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# Newsletter

Chagas Disease Clinical  
Research Platform



## Celebrating 20 years of working in partnership to provide better treatments to people with Chagas

The Chagas Disease Clinical Research Platform was launched in 2009 to address research gaps for this neglected disease which causes up to 14,000 deaths every year, mainly in Latin America. As in other neglected diseases, the resources available to advance research are often limited. Therefore, a space is needed which brings together different people so they can collectively identify barriers and strategies and pool knowledge, expertise, and resources toward common goals.

The Chagas Platform is first and foremost a network of people from throughout the world who share a commitment to improving the life of the people with Chagas disease while ensuring that the disease itself, and those affected by it, remain visible to the world. The Platform is a broad network that includes over 500 members from patient associations, representatives from governments, healthcare professionals, and experts in all aspects of Chagas disease, from drug discovery to diagnostics, and from clinical research to the social sciences, representing over

150 organizations from 23 countries.

In 2023, DNDi celebrates 20 years of work to assure that the most vulnerable people have access to the products of the best science. It is a time for reflection on the many lessons learned recently in global health – from unprecedented acceleration of drug development processes to increased global awareness of the role of structural racism in health outcomes, and to a renewed understanding of the critical importance of international cooperation to overcome public health challenges. How can these lessons be applied to Chagas to help us achieve the ambitious goals put forth by the WHO to control the disease as a public health problem by 2030?

Progress is being made toward better diagnostic and therapeutic options, as well as for greater visibility for people with Chagas, but many difficult challenges remain. The Chagas Platform will continue to provide a space for interdisciplinary, international, multistakeholder cooperation. ◦



## Summary

# Some thoughts on the Chagas Platform in DNDi's 20 years

Isabela Ribeiro and Sergio Sosa-Estani (DNDi)

Since its foundation, DNDi has prioritized Chagas disease, focusing on research into new compounds and repurposing other drugs. A key moment was when, in 2005, several researchers sent a letter to Simon Croft, Director of Research and Development, recommending that DNDi take action to address a significant gap at that time: the absence of a pediatric formulation. The letter prompted an exploratory assessment by DNDi and several exchanges with different stakeholders, culminating in a meeting in Rio de Janeiro in 2006 with various experts. DNDi then began to support a Federal Laboratory of Pernambuco (LAFEPE) project seeking to develop a pediatric formulation, while also exploring azoles, a promising class of drugs, through preclinical and clinical studies.

To successfully develop the pediatric formulation and new clinical trials, a number of other related issues needed to be addressed. Several topics were discussed in technical meetings, such as the epidemiological scenario, the need for a tool to estimate demand for treatments, limitations in diagnosis, and the pharmacokinetic model, among others. Important outputs were obtained from those initial discussions; notably, a demand estimation tool and the first Target Product Profile (TPP) for a treatment. During one of the most crucial meetings, a significant improvement in dynamics was achieved when the language was changed from English to Spanish. To help conduct clinical studies, a method for measuring therapeutic response was published, and the most appropriate preclinical and clinical study designs were discussed. These have since been adapted by most clinical trials on Chagas.

The need for a shared space where the various partners and other stakeholders could strategically discuss possible solutions was also identified. By then, DNDi already had a positive experience with disease platforms in Africa, and it was thought that this model could work in the context of Chagas. The Chagas Platform was formally launched in 2009 in Uberaba, Brazil. One of the most important contributions of DNDi and the Chagas Platform was bringing together different areas of knowledge. At the time, the scientific community around Chagas was composed mainly of academic scholars. DNDi and the Platform brought together experts from other sectors, such as regulatory agencies and the pharmaceutical industry. It also offered a space to discuss access issues with patient associations and decision-makers of health care programs, among other actors.

The diversity of voices has grown, enriching the Platform and scientific research, but there is still much room for improvement to make patient-centered research a systematic practice, and not only a discourse.

Today, the Platform represents an efficient model adapted to the Chagas context, serving as an example for platforms of other diseases at DNDi and also learning from them. It continues to provide an essential space that brings together perspectives from the Chagas global community. ◦

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# Coordination between the Benlatino and NuestroBen clinical trials

Tayná Marques (DNDi), Israel Molina (Vall d'Hebron Research Institute - VHIR), and Colin Forsyth (DNDi)



The current treatment for people with Chagas disease presents several key barriers, including long duration and frequent side effects, which cause about 20% of patients to discontinue the medication, while requiring laboratory testing and numerous healthcare visits. This creates complications for healthcare providers and can make adherence difficult for patients. Conversely, a shorter, safer treatment could improve access and enable easier scale-up of Chagas disease programs.

Several clinical trials have recently explored or are exploring alternative regimens of benznidazole (BZN) and/or nifurtimox, including TESEO, BETTY, MULTIBENZ, and EQUITY. Additionally, two new Phase III clinical trials of shorter treatments of benznidazole are on the horizon. The first, Benlatino, is led by the Oswaldo Cruz Foundation (Fiocruz) as part of the UNITAID-funded CUIDA Chagas project in Bolivia and Colombia. The other, NuestroBen, is sponsored by ELEA Phoenix S.A., under the technical-scientific management of DNDi, in six clinical sites in Argentina. Both studies are evaluating 2- and 4-week treatments of benznidazole (100 mg TID) compared to the standard 8-week regimen (100 mg TID).

During a May 2022 technical meeting hosted by DNDi, where investigators discussed key questions on the research of new treatments of benznidazole and nifurtimox for Chagas disease, one of the key recommendations was to explore the possibility of alignment between the two studies to increase power and comparability, among other advantages. Subsequently, investigators from the two studies held several important discussions and came to the following agreements:

- Study population of adults in the chronic phase of Chagas disease with the indeterminate form or mild cardiac progression;
- Harmonization of all PCR timepoints during the first 12 months of follow-up: 1, 4, 6, 8 and 12 months after the end of treatment;
- Serial qualitative PCR results as six negative results: duplicate PCR testing from three independent DNA extractions of 5-ml blood sample aliquots treated with Guanidine per visit;
- Use of the same commercial PCR kit (Fiocruz's NatChagas), and quality control among the central laboratories of both studies coordinated by Fiocruz;
- Same dosage scheme (100 mg tablet taken three times daily);
- Employment of a "dynamic borrowing" analysis, where efficacy results from each study will be enhanced by borrowing data from the other study. Each study's own data will be more heavily weighted during the analysis.

In this sense, study designs were made comparable in terms of study population, statistical analysis, and all related to the performance of the PCR as the primary endpoint of both studies. Both designs were presented during the Plenary Meeting of the Chagas Research Platform in Bogota on September 23, 2022, where the plan to coordinate the studies was announced. Each study will continue to operate independently, but the agreement to coordinate the above points will help foster robust scientific evidence for the potential adoption of a new BZN treatment for Chagas disease in Latin America. ◦

## New Treatment Alternatives for Infectious Diseases Program: an opportunity to find new drugs against *Trypanosoma cruzi*

Bertha J. Espinoza Gutiérrez, Department of Immunology, Institute of Biomedical Research, National Autonomous University of Mexico

A multidisciplinary group of researchers has been formed at the Institute of Biomedical Research and other research institutes of the National Autonomous University of Mexico to study new drugs and treatments for infectious diseases. The “New Treatment Alternatives for Infectious Diseases” program is supported by the Coordination of Scientific Research of the University, and in the case of Chagas disease and leishmaniasis by the National Council of Science and Technology of Mexico (CONACyT, 160671).

Our collaborators from different institutes are experts in purifying natural compounds from the national flora, from research of local plants and field work for their collection to laboratory work to obtain pure compounds. Likewise, other groups can synthesize new molecules. The use of computational chemistry to select molecules with the characteristics required to bind to a target of interest is ongoing. Also, this project has worked on modifying drugs that are available on the market, which greatly helps to advance their possible application, since the drugs are already authorized by regulatory agencies.

Once a molecule is obtained, tests for its activity against the pathogen and its cytotoxic activity against mammalian cells are carried out in parallel. To evaluate *in vitro* activities, the group uses several standardized assays, such as the MTT viability assay, growth reduction, and observation of morphological and structural changes using transmission electron microscopy, among others.

Once promising results are obtained regarding the effect of a new compound at appropriate LC50 concentrations, it needs to be tested in *in vivo* models. Our group has valuable infection models of *T. cruzi* and *Leishmania sp.* in rodents.

An example of a promising compound of natural origin found by our group is mammea A/BA, obtained from the *Caluphyllum*



*brasilense* tree, which demonstrated potent action on *T. cruzi* epimastigotes and trypomastigotes (LC50 13.4  $\mu$ M and 17.6  $\mu$ M respectively), as well as reduced parasite infection *in vitro*. This compound produces oxidative stress in the parasite, changes in the cell cycle, and induced apoptosis, as demonstrated by biochemical studies and transmission electron microscopy.

Also, a drug modified from amphotericin B, named A21, has been very effective in combination with benzimidazole to rescue mice from damage and death caused by a virulent strain of *T. cruzi*. A patent has been obtained for this compound.

Further studies on these compounds are currently in progress. We hope that this joint effort will soon allow us to find other effective compounds against this infection that affects large sectors of our populations in Latin America. ◦

## Early molecular diagnosis of vertical Chagas disease: transfers to maternity hospitals from public healthcare institutions in Latin America

Silvia Longhi (INGEBI-CONICET), Lady García-Casares (INGEBI-CONICET), Arturo Muñoz-Calderón (INGEBI-CONICET), Julio Alonso-Padilla (CIBERINFEC, ISGlobal and Hospital Clínic – University of Barcelona), Alejandro G. Schijman (INGEBI-CONICET), and Chagas-LAMP group



Preventing mother-to-child transmission of *Trypanosoma cruzi*, the cause of vertical Chagas disease (VCh), is a public health priority, as this type of transmission is more common in places where vector control has been successful and in non-endemic areas. Moreover, the disease can be identified at birth and, more importantly, treated.

Within the framework of the Chagas-LAMP G2020-2030 projects, a public-private international consortium funded by GHIT and co-funded by the Mundo Sano foundation with TDR (LEG 22-0062) grants from PAHO, we are evaluating the loop-mediated isothermal amplification (LAMP) method for fast molecular diagnosis of VCh using ultrafast DNA extraction, which can be adapted to the conditions of the labs located in maternity hospitals in endemic areas. We followed the procedures used in neonatal research projects and established standard operating procedures (SOP) for detecting the infection in small blood sample volumes treated with the anticoagulant heparine (30  $\mu$ ls) and in blood obtained with filter-paper FTA. Then, we sent the two SOPs to five maternity hospitals in Bolivia, two in Paraguay and four in Argentina.

Staff training involved three stages. The first stage provided a theoretical view of the technique and the reagents used in it. The second was a day of lab work with samples from artificial panels of human blood that tested negative for *T. cruzi* and were inoculated with known quantities of the parasite from *in vitro* cultivation. The purpose of this stage was to evaluate the performance of the operators working in each participating lab. The final stage required that the trained operators process blood samples from the newborns of women with *T. cruzi* and who were enlisted in the projects. The purpose of this last stage was to evaluate how they interpreted and entered the results in the respective databases.

We also set up capability panels for external quality control of the LAMP for the participating labs, to help provide a global performance evaluation of the teams and the technique on the field.

Conclusion: the LAMP methodology used for the diagnosis of VCh was transferred to maternity hospitals in endemic areas, which are the places where clinical validation is done. If it shows similar diagnostic certainty to that of real-time PCR, the methodology could be incorporated into the diagnostic algorithm and become an agile and accurate alternative for the early detection of VCh. ◦

## PARACHUTE-HF, a clinical trial for chronic Chagas cardiomyopathy

Caroline Demacq, Claudio Gimpelewicz, and Renato Lopes, on behalf of the PARACHUTE-HF team



Chronic Chagas cardiomyopathy (CCC) is the most severe clinical manifestation and the main cause of death due to Chagas disease. It is estimated that approximately 20-30% of affected people will develop CCC. However, considering the limitations in the diagnosis and treatment of Chagas disease, the real prevalence of CCC may be underestimated. Often, the diagnosis is made when the patient already has advanced forms of the disease and presents with signs and symptoms of heart failure, stroke or severe arrhythmias. Sudden cardiac death may be the first manifestation of the disease. In addition, there is no biomarker to identify subjects at higher risk of progression to CCC.

Compared to other etiologies of heart failure with reduced ejection (HFrEF), CCC presents at a younger age and has fewer associated comorbidities, such as hypertension, diabetes, and atherosclerotic cardiovascular disease. Nevertheless, it carries higher mortality and hospitalization rates, high prevalence of stroke, arrhythmias requiring device implantation, and worse health-related quality of life. Importantly, this population is not well represented in the clinical trials for cardiovascular drugs and the current treatment is based on extrapolation from other etiologies.

Considering this significant unmet need, Novartis, in cooperation with the Brazilian Clinical Research Institute, an ac-

ademic research organization from Brazil, implemented the PARACHUTE-HF study (Prevention and Reduction of Adverse Outcomes in Chagasic Heart Failure Trial Evaluation - [NCT04023227](#)). This Phase IV, multinational, prospective, randomized, open-label with blinded-endpoint adjudication study is ongoing and enrolling participants in more than 80 sites in Argentina, Brazil, Colombia, and Mexico. The primary objective is to evaluate if sacubitril/valsartan is superior to enalapril in improving the composite endpoint of cardiovascular (CV) events (CV death or the occurrence of first heart failure hospitalization) and reducing NT-proBNP (N-terminal fraction of the pro-B type natriuretic peptide) at week 12 in patients with HFrEF caused by Chagas disease.

Participants are adults with Chagas disease confirmed by at least two different serological tests, with HFrEF  $\leq$  40%, and increased NTproBNP or BNP. Patients with a severe gastrointestinal form of Chagas disease or with cardiovascular conditions that suggest a primary etiology other than Chagas are not included.

The PARACHUTE-HF study also includes imaging and biomarker sub-studies that will contribute to increase the knowledge of the underlying pathophysiology of this complex and neglected tropical disease. ◦

## “Red Atendiendo Chagas”: a connection between patients and healthcare professionals

Carolina López Ferloni (Mundo Sano Foundation)

In 2019, the Mundo Sano Foundation created “Atendiendo Chagas,” a global advocacy network for diagnosis and treatment of Chagas disease. The idea originated with the identification of an actual need: a space for collaboration and exchange of experiences between healthcare teams and professionals dedicated to the diagnosis and treatment of Chagas disease, and, at the same time, a connection between those healthcare professionals and the patients. Today, the platform brings together more than 330 healthcare professionals and team members that work every day on this issue, mainly in the Americas, but also in Europe and Asia.

“The network enables us to establish a link between Chagas patients, or those who think they may have the disease, and the professionals who are committed to their treatment, which is the case of every member of the network,” highlights Marcelo Abril, Executive Director of the Mundo Sano Foundation.

“Atendiendo Chagas” is open to physicians, biochemists, social workers, nurses, veterinarians, and other healthcare team members. Each one, working from their own position, can help make the treatment of Chagas disease a reality. The main goal is to facilitate access to diagnosis and treatment of Chagas disease for all those who are affected by it, but also to serve as a space for healthcare professionals to share their experiences and best practices in the spirit of mutual exchange and collective consultation. The network

If you are interested in joining this initiative and want to know more about the network, please register at [Atendiendo Chagas website](#) or through the [WhatsApp channel +54911- 50384515](#).

In 2022 we held the First Meeting of the Red Atendiendo Chagas, with 65 members in attendance. Physicians from the Mundo Sano Foundation and researchers from CONICET and the Instituto Nacional de Parasitología “Dr. Mario Fatała Chabén” talked about treating people with the disease, diagnostic techniques and the practical aspects of the etiological treatment. Medical practitioners also shared their work experiences, challenges and breakthroughs in treating the disease.



makes available to its members the prevailing norms, laws and guidelines, as well as scientific journals dedicated to the theme, and promotes activities, training and events of interest to network members.

This digital platform, which is available in Spanish and English, is appealing because it works as a space in which professionals can meet, debate, and share news and scientific advances through forums. In addition, they can have access to extensive literature with research papers and books in electronic format and stay up to date on the latest advances and news about the disease. The network also has a space for frequently asked questions for basic clarifications.

In the medium term, “Atendiendo Chagas” intends to keep growing and aims to become the largest global platform dedicated to the treatment of Chagas disease. ◦

# A pharmacometric platform for Chagas disease

Cintia Cruz (MORU Tropical Health Network)



The CHARM (CHAgas phaRMacometric platform) collaborative group aims to develop a pharmacometric methodology platform for Phase II studies of Chagas disease centered on pharmacometric determinants. This interdisciplinary group is part of the Wellcome HIT initiative for neglected diseases, which researches new drugs for Chagas disease and leishmaniasis.

Pharmacometrics quantifies the ratio between the dosage and the pharmacologic response. CHARM's main hypothesis is that serial qPCR analyses would allow the creation of a dosage-response curve to optimize treatment regimens for Chagas disease. CHARM's objectives are organized into five working groups:

## Pharmacodynamic model, led by James Watson, PhD (University of Oxford)

In theory, the simplest pharmacodynamics model of chronic infection by *T. cruzi* (without re-infection) has two "compartments": one for tissues and another for blood (Figure 1). Tissue parasites multiply at rate  $\alpha$  (e.g., they double every 12 hours). Blood parasites do not replicate. They have an immunological elimination rate  $\lambda$  and re-infect tissues at rate  $\gamma$ . A stationary parasitemia suggests that  $(\alpha - 1)\gamma = \lambda$ .

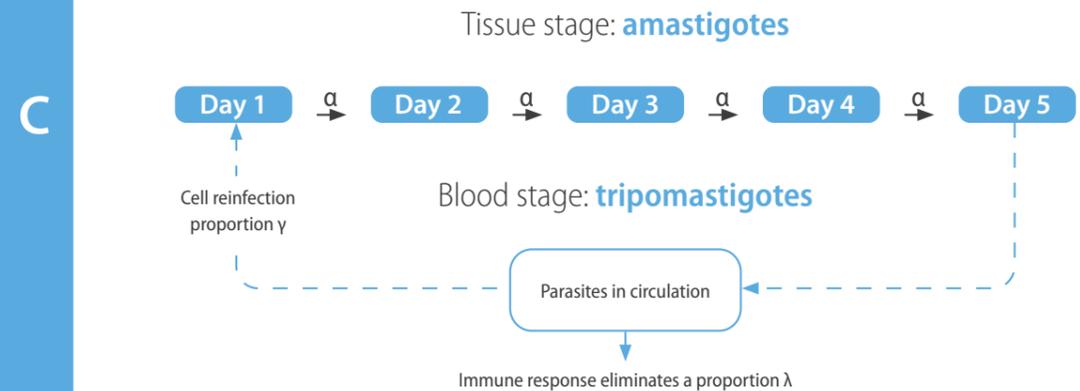


Figure 1 – Simple pharmacodynamics model of chronic infection by *T. cruzi* in human beings.  $\alpha$ : parameter representing parasite multiplication in tissues;  $\lambda$ : elimination by the immune system;  $\gamma$ : tissue reinfection. This model does not include the latent stage.

## A

**Chagas Data Platform and standard CDISC with IDDO (Infectious Diseases Data Observatory)**, led by Prof. Philippe Guerin (University of Oxford)

IDDO is currently the largest data platform for the study of infectious diseases and will coordinate the Chagas Data Platform development and maintenance. Initially, IDDO will perform the following activities:

- Development of the standard report form for “CDISC.”
- Creation of the study group “Pharmacokinetic analysis of nifurtimox and benznidazol,” calling for contributions in the form of pharmacokinetic studies.

## B

**Pharmacometric meta-analysis**, led by Cintia Cruz (Mahidol Oxford Research Unit - MORU) and Dr. Jaime Altchek (Ricardo Gutierrez Children's Hospital)

Seroconversion is the current gold standard for a diagnostic assessment of cure after treatment for Chagas disease. However, seroconversion is a variable phenomenon; it can take many years, is not specific for cure, and it relies on the measurement of antibodies and their sensitivity.

The meta-analysis will have three components:

- A population-based pharmacokinetic model combining nifurtimox and benznidazole;
- A new analysis of cohort samples with extended follow-ups using standard and unified techniques;
- A meta-analysis of serology and qPCR results using the exposure to a compound as the predictive variable.

## D

**Pilot Phase II adaptive clinical study to determine the dosage-response ratio for existing Chagas disease drugs**, led by Israel Romero, MD PhD (Fiocruz/ Vall d'Hebron University Hospital)

CHARM's main hypothesis will be tested through extensive clinical analysis with a group of adults with chronic Chagas disease and high parasite density, at three consecutive instances:

- Determination of the parasite dynamics in stationary state;
- Evaluation of parasite clearance after one treatment dose (which will vary in an adaptive way);
- Complete treatment after the parasite reappears.

## E

**Complete *T. cruzi* genome sequencing**, led by Louisa Messenger, PhD (LSHTM/University of Las Vegas, Nevada)

The genomic data will help understand the source of rebound in relation to the primary infection and identify if latency is important for this rebound. We will seek to determine if treatment reduces parasite diversity and if we can use this to measure efficacy.

Pharmacometry is supervised by doctors Facundo Garcia Bournissen (Schulich School of Medicine & Dentistry at Western University), Joel Tarning, and Richard Hoglund (MORU). Prof. Sir Nicholas White (MORU) is in charge of the overall direction of the project.

# Implementing chronic Chagas disease notification in Brazil: updates and challenges

Veruska Maia, Mayara Lima, Swamy Palmeira, Milton Neto, and Rafaella Silva  
(Chagas Disease Technical Group – Brazilian Ministry of Health)

After 114 years since the discovery of Chagas disease, Brazil has made considerable progress due to the adoption of national policies aiming at the prevention and control of the disease. However, the infection by *Trypanosoma cruzi* that affected thousands of people until the 1980s currently has led to more than a million people living with the disease in almost all Brazilian states. This situation reveals the magnitude of the chronic stage of the disease, which represents:

The **4<sup>th</sup>** leading cause of death among all infectious parasitic diseases in the country

The basic cause of approximately **4,500 deaths/year**

**7,402,559 years** of life lost, adjusted by disability (DALY)

Moreover, we should note a change in the epidemiological profile of the disease. The traditional scenario of vector transmission in the home has given way to transmission linked to the parasite's cycle in the wild, and currently it is centered in the Amazon Region. The acute phase of the disease represents:

Approximately **280 new cases/year**

**80%** of the cases caused by ingesting contaminated food (oral transmission)

A statistically significant increase in the number of cases in the **North** of the country, as shown by a 10-year trend analysis

Regarding **congenital transmission**, despite lower notification rates and the challenges in identifying cases, estimates from 2010 have shown:

**1.1% infection** prevalence in pregnant women

**589 children** with congenital infection

Therefore, the disease in its acute phase has become important for public health at the national level due to the unexpected epidemiological conditions related to concurrent forms of transmission. Considering the traditional assumption that for each acute case of the disease there are twenty silent infection cases (non-apparent transmission), we should consider immediately testing chronic patients in the North Region. Although the main form of concurrent transmission is indirect (oral), vectors from outside the home are almost always involved, revealing a potential for silent transmission at a level that has not yet been measured.

It is clearly important to undertake efforts to articulate health monitoring actions with multisector involvement, especially focusing on the effective participation of the healthcare network of the Brazilian healthcare system. Thus, we took a great step forward in 2020 when the chronic phase of Chagas disease was added to the national report mandate (Directive 1,061, of May 18, 2020), as only the acute phase was previously included in the National List of Diseases Subject to Compulsory and Immediate Notification.

Due to the health emergency posed by COVID-19, the policy of notification of chronic cases only became effective after the implementation of the notification form in the Ministry of Health electronic system (e-SUS Notifica) on January 6, 2023. The following month, the notification of chronic cases was released through a webinar with the goal of raising the awareness of health professionals. The webinar was also attended by members of the National and Municipal Councils of Health Secretaries. There are other strategies under consideration and being implemented, such as in-person training, educational videos, and a plan to discuss and execute measures and goals for monitoring and evaluating this new type of control.

We hope that this new policy will better respond to the needs of those affected by this disease, so we can know how many there are and where they live, focusing on equity and comprehensive healthcare, and ensuring a better quality of life for them. ◦

## Seroprevalence and clinical evaluation of infection by *Trypanosoma cruzi* in three Venezuelan states where Chagas disease is endemic

**Raúl Espinosa** (Dr. Miguel Pérez Carreño Hospital - Venezuelan Social Security Institute), **Edmundo Figuera** (Institute of Biomedical Research and Applied Sciences - Universidad de Oriente), **Edgar Marchán** (Institute of Biomedical Research and Applied Sciences - Universidad de Oriente), **Hernán Carrasco** (Institute of Tropical Medicine "Dr. Félix Pifano" - Central University of Venezuela), **Clara Martínez** (Institute of Tropical Medicine "Dr. Félix Pifano" - Central University of Venezuela), **Lourdes Figuera** (Institute of Biomedical Research and Applied Sciences - Universidad de Oriente), **Leidi Herrera** (Institute of Tropical Medicine "Dr. Félix Pifano" - Central University of Venezuela) and **Marianela Torres** (Dr. Miguel Pérez Carreño Hospital - Venezuelan Social Security Institute)

The main cause of parasitic cardiomyopathy in Venezuela, the cardiomyopathy caused by *Trypanosoma cruzi* infection, or Chagas disease (CD), had its transmission somewhat under control in the last decade of the 20th century. The seroprevalence in rural areas of 19 states decreased gradually from 44.5% to 9.2% in the period from 1958 to 1998. In the age group of 0-9 years, it decreased from 20.5% to 0.5%; and in the age group of 10-19 years, it decreased from 18.4% to 1.8%<sup>1</sup>.

In the context of a multicenter study with serological, parasitological and molecular analyses for infection and parasite detection in blood samples from people living in eight endemic communities in three states (Sucre, Guárico and Portuguesa), a clinical-electrographic evaluation and follow-up (2006-2012) of a representative number of those communities was carried out. Of the 1,259 patients of both genders who were participants in the study, 16.04% (202 patients) were found to be seropositive based on two exams (ELISA and indirect hemagglutination); of the seropositive patients, 138 were also clinically evaluated. The average age (years) was  $32.64 \pm 15.75$  for ♂ and  $39.24 \pm 8.72$  for ♀, with a prevalence of 12.3% for patients younger than 10 and 28.2% for patients younger than 20 years of age (insipient chronic Chagas). Of the total number of patients evaluated, 88.4% corresponded to group I (no evidence of cardiomyopathy), 10.9% to group II (advanced damage) and 0.7% to group III (congestive cardiomyopathy). During the follow up, four patients from GI advanced to GII and one from GII advanced to GIII. Five

patients died: three from GII of sudden death, one from GIII of heart failure, and one of non-cardiac causes.

This retrospective study demonstrated an upturn of parasite infections in these endemic regions, with the presence of vectors both inside and around homes, perhaps attracted by overcrowding in poor housing conditions, by the light and by ongoing deforestation<sup>2</sup>.

The increase in severe cases due to vector transmission and the flare-up of oral transmission cases, both in the capital region and in other states, highlights the need for increased vigilance. Our study has shown, by means of the prevalence in patients under 10 years of age, a reemergence of the active transmission of the infection in the last two decades. Researchers from the University of the Andes found similar results in a sample of 3,343 individuals of both genders from 17 states, with a seroprevalence of 10.7%, and for the group of children under 10, of 6.9%<sup>3</sup>. The results above contradict what was reported by the Chagas Disease Control Program for 2011, based on a sample of 5,451 people from 16 states, which found a prevalence of 3.69%, and for the group of children under 10, of 1.85%<sup>4</sup>.

The difference between the results found by the National Chagas Disease Control Program for 2011 and the studies by Añez and ours highlights the need for a national study, jointly conducted by the Ministry of Health and academia, to determine the real prevalence rate and the current status of Chagas disease in the country. ◦

<sup>1</sup>Alberto Ache. Interrupting Chagas disease transmission in Venezuela. *Rev Inst Med Trop S Paulo* 2.001; 43(1): 50,000-100,000

<sup>2</sup>Herrera L. (2.014). *Trypanosoma cruzi*, the Causal Agent of Chagas Disease: Boundaries between Wild and Domestic Cycles in Venezuela. *Front Public Health* 2: 259. doi: 10.3389/fpubh.2014.00259

<sup>3</sup>Añez N, Crisante G, Rojas A y col (2.020). Update on Chagas disease in Venezuela during the period 2003-2018. A review. *Acta Tropica*. 203: 105310

<sup>4</sup>Benítez J A, Araujo B, Contreras KW y col (2.013). Urban outbreak of acute orally acquired Chagas disease in Táchira, Venezuela. *J Infect Dev Ctries*. 7(8): 638-41

## The Bogotá Manifesto: six commitments for the elimination of Chagas as a public health issue

Diogo Galvão (DNDi) and Javier Sancho (Chagas Coalition)

Since 2018, the Global Chagas Coalition and the Chagas Platform have agreed on a framework of commitments in which their partners, allies, and public and private institutions can contribute to achieve the goal of eliminating the disease as a public health issue. After a first document jointly developed in Santa Cruz de la Sierra, Bolivia, some of the progress made at the global level was reviewed, such as the approval of the World Chagas Disease Day or the emergence of new initiatives to control congenital transmission. Therefore, on September 23, 2022, during the meeting of the Chagas Platform in Bogotá, Colombia, a new document — the Bogotá Manifesto — was agreed upon. It records the most important commitments for the current moment and decade.

In summary, the Bogotá Manifesto calls on governments and organizations to intensify their efforts in six areas of priority:

1. Access to comprehensive care by improving the decentralization of health services to bring them closer to the affected population. This is possible, for example, through simplified diagnostic algorithms and the systematic implementation of screenings in women of reproductive age, pregnant women, and babies. This is intended to not only stop congenital transmission, but also to ensure the timely detection and care of all cases in the affected communities.
2. Encouraging investment in R&D for new diagnostic and therapeutic tools, as well as for facilitating access to current tools.
3. Improving mandatory reporting systems for cases and their clinical complications.
4. Strengthening access to training and consultation tools for healthcare providers and affected people.
5. Encouraging coordination among all the actors involved in providing care and ensuring the participation of affected people and their associations in the design and implementation of strategies.
6. Supporting actions to raise visibility centered on World Chagas Day.

We invite you to join and embrace these commitments to support the elimination objectives set at the national, regional and global levels.

The manifesto is available for consultation, adoption and dissemination at the [Global Chagas Coalition website](#). ◦

# #VocesDelChagas: process and protagonists

Laura Giménez and Leonardo de la Torre (ISGlobal)



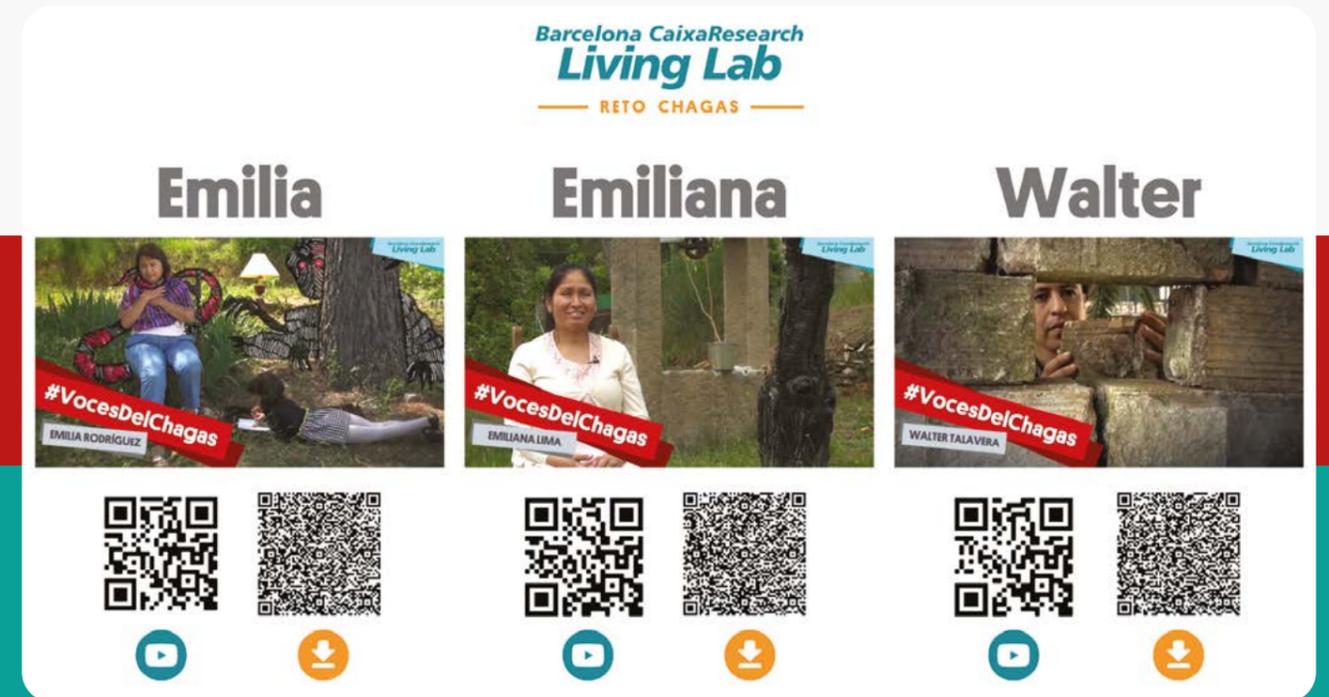
**#vocesdelchagas**  
isglobal.org/vocesdelchagas

An experienced community that had been asking to be part of an impactful adventure; perhaps that was the key to the process that led to #VocesDelChagas.

Our invitation to conceive proposals in the face of the well-known barriers to access would have come to nothing if a diverse group of people affected by Chagas disease had not responded to it with a clear desire to participate. Through the advocacy work of the Association of Friends of People with Chagas Disease (ASAPECHA) and the previous project, “¡Pasa la voz!,” these people had already demonstrated their ability to overcome the condition of “patients” and become protagonists of an increasing access to Chagas care within their communities.

Working with the team of the Unitat de Salut Internacional Drassanes (Vall d’Hebron-PROSICS), the Living Lab asked these protagonists: *How do you face the disease here and there?* The touching answers to this question, describing various practices deployed in Barcelona and in each participant’s place of origin, put in motion the process that took us through the following stages, each of them open to co-creation: mapping actors and identifying needs; designing objectives (agenda); co-creating solutions; implementation and evaluation.

To date, there have been eight workshops and many regular meetings where the process has continued to be underscored and redirected. Another keyword? Validation. In each workshop, agreements were reached by demonstrating that all ideas were really being heard.



Based on experience, the participants considered themselves capable of co-creating materials for communication, destigmatization and awareness in relation to Chagas. Thus, they set out to select testimonies that could be shared naturally “here and there” on social networks.

The stories of Emiliana, Emilia and Walter were chosen because of their potential to address: a) the myth of disability, migration and agency to overcome vertical transmission; b) fear and its transformation with monitoring and information; and (c) the “unfinished business” of overcoming the wall of silence.

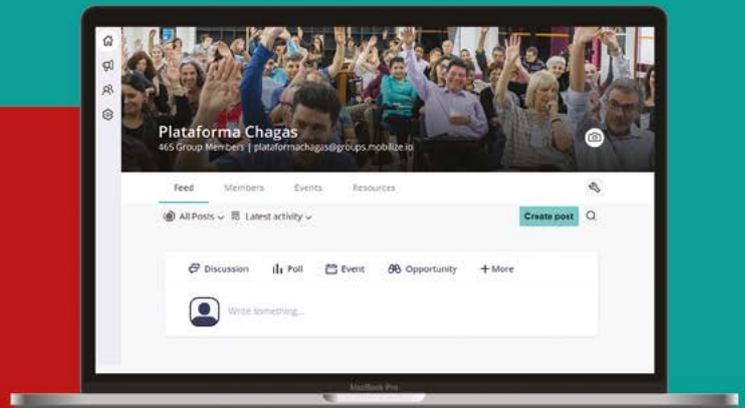
The videos were professionally produced by Pequeños Dibujos Animados (PDA) and ended up becoming the pillars of the #VocesDelChagas campaign, whose name was chosen after the first viewing of the material.

Community involvement did not end with the production: the protagonists also helped spread the campaign in various scenarios and forums. In the final stage, a study was initiated to assess the scope of the campaign with a protocol approved by the Ethics Committee of the Hospital Clínic de Barcelona.

The criteria for this evaluation were not provided by a team made up only of officials from a research center. Consistent with the spirit of #VocesDelChagas, it was proposed that the impact assessment be carried out in accordance with the objectives that all its stakeholders agreed on from the outset. The videos are analyzed from the perspective of groups at risk, associations of people affected by Chagas and the civil society group that took part in the co-creation process. ◦

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