A photograph of a woman with dark hair tied back, wearing a green shirt, holding a baby wrapped in a light blue cloth. A young girl with dark hair in pigtails, wearing a white t-shirt, stands next to her, looking out a window with metal bars. The scene is dimly lit, with light coming from the window.

# New Horizons in Treatment and Care for People Living with Chagas Disease

*Colin Forsyth  
World Chagas Day  
San Diego, California, USA  
April 14, 2023*





**DNDi was created in response to the frustration of clinicians and the desperation of patients faced with medicines that were ineffective, unsafe, unavailable, unaffordable, or that had never been developed at all.**

### **The root of the problem?**

The prevailing profit-oriented model for medical research and development (R&D) leaves little incentive to develop drugs for the poorest and most vulnerable communities.

## INNOVATING TO SAVE LIVES

We discover, develop, and accelerate access to **urgently needed treatments for neglected patients**, focusing on gaps for neglected tropical diseases and viral diseases that fuel cycles of poverty and disease in resource-constrained settings.



### **Sleeping sickness**

Accelerate sustainable disease elimination



### **Leishmaniasis**

Deliver safer, simpler treatments to save lives and reduce social stigma



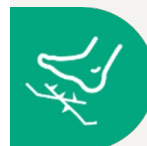
### **Chagas disease**

Contribute to eliminating Chagas as a public health problem



### **Filaria (river blindness)**

Advance progress toward breaking the cycle of transmission



### **Mycetoma**

Prevent devastating amputation and disability



### **Dengue**

Accelerate R&D to address the most prevalent mosquito-borne viral disease



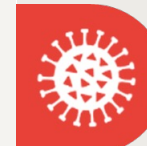
### **HIV**

Ensure access to life-saving treatment for children and people with advanced HIV



### **Hepatitis C**

Help make treatment a reality for millions of people waiting for a cure



### **COVID-19/ pandemic-prone diseases**

Speed tools to save lives, especially in resource-limited settings



### **New areas to be explored:**

Schistosomiasis, snakebite, rabies





# CHAGAS DISEASE

ACCELERATING ACCESS TO BETTER TREATMENT  
AND IDENTIFYING NEW DRUG CANDIDATES

## FACTS

**>6 million**  
people living with  
Chagas

**21**  
endemic  
countries in Latin  
America

**33%**  
of people  
infected suffer  
cardiac damage

## CHALLENGES

Current treatments were **discovered over 50 years ago**, last at least 8 weeks, and can have serious side effects.

Only **1%** of those infected have **access to diagnosis and treatment**.

## OUR WORK

**2011:** First age-adapted **formulations** of the drug benznidazole **for infants and children**

**2018:** Simplified test-and-treat approaches piloted in Colombia are now being replicated in other Latin American countries

## OUR GOALS

**2021-2028:** Contribute to eliminating Chagas as a public health problem

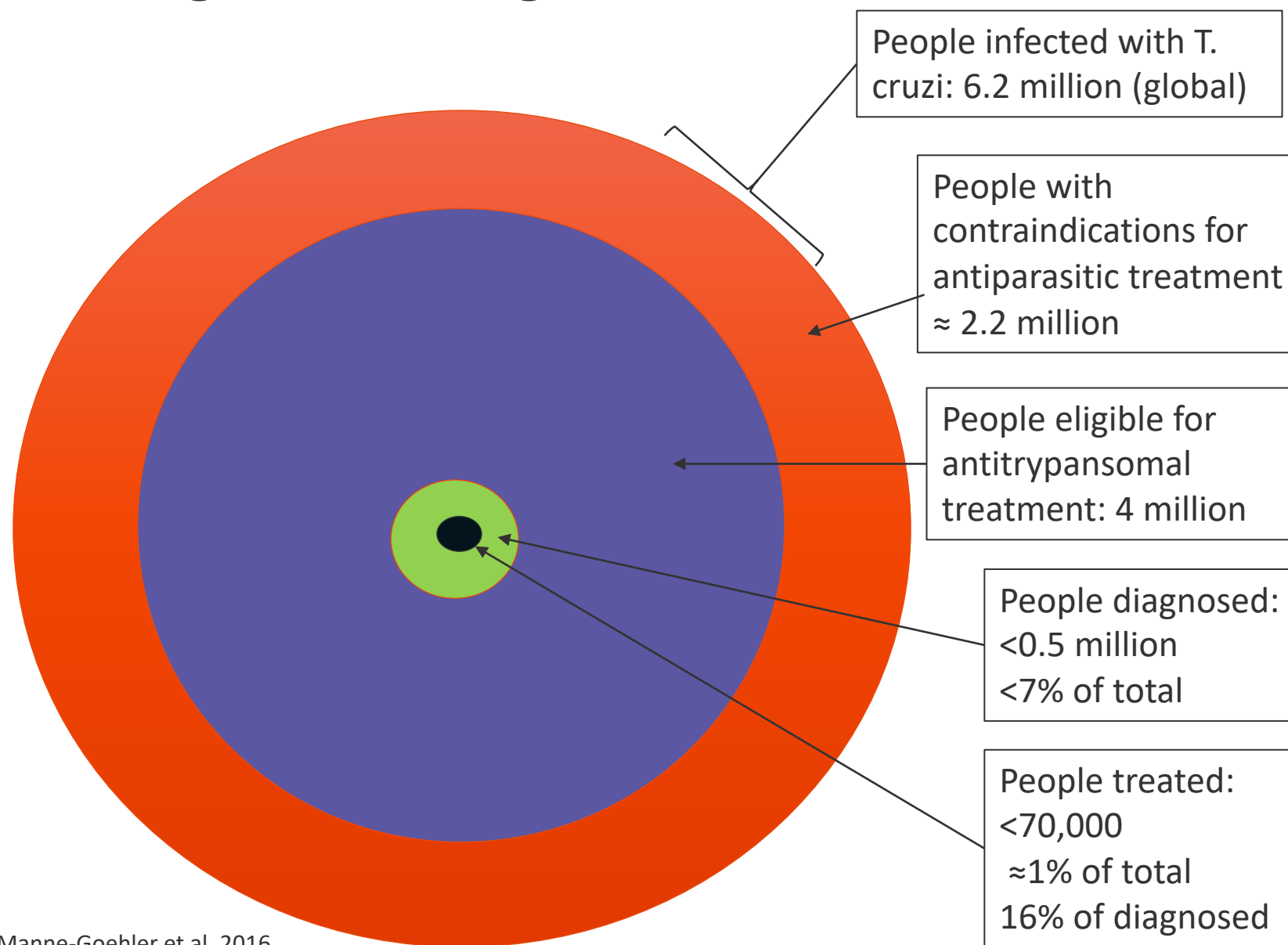
- Develop a **safer, shorter treatment** with benznidazole
- Make progress towards an **entirely new drug for Chagas**, with one new chemical entity entering Phase III trial
- **Reduce mother-to-child transmission** and accelerate roll-out of **test-and-treat strategies**



**MAIN PARTNERS:** Eisai, ELEA, Fiocruz, Fundación Mundo Sano, ISGlobal, Ministries of Health of Argentina, Brazil, and Colombia



# Global Neglect of Chagas Disease\*



\*Sources: WHO 2015; Basile et al. 2011; Manne-Goehler et al. 2016

**Without a change in the current situation, over the next 10 years, according to current estimates, we can expect:**

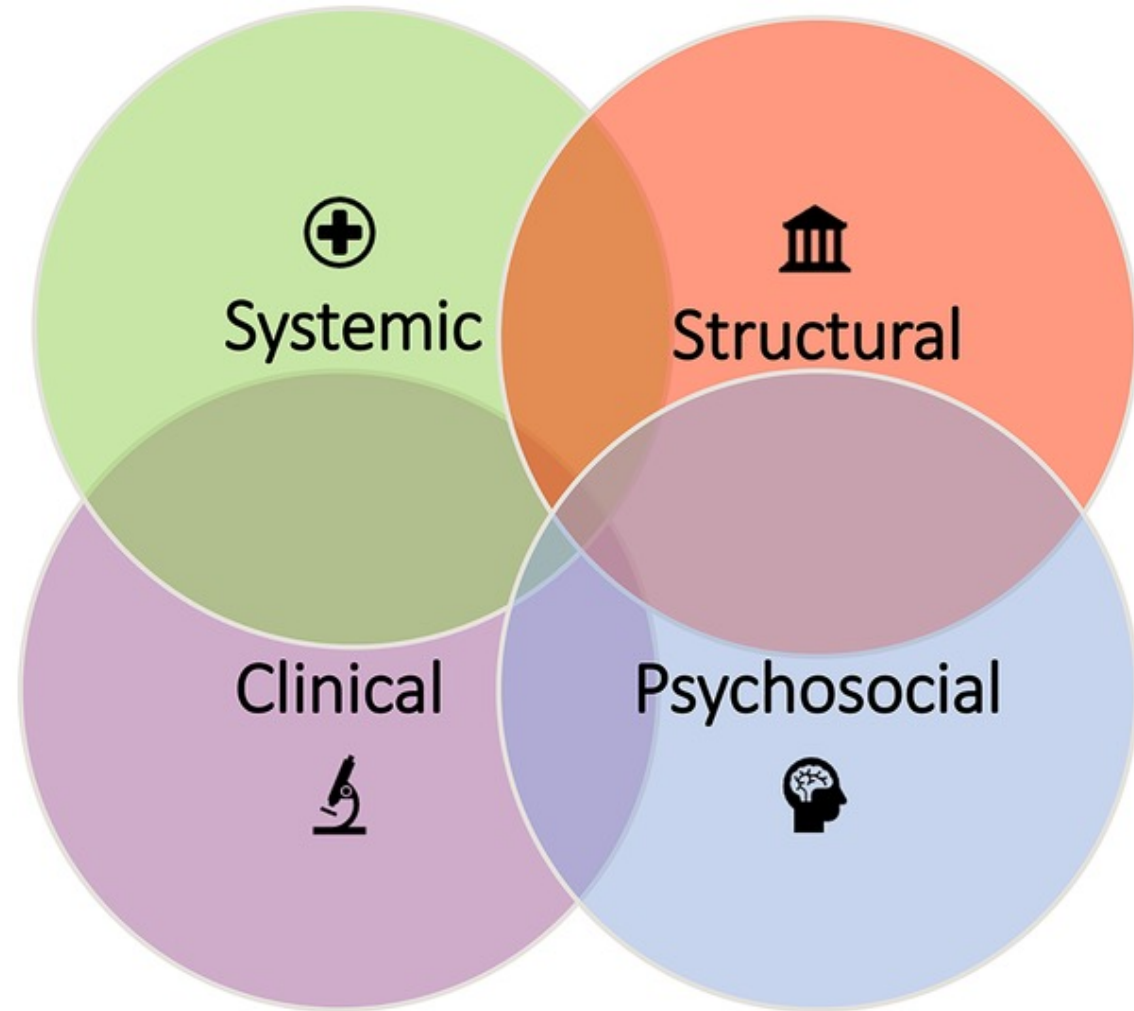
- 75,000-100,000 premature deaths due to Chagas disease and 8 million DALYs lost
- Nearly 300,000 new cases due to vector transmission and 85,000 due to congenital transmission
- 800,000-1.2 million new cases of cardiomyopathy
- US\$7 billion in healthcare costs and \$80 billion in economic losses



## How can we change the status quo?

1. Improve Chagas disease treatment
2. Strengthen healthcare system capacity
3. Simplify testing processes
4. Improve access to testing and treatment
5. Advocate to end the neglect

# Multidimensional Barriers to Diagnosis and Treatment of Chagas Disease



Forsyth C, Meymandi S, Moss I, Cone J, Cohen R, et al. (2019) Proposed multidimensional framework for understanding Chagas disease healthcare barriers in the United States. PLOS Neglected Tropical Diseases 13(9): e0007447. <https://doi.org/10.1371/journal.pntd.0007447>



# 1. Improving Chagas Disease Treatment

*In my case they can't give it to me because it's very strong and if the medicine were a little milder I could take it. (Jorge)*

# Problems with Current Chagas Disease Treatment

- Only two drugs with proven efficacy, benznidazole and nifurtimox
- No new drugs in over 50 years
- Long treatment (2-3 months)
- Problems
  - Effectiveness
  - Safety
- Costs





# The R&D pipeline explained



## DISCOVERY

- Chemical compound screening, evaluation & optimization



## TRANSLATION

- Drug candidate assessment
- Testing in healthy volunteers



## CLINICAL DEVELOPMENT

- Large-scale clinical trials



## IMPLEMENTATION

- Drug regulatory review & national registration
- Ongoing surveillance
- Tackling barriers to treatment access

Working with partners at every step of the way



Patients & communities



Health Ministries



Academia



Pharmaceutical industry



Treatment providers



# Lead Optimization Latin America (LOLA) Consortium



## Our Drug Discovery Partners in Latin America

- University of Campinas (UNICAMP)
- University of São Paulo (USP)
- Phenotypic Screening Platform, Institute of Biomedical Sciences, University of São Paulo (ICB-USP)
- The Centre for Medicinal Chemistry (CQMED-UNICAMP)
- Structural Genomics Consortium (SGC)
- Centro de Inovação e Ensaios Pré-Clínicos (CIEEnP)
- São Paulo Research Foundation (FAPESP)



# Toward a Safer, Effective Treatment for Chronic Chagas Disease: Shortening Current Treatment



## The BENDITA study

A Phase II study to assess safety, tolerability, and efficacy of different benznidazole regimens, alone and in combination with fosravuconazole

**DNDi**  
Drugs for Neglected Diseases *initiative*



BENLATINO

## NuestroBen (Nueva Esquema para Tratamiento con Benzonidazol )



Mundo Sano

Laboratorio  
**ELEA PHOENIX**

**DNDi**  
Drugs for Neglected Diseases *initiative*

**DNDi**

# Toward a Safer, Effective Treatment for Chronic Chagas Disease: Clinical Trials of New Drugs



**ISGlobal**



FEXI-012

# The Chagas Clinical Research Platform

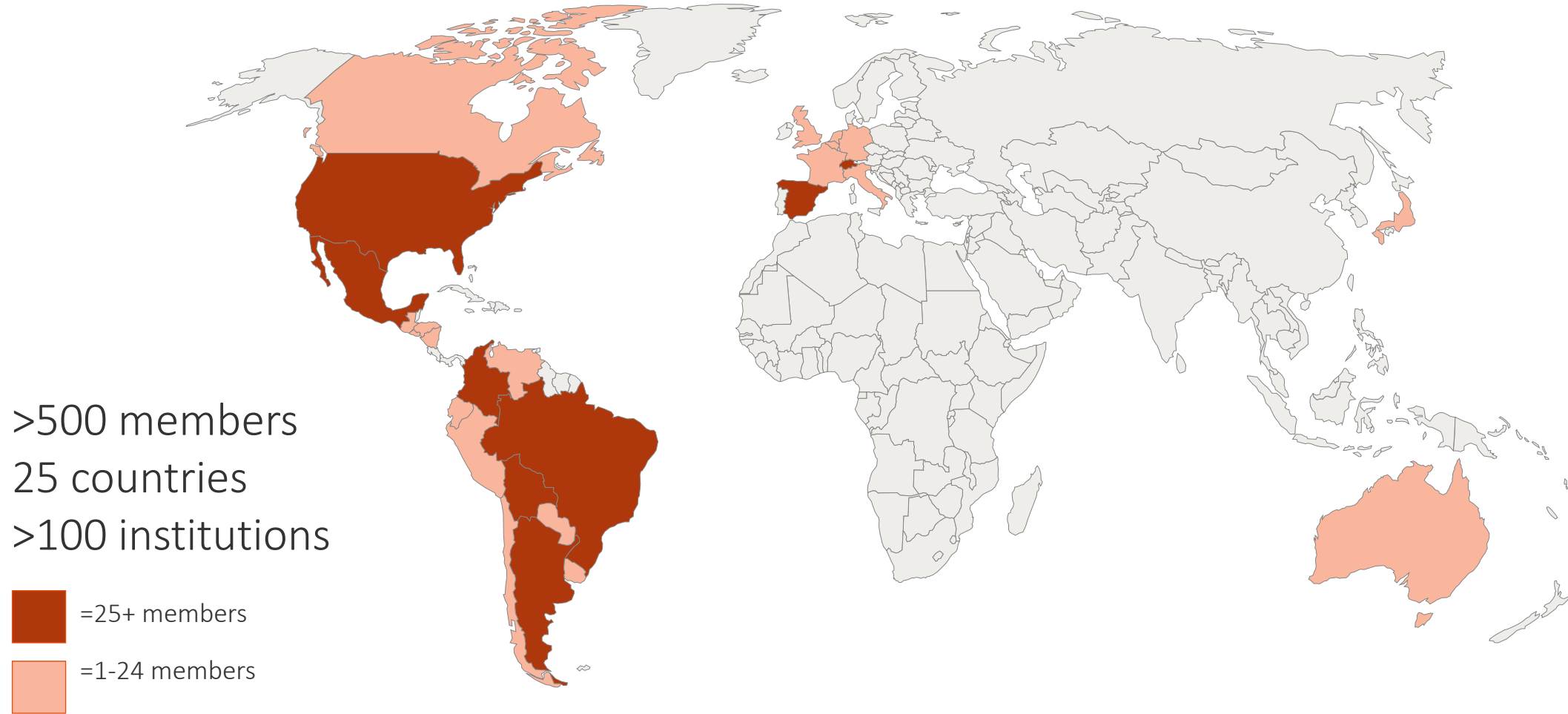


- Unify the Chagas clinical and research community in serving the needs of people with Chagas disease, their families, and communities.
- Provide a forum for discussions on research priorities, and alignment on collaborative action
- Promote communication and sharing of new research





# Chagas Clinical Research Platform



## 2. Strengthening Healthcare System Capacity to Care for Patients with Chronic Chagas Disease

*There is not a lot of awareness. I think every health center should give talks about this disease to train the nurses and everyone else because they don't have knowledge about it. (Roberto)*





## Activities to Strengthen Health System Capacity



iChagas app

1. Training healthcare personnel in diagnosis and treatment
2. Updating manuals and recommendations
3. Improving information resources

### 3. Simplifying Testing Processes to Make Testing More Accessible

*Include it in annual physicals or provide the test for free. I would find a way to provide free Chagas testing in more places. (Renata)*



# Simplifying Testing Processes



- Studies to better understand the performance of current diagnostic tools
- Working with partners to improve the available diagnostic tools
- Incorporating rapid, point-of-care tests

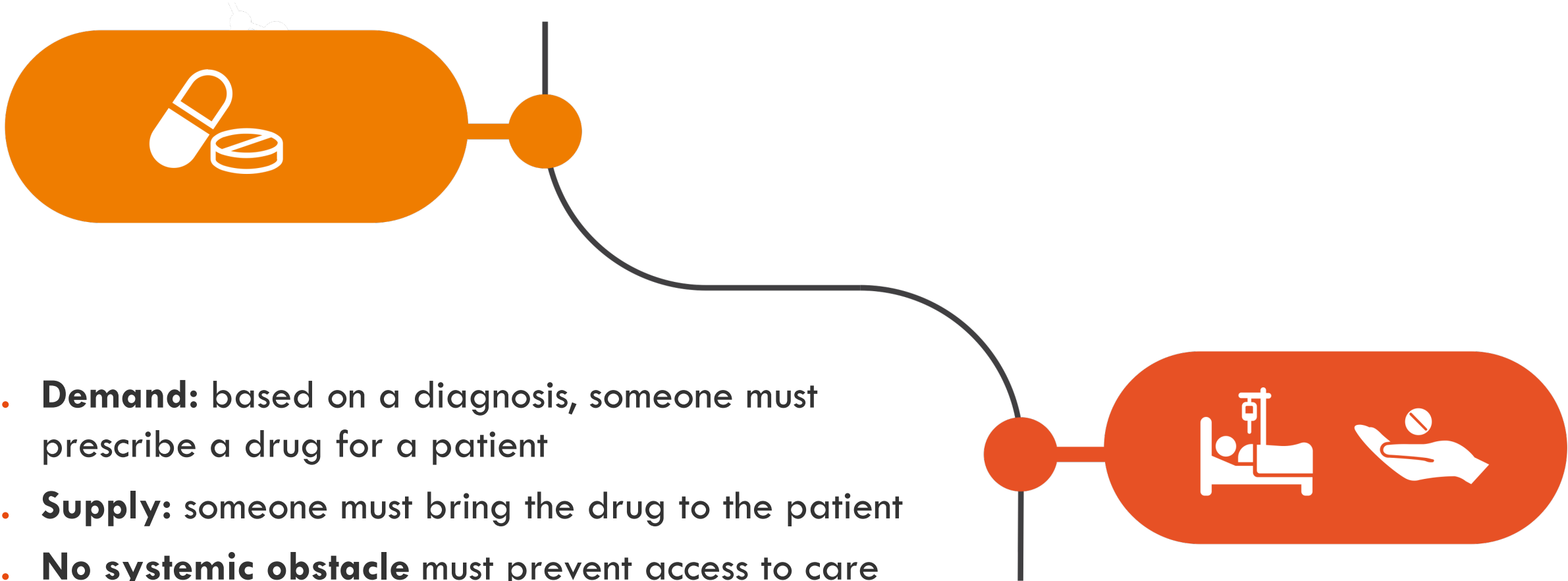


## 4. Improving Access to Testing and Treatment

*Make treatment more accessible. Thank God we have insurance and were able to go to this clinic, but maybe if there were more clinics and better informed doctors it would be easier. (Eleana)*



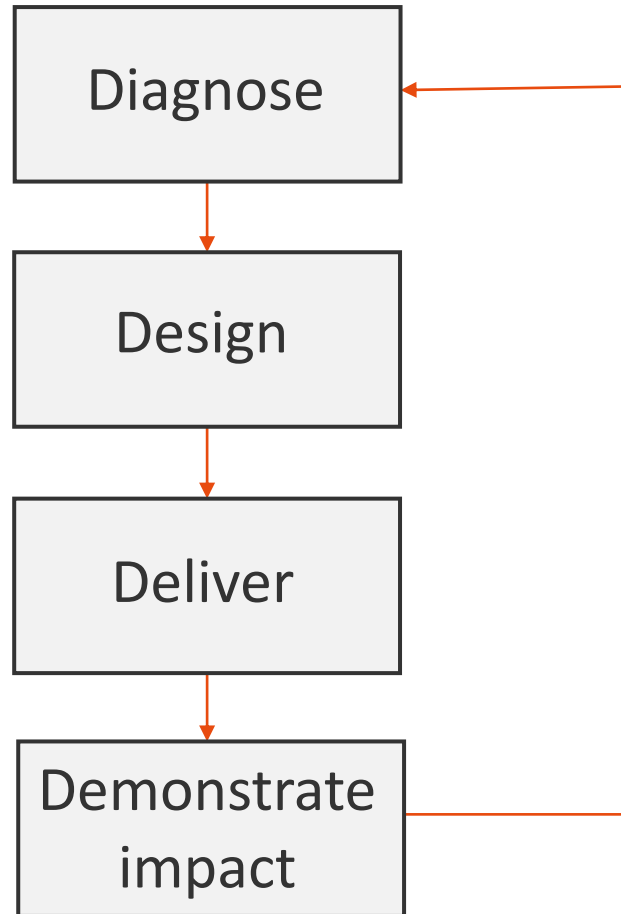
# Simplified access framework across diseases and countries



1. **Demand:** based on a diagnosis, someone must prescribe a drug for a patient
2. **Supply:** someone must bring the drug to the patient
3. **No systemic obstacle** must prevent access to care
4. **Financing:** all costs must be covered



## 4D Access Approach



### 4D Pilot Project Impact in Colombia

- Simplified testing process with 92% reduction in wait times for test results
- Scaled up to 22 new municipalities in Colombia so far
- Fivefold increase in people tested per year compared to baseline

# Improving Access to Information for People at Risk



La salud es de todos Minsalud

**¡Que tu corazón crezca de felicidad y emoción! Pero que nunca sea por Chagas.**

El Chagas es una infección causada por un parásito, la cual puede presentarse al comienzo con síntomas como fiebre mayor a 7 días y malestar general. Y, luego puede pasar sin manifestarse durante años, pero cuando se desarrolla la enfermedad puede causar daños principalmente en el corazón y en ocasiones en el sistema digestivo (intestinos y esófago).

**¿Cómo se transmite el parásito?**

 Por contacto con la materia fecal del pito.	 Consumo de alimentos contaminados o de animales infectados.	 De mamá infectada con Chagas o su hijo durante el embarazo.	 Transfusiones de sangre o trasplante de órganos de personas con Chagas.
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\*El Chagas solo puede ser transmitido en su momento, cuando el pito está con los síntomas.

Si en tu casa hay o ha habido pitos, o si tienes familiares con Chagas, acércate al centro de salud, pide tu cita médica y solicita el examen. Si sales positivo, sigue el tratamiento.

**El diagnóstico y tratamiento temprano del Chagas evita complicaciones futuras y daños irreparables.**

INSTITUTO NACIONAL DE SALUD GOBIERNO NACIONAL COALICIÓN CHAGAS DNDi

# DNDi and Partners: Chagas Treatment Access Project



## Funding



- 4 =4D approach
  - Microscope icon =DNDi clinical trial
  - DNDi logo =DNDi regional office
- DNDi

## 5. Advocate to end the neglect





# The Bogotá Manifesto: Six commitments to advance towards the elimination of Chagas disease as a public health problem

1. **Improve access** to Dx, Tx and comprehensive care for people affected by CD, **through decentralized routes of care**, which allow the provision of care and follow-up in **the primary healthcare level**; adoption of simplified diagnostic algorithms and implementation of screening in women of reproductive age, pregnant women, and infants.
2. Encourage investment in **research and development** to obtain simpler, safer diagnostic and therapeutic tools, as well as facilitate access to existing technologies.
3. Strengthen and facilitate **access to training and information resources** for both healthcare personnel and affected people, facilitating the provision of up-to-date, high-quality care.








4. Promote **coordination** between all the actors involved in **routes of care** and guarantee the participation of **affected people and their associations** in the design and implementation of strategies.
5. Continue to support activities related to **World Chagas Day**.
6. Improve surveillance and control of the disease, **expanding systems of mandatory notification** of Chagas cases and clinical complications. **DNDi**



# Thank you! Obrigado! Gracias!



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