treatment - 0% catastrophic expense
Improve efficiency	- Target population (100% of treatable cases treated)

Maximising the likelihood that this scenario will be possible is in our hands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Appendices

APPENDICES

Case studies were carried out to provide a picture of the situation in three different countries. Each one presents the data on Chagas disease and a description of the project. All three projects were based on the six system-building blocks of the WHO Health Systems Framework. The studies describe the actions associated with each building block, the goals pursued and the results achieved in each case. The challenges in each country are described and analysed. The final section of each study presents a series of recommendations based on the lessons learned. Comments from people who participated in the programmes are also included.

1. Diagnosis and Treatment in a Non-Endemic Area: The Case of La Plata, Argentina

1.1. Introduction

As a result of migratory flows, Chagas disease, once a problem confined to endemic areas of the Americas, has spread to areas where the disease is not endemic, such as the city of La Plata, capital of Buenos Aires province. The vector that transmits Chagas disease is not found in La Plata. However, due to the presence of migrants from places with high rates of Chagas infection—other parts of Argentina and neighbouring countries—the prevalence of *T. cruzi* infection in pregnant women in Buenos Aires province was 1.75% in 2010.

The Mundo Sano Foundation, in collaboration with the La Plata Department of Health and Social Medicine, runs a programme for the early detection and treatment of Chagas disease in the city. The programme was launched at two health centres in 2010 and was expanded in 2014. All 46 of La Plata's health centres now actively seek out patients at risk for Chagas infection. Programmes to detect those at risk are also carried out in all of the city's public schools.

As of November 2015, this innovative programme had tested 11,922 people for *T. cruzi* infection, diagnosed 976 and treated 802*.

*Pregnant women, patients older than 50 years of age, and patients with severe organ involvement—in whom treatment is contraindicated—account for the difference between the number of patients diagnosed and the number of patients treated.

Argentina in Numbers[2, 38, 39, 40]:

- **Estimated number of people infected:** 1,505,235
- **Prevalence:** 3.6%
- **Number of people at risk:** 2,242,528
- **Treatments ordered in 2013:** 8,761, (173% more than in 2010, sufficient to treat 4,380 patients)
- **Births per year:** 750,000
- **Pregnant women screened for *T. cruzi* infection in 2013:** 265,098 (38%)
- **Newborns infected with T cruzi (estimated):** 1,457 per year
- **Detection and follow-up of newborns (2013):** 55.29%
- **Percentage of blood screened for Chagas disease at blood banks:** 100%

1.2. Chagas Disease: Regulatory and Policy Framework

Argentina has a legal and regulatory framework for the prevention and control of Chagas disease (see Box 1) and a strong national programme that recognises the need not only to diagnose but also to treat patients. Vector control activities have been underway for some time in endemic areas, and some of Argentina's provinces have been declared vector-free. The national Chagas programme now faces new challenges, such as detecting cases in non-endemic areas and finding the right formula to increase the number of patients diagnosed and treated.

Box 1. Legal and Regulatory Framework in Argentina

- **Chagas Act 26.281, 2007**. This law prioritises school-age children as well as pregnant women and newborns.

- **Guidelines:** Guidelines for the care of patients with *T. cruzi* infection (Chagas disease). Argentine Ministry of Health, Buenos Aires. http://www.msal.gov.ar/chagas/images/stories/Equipos/Guia_Nacional_Chagas_version_27092012.pdf

- **Recommendations:** The Argentine Ministry of Health (2012) **recommends treating** congenital, acute, early chronic and late chronic Chagas disease. The ministry also maintains that treatment is probably advisable in patients with incipient heart disease and in indeterminate chronic cases and cases of reactivation in immunocompromised patients.

At the local level, the project is implemented by the La Plata Department of Health and Social Medicine. It is important to note that the Chagas programme is cross-cutting, that is, it is integrated into other national health programmes: PROSANE (a school-based health programme), REMEDIAR (a programme that guarantees drug supplies and distributes kits to health centres), MÉDICOS COMUNITARIOS and SUMAR. Some health centres are also participating in a pilot project designed to test whether adding benznidazole to the list of drugs supplied through REMEDIAR could improve access to treatment and pharmacovigilance.

1.3. Intervention Model

The model was designed on the basis of the principles of **stability, sustainability, scalability and reproducibility** and takes into account that the jurisdiction of the municipal authorities only extends to primary health care centres. It was therefore essential to create a network capable of dealing with different levels of complexity in order to provide patients the medical services they need at all levels.

With a focus on primary care, the programme is integrated into existing public health services and ensures the routine provision of services related to Chagas disease. The approach is horizontal—focusing on the patient rather than on the disease or the structure of the health system—and covers many different aspects, including clinical care, health care management and policy, promotion, prevention, and cure.

At-risk persons are detected on the basis of an epidemiological profile in the primary care setting, either on demand or during prenatal visits. Cases are also detected through the PROSANE school-based health programme. Health centre personnel and network coordinators also organise activities to raise awareness about Chagas disease among pregnant women, women of childbearing age, and in the paediatric setting. Activities are also organised in at-risk communities and neighbourhoods with large migrant populations.

Care relating to Chagas disease is provided to all age groups, and members of priority groups (pregnant women and children) are followed up. Patient diagnosed with the infection start treatment within a maximum of 15 to 20 days unless treatment is contraindicated. Mobile electrocardiograph (ECG) and laboratory services—not only for Chagas patients but for all diseases—are available at each health centre and patients do not have to visit a different facility for additional testing (blood test or ECG).

Although the programme forms part of the public health service, integration is incomplete because existing protocols do not regulate the referral and counter-referral of patients to higher levels of care and rehabilitation is not included.

1.4. Supplies: Diagnostics and Drugs

The first- and second-line treatments—benznidazole and nifurtimox—and medicines to treat adverse effects are provided to patients at no charge by the National Chagas Disease Programme. In 2011, the programme was paralysed for several months due to an interruption in the supply of benznidazole from LAFEPE, the only producer at that time. ELEA—a manufacturer that entered the market at the request of the Argentine Ministry of Health—currently guarantees production of benznidazole. Under the trade name Abarax, the drug has been approved for sale in Argentina.

1.5. Human Resources

All the personnel engaged in Chagas care are employees of the national health service and no additional personnel are needed. The Chagas network is coordinated by four people employed by the health centres. These coordinators receive extra pay to compensate them for the additional responsibility. An in-service training programme provides both distance and face-to-face training, and a network of experts provides ongoing support to health centre personnel.

1.6. Funding and Sustainability of the Model

The project has four sources of funding: the La Plata city government (through taxes), the province of Buenos Aires (via revenue sharing), the Mundo Sano Foundation, and the Argentine government. The government participation is channelled through national programmes, such as MÉDICOS COMUNITARIOS (to ensure the availability of human resources) and PROSANE (to reach children and adolescents).

It is too early to know whether future sustainability can be guaranteed. However, following changes in the health care structure and after the Argentine government changed hands in late 2015, the new authorities undertook to continue the programme. If there is no change in policy, the programme could become state policy—rather than government policy—provided that future administrations prioritise its continued existence.

La Plata Project Outline Based on the Six-Building-Block Health System Model

Building Block	Action
Service delivery	- Diagnostic testing and treatment are provided at existing primary care centres - Health promotion activities are organised - Early diagnosis is available through the national health service
Health workforce	- No additional human resources are used; the existing health service workforce is strengthened, coordinators are given incentives and staff are trained
Information systems	- The project has its own data-collection system - Cases are reported to the Health Department, which records data in the health information system - Pilot plan with REMEDIAR to test delivery of benznidazole
Financing	- La Plata city and provincial authorities, Argentine government, Mundo Sano Foundation
Access to diagnostics and medicines	- Laboratory services available on site - Programme supplies benznidazole (purchased from ELEA) - Nifurtimox (donated by Bayer) used as second-line treatment - Free diagnostic testing and treatment
Leadership and governance	- Strong leadership provided by the La Plata Health Department and the Mundo Sano Foundation

Coverage of Access to Testing and Treatment

- 100% of patients seeking testing covered. (Demand is not high.)
- 25% of the total target population
- 100% of health centres offer diagnostic testing and treatment

Quality and Safety

- 0% reinfections
- 19.5% adverse effects during treatment
- 2 different treatment regimens available
- 0% serious safety incidents

Results as of Nov. 2015

Goal	Overall Results
Improve health	**802** people have completed treatment since 2010, preventing around 30% of them from developing cardiac or intestinal problems.
Guarantee response capacity	Response for infected people and cure for infected newborns are provided more rapidly. Programme data are monitored, allowing strategies and forecasts of demand to be adjusted accordingly.
Financial and social protection	The tools and medicines needed to treat patients free of charge are currently available.
Improve efficiency	Target population = 47,688

Mundo Sano

1.7. Conclusions: Keys to Success, Challenges and Lessons Learned

As of November 2015, the programme had screened 11,922 at-risk individuals, diagnosed 976 people with *T. cruzi* infection and treated 802 patients*, 11% of whom were children under 19 years of age. For various reasons (travel, intolerance, coinfection), 8.13% of those treated failed to complete 30 days of treatment. All pregnant women who received care through the municipal primary care system were screened for Chagas disease with two blood tests.

*Pregnant women, patients older than 50 years of age, and patients with severe organ involvement—in whom treatment is contraindicated—account for the difference between the number of patients diagnosed and the number of patients treated.

In my opinion, the experience of La Plata has shown that most patients can be treated in the primary care setting. Training the workforce involved in patient care and the clinical management model used are very important factors that guarantee the efficiency and quality of the service and ensure adherence to treatment and appropriate follow-up. This experience has also shown us that public-private partnerships are not only possible, but in fact very fruitful for both parties.

Dr Ana Pereiro, Project Coordinator, Mundo Sano Foundation

The **model has been successful** in gradually scaling up access to diagnosis and treatment. The fact that the programme was integrated into the health system and required no additional resources facilitated its implementation. Other key factors in the success of the programme were the strong leadership of the La Plata Department of Health and Social Medicine, the support of the national Chagas programme and of the Mundo Sano Foundation, and the motivation of the staff involved and in particular of the coordinators. The emergence of a second benznidazole manufacturer has, since 2012, made it possible once again to guarantee free access to the drug.

The main **problems** faced by the programme:

- Interruption of the benznidazole supply in 2011.
- Public-private integration as a work model in public health.

The main **challenges** that lie ahead:

- Health centres do not always have sufficient resources to meet the demand.
- Commitment levels and results vary across the 46 health centres.
- The coverage of screening for congenital Chagas disease needs to be improved because the municipal health system has no maternity clinics and the diagnosis of newborn babies has to be confirmed by serology when the infant reaches 10 months of age.
- Continued collaboration will be necessary to improve the capacity for care of the primary network and to continue to provide mobile ECG and laboratory services.
- The treatment of patients in the chronic and symptomatic phase of the disease needs to be integrated into the programme because there is no formal protocol regulating the referral of patients who require more complex care.

The main lessons **learned (with a view to replicating the programme elsewhere)**:

- It is essential to define the geographical scope of the intervention. A preliminary analysis should be carried out to gain an understanding of the high-risk group and estimate the extent of the problem. The demand for—and delivery of—services and the target population's access to the care centres should also be studied.
- It is important to assess the strengths, weaknesses and operational capacity of the health service. Special attention should be paid to laboratory and ECG services, available human resources, and financial capacity.
- Screening of pregnant women proved to be a useful means of estimating prevalence in the area.
- It is essential to use existing services to integrate screening, diagnosis and treatment, as well as promotion and prevention activities at the health centres in order to eliminate the need for patients to visit other facilities and to ensure the greatest possible access.
- It is important to ensure that information reaches all levels of coordination so as to ensure appropriate prioritisation and epidemiological surveillance and to accurately forecast the demand for drug.
- Leadership, political commitment and motivated staff are key factors in achieving success.

2. The Case of Bolivia: The Platform for the Comprehensive Care of Patients With Chagas Disease and Its Expansion to the Clinics of the National Health Service

2.1. Introduction

Chagas disease has been known in Bolivia for many years and is endemic across 60% of the country. Every year, more new cases of vector-borne Chagas disease occur in Bolivia than in any other country in the Americas[41]. Prevalence is estimated at 6.1% nationwide but varies widely across different regions. In some parts of the Gran Chaco region, for example, prevalence exceeds 40%. Therefore, in addition to the work of Bolivia's national Chagas programme, the country continues to receive significant financial and technical assistance to support efforts to control the disease, mainly through prevention activities but also through diagnosis and treatment.

For many years, the main focus of the Bolivian National Chagas Programme—the entity responsible for the health ministry's Chagas prevention and management efforts—was to reduce infestations of kissing bugs or *vinchucas* (the insects that carry the parasite).

Over the past decade, greater emphasis has been placed on the diagnosis and treatment of infants and children under 15 years of age. In 2009, ISGlobal and the CEADES Foundation created the Platform for the Comprehensive Care of Patients With Chagas Disease with the aim of diagnosing and treating adults, providing training in the management of Chagas disease and undertaking R&D projects. The Platform currently has six health centres in three Bolivian departments (an administrative division): four in Cochabamba (Hospital Viedma, Hospital Punata and clinics in Sacaba and Villa Tunari); one in Chuquisaca (Sucre); and one in Tarija. A protocol-based care model encompassing various areas of activity has been consolidated over the past four years. This model is now being expanded to health centres belonging to Bolivia's National Health Service. The expansion of the model—mostly to primary and secondary level facilities—involves training the staff of the centres and encouraging them to incorporate comprehensive care of Chagas disease into their routine activities.

As of December 2015, **24,744** people had been tested at the Platform's centres, **21,387** of whom were diagnosed with *T. cruzi* infection. In total, **10,454 patients have started treatment** and 80% have completed the course.

Bolivia in Numbers[2, 42]

- **Percentage of the country considered endemic (presence of triatoma):** 60%
- **Estimated number of people infected:** 607,186
- **Prevalence:** 6,104% countrywide, but as high as 40% in certain areas
- **Number of people at risk:** 586,434
- **Estimated number of new cases annually due to vector-borne transmission:** 8,087
- **Percentage of blood screened for Chagas disease at blood banks:** 100%

Diagnosis and Treatment in 2013

- **Number tested (children and adults):** 50,842
- **Positive for infection:** 12,945
- **Treated:** 2,274
- **Pregnant women screened:** 71,003
- **Pregnant women testing positive:** 15,461
- **Positive cases in newborns per year (estimated):** 616
- **Detection and Follow-up of Newborns in 2014:** Screened 12,578 and diagnosed with *T. cruzi* infection 182

2.2 The Context: National and Provincial Policies Relating to Chagas Disease

There is a legal and regulatory framework for the management of Chagas disease in Bolivia (Box 2). The National Chagas Programme (which operates at the national and departmental levels), the Departmental Health Services and the Municipal Health Councils are the bodies responsible for the prevention, diagnosis and treatment of Chagas disease. The National Chagas Programme provides free treatment at the health centres of the National Health Service. However, the cost of one of the diagnostic tests is not covered and drugs and other supplies are not always available for various reasons. Moreover, although efforts have been made locally to improve the provision of diagnostic and treatment supplies, the resources made available by the National Health Service fall short of the potential demand for diagnosis and treatment if all people with *T.Cruzi* infection in Bolivia are taken into account.

Box 2. Legal and Regulatory Framework in Bolivia

- **Chagas Act:**
  - Law No. 3374, dated 23 March 2006, declares the prevention and fight against Chagas disease to be a national priority in all the country's departments.
  - Departmental Law No. 34, dated 23 September 2011, provides for "the promotion of human development through the construction and improvement of homes and the education of citizens in the prevention of Chagas disease".
- Diagnosis and treatment are free for all in health centres.
- **Disease management guidelines:** Guidelines for the management of congenital and paediatric (up to age 15 years) Chagas disease have been published and were revised in 2015. Guidelines for adult patients are forthcoming.

Recommendations: The Bolivian Ministry of Health **recommends treating** congenital, acute, early chronic and late chronic Chagas disease when the patient does not present heart disease or serious complications.

2.3. Intervention Model

The Platform's centres provide care for patients with Chagas disease to build up a comprehensive approach (prevention, diagnosis and treatment). They also train health professionals in the management of Chagas disease and conduct research to generate knowledge that can benefit the affected population. These centres also organise activities to raise awareness among people who might have the disease or know someone who does to encourage them to seek diagnosis and, if necessary, treatment.

The **direct care** provided by the centres includes services for adult patients with chronic disease without distinction as to the sex or nationality of the patients. The Platform's centres provide a vertical service focused on Chagas disease. Thanks to the expansion of the Platform's activities to facilities operated by the National Health Service, protocol-based care is now being integrated into the health system and Chagas disease will become just one more condition treated at all health care levels.

Since 2015, the Platform has been working to help the National Health Service facilities to adapt the proposed protocols for the comprehensive care of Chagas disease and to create a network and define a system for referrals and counter-referrals between levels of care. The network is also being strengthened by way of strategies that entail joint supervision together with the key stakeholders with responsibilities at the local level (National Chagas Programme, Departmental Health Services, and the coordinating bodies responsible for the NHS network).

The Platform uses an integrated approach that takes into account **gender** and **interculturality** in order to improve coverage and quality of care. This approach enables the Platform to respond adequately to gender- and ethnicity-related constraints that prevent vulnerable populations from gaining access to health services.

"We have always lived with vinchucas since we were children living in an adobe house. I'm studying biochemistry and I heard about the disease and the *vinchucas* in the faculty. Remembering my childhood, I realised I should get tested. And I tested positive. I was treated at the Platform. I didn't have an allergic reaction or anything. They told me everything I needed to know about the medicine, and everything went fine. The medical care at the Platform is very good. They're flexible about scheduling, to make sure you don't miss your appointments. They give you the full treatment for free, and we're very grateful for0,2117s a great help.

My only concern is that more people need to be made aware of the danger. The topic should be on the news to encourage more people to come for testing. So many people must have [the disease] and in the long run they run serious risks. But they simply don't know".

César Jhonny Hidalgo (27) from Vinto, Cochabamba

Recognising the crucial role that at-risk populations must play in the fight against Chagas disease, the Platform organises campaigns to provide basic **information** and **raise awareness** about epidemiological surveillance, prevention measures and access to health services. The objective is to encourage people to seek timely diagnosis and treatment or disease management, as appropriate.

The lack of knowledge among health professionals about Chagas disease and how it should be managed is a major barrier to care for people diagnosed with *T. cruzi* infection. To remedy this situation, the Platform provides **training** to update and expand the knowledge, skills and competencies of those working with at-risk populations and patients with Chagas disease.

"This was the first time I've attend a training course like this one. The truth is, I have never dared to treat patients with Chagas disease for fear of causing the side effects I'd heard about. During the week I've spent here at the Platform, I've seen hundreds of patients who are being treated without incident. They're fine. Patients who have had a reaction are monitored more closely and they complete treatment without too much difficulty. As soon as I get back to my community I will start treating patients. Now I feel more confident. But we also need to inform the people as well. We all need to improve our awareness and learn more, don't you think? We're going to coordinate with the nurses here at the centre to move in this direction".

Dr Mario Ponce Flores, interviewed at the Chagas Platform's Pocona Centre in Cochabamba

Finally, the Platform is working on three lines of **research**:

1) Studies to identify biomarkers of early treatment response and disease progression,
2) Clinical characterisation of cardiac and digestive complications in Bolivia, and
3) Assessment of the results of vector control efforts within the project area.

2.4. Supplies: Diagnostics and Drugs

Benznidazole and nifurtimox are both on the essential medicines list in Bolivia. Benznidazole—which is approved by the national drug regulatory agency—is the first-line treatment. Currently, the only supplier of benznidazole in Bolivia is the National Chagas Programme, which centralises procurement of the drug and provides it free of charge. Nevertheless, benznidazole is not always available at health centres. The centres run by the Platform provide all diagnostic tests, treatments and follow-up visits free of charge. At National Health Service centres, however, the conditions are different. The first diagnostic test and the drugs to treat the infection are provided at no cost. However, the second test required by protocol, follow-up visits during treatment, and the drugs used to control the side effects of benznidazole are not free.

Benznidazole is currently being purchased from ELEA, and it has also been provided through the Bolivian Strategic Fund. The drug was previously purchased from LAFEPE. Access to medicines is clearly the main challenge for Bolivia. According to the head of Cochabamba's Departmental Chagas Programme, the country's benznidazole stock in 2015 fell far short of the demand. Orders were made for 500,000 tablets but only 50,000 were received, mainly because the budget allocated by the ministry for the management of Chagas disease was limited despite the fact that the government had declared the disease a top-priority health issue. Paradoxically, the budget for 2015 was cut because the 2014 allocation had not been used in its entirety owing to problems with supply. According to the authorities—who are making an effort to improve the situation—the higher price of Abarax (the drug currently in use) has had a direct impact on the number of patients who can be treated under the existing budget.

2.5. Human Resources

Thirty-five people work in various capacities at the Platform's six centres. Although some members of the staff are assigned to the programme and paid by the Chuquisaca Departmental Health Service (four workers in Sucre) or the University of Tarija (eight workers at the university health centre), the budget for all the others comes through CEADES-ISGlobal under an agreement funded by the Spanish Agency for International Development Cooperation (AECID). The new centres being added to the network are manned by the employees of the National Health Service. In those centres no additional staff have been taken on and no incentives are provided, but the people involved are offered an internship at one of the Platform's centres. The employees of the Platform's own centres are highly trained; in fact, they train the trainers who go on to give courses to other professionals working in the health care network.

2.6. Funding and Sustainability of the Model

Much of the Platform's budget is provided by foreign donors, mainly the AECID. Some local partners make in-kind contributions, such as spaces in hospitals, health centres and university facilities. Since most of the funding comes from a single source (AECID), the future sustainability of the Platform is not guaranteed. The expansion of the model to include National Health Service centres should, in the future, result in an adequate and sustainable network, provided that diagnosis and treatment are included among the services provided.

Bolivia Project Outline Based on the Six-Building-Block Health System Model

Building Block	Action
Service delivery	- 6 centres created: 4 in secondary-level or rural hospitals, 1 at a university and 1 at a departmental health centre (SEDES) - Care for adults at-risk for Chagas infection plus information and prevention activities - Training platforms for health workers - Investment and capacity-building for R&D - Provision of care at primary care facilities
Health workforce	- 23 workers empoyed by ISGlobal-CEADES - 4 workers assigned by departmental health services - 8 workers assigned by a university
Information systems	- Data shared systematically with the departmental Chagas programme and the Platform is represented on indicator-monitoring committees and the health board - Platform collects data and reports to the Ministrry of Health
Financing	- Competitive: AECID + Catalan Government + research grants - Contributions from local partners - Free diagnostic testing and treatment
Access to diagnostics and medicines	- Provision of the diagnostic and medical supplies required to meet demand is guaranteed - The entire process (treatment and care) is provided free of charge
Leadership and governance	- Leading institution: CEADES + ISGlobal - Partners: National Chagas Programme, Departmental Chagas Programme, Departmental Health Services, Universities (UMSS and UAJMS), network managers (Departmental Health Services)

Coverage of Access to Testing and Treatment

- 5% of adults in the catchment area are covered
- Diagnostic testing and treatment are offered at 12 centres, 6 of which belong to the National Health Service

Quality and Safety

- Treatment discontinued in 13.3% of patients (due to side effects of benznidazole/nifurtimox in 98% of cases)
- 0% serious safety incidents

Results as of Nov. 2015

Goal	Overall Results
Improve health	**24,744 patients** (adults) have been tested **74% (17,660)** have tested positive for *T. cruzi* **9,210** have started treatment (80% have completed) **737** health professionals have been trained **10** R&D projects have been completed
Guarantee response capacity	Adults with Chagas disease who normally would not be included or prioritised by the health system have received treatment.
Financial and social protection	Diagnostic testing and treatment are provided at no cost to the patient.
Improve efficiency	The number of adults diagnosed and treated has increased in three Bolivian departments where the disease is endemic.

CEADES ISGlobal

2.7. Conclusions: Keys to Success, Challenges and Lessons Learned

As of 2015, **24,744 adult patients** have been seen in the Platform's centres, of whom 21,387 (86%) have been diagnosed with T cruzi infection. So far, **10,454 patients** have started treatment and, on average, 80% have received the complete course.

Ninety health professionals are affiliated with the Platform and 737 more have received training. More than 400 people have attended an informative session. Twenty-three talks have been organised in rural areas, more than 300 reports of insect vectors have been received, and over 25,000 people have received information about Chagas disease at the Platform's centres or in their communities. Around a dozen R&D projects have been carried out.

The main past and future **challenges** faced by the Platform are as follows:

- Many people diagnosed with Chagas disease never receive treatment.
- An interruption in the supply of benznidazole in 2011 led to the build-up of a waiting list for treatment.
- There have been various problems with the supply of drugs to treat Chagas disease in Bolivia.
- Demand for the diagnosis and treatment of Chagas disease exceeds the current capacity to provide services (as evidenced by waiting lists).

- Health centres have limited autonomy in areas that depend on other actors, such as vector control activities, efforts to strengthen the health care network, and the equipment and other resources allocated to the centre.
- Progress in the health centre network depends on the capacity of the system as a whole.
- To ensure the continuum of care in Bolivia, it will be essential to develop a countrywide network of centres that can identify potential patients and provide care for those diagnosed with Chagas disease. This network will include the Platform's own centres and those of the National Health Service, including facilities providing higher levels of care.
- Leadership changes affecting the National Health Service give rise to delays in the revision and updating of guidelines and protocols, coordination difficulties, and other problems.

The main **lessons learned** (with a view to replicating the programme elsewhere):

- It is essential to collaborate and coordinate with primary care networks and with the Chagas programme at the departmental and national level.
- The programme should be introduced initially in places where strategic alliances can be established with stakeholders committed to taking action.
- It is advisable to ensure the supply of the necessary drugs before launching a diagnosis and treatment campaign. Diagnostic testing should not begin until the supply of drugs can be guaranteed.
- Centres should be able to provide additional testing on-site rather than referring patients elsewhere (laboratory tests, ECG, etc.).
- A system to manage referrals and counter-referrals should be established.
- Extending the network of centres offering Chagas services is crucial to scale up access to care.

3. The Case of the USA: Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center

3.1. Introduction

The United States of America (USA) is considered to be a non-endemic country for Chagas disease. Despite the presence of triatomine bugs in the country, vector-borne transmission of *T. cruzi* is rare in the USA and almost all reported cases of the disease involve immigrants from endemic countries or the children of women from those areas. According to the most recent US census

data (2010), **there are around 21 million Latin American immigrants currently living in the USA**, of whom 10 million live in California. It is estimated that one in every five patients with heart failure in the County of Los Angeles is infected with the ***T. cruzi*** parasite.

Although Chagas disease is treatable, infection must first be detected. The barriers to diagnosis and treatment in this population include language, immigration status, lack of medical insurance, lack of information, and the difficulty of requesting time off work. All of these aspects should be taken into account in the design of any intervention undertaken to combat this disease.

When the Olive View-UCLA Medical Center in Los Angeles county (Southern California) opened a Center of Excellence for Chagas Disease in 2007, it was **the first clinic in the USA for the diagnosis and treatment of this parasitic** disease. The clinic also runs a free outreach programme in the community, offering mobile medical services to educate the public about the disease and ensure early diagnosis. In total, between the clinic and the community outreach programme, **7,357** people have been tested; of these, **200** had a positive result for *T. cruzi* infection and **162 have completed treatment**.

As well as providing medical care, the clinic also conducts important clinical research, studying prevalence, conduction disorders, infection in pregnant women, and congenital transmission.

The USA in Numbers: As Chagas disease is not a mandatory reportable disease and is still little known, scant data is available on its prevalence in the USA. Even so, the US CDC estimates that **some 300,000 people with *T. cruzi* infection live in the USA**.

The **prevalence of the infection** in Los Angeles county is estimated to be **1.14%**.

Donated blood is screened systematically for *T. cruzi* in 100% of US blood banks.

3.2 Political Aspects and Legal Framework

As health care is not generally free for people living in the USA, residents require insurance to cover health care spending. In Los Angeles county, My Health LA, a programme set up under the Affordable Healthcare Act, provides health care at no cost even to undocumented immigrants. As most of the patients with Chagas disease are immigrants, they are often underinsured or not insured, a situation that represents a crucial obstacle to treatment.

Another major barrier is the lack of national guidelines on the diagnosis and treatment of Chagas disease in the USA. There is a general lack of information, knowledge and awareness of the disease among medical professionals and the affected community. Consequently, access to diagnosis and treatment is difficult. The fact that medical professionals are not familiar with the drugs and regimens used to treat Chagas disease or how to manage potential adverse effects is an additional obstacle.

Given the lack of national guidelines, a generally used reference is the article by Bern et al., published in the Journal of the American Medical Association: "Evaluation and Treatment of Chagas disease in the United States: A Systematic Review".

While blood banks do screen for *T. cruzi* infection, it is not mandatory to report the disease and many patients who are diagnosed are not referred for treatment. The exception is the Red Cross in Los Angeles, which provides donors who have tested positive with the contact details of the Center of Excellence for Chagas Disease at Olive View Medical Center.

3.3. Intervention Model

Olive View-UCLA is the first national centre of excellence for the evaluation and treatment of Chagas disease in the USA. The initiative works closely with the Red Cross and the CDC. The treatment model is based on a multidisciplinary team made up of cardiologists, infectious disease specialists, paediatricians and obstetricians.

In Olive View-UCLA Medical Center, screening for infection with *T. cruzi* is routine in certain patients:

- Patients with heart disease
- Patients with conduction abnormalities on electrocardiogram (ECG)
- Pregnant women
- Newborn children of mothers who have tested positive for infection

Once or twice a month, volunteers from the centre go out into the community to offer free Chagas screening at health fair events held in public meeting places, such as churches, parks, and civic centres.

The clinic's activities also include:

- **Community-based prevalence studies:** A study enrolling more than 5,000 people undertaken to determine the prevalence of Chagas disease in the community. The study is being conducted in the San Fernando Valley. To date, 4,475 patients have been tested of the 5,000 required by the study protocol.

- **Hospital-based prevalence studies:** Studies are also being carried out to determine the prevalence of the infection among several specific populations who come to the hospital, such as patients with end-stage congestive heart failure or cardiomyopathy, asymptomatic patients with early-stage cardiac disease, pregnant women, and HIV-positive individuals. Other studies have focused on patients in whom lesions have been assessed in various stages of the disease and patients who underwent assessment prior to antiparasitic treatment.

- **Treatment of positive cases:** once a diagnosis has been confirmed, the patient is offered treatment through the CDC. Currently only two drugs—nifurtimox and benznidazole—are available in the USA and, unfortunately, neither has been approved by the competent regulatory agency—the US FDA.

- **Assessment of fibrosis (scar burden) using magnetic resonance imaging (MRI) in patients with myocardia in various stages of the disease:** Before they receive treatment, all patients diagnosed with *T. cruzi* infection are assessed to determine whether damage has already been caused by the parasite and to establish whether a defibrillator is necessary.

- **Evaluation of scar burden before and after antiparasitic therapy:** Scarring detected on MRI has been shown to be the first sign of organ involvement in Chagas disease. Such scarring can cause cardiac arrhythmias, and early detection allows the medical team to intervene to prevent complications and even sudden death.

- **Guidance to other medical professionals:** Recognising how difficult it can be for people in other parts of the USA to come to the clinic for treatent, the centre offers guidance to physicians and health care providers in other parts of California and other US states to help them to provide treatment for patients with Chagas disease.

"We met a woman at the outreach clinic some weeks ago who explained that her husband had been diagnosed with Chagas disease 10 years ago but had never received treatment. They had no legal status and, until recently, no health insurance. The primary care physicians they contacted knew nothing about the disease and were unable to help him. The woman came to our outreach centre looking for information about treatment for her husband. We will assess her husband and offer him the treatment he needs. This is a common story and we really hope that with improved knowledge we can ensure that people are treated sooner".

Dr. Salvador Hernandez, Cardiologist, Olive View–UCLA.

3.4. Supplies: Diagnostics and Drugs

Population screening and testing is currently performed using venous blood samples and laboratory techniques. The reagents are bought by the centre from a supplier in Argentina and sent to the CDC laboratory, where the blood is tested using ELISA and TESA blot. Rapid diagnostic tests are not used because of their low sensitivity and specificity.

As the drugs are only available through the CDC, obtaining them is labour-intensive for anyone unfamiliar with the process. Upon receipt of confirmation from the CDC that the test is positive, the physician must complete an initial application including demographic data, laboratory results and a signed patient consent form. The drug is dispensed when these formalities have been completed and the physician is also obliged to submit a report when the patient has completed the course of treatment.

3.5. Human Resources

The staff of the centre varies from nine to twelve people, including two cardiologists, nurses, phlebotomists, and the staff in charge of data collection and logistics.

Project Outline Based on the Six-Building-Block Health System Model
Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center

Building Block	Action
Service delivery	Diagnosis and treatment of Chagas disease through community outreach activities (mobile clinics)
Health workforce	Additional personnel required to carry out the programme
Information systems	Centers for Disease Control (CDC) database—only cases confirmed by laboratory testing are reported, which means the data does not include screened patients. (Chagas disease is not a reportable disease.)
Financing	Los Angeles county provides the supplies needed for sampling (phlebotomy) and covers the cost of sending the samples to the CDC for confirmatory testing. The clinic is financed by funds obtained by Dr Meymandi in return for carrying out clinical trials.
Access to diagnostics and medicines	Diagnosis is made using two serologic tests: ELISA and TESA blot. Diagnosis is confirmed by the CDC. Benznidazole and nifurtimox are provided free of charge by the CDC on a case by case basis.
Leadership and governance	The Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center and the Centers for Disease Control and Prevention (CDC)

Coverage of Access to Testing and Treatment

- Coverage of the Hispanic community in Los Angeles county
- Coverage of at-risk women and their newborns

Quality and Safety

- 100% of adverse effects closely monitored and treated
- 0% serious adverse events

Results as of Nov. 2015

Goals	Overall Results
Improve health	**7,357** people tested, **200** people diagnosed with Chagas disease and **162** treated
Guarantee response capacity	- Treatment on case-by-case basis of cases reported to the CDC - Diagnosis and treatment were previously unavailable
Financial and social protection	- 100% of screening, diagnosis and treatment now free of charge
Improve efficiency	Target population

3.6. Funding

Los Angeles county provides the supplies needed to take blood samples and covers the cost of sending them to the CDC. There is no additional funding at present. Funds generated by Dr Meymandy from clinical trials are used to support the work of the centre. The community outreach activities represent no additional cost because the work is carried out by volunteers. The centre is currently seeking additional funding to support its work.

3.7. Conclusions: Keys to Success, Challenges and Lessons Learned

Between hospital patients and those screened as part of the community outreach programme, some 7,357 people have been tested and 200 have been diagnosed with *T. cruzi* infection; 162 of those received treatment.

The following table shows the details of the patients diagnosed.

Patient Group	Diagnosed	Positive	%
Patients with ECG conduction abnormalities	377	15	4.0%
Patients with heart disease	364	48	13.2%
Relatives of patients with *T. cruzi* infection	183	12	6.6%
Pregnant women	408	1	0.2%

The Center of Excellence for Chagas Disease works closely with the CDC and the Red Cross. All Red Cross blood donor banks in Los Angeles county now refer donors who test positive to the clinic.

In the near future, the Center hopes that the Department of Health Services (DHS) will introduce screening for Chagas disease into all of its facilities, including four primary care clinics and nineteen outpatient clinics. To facilitate this, the laboratory at Olive View-UCLS Medical Center will become part of the Center of Excellence, so that the first test for Chagas disease can be done at the hospital. All other DHS facilities would send blood samples to this laboratory for testing. Until the drugs used to treat the disease have obtained FDA approval, the confirmatory testing would still be done at the CDC laboratory.

The following are the main **challenges** encountered by this project:

- Lack of knowledge about the disease among primary health care physicians. This poses two problems: first, the patients consulting primary care physicians are not being screened or informed that they may have Chagas disease; and second, patients seeking treatment because they have been diagnosed (for example, after giving blood) do not receive appropriate help or treatment.
- Access to the drugs. Until the two available drugs—benznidazole and nifurtimox—are FDA approved, access to treatment will remain complicated.
- Lack of consensus on the use of rapid diagnostic tests complicates screening activities and prolongs patient follow-up.
- Lack of knowledge and awareness of the disease in the community explains the lack of active demand for diagnosis and treatment.
- Patients without medical insurance may not seek medical care even though diagnosis and treatment are provided at no cost at Olive View.
- Language barriers hinder access to treatment.
- Long-term funding is needed to ensure the continuation of the programme.
- Chagas disease is not a reportable disease and patients who are diagnosed do not know where to seek medical care and treatment.
- The lack of recommendaitons or protocols for screening pregnant women at risk means that congenital transmission is not prevented.

The main **lessons learned** that may be relevant to reproducing the project elsewhere are as follows:

- People living in the USA usually donate blood during their last year of secondary schooling (senior year in high school). A programme could be designed to take advantage of this by providing information to this group before they donate and being prepared to deal with cases of Chagas.
- Many people diagnosed through blood donor banks do not know where to go for treatment and look for information online. It is important to ensure that complete information is easily searchable and accessible online.
- Primary care physicians must receive training on the diagnosis and treatment of Chagas disease to enable them to deal with cases they may encounter.
- Primary care physicians should also be at the frontline of screening the Hispanic community and providing treatment.
- Recommendations on the need to screen pregnant women are needed.
- Diagnosis and treatment programmes should be accompanied with information, education and communication campaigns aimed at the target population. Fear of stigma and ignorance of the disease and its potential complications discourage patients from being tested.
- It is important to find ways to communicate effectively with patients who may struggle with language barriers or not have a high level of literacy.
- A close relationship between between patients and staff at the clinic is crucial.
- Consideration must be given to patients who live a long way from the clinic (some of whom may have to travel for 2 to 3 hours by bus to access treatment).
- It is important to establish an effective process for obtaining benznidazole and/or nifurtimox from the CDC and to make it available to any pharmacy.
- A stong patient group that can lobby for change and raise awareness about the disease makes a big difference.

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