Access to Care for Chagas Disease in the United States: A Health Systems Analysis

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Abstract. There are 300,000 estimated cases of Chagas disease in the United States but limited data on access to care. This study analyzed trends in access to care for Chagas disease in the United States and assessed the national and state barriers to access. Data on cases in blood donors and drug releases were obtained from the AABB (formerly American Association of Blood Banks) and U.S. Centers for Disease Control and Prevention (CDC), respectively. Semi-structured in-depth interviews were conducted with 30 key informants at the national level and in five states where treatment had been released. Interview responses were analyzed according to the health systems dimensions of regulation, financing, payment, organization, and persuasion. Data indicate that 1,908 cases were identified in the blood donation system from 2007 to 2013 and that CDC released 422 courses of benznidazole or nifurtimox during this period. The barriers to access at the national level include limited diagnostic and institutionalized referral and care processes, lack of financing for patient-care activities, and limited awareness and training among providers. This study demonstrates that access to treatment of Chagas disease in the United States is limited. The lack of licensing is only one of several barriers to access, highlighting the need for a health systems perspective when scaling up access to these essential medicines.

BACKGROUND

Chagas disease is a neglected vector-borne disease with an estimated burden of 8–10 million cases worldwide. Infection with *Trypanosoma cruzi*, the etiologic agent of Chagas disease, and its clinical sequelae of Chagas cardiomyopathy and gastrointestinal disease are responsible for as many as 15,000 deaths each year.^{1,2} Despite this substantial burden, recent estimates suggest that less than 1% of infected patients receive treatment with benznidazole or nifurtimox, the two antitrypanosomal medicines currently available to treat Chagas disease.^{3–5}

The burden of Chagas disease has historically been concentrated among the poor in Latin America, in particular, because of substandard housing and living conditions that create suitable vector habitats for repeated domestic transmission. In addition to vector-borne transmission, the *T. cruzi* parasite can be transmitted congenitally from infected mother to child and through blood and organ donation. In recent years, human migration has resulted in increasing prevalence of this disease in developed countries such as the United States, Switzerland, and Spain.^{6–8} Although prevalence data are limited, the most recent estimate suggests that about 300,000 individuals living in the United States are infected with *T. cruzi* and that the majority of these cases are chronic infections in people who have migrated from high-prevalence regions of Latin America.⁷ Detection of infection has increased in the United States since screening of the blood supply was initiated in 2007, but there remains relatively limited understanding of access to care for Chagas disease.⁹

This study analyzes access to care for Chagas disease in the United States, defined as diagnosis, clinical evaluation, and treatment where appropriate, and examines the barriers to access. Using a Health System Reform Framework proposed by Roberts and others, we assess the barriers to care from the perspective of health-care providers in terms of five policy interventions—financing, payment, organization, regulation,

and behavior—and offer strategies to increase access based on this analysis.¹⁰

METHODS

Theoretical framework. The Health System Reform Framework by Roberts and others was selected for this analysis because it allows one to identify health-system deficiencies and derive strategies to improve health-sector performance directly.¹⁰ This analysis focuses on access, one of the three intermediate performance goals of a health system. In this study, access was defined as “the ability to obtain and appropriately use a good quality health technology when it is needed.”¹¹ Access to antitrypanosomal treatment as an intermediate performance goal can be linked to the ultimate performance goal of health status via the established relationship between treatment with antitrypanosomal therapy and improvements in the health status of *T. cruzi*-infected patients.¹² Prior research has shown that antitrypanosomal therapy with benznidazole or nifurtimox prevents or slows the progression of chronic Chagas disease and increases quality-adjusted life expectancy, though some patients may not be appropriate candidates for this treatment based on their age, disease severity, and comorbidities, which can increase the risks of treatment.^{13,14} We directly adopted definitions for the five policy interventions—namely, financing, payment, organization, regulation, and behavior—from the Framework.

Data collection. In this study, two different methodological approaches were used: 1) confirmed cases of Chagas disease and treatments released by state were quantified through a) blood donor registry and b) CDC drug release data and 2) primary data were collected through key informant interviews at the national, state, and local levels.

Analysis of secondary data from blood donors and treatment releases. Data on confirmed cases of Chagas disease between 2007 and 2013 were requested from the AABB (formerly the American Association of Blood Banks). These data include cases reported by all laboratories that use U.S. Food and Drug Administration (FDA)-licensed tests to screen blood donors for the *T. cruzi* antibody and account for about 65% of the total blood donated in the United States. It is important

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to note that reporting of confirmed cases to AABB is not mandatory and that some smaller blood banks may not have the expertise or capacity to upload cases to AABB. Because of the high rate of sero-discordance among different diagnostic tests, two separate diagnostic tests must be positive before a case of *T. cruzi* infection is confirmed. To assess the number of releases of benznidazole and nifurtimox to individuals, we requested information by state from the U.S. Centers for Disease Control and Prevention (CDC). On the basis of the AABB data, we chose five states (California, Florida, New York, Texas, and Washington, DC/Virginia) with the highest numbers of positive blood donors for further qualitative analysis. Descriptive analysis of data on patients diagnosed and treated in the United States was performed in Stata v 13 (College Station, TX).

Primary data collection through key informant interviews and analysis. Semi-structured in-depth interviews were conducted with 30 key informants, including nine national experts from the CDC or American Red Cross, 10 administrators from state or local Departments of Health (DoHs) or blood donation agencies, and 11 physicians each of whom had treated at least one case of *T. cruzi* infection. These physicians included specialists in cardiology, infectious diseases, and general adult internal medicine. The exclusion criteria were any person under the age of 18 or any person who has or is currently seeking treatment of Chagas disease. Finally, we also reviewed organizational guidelines or policy documents (not published in peer-review journals) on this subject where available. A snowball sampling approach was used such that additional experts were contacted on the recommendation of those who had already participated.

Data obtained in interviews and policy documents were analyzed according to the Health System Reform Framework. Reliance on multiple sources of written and oral information was used to triangulate the results and minimize bias that may be present in any one source. Verbal informed consent was provided for all interviews. This study was approved by the Boston University Medical Center Institutional Review Board (IRB) (Protocol H-32356).

RESULTS

Data on diagnosis and treatment of Chagas disease patients in the United States. The primary epidemiological data on estimated cases, confirmed cases among blood donors, and drug releases by state are shown in Table 1 for the 15 highest-burden states. These data demonstrate that treatment efforts have been geographically focal and not always congruent at the state level with the number of estimated cases or the number of cases identified among blood donors.¹⁵ In terms of treatment, CDC data on drug releases to physicians show that between 2007 and 2013 drug was released for a total of 422 cases. Among these, 253 (59.95%) patients received nifurtimox and 169 (40.05%) received benznidazole, though the number of benznidazole releases increased over the period from 3 in 2007 to 53 in 2013.¹⁶

Current approach to diagnosis, drug procurement, and treatment in the United States. *Diagnosis.* Our interviews found five primary routes by which patients with Chagas disease initially present to the health system (see Figure 1). In all states except New York, it was reported that blood donors who had received notification of a confirmed positive test for

TABLE 1

Estimated cases, confirmed cases in blood donors, and drug releases for Chagas disease for the 15 states with the highest estimated total cases, 2007–2013

State	Estimated cases	AABB cases	Drug releases
California	71,000	707	141
Texas*	37,200	176	41
Florida	18,200	260	23
New York	17,500	160	32
Illinois	9,200	22	12
New Jersey	8,800	32	7
Virginia	7,300	103	30
Arizona*	6,400	28	1
Georgia	5,600	37	4
North Carolina	5,400	41	16
Maryland	4,500	29	4
Nevada	3,700	25	2
Massachusetts	3,400	9	21
Washington	3,100	18	2
Colorado	3,200	4	6

AABB = American Association of Blood Banks.

Source: This table uses the authors' computed state-level estimates of Chagas disease prevalence based on data about foreign-born Hispanic populations in the United States as of 2011 provided by the Pew Research Center's Hispanic Trends Project (<http://www.pewhispanic.org/>) and national prevalence estimates published by the World Health Organization (<http://www.bvsops.org.uy/pdf/chagas19.pdf>). Data on cases identified among blood donors were provided by the AABB. Data on drug releases by state were provided by the U.S. Centers for Disease Control.

*Texas, Tennessee, and Arizona are three states in which Chagas disease is a mandatory notifiable condition as detailed in <http://www.cdc.gov/parasites/chagas/resources/chagasdiseaseintheamericas.pdf>. Tennessee does not appear in Table 1 because it does not fall in the top 15 states by estimated total cases of Chagas disease.

T. cruzi infection constituted a minority of those who ultimately presented for further diagnostic testing.

The initial test for *T. cruzi* infection was often performed in-house or through a private laboratory. In cases where the clinical suspicion for infection was high or the patient was uninsured, the initial diagnostic sample was sometimes sent directly to CDC to expedite a confirmed diagnosis at low cost. Regardless of where the initial test was performed, confirmatory diagnostic testing was performed by CDC.

Drug procurement and release. Both benznidazole and nifurtimox are available through CDC under FDA investigational protocols for “expanded access to investigational drugs for treatment use.” This regulatory mechanism seeks to “facilitate the availability of drugs to patients with serious diseases . . . when there is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the patient’s disease or condition.”¹⁷ The investigational protocol was established for nifurtimox in 1986 and benznidazole in 2010. Both protocols are approved by the CDC IRB and reviewed for renewal of approval every year. Individual physicians may join each protocol as coinvestigators when administering treatment to Chagas patients.

In terms of drug procurement, the CDC forecasts, procures, and maintains a supply of both benznidazole and nifurtimox. As defined in the protocols, drug is released to physicians on a per-patient basis. After a case is confirmed, the CDC works with the treating physician to assess patient eligibility for treatment.² Most physicians reported a preference for using benznidazole as a first-line therapy. Studies to date suggest that benznidazole is better tolerated by patients and associated with a more favorable side effect profile, which could influence the prescribing decisions of physicians.

Interviews also suggested a generally limited role for state and local DoHs in the diagnosis and treatment of Chagas disease patients. Currently, Chagas disease is only a reportable health condition in only three states (Arizona, Tennessee, and

FIGURE 1. Generalized flow diagram of Chagas disease diagnostic and treatment procedures in the United States.

Texas), which may contribute to the limited ability of state DoHs in referring cases to health-care providers. Respondents indicated that the primary activity of state DoHs with respect to treatment is to refer positive blood donors or other patients who call with questions to either CDC or local physicians. Key informants reported a lack of financial support for DoHs to undertake education or public awareness campaigns for Chagas disease, even in states where Chagas disease is a reportable condition.

Barriers to access. Barriers to access are discussed according to the policy interventions of financing, payment, organization, regulation, and behavior. These are summarized in Table 2.

Financing and payment. The results of this study indicate that financing is a significant barrier to care for many patients with Chagas disease in the United States. Interview data suggested that most patients infected with *T. cruzi* are uninsured and that, given the very limited resources available to care for them, their physicians often went to extraordinary lengths to develop ad hoc financing systems to provide this care. These physicians reported financing their clinical activities through a combination of research grants, personal funds, and publicly funded health programs or facilities. For instance, several

physicians used research grant funds or personal funds to purchase diagnostic kits. Others reported using personal funds to ship these samples and even to buy medical equipment such as electrocardiogram (ECG) machines for use in clinical evaluation of infected patients.

To finance clinical visits, several physicians searched for alternative ways to enroll patients in local clinics that provide free or subsidized health care to the uninsured and relied on publicly funded hospitals to subsidize the costs of care. Some physicians reported fear that uninsured patients would require hospitalization for an adverse drug effect, as it was unclear what, if any, source of financing could be mobilized to cover the costs of such a hospitalization. For patients who were insured, financing of these clinical activities was usually available through insurance. These findings also showed that payment of the drug supply for treatment is a minor concern to clinicians and patients who work with CDC, because CDC bears the cost of purchasing and delivering both drugs.

Organization. The interviews indicated that the organization of patient care activities mirrors the local, ad hoc nature of financing systems where providers look for ways to overcome system barriers to access. Four major organizational challenges to diagnosis were reported: 1) an inability to place

TABLE 2
Health systems barriers to diagnosis and treatment of Chagas disease in the United States

Policy intervention	National level	Local level
Financing	CDC finances confirmatory diagnostic testing (diagnostic kit + labor) CDC finances all costs of medicine procurement and distribution including all administrative costs	Lack of patient access to health insurance (LA, DC, NYC, MIA) Insufficient financing for patient care activities for uninsured leading to reliance on ad hoc financing schemes (for diagnostic kits, shipping costs, EKGs, provider time, etc.) using grant funding, personal or institutional donations of health-care resources or reliance on free clinics and public programs (LA, DC, NYC, MIA)
Payment	None	Depending on visa and insurance status, patient may be responsible for costs of treatment-related visits (LA, NYC) Patients assume risk of payment for hospitalization for secondary events (DC)
Organization	Single national laboratory to perform confirmatory testing for <i>Trypanosoma cruzi</i> diagnostic samples Poor connection to follow-up care for positive blood donors Diagnostic test reliability is variable Time consuming coordination with WHO and suppliers to maintain sufficient supply at CDC Time-consuming updates to research protocols	Inability to order or process diagnostic tests within local institutions (DC, LA) Separate institutional IRB approval required (MIA) Inability to forecast drug requirements or maintain drug supply within institutions (LA)
Regulation	Benznidazole and nifurtimox not FDA approved, available only through CDC under investigational protocols Drugs can only be released on a per-patient basis	High barrier to entry to establish local treatment system because of time required for administrative processes preceding drug release
Behavior	Lack of a clear, evidence-based screening guidelines Limited funding for health education or research Limited physician awareness or knowledge of disease, its diagnosis, and treatment Limited patient information about where to obtain diagnosis and treatment	Limited physician awareness or knowledge of disease, its diagnosis, and treatment (LA, DC, NYC, MIA) Limited funding for health education or research (LA, DC, NYC, MIA)

CDC = U.S. Centers for Disease Control and Prevention; EKG = electrocardiogram; FDA = U.S. Food and Drug Administration; IRB = institutional review board; WHO = World Health Organization; LA = Los Angeles; DC = Washington, DC; NYC = New York City; MIA = Miami.

orders for Chagas disease diagnostic tests in institutional laboratory ordering systems, 2) heterogeneity in available diagnostic tests, 3) a limited capacity to conduct definitive confirmatory diagnostic testing, and 4) poor follow-up of positive blood donors. Several physicians reported that their affiliated hospital laboratories refused to order diagnostic test kits or process diagnostic samples, reinforcing reliance on the CDC for confirmatory diagnosis. Furthermore, both national and local policymakers and physicians expressed concern about the lack of understanding about why positive blood donors do not seek follow-up clinical evaluation. Interviewees from the American Red Cross indicated a follow-up rate of only 26.5% among positive blood donors enrolled in a study they conducted. Moreover, local public health administrators reported that in some cases, positive blood donors who did present to their physician with this information were not offered clinical work-up or treatment. This finding was reinforced by a recent pilot study of 17 positive blood donors, among whom only 25% were offered electrocardiography and one was offered treatment.

The following organizational challenges were mentioned: 1) the lengthy, often complicated process of obtaining an internal IRB approval from institutions that required it and 2) a lack of reliability in the health-care infrastructure. In some cases, physicians interviewed reported that they were unable to successfully establish a local treatment capacity in their facility and therefore referred infected patients to

colleagues at neighboring institutions who had been able to do so. Finally, interviewees also indicated substantial fragmentation of both public health and patient care activities for Chagas disease.

Regulation. According to respondents, lack of market approval for nifurtimox and benznidazole was not perceived as a significant barrier to care for Chagas disease. Instead, they reported a “barrier to entry” for physicians in establishing a system for diagnosis and treatment, based on regulatory procedures. Treating physicians required a substantial time commitment to complete the administrative process preceding medication release by the CDC. In some cases, a separate IRB approval was required from a physician’s own institution, further complicating and at times delaying treatment initiation (usually for at least 1 month and often longer). These respondents almost universally reported that, once initiated, the process of confirming a diagnosis through the CDC and obtaining medication for treatment where appropriate was straightforward and timely.

Behavior. Respondents expressed widespread agreement that a lack of awareness and clinical knowledge about Chagas disease among health-care providers and a lack of funding for education and research were the two most important barriers to access to care for these patients. Moreover, several respondents expressed frustration at what they perceived as a resistance on the part of physician colleagues to seriously consider this diagnosis, even in high-risk groups.

DISCUSSION

This study offers three important contributions to knowledge about access to care for Chagas disease in the United States. First, it offers evidence to suggest a substantial gap in access to care for this disease. Next, this study describes substantial health-system barriers that prevent access to care for patients with Chagas disease, which help to explain the existing gap. Finally, it proposes solutions to these health-system failures.

With respect to quantifying the gap in access, this study demonstrates that from 2007 to 2013 only a small fraction (< 1%) of estimated cases in the United States were identified among blood donors, the only source of national case data. Moreover, data from the CDC on patient drug releases shows that 422 cases were treated from 2007 to 2013. Many of these 422 treated cases were not positive blood donors, but rather patients identified through one of several other avenues described, such as clinic-based screening in certain geographic regions or clinical presentation to a health facility with signs or symptoms of Chagas disease. Although not all of the estimated 300,000 cases would be eligible for or would benefit from treatment of the primary infection, it suggests a very large treatment gap.

Four major health-system barriers to care for Chagas disease were identified, which likely contribute to this large gap in access: 1) limited diagnosis of Chagas disease and follow-up of positive cases; 2) a reliance on local, ad hoc systems to finance and deliver care for a largely uninsured patient population (financing and organization); 3) a lack of physician awareness and knowledge of the disease (behavior); and 4) lack of funding for both education and research (behavior). Although market authorization of both medicines would be helpful to improve access, these results suggest that it alone would not resolve low access to treatment of Chagas disease.

Limited diagnosis and follow-up of Chagas disease. Very limited diagnosis of Chagas disease in the United States is a complex problem that represents an important barrier to care. The reasons for this include broad policy issues such as the absence of a single, clear screening recommendation and limited physician awareness of the disease or consideration of Chagas disease as a potential diagnosis. Additional factors are the lack of in-house diagnostic testing in many hospital laboratories and the heterogeneity in test reliability that was mentioned by the physicians interviewed.

Limited diagnosis is further compounded by poor follow-up to care among blood donors who screen positive for *T. cruzi* infection. Our key informants did not have good information on the reasons for the lack of follow-up. CDC researchers recently conducted one study of patient perspectives and found contributing factors included patient concerns about immigration status and limited access to health care at free clinics serving immigrant populations, including problems of long wait times and overcrowding. Given that this study was limited by low participation (only 14 of 30 invited positive blood donors participated), further research is needed to explain poor follow-up by positive blood donors.

Reliance on local, ad hoc systems to finance and deliver care. This study shows that the financing and organization of care for uninsured patients with Chagas disease currently relies on ad hoc, often informal mechanisms initiated by individual physicians with an interest in this disease. The interview results demonstrate an high level of personal commitment on the part of health-care providers who use personal funds or research

grants to support their efforts to care for patients with Chagas disease. Providers expressed great frustration that the clinical infrastructure is often insufficient, unreliable, or unsustainable. The high degree of fragmentation in the health-care institutions associated with this disease adds another layer of organizational complexity to care delivery.

Limited physician awareness and knowledge of the disease. This study found widespread agreement that limited physician awareness and knowledge about Chagas disease represent a major barrier to access to care. These findings are consistent with a recent survey that showed that 68.8% of obstetricians-gynecologists, targeted due to their important role in preventing congenital transmission, had “very limited” knowledge of Chagas disease and that 77.9% had “never considered” this diagnosis among patients from endemic countries.^{9,18} These studies also suggested a substantial knowledge deficit among physicians in other subspecialties including primary care and cardiology, though the knowledge gap was most pronounced among obstetricians and gynecologists.

Limited funding for both education and research. Finally, the study found that almost all respondents considered a lack of funding for provider or patient education and research as a key barrier to care. The most recent estimate of research funding for Chagas disease by the Global Funding of Innovation for Neglected Diseases report showed that the three major kinetoplastid diseases (leishmaniasis, African sleeping sickness, and Chagas disease) represented 4.4 million disability-adjusted life years (DALYs) as of 2010 but together received only US\$136.3 million in research funding in 2012, as compared with dengue that represented about 800,000 DALYs as of 2010 but received nearly double the amount of research funding, US\$248.9 million, in 2012.¹⁹

This study has several limitations. First, the use of data on cases of Chagas disease identified among blood donors offers only partial insight into the total distribution of cases diagnosed in the United States. In particular, patients at the highest risk of infection, specifically foreign-born populations from endemic regions of Latin America, are underrepresented in the blood donation system because of community norms, lack of health insurance, and immigration status.²⁰ Though less common, autochthonous cases of disease transmission have also been identified in the United States, which raises the risk of improper diagnosis and treatment since these patients do not have the travel history and traditional risk factors commonly associated with Chagas disease in the United States.^{21,22} In addition, blood donation is just one of several avenues by which infections are newly diagnosed; the other common routes to diagnosis mentioned earlier are not included in the case data from the blood donation system. A second limitation of this study is the inability to directly address the patient perspective through interviews. However, by interviewing physicians and local policymakers, we were able to assess the structure and function of the health system in relation to Chagas disease from those whose experience was most proximal to that of patients. Finally, a third limitation of this study was the dearth of data on clinical outcomes.

Based on this analysis, we propose six health systems recommendations to increase access to care for Chagas disease in the United States:

1. Create a U.S. Task Force on Chagas disease: To reduce fragmentation and unify efforts to address Chagas disease

across institutions, we propose the creation of a U.S. Task Force on Chagas Disease. The objective of this task force would be to develop a clear screening guideline, create a physician referral network and searchable patient registry, and facilitate a national education campaign for physicians.

2. Establish a screening guideline and improve diagnostic infrastructure: To address the limited diagnosis of Chagas disease in the United States, the U.S. Task Force on Chagas Disease, in collaboration with the CDC, should establish a clear screening guideline and advocate for increasing the capacity to process diagnostic samples for Chagas disease.
 3. Create a provider referral network and patient registry to track health outcomes: To address the high barrier to entry for health-care providers and challenges in the organization and financing of local systems of care, we recommend the creation of a formal physician referral network and patient registry for Chagas disease. This referral network should include facilities that have been successful in establishing a local treatment infrastructure for patients irrespective of insurance status, and the registry should be deidentified to ensure patient privacy. Currently, there is one "Center of Excellence" for Chagas disease in the United States; similar centers could be established in other geographic regions with strong support from state DoHs under national guidance.
 4. Establish a national research agenda: The U.S. Task Force on Chagas disease, with support from the National Institutes of Health (NIH) and CDC, should establish a research agenda beyond the much-needed development of new and better diagnostics and therapeutics. This should include representative epidemiologic studies in the United States and studies to better understand poor follow-up among blood donors.
 5. Initiate a national provider education campaign: To address limited physician knowledge of this disease, the U.S. Task Force on Chagas disease together with professional associations and medical schools should lead a national education campaign for health-care providers.
 6. Increase funding for Chagas disease: To address the lack of funding for both education and research on Chagas disease, a U.S. Task Force on Chagas disease should advocate for greater attention to and funding for these activities.
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