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MAJOR ARTICLE

Recommendations for Screening and Diagnosis of Chagas Disease in the United States

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Background. Chagas disease affects an estimated 326 000–347 000 people in the United States and is severely underdiagnosed. Lack of awareness and clarity regarding screening and diagnosis is a key barrier. This article provides straightforward recommendations, with the goal of simplifying identification and testing of people at risk for US healthcare providers.

Methods. A multidisciplinary working group of clinicians and researchers with expertise in Chagas disease agreed on 6 main questions, and developed recommendations based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, after reviewing the relevant literature on Chagas disease in the United States.

Results. Individuals who were born or resided for prolonged time periods in endemic countries of Mexico and Central and South America should be tested for *Trypanosoma cruzi* infection, and family members of people who test positive should be screened. Women of childbearing age with risk factors and infants born to seropositive mothers deserve special consideration due to the risk of vertical transmission. Diagnostic testing for chronic *T. cruzi* infection should be conducted using 2 distinct assays.

Conclusions. Increasing provider-directed screening for *T. cruzi* infection is key to addressing this neglected public health challenge in the United States.

Keywords. Chagas disease; *Trypanosoma cruzi*; diagnosis; neglected diseases.

Chagas disease (CD) is a neglected tropical disease of substantial public health importance. In the United States, >300 000 people are estimated to be infected with *Trypanosoma cruzi*, the protozoan that causes the disease [1, 2]. The vast majority were infected while living in endemic areas of Latin America and are in a chronic phase of the disease. While most remain asymptomatic for life, 20%–30% eventually develop Chagas cardiomyopathy, and up to 10% may suffer damage to the gastrointestinal or nervous systems [3]. CD causes a heavy burden of morbidity and mortality, resulting in an estimated global annual loss of >800 000 disability-adjusted life-years, including >27 000 annually in the United States [4]. Only about 1% of estimated US cases have been identified, usually through blood donor screening [5]. Most people are unaware they are infected with *T. cruzi*. Provider-directed screening is essential because early diagnosis and treatment can improve outcomes and limit mother-to-child transmission. Screening programs for CD are highly cost-effective [6], but with the current paradigm of limited testing, estimated total annual healthcare costs from CD in the United States exceed $130 000 000 [4]. However, not all US providers are aware of CD [7] and testing poses certain challenges.

The Pan American Health Organization has provided overall guidelines on diagnosis and management of CD [8]. The US Centers for Disease Control and Prevention (CDC) website also provides specific recommendations for healthcare providers [9–11]. Here we examine considerations for screening and diagnosis of CD in the United States.

METHODS

A group of experts on CD screening and management in the United States, including clinicians, researchers, and public

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health experts, prepared these recommendations. Group members had previously participated in meetings on challenges in diagnosis of CD. The working group was organized to provide a straightforward, quick-reference tool to facilitate CD testing by primary healthcare providers, hospitals, infectious disease specialists, and laboratories. Diagnostic guidance was constructed via both expert consensus and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology [12]. The group agreed on 6 main questions based on the PICO method (Population, Intervention, Comparison, and Outcome) and divided into subgroups to discuss each and propose initial recommendations, which were then shared and validated within the larger group. Literature searches were conducted on CD screening and prevalence in the United States and the 4 assays that are currently Food and Drug Administration (FDA)-cleared for clinical use (Table 1).

The GRADE methodology provides 2 types of ratings. The strength of the recommendation (strong or conditional, either for or against a recommendation) is based on the public health priority, potential benefit, feasibility of implementation, acceptability to patients, and costs in terms of resources. An additional rating is provided for the quality of available evidence supporting the recommendation (high, moderate, low, very low), which considers previous study designs, effect size, relevance, sources of bias, and other factors. Two key limitations should be noted: (1) the evidence on US CD has significant gaps, and (2) while the GRADE methodology provides a structured, evidence-based framework, this does not completely rule out subjectivity in determining ratings.

RESULTS

Who Should be Screened for Chagas Disease in the United States?

Are There Populations at Risk That Should be Screened?

Recommendations.

1. Screening people who were born or lived for a prolonged period (>6 months) in areas of Mexico, Central or South America with endemic CD can effectively identify new cases (strong, low) (Table 2).

Within the US population, people who were born or lived for a prolonged period in areas with endemic CD in Mexico, Central, or South America are at greatest risk of *T. cruzi* infection (Table 3). One community-based study of over 4000 Latin-American born immigrants living in Los Angeles showed a seroprevalence of 1.24% [16]. Among people who were born or lived for a prolonged period in Latin America, the seroprevalence has been higher still in those with evidence of characteristic findings on electrocardiogram (ECG) including bundle-branch blocks, nonischemic cardiomyopathy, or pacemaker placement [17–20]. This supports the assertion that screening people who were born or lived for a prolonged period in areas with endemic CD—Mexico and Central and South America—is a viable approach to identifying new cases. Generally, people will need to be screened even though they do not exhibit visible signs or symptoms of CD.

2. Screening close (first-degree) relatives of people previously diagnosed with CD can effectively identify new cases (strong, low).

Limited evidence shows a substantial prevalence of *T. cruzi* infection among close relatives of people previously diagnosed with CD. A Los Angeles study found a prevalence of 7.4% among family members of CD patients [14]. Screening the relatives of people who have been previously diagnosed with the disease is another way to identify individuals with CD. When a patient is confirmed positive, healthcare providers should encourage the patient to advise family members to seek testing. (Contact information for US providers with expertise in CD can be found at https://uschagasnetwork.org/providers).

3. Screening people with documented exposure to triatomines in states with known presence of triatomine species capable of transmitting *T. cruzi* (conditional, low).

Autochthonous transmission can occur in the United States, with cases reported in at least 8 states as of 2020. Most confirmed or suspected autochthonous cases were detected via screening of blood donors, and often these cases face barriers

Table 1. *Trypanosoma cruzi*-Specific IgG Antibody Assays With Food and Drug Administration Diagnostic Clearance[a]

Test	Antigen	Availability	Manufacturer
Hemagen ELISA	Purified antigens from parasite culture	Commercially available	Hemagen Diagnostics, Columbia, MD
InBios Chagas Detect Plus	Recombinant multiepitope fusion antigen	Commercially available point-of-care test	InBios International, Inc, Seattle, WA
Ortho *T. cruzi* ELISA	Purified antigens from parasite culture	Not commercially available for diagnostic use; only marketed for blood and organ donor screening	Ortho Clinical Diagnostics, Inc, Raritan, NJ
Wiener Chagatest ELISA recombinante v0.3.0	Recombinant trypomastigote-shed acute-phase antigens	Commercially available	Wiener Lab Group, Rosario, Argentina

Abbreviation: ELISA, enzyme-linked immunosorbent assay.

[a]As of June 2021.

Table 2. Recommendations for Screening and Diagnosis of Chagas Disease in the United States

Recommendation	Strength	Quality of Evidence
Who should be screened for Chagas disease in the United States?		
People who were born or lived for a prolonged period (> 6 mo) 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 *Trypanosoma 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 Mexico, South or Central America with endemic Chagas disease	Strong	Moderate
Which clinical conditions warrant diagnostic testing for Chagas disease in people from endemic countries of Latin America?		
Electrocardiogram abnormalities suggestive of infection, even in the absence of symptoms. These include first-degree atrioventricular block, premature ventricular contractions, atrial fibrillation, right bundle branch block, left anterior fascicular block, 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
What is the diagnostic algorithm for testing neonates and infants (<1 y old) who are born to infected mothers?		
Infants in whom congenital Chagas disease is suspected should undergo evaluation using existing CDC-based recommendations	Strong	Moderate
What is the recommended algorithm for diagnosing Chagas disease in the United States?		
Diagnostic testing for chronic *T. cruzi* infection should be conducted using 2 distinct assays based on different antigens or in different formats following PAHO and CDC guidelines. If the results are discordant, a third distinct test should be performed. Confirmed diagnosis requires positive results by at least 2 tests	Strong	Moderate
Screening by clinical and public health laboratories in populations with low *T. cruzi* infection prevalence should be conducted using a high-sensitivity test, bearing in mind the anticipated false-positive rate of (1 – specificity). Individuals with positive results by the screening test require confirmatory testing as outlined in the above recommendation	Strong	Moderate
What is the next step after a patient has a confirmed diagnosis of Chagas disease?		
Even if asymptomatic, individuals who test positive for *T. cruzi* infection should receive:		
Electrocardiogram	Strong	High
Echocardiogram	Strong	Low
Chest X-ray	Conditional	Low

Abbreviations: CDC, Centers for Disease Control and Prevention; PAHO, Pan American Health Organization.

to obtaining treatment [21, 22]. Triatomines (kissing bugs) have been identified in 29 states in the southern United States and limited studies have shown that most can harbor *T. cruzi* at varying rates [23, 24]. Some infected triatomines feed on humans, based on the finding of human blood in their gut [24, 25]. Because autochthonous transmission has been demonstrated and naturally infected triatomines reside in the United States, screening people who have highly suspected exposure to triatomines (eg, entomological confirmation of triatomines in the home) in states where the vector is known to reside is a reasonable approach to identifying potential cases of autochthonous CD [26].

Table 3. Studies on Prevalence of Chagas Disease in Latin American-Born Populations in the United States (2010–2020)[a]

Study	Population	Prevalence, %
Castro-Sesquen et al 2020 [13]	1514 people in the greater Washington, DC metropolitan area (community screening program)	3.8
Hernandez et al 2019 [14]	189 relatives of 86 previously diagnosed patients with Chagas Disease	7.4
Manne-Goehler et al 2019 [15]	5125 people from endemic regions screened in primary care setting in East Boston	1.0
Meymandi et al 2017 [16]	4755 Latin American-born residents of Los Angeles (community screening program)	1.2
Traina et al 2017 [17]	327 hospital patients with electrocardiogram abnormalities	5.2
Park et al 2017 [18]	80 patients with pacemakers	7.5
Traina et al 2015 [19]	135 hospital patients with nonischemic cardiomyopathy	19.0
Kapelusznik et al 2013 [20]	39 hospital patients with nonischemic cardiomyopathy	13.0

[a]All study populations consist of people who were born or lived a significant amount of time in endemic countries of Latin America.

4. Travelers with confirmed exposure to triatomines or associated risk factors in regions of Latin America where CD is endemic may be tested to rule out possible *T. cruzi* infection (conditional, low).

Acquisition of CD is thought to occur rarely among travelers, but evidence is limited. Risk factors for travel-acquired CD include confirmed or suspected exposures to triatomines, staying in a rural setting in housing constructed of mud, adobe, thatch, or other natural materials, and consumption of raw or unpasteurized food or beverages, such as sugar cane extract, guava and bacaba juice, açaí pulp, or palm wine [27]. Such travelers may have nonspecific symptoms including fever, malaise and myalgias; acute CD should be considered in addition to other infectious diseases. We advise travel medicine specialists to consider the risk and include advice on preventive measures for individuals with high-risk travel that might expose them to the *T. cruzi* vector.

Should Women of Childbearing Age From Latin America be Screened?

Recommendation.

1. Screening women of childbearing age who have lived in a region of Mexico, South or Central America with endemic CD can effectively identify cases and prevent congenital transmission of the disease (strong, moderate).

Congenital transmission of CD from infected mother to unborn child is a potentially important mode of disease transmission in the United States. Several US surveys in pregnant women from high-risk groups have shown a substantial prevalence of *T. cruzi* infection (Table 4). From a public health perspective, treatment of women before pregnancy can prevent congenital transmission and provide health benefits for the mother [32]. Targeted and universal screening for CD in US mothers is cost-saving for all rates of congenital transmission >0.001% and all levels of maternal prevalence >0.06%, compared with no screening [6].

Table 4. Key Studies on Congenital Transmission of Chagas Disease in the United States

Study	Key Finding
Perez-Zetune et al 2020 [6]	In the US, congenital Chagas disease screening is cost-saving for all rates of congenital transmission ≥ 0.001% and all levels of maternal prevalence ≥ 0.06%. Targeted screening saves $1314 per birth
Yarrington et al 2019 [28]	0.5% prevalence in screening of 619 Latina[a] pregnant women in East Boston
Edwards et al 2015 [29]	0.25% prevalence in screening of 4000 Latina[a] mothers in Texas at delivery
CDC 2012 [30]	First US documented case of congenital Chagas disease in Virginia
Di Pentima et al 1999 [31]	0.3% prevalence in screening of 3765 pregnant women in Houston (Latina and non-Latina)

[a]Latina refers to ethnicity, not necessarily birth in a Chagas disease-endemic country in Latin America.

Which Clinical Conditions Warrant Diagnostic Testing for Chagas Disease in People From Endemic Countries of Latin America?

Recommendation.

1. *T. cruzi* serologic testing should be performed in individuals with epidemiological risk factors who present with the following clinical syndromes:
   a. Electrocardiographic abnormalities suggestive of infection, even in the absence of symptoms. These include first-degree atrioventricular block, premature ventricular contractions, atrial fibrillation, right bundle branch block, left anterior fascicular block, bifascicular block, and low voltage QRS (strong, low)
   b. Bradyarrhythmias (strong, low)
   c. Tachyarrhythmias (atrial fibrillation/ventricular tachycardia), including sudden cardiac death (strong, low)
   d. Regional wall motion abnormalities (particularly basal inferolateral, apical aneurysm) (strong, low)
   e. Thromboembolic phenomenon (strong, low)
   f. Congestive heart failure and/or a reduced ejection fraction (strong, low)
   g. Megacolon/megaesophagus (strong, low).

Screening Latin American-born individuals with the above syndromes for CD has ramifications for the evaluation, treatment, and prognosis of the individual. Because of limited screening for CD in the United States and profound healthcare barriers for the at-risk population, many individuals with CD first receive medical attention after developing a clinical syndrome of the illness. However, estimates suggest <1% of people with signs/symptoms suggestive of CD actually receive CD testing [33]. An estimated 30 000–45 000 people in the United States suffer from CD cardiomyopathy [2]. In 2 small studies of Latin American-born patients with nonischemic cardiomyopathy, 5/39 in a New York hospital and 26/135 in a Los Angeles hospital network were seropositive for *T. cruzi* infection [19, 20]. Other Los Angeles studies in Latin American-born patients found a prevalence of 7.5% among those with pacemakers and 5.2% in those with conduction abnormalities [17, 18].

Screening and Diagnosis in Immunosuppressed Patients

Immunosuppressed hosts with acute *T. cruzi* infection (eg, donor-derived infection) are at risk for severe manifestations such as meningoencephalitis or acute myocarditis. Recipients of blood components, organ, or tissue from an infected donor should be monitored by serial polymerase chain reaction (PCR) in blood weekly during months 1–2, every 2 weeks during months 3–4, monthly during months 5–6 posttransfusion or transplant, then based on the clinical scenario [10].

Immunosuppression in an individual with chronic *T. cruzi* infection may lead to reactivation, characterized by a return to high levels of parasitemia. In transplant recipients, manifestations of reactivation vary depending on host characteristics and immunosuppressive regimen; reactivation myocarditis can be life threatening. A positive PCR result does not constitute a diagnosis of reactivation, because this occurs in patients with chronic infection in the absence of reactivation. Serial monitoring by quantitative PCR, using a schedule similar to that outlined above, provides early detection of reactivation based on falling cycle threshold (Ct) values, reflecting rising parasite loads [34, 35]. The US CDC provides consultation on the management of patients and acts as a reference laboratory to monitor for reactivation by serial PCR. The most common manifestations of reactivation in human immunodeficiency virus (HIV)-*T. cruzi* coinfected patients include central nervous system (CNS) mass lesions, with or without meningoencephalitis, and myocarditis. Diagnosis varies depending on the clinical scenario; in CNS reactivation, parasites may be detectable by microscopy or PCR of cerebrospinal fluid.

What Is the Diagnostic Algorithm for Testing Neonates and Infants (<1 Year Old) Who Are Born to Infected Mothers?

Recommendation.

1. Infants in whom congenital CD is suspected should undergo evaluation using existing CDC-based recommendations (strong, moderate).

Edwards et al 2019 [11] provides a comprehensive review of diagnosis and treatment of congenital CD that is summarized below. Infants born to women with suspected or confirmed CD, and infants with clinical features of congenital infection born to women at risk for CD, should undergo evaluation as soon as possible after birth to detect hepatomegaly, splenomegaly, anemia, or thrombocytopenia and, as indicated, pneumonitis, heart failure, cardiac arrhythmia, or meningoencephalitis (Figure 1) [11, 36, 37]. The cure rate for treatment in the first year of infection exceeds 90%, and treatment is well tolerated [36, 38, 39].

If the mother's infection status is unknown, serologic testing for *T. cruzi* immunoglobulin G (IgG) antibodies should be performed to determine infant risk. Diagnosis of congenital infection relies on detection of motile trypomastigotes through microscopic examination of a wet mount of fresh anticoagulated blood or buffy coat specimen (collected in a microhematocrit tube), detection of parasites on Giemsa-stained blood smears, and/or PCR testing for *T. cruzi* DNA in whole blood from the infant. This testing is available through the Parasitic Diseases Reference Laboratory at the CDC. Histopathologic examination of the umbilical cord and examination of cerebrospinal fluid in at-risk infants with meningoencephalitis may also reveal the parasite [40]. Because maternal blood contamination has been reported in a small number of infants born to infected mothers, a positive PCR result in an infant should be confirmed by repeat testing

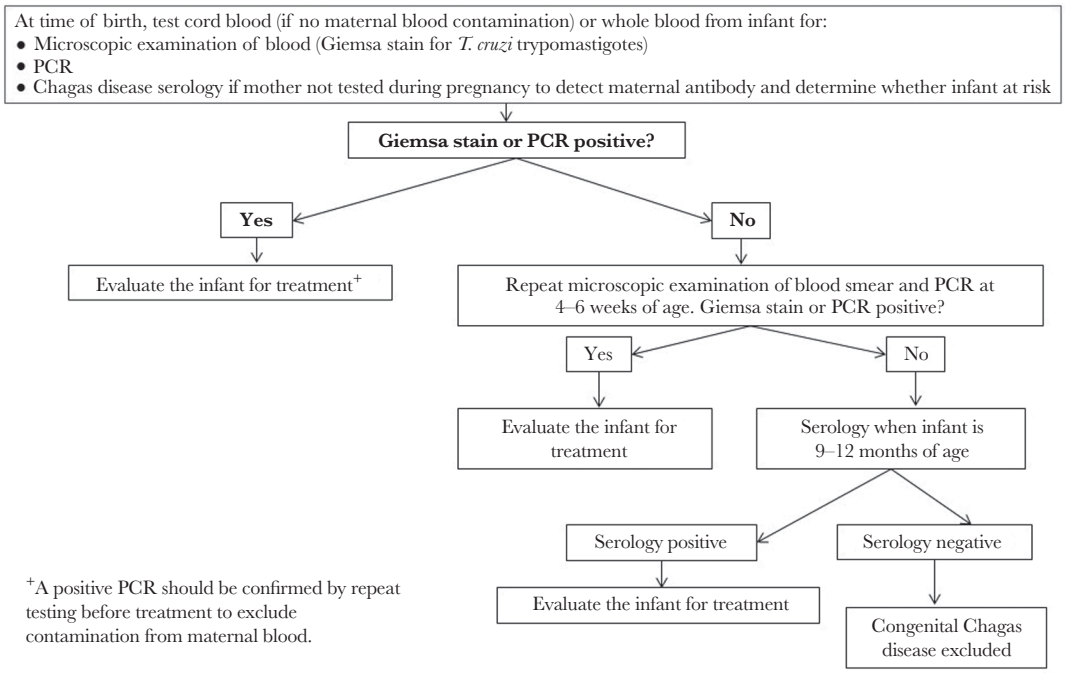

Figure 1. Algorithm for evaluation of congenital Chagas disease for infants ≤ 3 months of age born to a mother with suspected or confirmed Chagas disease, or infant with symptoms of congenital Chagas disease born to an at-risk mother with serological status unknown. Source: Centers for Disease Control and Prevention (https://www.cdc.gov/parasites/chagas/health_professionals/congenital_chagas.html) [36]. Abbreviations: CCD, congenital Chagas disease; PCR, polymerase chain reaction.

(Figure 1). If a second PCR is positive, the diagnosis of congenital CD is confirmed and the infant should undergo clinical evaluation for features of congenital CD (such as cardiac arrhythmias), laboratory evaluation, and initiation of treatment. For mothers who are seropositive for *T. cruzi* infection whose infants are PCR negative, infants should undergo repeat testing at 4 to 6 weeks of age to confirm absence of infection [40, 41].

Because parasitemia levels can fluctuate, the serologic status of infants born to mothers with chronic CD should be monitored even if the infant has negative PCR results early in life. Transferred maternal IgG antibodies persist in infants for up to 12 months [42, 43]. If an infant first evaluated at 3 months of age or older has a positive CD screening *T. cruzi* IgG test, performed through a commercial laboratory, repeat screening should be performed when the infant reaches 9 to 12 months of age. If antibody remains detectable, confirmatory serologic testing through CDC is appropriate to establish or exclude congenital infection (Figure 2) [36]. An increase in antibody titer over time after 9 months of age, documented at CDC, indicates congenital infection.

What Is the Recommended Algorithm for Diagnosing Chagas Disease in the United States?

Recommendations.

1. Diagnostic testing for chronic *T. cruzi* infection should be conducted using 2 distinct assays, based on different antigens or in different formats, following Pan American Health Organization and CDC guidelines. If the results are discordant, a third distinct test should be performed. Confirmed diagnosis requires positive results by at least 2 tests (strong, moderate).
2. Screening by clinical and public health laboratories in populations with low *T. cruzi* infection prevalence should be conducted using a high-sensitivity test, bearing in mind the anticipated false-positive rate of (1 – specificity). Individuals with positive results by the screening test require confirmatory testing as outlined in the above recommendation (strong, moderate).

Confirmation of chronic *T. cruzi* infection requires positive results by 2 different tests, preferably based on different antigens, to optimize sensitivity and specificity [8]. However, most commercial laboratories in the United States only utilize 1 assay. If positive based on commercial laboratory results, sending samples to CDC for confirmation assures that the criteria of 2 distinct assays is met. More confirmatory testing options may become available in the future. Clinicians should check with their healthcare system's clinical laboratory for current or preferred confirmatory testing options.

Providers can contact CDC with questions about CD (parasites@cdc.gov, 404–718–4745). Requests for CDC testing should be coordinated with the state or local health department.

FDA-Cleared Serological Tests for Chagas Disease

Four IgG serological tests have FDA clearance for diagnosis of chronic *T. cruzi* infection (Table 1), 2 are *T. cruzi* lysate-based enzyme-linked immunoassays (ELISAs; Ortho *T. cruzi* ELISA and Hemagen Chagas' kit ELISA); a recombinant antigen-based

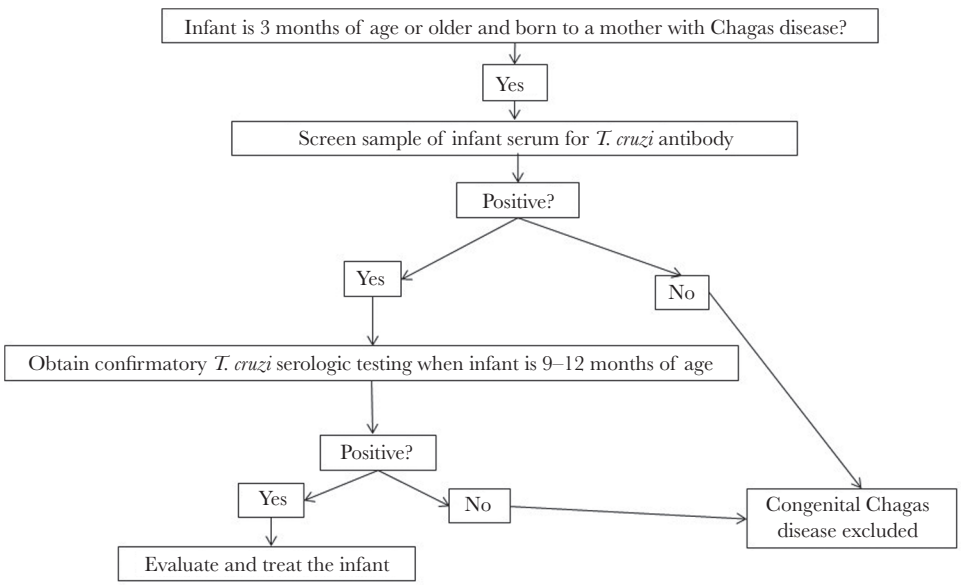

Figure 2. Algorithm for evaluation of congenital Chagas disease (CCD) for infants ≥ 3 months of age. Source: Centers for Disease Control and Prevention (https://www.cdc.gov/parasites/chagas/health_professionals/congenital_chagas.html) [36].

ELISA (Wiener Chagatest Recombinante 3.0); and a recombinant antigen-based immunochromatographic strip test (InBios Chagas Detect Plus). All 4 tests have high manufacturer-reported sensitivity and specificity, but postclearance performance data are sparse, especially in US-resident populations (Supplementary Table 1). In US-based evaluations, the Wiener Chagatest Recombinante 3.0 assay consistently showed high specificity and intermediate sensitivity [13, 29, 44]. Investigations also confirm variation in assay performance by geographic origin of infections, with sensitivity generally highest in specimens from South America, intermediate in Central America, and lowest in those from Mexico, Panama, and southern Peru [13, 44–47]. These differences are often attributed to *T. cruzi* genetic differences, but do not correlate entirely with the predominant lineages as currently identified [48]. Further diagnostic test evaluations in robust sets of specimens from at-risk US populations are needed to provide an adequate evidence base for recommendations for use of specific assays.

However, prospective parallel testing by multiple assays in population-level screening may be prohibitively expensive. In a serial testing scenario, the population is screened by a single test and only those with positive results receive a second, confirmatory test; when the results are discordant, a third test is used as a tiebreaker. Algorithms should be designed with test performance characteristics in mind; a deliberate choice must be made regarding the acceptable number of missed infections versus the cost of additional testing (and the logistics of having patients return for testing) required to rule out false positives. Figure 3 provides a basic framework of the testing process, from identification of risk factors to diagnostic confirmation.

What Is the Appropriate Course of Action if the Screening and Confirmatory Tests for Chagas Disease Are Discordant?

The lack of a gold standard CD test necessitates multistep serological testing to confirm chronic *T. cruzi* infection. Discordant test results can be expected due to imperfect test performance and will be a large proportion of total results given CD's overall low prevalence in the United States. When the results of the first 2 assays are discordant, a third test is required to assign a consensus positive or negative status for the presence of IgG antibodies to *T. cruzi* in the individual.

Diagnostic serologic testing in the United States is primarily available at commercial reference laboratories and CDC. Currently, CDC performs an ELISA (Chagatest Recombinante v0.3.0; Wiener Laboratories) and an immunoblot using trypomastigote excreted-secreted antigens (TESA) when CD serology is requested. If results are discordant, a second sample is requested; if results are again discordant, a third serologic test is run (immunofluorescence assay [IFA] based on slide-fixed epimastigotes) [49, 50]. At CDC, the TESA and IFA assays are laboratory-developed tests and all tests are run under the Clinical Laboratory Improvement Amendments (CLIA). Currently, the FDA does not clear or approve laboratory-developed tests [51], but their validation and performance is reviewed during laboratory inspections to maintain CLIA certification. There are no published diagnostic evaluations for the CDC TESA and IFA tests in infected populations of the United States, but these test formats have been widely used throughout Latin America.

Most testing currently begins with a commercial laboratory, where typically only one IgG assay is used. Commercial laboratories periodically change the tests they employ due to

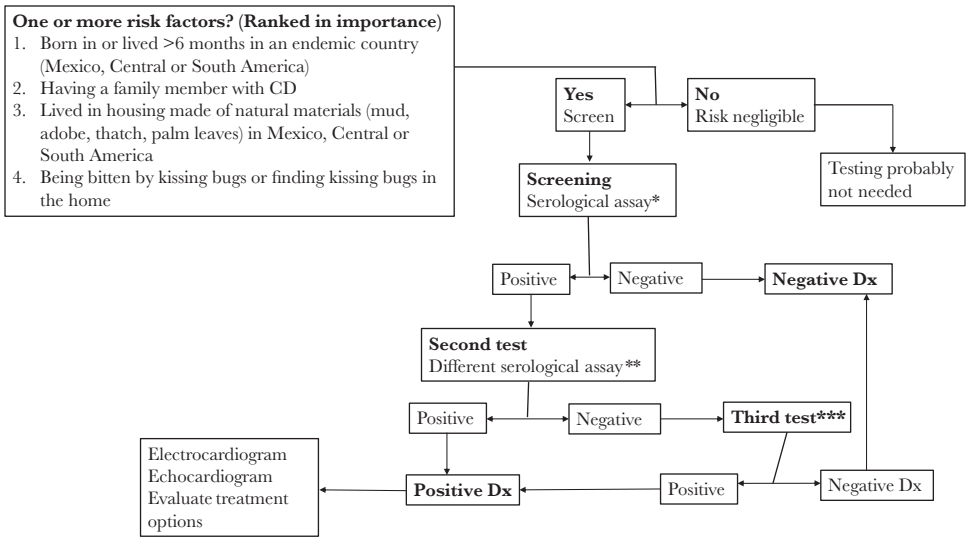

Figure 3. Algorithm for screening and diagnostic confirmation of Trypanosoma *cruzi* infection in the United States. *There could be rare exceptions, but infection is unlikely in individuals without 1 of these risk factors. **Not all commercial laboratories run a second serological test at this time. Samples should be sent for confirmation to CDC. ***Confirmatory testing for discordant results is available at CDC. Abbreviations: CD, Chagas disease; CDC, Centers for Disease Control and Prevention; Dx, diagnosis.

commercial availability, cost, and testing format and performance. To ensure that 2 different serologic assays are used, it will be necessary to confirm which assay is being performed. In general, a sample should then be sent to CDC for confirmation.

What Is the Next Step After a Patient Has a Confirmed Diagnosis of Chagas Disease?

Recommendation.

1. Even if asymptomatic, individuals who test positive for *T. cruzi* infection should receive:
   a. Electrocardiogram (strong, high)
   b. Echocardiogram (strong, low)
   c. Chest X-ray, if an echocardiogram is unavailable (conditional, low).

Individuals with *T. cruzi* infection may have no evidence of organ involvement (indeterminate form) or organ involvement with or without noticeable symptoms. Individuals with any of these forms would be expected to be seropositive. Determining whether the patient has the indeterminate form of CD or has progressed to Chagas cardiomyopathy or other end-organ involvement is important for establishing a treatment plan. A normal echocardiogram and ECG indicate an indeterminate form of CD [52]. In settings where an echocardiogram is not available, a chest X-ray may be considered instead. The ECG should be repeated annually to detect signs of progression to Chagas cardiomyopathy, even in individuals who receive antitrypanosomal treatment [52]. Echocardiogram may be repeated depending on the patient's clinical status. Those with cardiac symptoms and/or abnormalities on 1 or more of the above tests should be referred to a cardiologist for more extensive testing [53]. Patients with immunosuppressive conditions require special consideration due to the risk of reactivation and should be referred to an infectious disease specialist. Patients from southern Cone countries of South America (Argentina, Bolivia, Brazil, Chile, and Paraguay) may be more at risk for gastrointestinal complications. Steps for diagnosis and management of gastrointestinal CD are provided by Pinazo et al [54].

DISCUSSION

Uncertainties and complexities around current CD testing processes in the United States pose a major barrier to increasing screening coverage, perpetuating a situation where <1% of the estimated population with the disease has been tested. This document provides clear, straightforward guidance to healthcare personnel to facilitate screening and diagnosis of the people at risk, so that they can receive timely and appropriate care. While more research is needed, both on the epidemiology of CD in the United States, including congenital and vector-borne transmission and the burden of disease in specific populations, and on the performance of diagnostic tools in the heterogeneous US patient population, this document presents practical recommendations based on the best information currently available. Ensuring proactive screening of patients will require concerted efforts to increase provider awareness, convey accurate information to the public about CD and its risks, and improve access to and performance of diagnostic technology and tools.

Notes

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