Increasing Access to Testing and Treatment for Chagas Disease in the United States: Understanding Patient and Community Perspectives

ECHO: Extension for Community Healthcare Outcomes

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BEST SCIENCE
FOR THE MOST NEGLECTED

DNDi
Drugs for Neglected Diseases *initiative*

DND*i*: 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

HIV
Ensure access to lifesaving treatment for children and people with advanced HIV

Hepatitis
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:
Dengue, schistosomiasis, snakebite

Center of Excellence for Chagas Disease (CECD)

- Founded in 2007: 1st US center to provide comprehensive care for Chagas disease
- Located within Olive View-UCLA Medical Center, a safety-net facility in Los Angeles, California
- Sources of patients
  - Community-based screening program
  - Referrals from Red Cross
  - Screening of Olive View patients (obstetrics, cardiology)
  - Patient family member referrals
  - Inquiries from patients and providers in L.A.
- over 8,000 screened, over 300 treated
- volunteer-driven

Topics

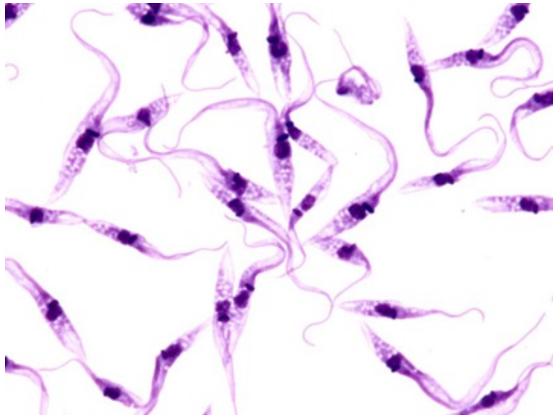
1. Why does Chagas continue to be a neglected disease in the U.S.?

2. What are the current testing recommendations?

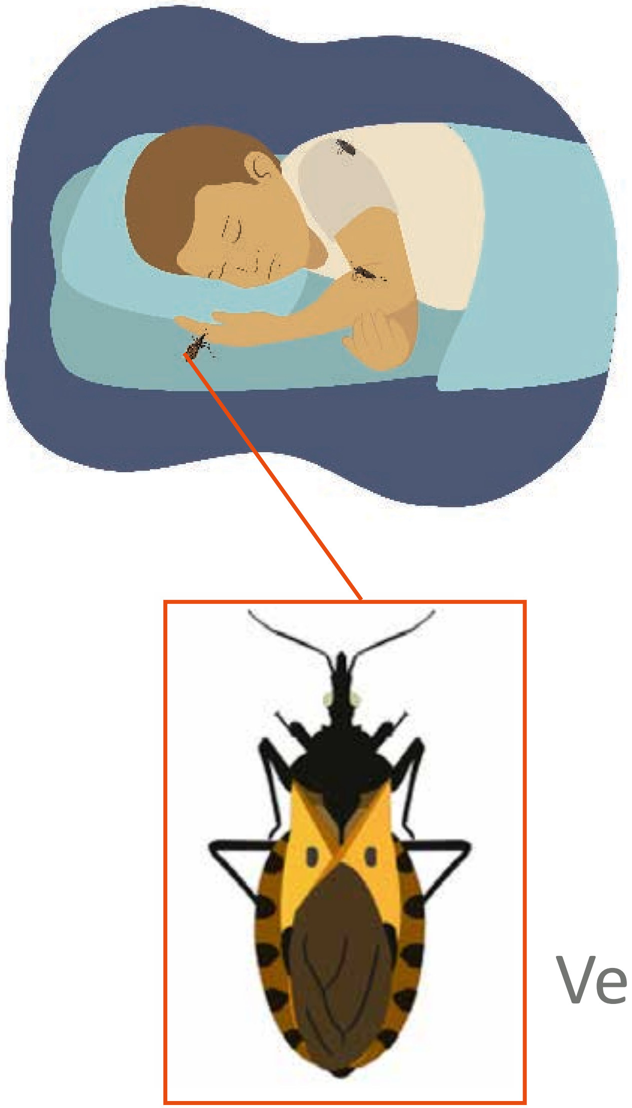
3. How can we increase access to testing and treatment?

Chagas Disease-Quick Facts

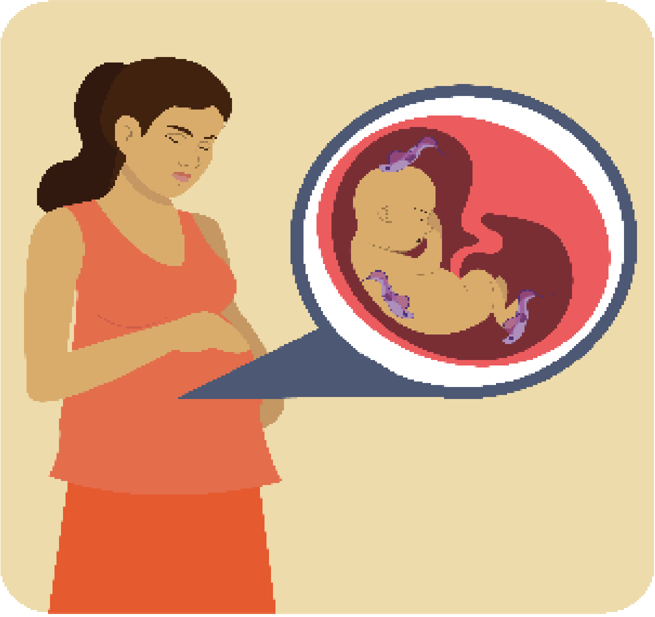
- Caused by *Trypanosoma cruzi*, a flagellate protozoan
- Affects an estimated 6-7 million people worldwide (WHO 2015)
  - An estimated 1.2 million have developed cardiomyopathy
- Most people are not aware they are infected
- Disproportionately affects vulnerable populations
- Annual global economic burden>$U.S. 8 billion (Lee et al. 2013)



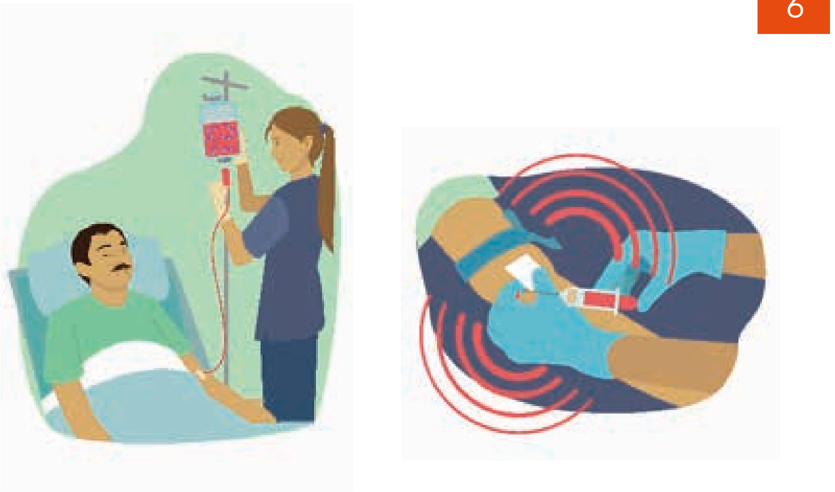
Chagas disease, forms of transmission



Vector (triatomines)



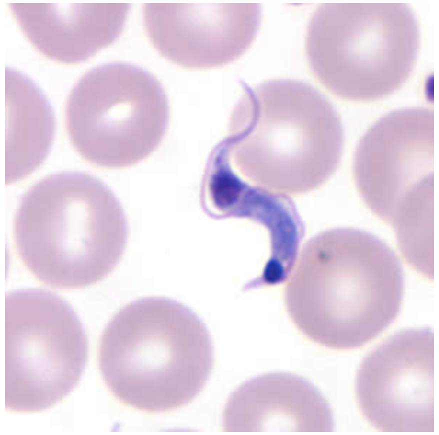
Congenital



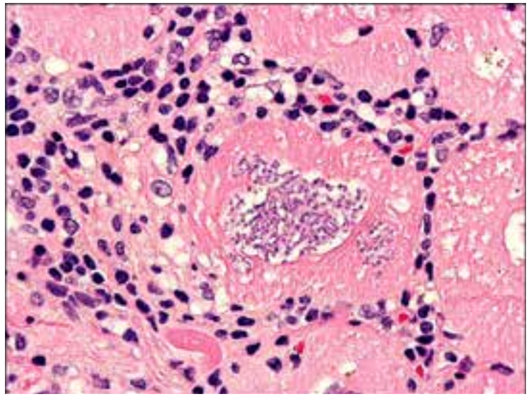
Transfusion/transplant

Oral

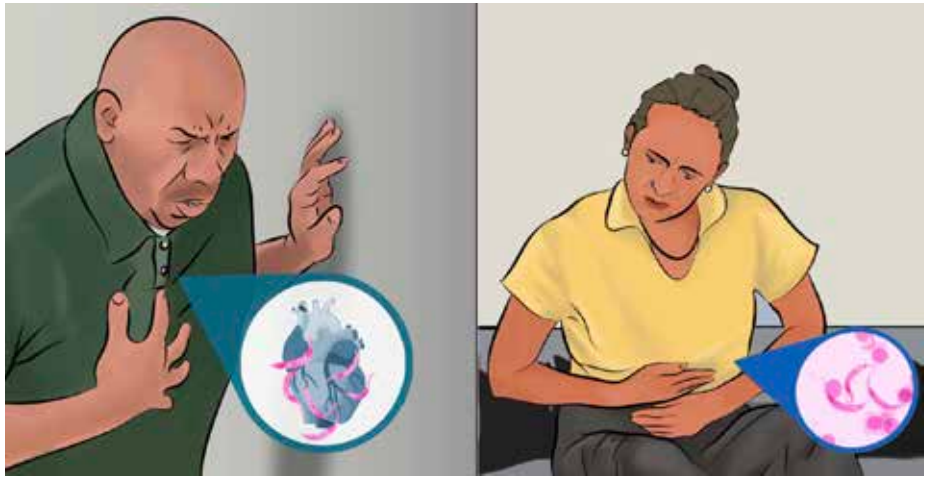
Phases of Chagas Disease



1. Acute Phase:
- Several days after transmission
- Resolves in a couple weeks
- Usually no symptoms
- But, can be fatal
- Parasites in the blood

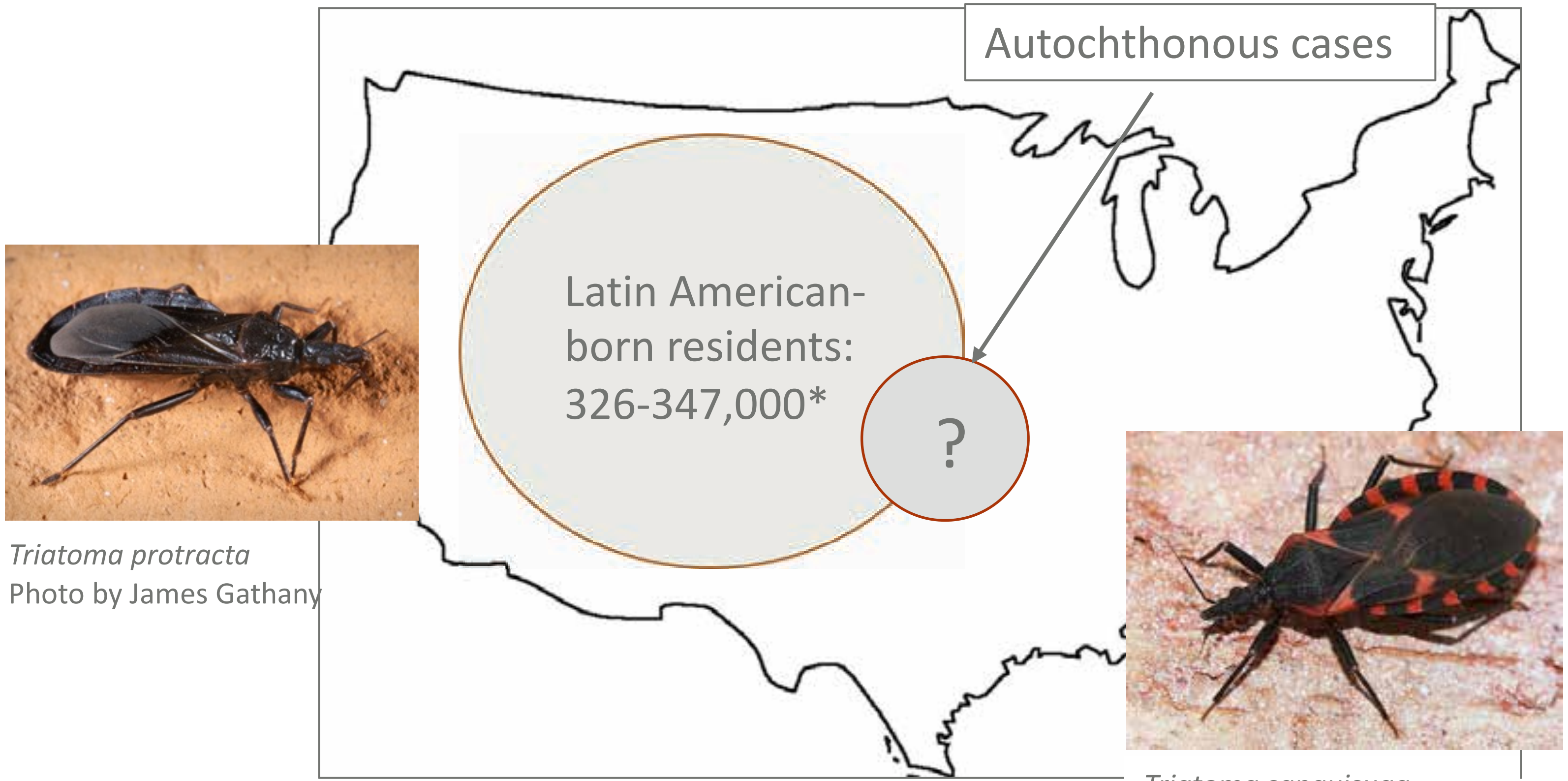


2. Chronic Phase (indeterminate):
- After acute phase
- No symptoms
- Parasites are hidden



3. Chronic Phase (advanced):
- 10-30 years after infection
- 30-40% of infected
- affects the heart, digestive system, and/or nervous system

Current Epidemiological Landscape



Autochthonous cases

Latin American-born residents: 326-347,000*

?

Triatoma protracta
Photo by James Gathany

Triatoma sanguisuga
Photo by Sam Houston

< 1% diagnosed*
<0.2% treated*

*Manne-Goehler J, Umeh CA, Montgomery SP, Wirtz VJ. Estimating the Burden of Chagas Disease in the United States. PLOS Neglected Tropical Diseases. 2016;10(11):e0005033.

1) True or false:

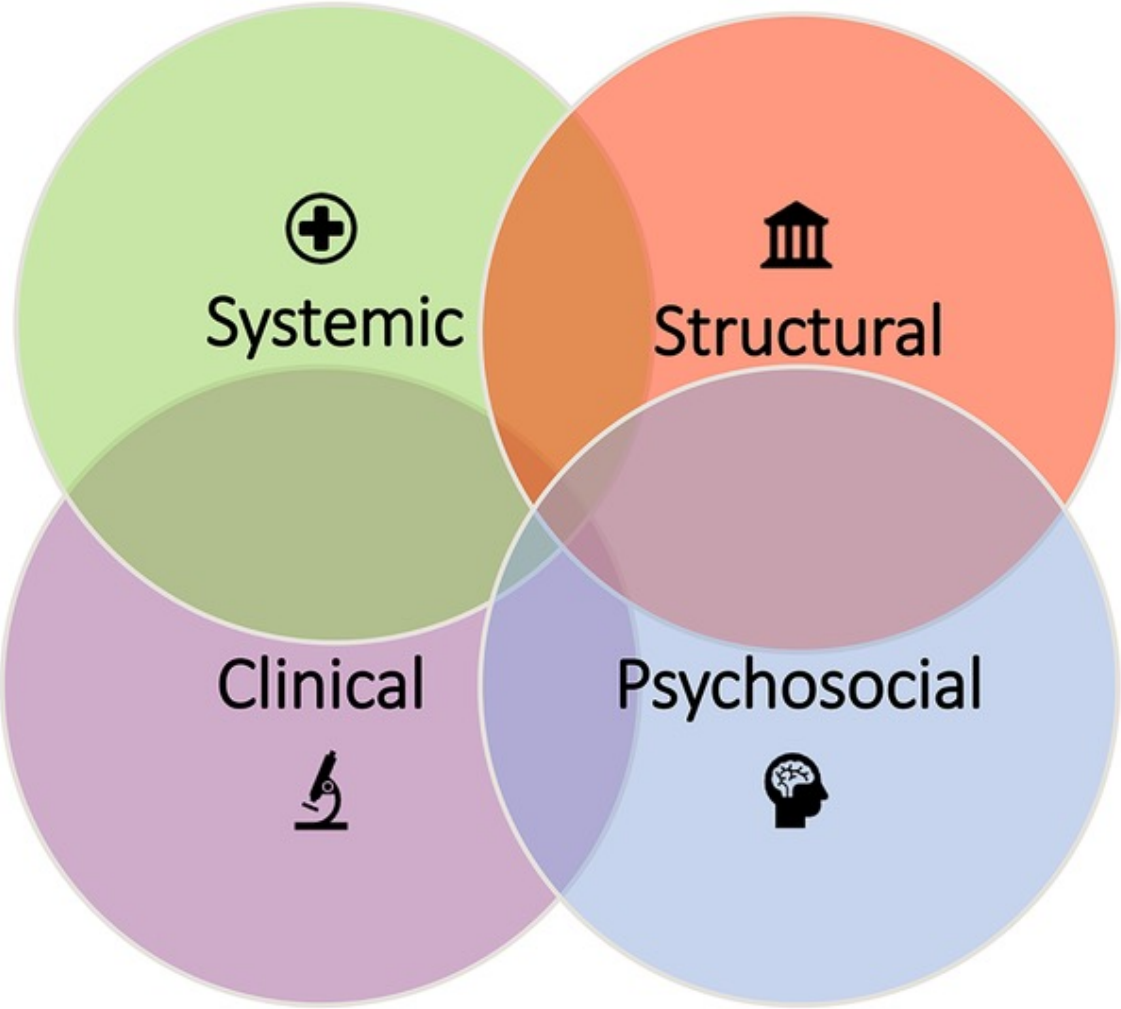
Testing for Chagas disease only makes sense for people who have resided in Latin America within the last 10 years.

Studies on Prevalence of Chagas Disease in Latin American-born Populations in the U.S. (2010-2020)*

Study	Population	prevalence (%)
Castro et al. 2020	1,514 people in the greater Washington, DC metropolitan area (community screening program)	3.8
Hernandez et al. 2019	189 relatives of 86 previously diagnosed patients with CD	7.4
Manne-Goehler et. al. 2019	5,125 people from endemic regions screened in primary care setting in East Boston	1.0
Meymandi et al. 2017	4,755 Latin American-born residents of Los Angeles (community screening program)	1.2
Traina et al. 2017	327 hospital patients with electrocardiogram abnormalities	5.2
Park et al. 2017	80 patients with pacemakers	7.5
Traina et al. 2015	135 hospital patients with nonischemic cardiomyopathy	19.0
Kapelusznik et al. 2013	39 hospital patients with nonischemic cardiomyopathy	13.0

Source: U.S. Chagas Diagnostic Working Group, Recommendations for Screening and Diagnosis of Chagas Disease in the United States, The Journal of Infectious Diseases, 2021;, jiab513, https://doi.org/10.1093/infdis/jiab513

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

PLOS | NEGLECTED TROPICAL DISEASES

Clinical Barriers

Aspects of the disease or limitations in the current diagnostic and therapeutic technologies that hamper capacity to provide appropriate care to people with Chagas.

- Complexities in the diagnostic process
    - Variations in sensitivity and specificity between tests
    - Regionally patterned variations in immune response
    - Necessity of using multiple tests
- Genetic diversity of *T. cruzi*
- Lack of biomarkers to assess efficacy of treatment, or predict who will progress to a more severe form
- Side effects from benznidazole and nifurtimox

Systemic Barriers

Gaps or limitations in the healthcare system that limit the ability of people with Chagas disease to obtain care, or the ability of healthcare workers to offer care

- Low awareness among healthcare workers
- Lack of proactive screening as part of routine care
- Regulatory barriers
- Lack of health information, publicity

Structural Barriers

Access barriers rooted in inequalities in the political and economic system.

- Migratory status
- Lack of resources to pay for transportation
- Limitations in time off/work schedule flexibility
- Lack of insurance coverage
- Lack of political commitment in sustainable actions against Chagas disease

Psychosocial Barriers

Perceptions or attitudes about the disease, and its treatment, in patients or in society that hamper efforts to obtain medical care for Chagas disease.

- Stigmatization of the disease
- Stigmatization of immigrants as carriers of disease
- Fear of knowing, of being diagnosed
- Ignoring or “forgetting” the disease
- Anguish due to being diagnosed

Impact of COVID-19 on Screening/Diagnosis of Chagas Disease

Area	**Potential impact of SARS-CoV-2 on roadblocks**
Prevention	-Reduced commitment from governments -Diversion of clinical research to COVID-19 -Public health resources diverted to COVID-19 -Lower media interest in neglected diseases -Limitations on health fairs, campaigns, and community events
Diagnosis	-Decreased visits to healthcare facilities out of fear of contagion -Testing/laboratory resources strained by COVID-19
Psychosocial	-Increasing poverty due to economic impact of pandemic -Isolation from support networks -Fears about susceptibility to COVID-19 because of CD diagnosis

Zaidel EJ, et al. COVID-19: Implications for People with Chagas Disease. *Global Heart*. 2020; 15(1): 69. DOI: https://doi.org/10.5334/gh.891

Healthcare Provider Awareness-USA

Study	Sample	Key findings
Stimpert et al. 2010	1142 physicians (Medscape CME survey)	26% never heard of Chagas disease; 30% “not at all confident” in their knowledge
Verani et al 2010	421 OB/GYNs	91% unaware of risk of congenital transmission; >75% did not consider diagnosis in patients from endemic areas
Edwards et al. 2018	Pediatric Infectious Diseases Society	Risk of CD in babies born to patients from endemic areas seldom considered
Pacheco 2018	43 Texas physicians	Concerns around diagnostic process

The majority of doctors in the United States don’t know what Chagas is. I’ve gone to two cardiologists… and I had to show the doctor on Google what Chagas is.

-Omar, 41, El Salvador

They explained to me I had been bitten by a chinche… and not to worry too much, to talk to my doctor, but I started to search and nobody could help me because they didn’t know what the disease was.

-Denver, 42, El Salvador

It's a fatal disease, and yet you don't hear anything about it, it's like a phantom disease that is killing people but nobody knows it exists, until they tell you you have it. You always hear about diabetes, cancer, but [Chagas] disease is something that's never heard anywhere, not even in the media.
-Sara, 60, El Salvador

86% of 2,677 Latin American-born residents of Los Angeles had never heard of Chagas disease (Sanchez et al. 2014)

Sanchez DR, Traina MI, Hernandez S, Smer AM, Khamag H, Meymandi SK. Chagas disease awareness among Latin American immigrants living in Los Angeles, California. *Am J Trop Med Hyg*. 2014;91(5):915-919. doi:10.4269/ajtmh.14-0305

2) Where do most people in the U.S. find out they are potentially infected with Trypanosoma cruzi?

a) during prenatal care visits
b) after donating blood
c) during routine checkups
d) during hospitalization

What are the Main Difficulties or Concerns in Seeing a Doctor for Chagas Disease from Patients' Point of View?

- Not having a source of transportation
- Difficulty in getting time off from work
- Lack of insurance coverage
- Financial resources
- Bureaucracy/delays in the health system
- Having services close to home

Before I couldn't go [to the doctor], because I didn't know how to drive. I had to wait for someone to take me; I depended on someone giving me a ride as a favor. And then I didn't have money to pay for the appointment or the ride, or sometimes for lack of time, and I've had to neglect other tasks so I could go to the doctor.
-Renata, 36, Mexico

Forsyth CJ, Hernandez S, Flores CA, Roman MF, Nieto JM, Marquez G, Sequeira J, Sequeira H, Meymandi SK. "You Don't Have a Normal Life": Coping with Chagas Disease in Los Angeles, California. Med Anthropol. 2021 Aug-Sep;40(6):525-540.

Forsyth CJ, Hernandez S, Flores CA, et al. "It's Like a Phantom Disease": Patient Perspectives on Access to Treatment for Chagas Disease in the United States. *Am J Trop Med Hyg*. 2018;98(3):735-741. doi:10.4269/ajtmh.17-0691

Patient Reactions to Diagnosis

I know that nothing can be done, there's no cure, nothing, and I think the only way to go on with life is to not pay too much attention to it. I take care of myself, but apart from that nothing more can be done. (Abram, 55, El Salvador)

I just didn't worry about it because I didn't feel anything. No symptoms. If I would have been worried I would have taken time out of my day and gone to see what it was all about. (Juana, 44, Mexico)

My fear is I know that I am going to die but I don't feel anything, it is a death that is killing me inside. I sometimes tell myself, maybe, if I wouldn't have found out about the disease, everything would have been okay. Now that I found out, it is constantly in my head, it just makes me cry constantly. All I do is think about my daughters. (Julia, 39, El Salvador)

Questions from Newly Diagnosed Patients

Is Chagas disease sexually transmitted or contagious?

Are my children at risk?

Do I need further testing?

Should I change my diet/lifestyle?

How can I have a disease if I don't feel any symptoms?

My doctor said I was fine at my last checkup. How can I have a disease?

When will I feel symptoms?

How long will I have the disease?

Where can I find more information?

What are the treatment options?

My primary care doctor can't help me. Where can I go for treatment?

Can I get this treatment even if I am uninsured/undocumented?

I am frightened, worried, concerned. Who can I talk to?

Source: Stimpert et al., focus group study, Los Angeles (unpublished manuscript)

Screening and Diagnostic Recommendations for U.S. Healthcare Providers

- **Recently published by working group of Chagas experts**

https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab513/6384556

Objectives:

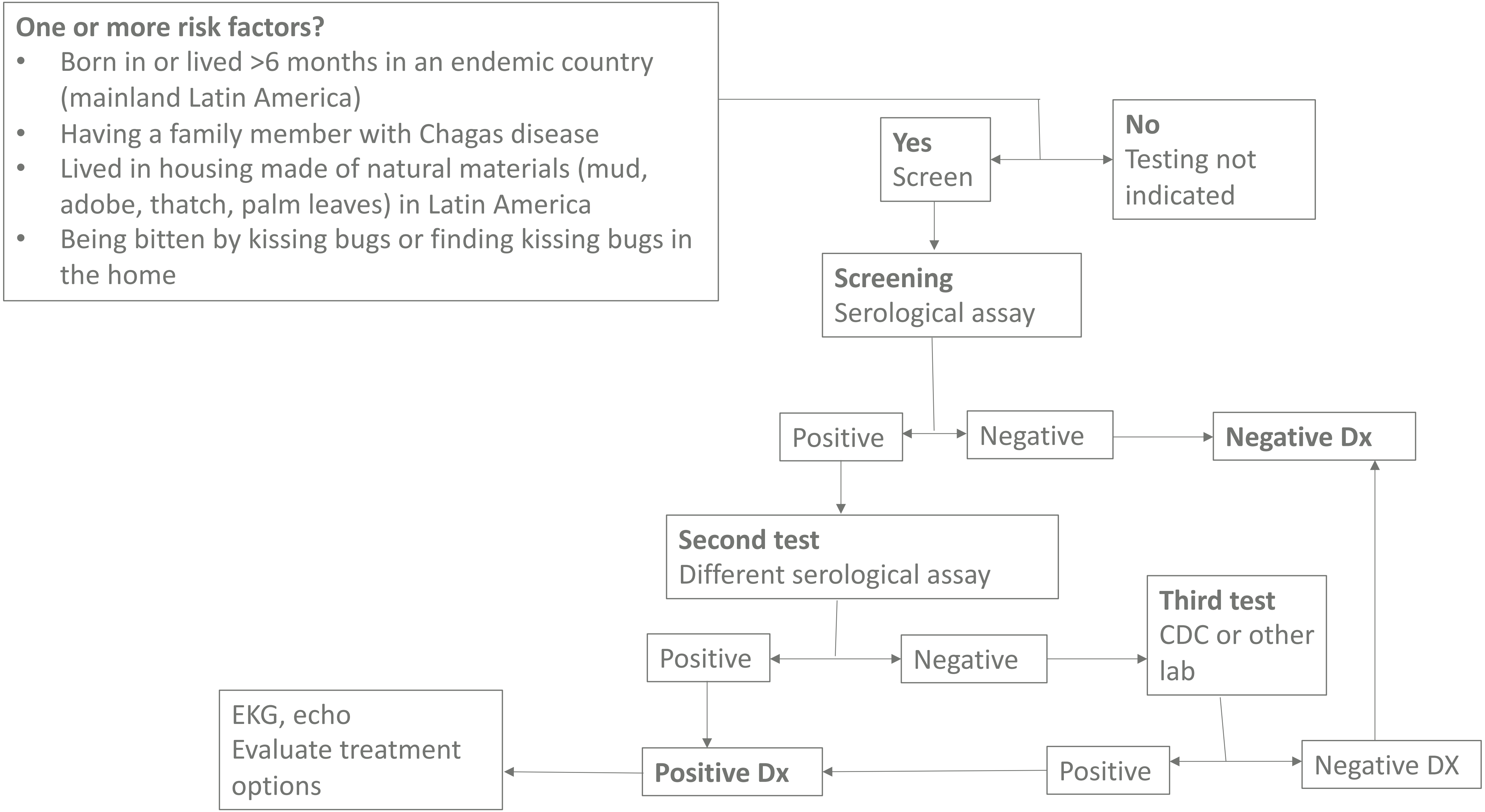
- Providing clear testing recommendations for primary healthcare personnel
- Help identify epidemiological and clinical risk factors
- Defining steps to simplify and strengthen current diagnostic algorithms
- Support increased testing for Chagas disease via healthcare providers

Screening Recommendations (Risk Groups)

Recommendation	**Strength**	**Quality of evidence**
I. Who should be screened for Chagas disease in the United States?		
People who were born or lived for a prolonged period in areas of Mexico, Central or South America with endemic Chagas disease.	strong	low
Close (first-degree) relatives of people previously diagnosed with Chagas disease	strong	low
People with entomologically confirmed or highly suspected exposure (bites and/or triatomines/kissing bugs found in the home), in states with known presence of triatomine species capable of transmitting T. cruzi.	conditional	low
Travelers with confirmed exposure to triatomines or associated risk factors in regions of Latin America where Chagas disease is endemic	conditional	low
Women of childbearing age who have lived in a region of South or Central America with endemic Chagas disease	strong	moderate

Risk Factors (Clinical)

Recommendation	**Strength**	**Quality of evidence**
II. Which clinical conditions warrant diagnostic testing for Chagas disease in people from endemic countries of Latin America?		
ECG abnormalities suggestive of infection, even in the absence of symptoms. These include first degree AV block, PVCs, atrial fibrillation, RBBB, bifascicular block, and low voltage QRS.	strong	low
Bradyarrhythmias and tachyarrhythmias	strong	low
Regional wall motion abnormalities (particularly basal inferolateral, apical aneurysm)	strong	low
Thromboembolic phenomenon	strong	low
Congestive heart failure and/or a reduced ejection fraction	strong	low
Megacolon/megaesophagus	strong	low



One or more risk factors?

- Born in or lived >6 months in an endemic country (mainland Latin America)
- Having a family member with Chagas disease
- Lived in housing made of natural materials (mud, adobe, thatch, palm leaves) in Latin America
- Being bitten by kissing bugs or finding kissing bugs in the home

Yes
Screen

No
Testing not indicated

Screening
Serological assay

Positive

Negative

Negative Dx

Second test
Different serological assay

Positive

Negative

Third test
CDC or other lab

Positive

Negative DX

Positive Dx

EKG, echo
Evaluate treatment options

3) Based on the recent publication of procedures for the screening and diagnosis of Chagas disease, in your opinion, which of the following ways would be most helpful for receiving this information? Please choose your top TWO choices:

- Read the full article
- 1-page summary
- Workflow diagram
- Workflow diagram with hyperlinks to information within the paper
- 1-page summary with hyperlinks to information within the paper
- A website with interactive hyperlinks to the paper
- Other? (Suggestions welcome)

If you were President, what would you do about Chagas disease?

Top solutions	N, (%)	In the patients' words
Provide more information **N=13**	13 (26)	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)
Find new/better medicines **N=13**	13 (26)	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)
Increase screening **N=9**	9 (18)	If I were President, I would 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)
More facilities, providers offering treatment **N=8**	8 (16)	Make treatment more accessible. Thank God we have insurance and were able to go to this clinic, but maybe if there were clinics and better informed doctors it would be easier. Because there's just one clinic, so far away and nobody else knows about this disease. (Eleana)
Provide free or more accessible treatment **N=7**	7 (14)	I would provide free services for all people with the disease, and explain to them what the disease is and how they can survive. (Flor)

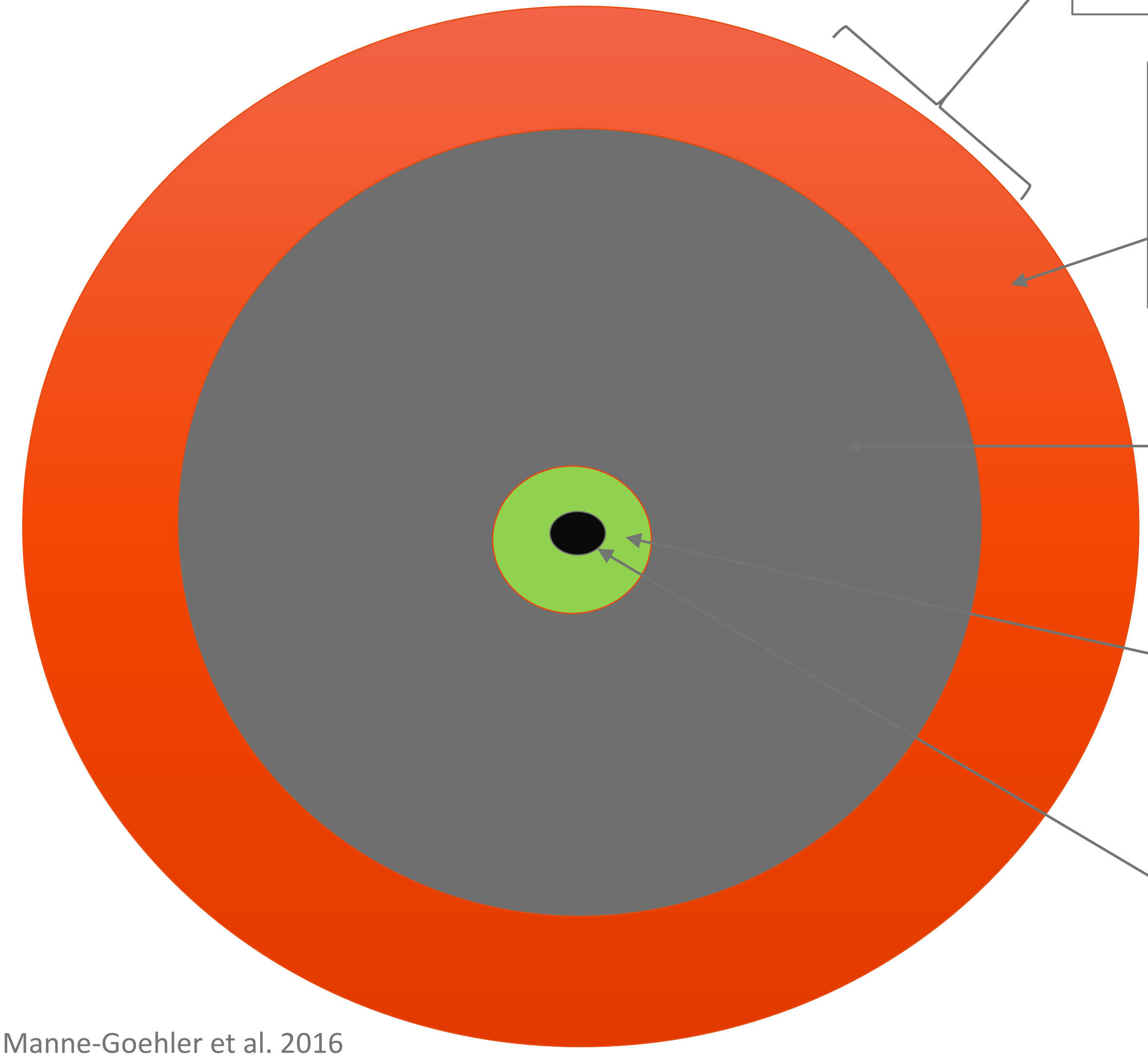
Thank you!

EXTRA SLIDES

Actions Needed to Strengthen Health Systems to Scale up Diagnosis and Treatment of CD in the US

Barrier	Actions Needed
Limited knowledge of disease burden.	Studies to better understand the burden of the disease in both urban and rural areas of the southern U.S., along with the incidence of autochthonous transmission among higher risk populations.
Few providers offering treatment.	Development of a statewide and/or national network of providers capable of offering treatment, along with a website where people can quickly identify nearby providers for testing and treatment.
Low provider awareness.	Increased health education measures and protocols for providers and greater incorporation of CD diagnosis and treatment in state medical schools.
Low patient awareness.	Public education program to raise awareness, especially among the Latin American-born population, and to stimulate demand for testing.
Absence of screening programs.	Routine screening program, ideally through primary care clinics, throughout the states identified as having the most-at-risk populations.
Limitations in current diagnostic capabilities.	Identification of a testing algorithm with high sensitivity and specificity for identifying patients infected with T. cruzi strains present in the southern US, Mexico, and Central America.
Access challenges for vulnerable at-risk populations.	Use of mobile clinics or telemedicine to help screen and treat people in rural areas.

Global Neglect of Chagas Disease*



People infected with T. cruzi: 6.2 million (global)

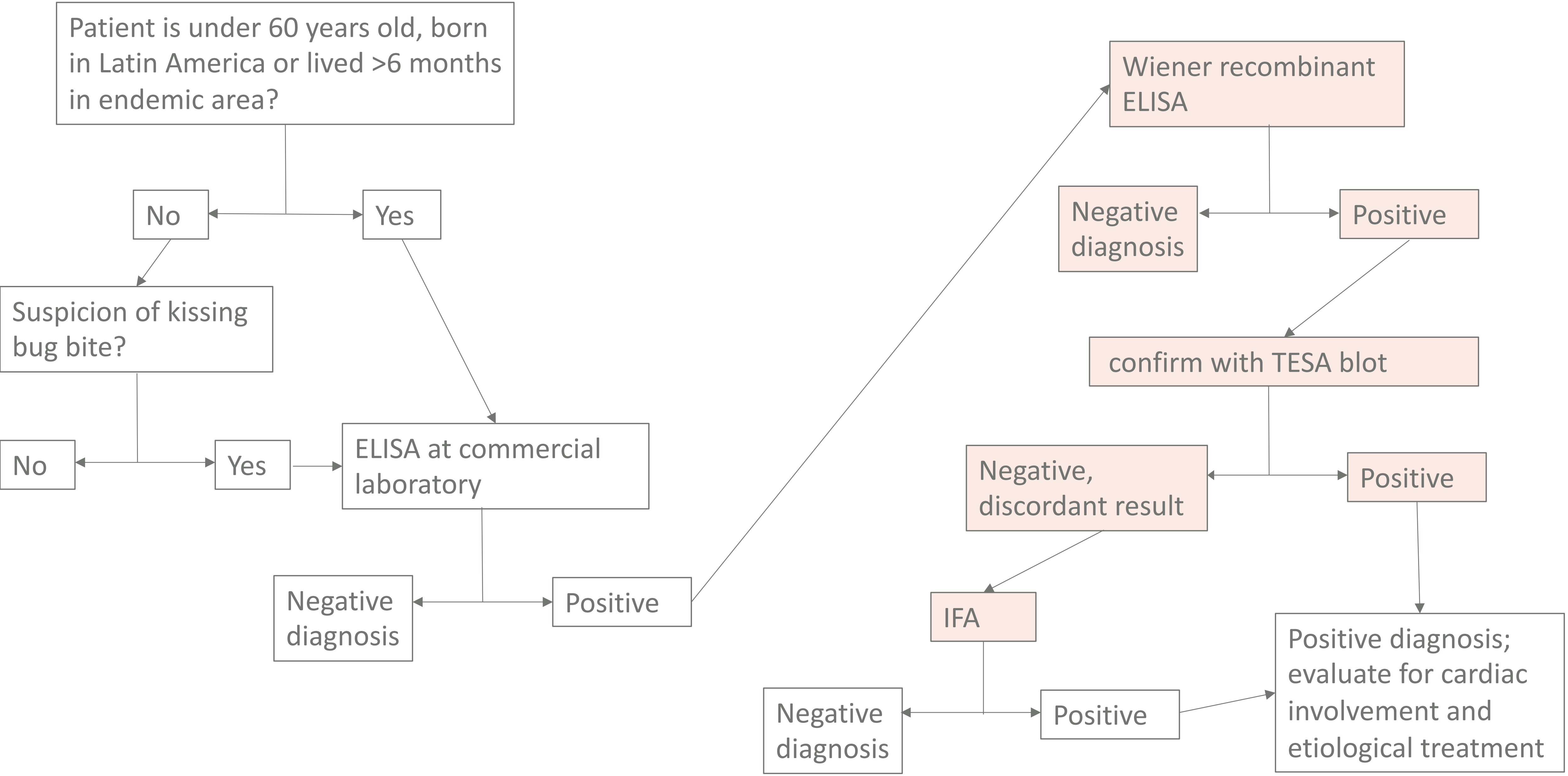
People with contraindications for antiparasitic treatment ≈ 2.2 million

People eligible for antitrypansomal treatment: 4 million

People diagnosed:
<0.5 million
<7% of total

People treated:
<70,000
≈1% of total
16% of diagnosed

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



Patient is under 60 years old, born in Latin America or lived >6 months in endemic area?

No

Suspicion of kissing bug bite?

No

Yes

Yes

ELISA at commercial laboratory

Negative diagnosis

Positive

Wiener recombinant ELISA

Negative diagnosis

Positive

confirm with TESA blot

Negative, discordant result

Positive

IFA

Negative diagnosis

Positive

Positive diagnosis; evaluate for cardiac involvement and etiological treatment