The Columbia University
JOURNAL of GLOBAL HEALTH

Chagas disease outbreaks in selected countries in South America from 2000 to 2022: A systematic review

Hillary V. Smith, MPH[1]

[1]College of Health, Oregon State University, Corvallis, OR, USA

ABSTRACT Chagas disease (CD), an emerging neglected tropical disease endemic to Latin America, causes 12,000 deaths annually. Its ecological and epidemiological complexities, including rural-urban shifts in disease distribution, have complicated outbreak control. Outbreak investigations of CD in selected countries in South America were reviewed and the investigative methods used across outbreaks were assessed to provide important insight into the disease epidemiology. The findings of this systematic literature review support further investments to improve disease surveillance and diagnostic tools and training and education in the health sector and impacted communities. Additionally, these findings support the global health movement towards improved management and control measures for Chagas disease.

KEY WORDS Chagas Disease, Neglected Tropical Disease, Chagas Disease Outbreaks, Global Health, Infectious Disease

INTRODUCTION

American trypanosomiasis, commonly known as Chagas disease, is endemic to twenty-one Latin American countries.[1,2] Estimates indicate that six to seven million people are infected with Chagas disease, resulting in approximately 10,000 to 12,000 deaths each year. Despite the large impact on human morbidity and mortality, Chagas disease and other diseases termed neglected tropical diseases by the World Health Organization were not prioritized in the global health agenda until the adoption of the Sustainable Development Goals in 2015.[3] Recent estimates have found that 75 million people are at risk of contracting Chagas disease within and outside of endemic regions,[1] and 30,000 new cases are detected annually, 8,600 of which are through mother-to-child transmission.[2]

Since their implementation in 1990, vector control measures, focused heavily on elimination, have been successful in managing Chagas disease in 17 of the 21 endemic countries.[2] Other control measures such as blood donor screening and diagnostic and treatment care have been improved across all endemic countries. However, the rate of infection and associated morbidity and mortality continues to warrant considerable public health concern.

In 2015, José Rodrigues Coura published an article reviewing three modes of Chagas disease transmission: vector, blood, and oral from an historical perspective, highlighting prominent associated outbreaks.[4] A 2017 review of select outbreaks associated with oral transmission of Chagas disease was published, focusing specifically on prevention mechanisms and prevention recommendations[5].[5] These publications provide important information

Send correspondence to: SMITHHI@OREGONSTATE.EDU

on various aspects of Chagas disease, but this systematic review of Chagas disease outbreaks gives further insight on current disease ecology, risk factors, incidence, and mortality and is especially important following 30 years of vector elimination and control measures.

EPIDEMIOLOGY OF CHAGAS DISEASE

Ecology and Risk Factors

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi,*[1] transmitted to humans by triatomine insect vectors commonly known as kissing bugs.[2,6] There are four primary vectors found in varying regions of Central and South America that are known to transmit *T. cruzi*.[2] These vectors include: (1) *Triatoma infestans* found in Argentina, Bolivia, Brazil, Chile, Paraguay, Uruguay, and Peru, (2) *Rhodnius prolixus* found in Colombia, Venezuela, and Central America, (3) *Triatoma dimidiate* found in Ecuador and Central America, and (4) *Rhodnius pallescens* found in Panama. Chagas disease also has a complex ecology involving wild and domestic animals, vectors, and human reservoirs.[2,7] Known animal reservoirs include rodents, marsupials, and other wild mammals, as well as domestic dogs and cats.

Risk factors for vector-borne infection include poorly constructed housing, habitation of rural, suburban, and urban areas in endemic regions, and low socioeconomic status.[8] Chagas disease is sometimes referred to as a disease of poverty as it disproportionately impacts populations of lower socioeconomic status.[9]People living in homes with cracked mud walls, thatched roofs, or unmortared brick in endemic areas and more specifically rural areas have a higher risk of disease.[10,11]

Signs, Symptoms, and Treatment

Chagas disease presents in two phases, acute and chronic, and has an incubation period of one to two weeks.[2] In the case of transmission through organ transplant or blood transfusion, the incubation period may be as long as 120 days.[10] The initial acute phase lasts two months and is characterized by high levels of parasites circulating in the blood.[2,10] If infection progresses to the chronic phase, it is known to persist throughout a lifetime.[10] *T. cruzi* may pass from human to vector during both the acute and chronic phases of disease.

During the acute phase, people who are infected may experience mild or non-specific symptoms or be asymptomatic.[10] Symptoms are present in 20% to 30% of cases and include fever, headache, nausea, diarrhea, vomiting, enlarged lymph glands, difficulty breathing, cough, and abdominal, muscle or chest pain.[2] Symptomatic cases may experience a rash and swelling at the site of inoculation known as Chagoma[2,10]/Romaña's sign, described as unilateral bipalpebral swelling caused by parasitic entry at the conjunctiva or eyelid.[10,12] In rare cases, acute infection can lead to myocarditis or meningoencephalitis with increased risk of mortality.[10]

In the absence of treatment, an estimated 20% to 30% of infections persist to the chronic phase.[2,10,13] During the chronic phase of the disease, parasitemia drops and acute symptoms subside.[10] Chronic symptoms of Chagas disease indicate heart, digestive system or nervous system tissue damage and may include enlargement of the gastrointestinal tract, organs, esophagus, colon, gastrointestinal, or gallbladder motor disorders, abnormal gastric emptying, cardiomyopathy, irregularities in heart rhythm, apical aneurysm, progressive deterioration of the heart muscle, and/or sudden heart failure or death.[2] Immunocompromised infected persons may experience reactivation of disease.[10]

There are two pharmaceutical treatment options available that act to eliminate *T. cruzi* infection: Nifurtimox and Benznidazole.[1,2] It is recommended to begin treatment early on, as it may become less effective over time.[2] When treatment is initiated during the acute phase of disease, both medications may be effective. The potential for adverse reactions, occurring in 40% of patients receiving treatment during the chronic phase, limits the benefit of later treatment. Neither medication is approved for treatment of women who are pregnant.

Transmission

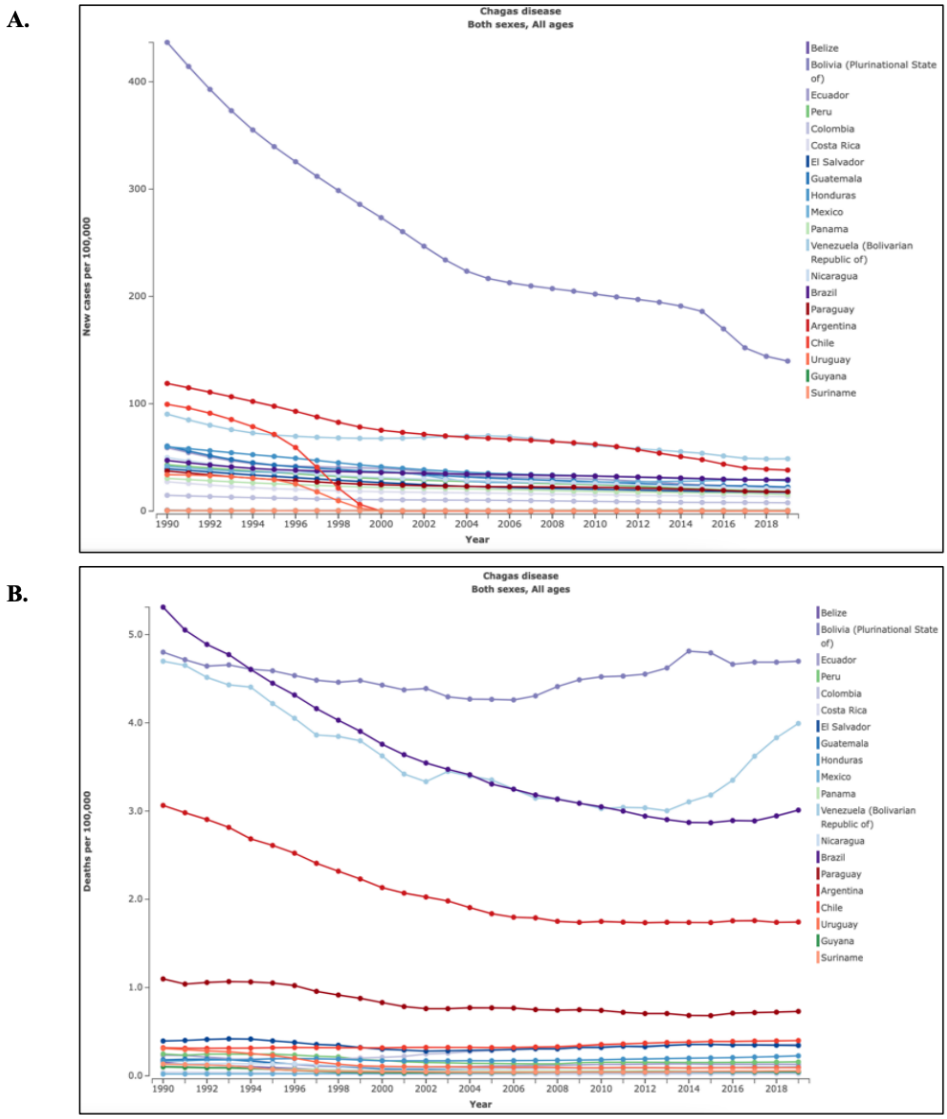
There are five modes of transmission for Chagas disease: (1) vector transmission through the feces or urine of triatomine insects, (2) oral/foodborne transmission, (3) vertical transmission from mother to child, (4) transmission through a transfusion or organ transplant, and (5) accidental transmission in laboratory settings.[1,2] Oral transmission occurs when foods or beverages contaminated by the vector or the vector's feces are ingested or by consuming raw meat of an infected animal reservoir.[14] Vertical transmission, transmission via organ transplant or transmission through blood transfusion can occur during either phase of disease.[10]

Global Health Concern

While Chagas disease is endemic to Central and South America and was primarily contained in this region, cases have now been detected throughout North America, Europe, and Australia, and in select countries in Africa and Asia.[15] Movement and migration of the human population has caused a rural to urban shift in geographic distribution, further influencing the global spread of Chagas disease.[15]

Data provided by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington indicate the population incidence of Chagas disease has decreased in every endemic country of Central and South America over time (data was not found on French Guiana).[16] In 2019, Bolivia had the highest incidence rate with 139.75 new cases per 100,000 persons among a group of twenty endemic countries (Figure 1A). Venezuela, Argentina, and Brazil followed with rates of 48.73, 38.14, and 29.11 new cases per 100,000 persons respectively. Chagas disease population mortality rates seem to also decrease over time; however, Brazil has shown an upward trend in mortality since 2017, and Venezuela has shown a similar but steeper trend upward since 2013 (Figure 1B).

FIGURE 1. INCIDENCE RATES (A) AND MORTALITY RATES (B) OF CHAGAS DISEASE IN TWENTY ENDEMIC COUNTRIES, 1990-2019, ACCORDING TO DATA PROVIDED BY THE INSTITUTE FOR HEALTH METRICS AND EVALUATION[16].



IHME data shows that incidence rates tend to be highest in younger populations of Central and South America (Figure 2A) while mortality rates tend to be highest in older populations in the regions (Figure 3B).[16] For example, the 2019 incidence rates in Brazil and Venezuela for persons aged 15-49 years were 34.64 and 64.54 new cases per 100,000 persons, respectively (Figure 2A). In contrast, that same year, incidence rates for persons aged 50-69 years were 20.04 new cases per 100,000 persons in Brazil and 20.32 new cases per 100,000 persons in Venezuela (Figure 2B). In 2019, the mortality rate for persons aged 50-69 years in Brazil was 6.61 deaths per 100,000 persons and in Venezuela was 7.71 deaths per 100,000 persons (Figure 3B). In comparison, the mortality rate for persons aged 15-49 years in Brazil was 0.62 deaths per 100,000 persons and in Venezuela was 0.45 deaths per 100,000 persons (Figure 3A).

FIGURE 2. INCIDENCE RATES OF CHAGAS DISEASE AMONG 15-49-YEAR-OLDS (A) AND AMONG 50-69-YEAR-OLDS (B) IN TWENTY ENDEMIC COUNTRIES, 2019, ACCORDING TO DATA PROVIDED BY THE INSTITUTE FOR HEALTH METRICS AND EVALUATION[16].

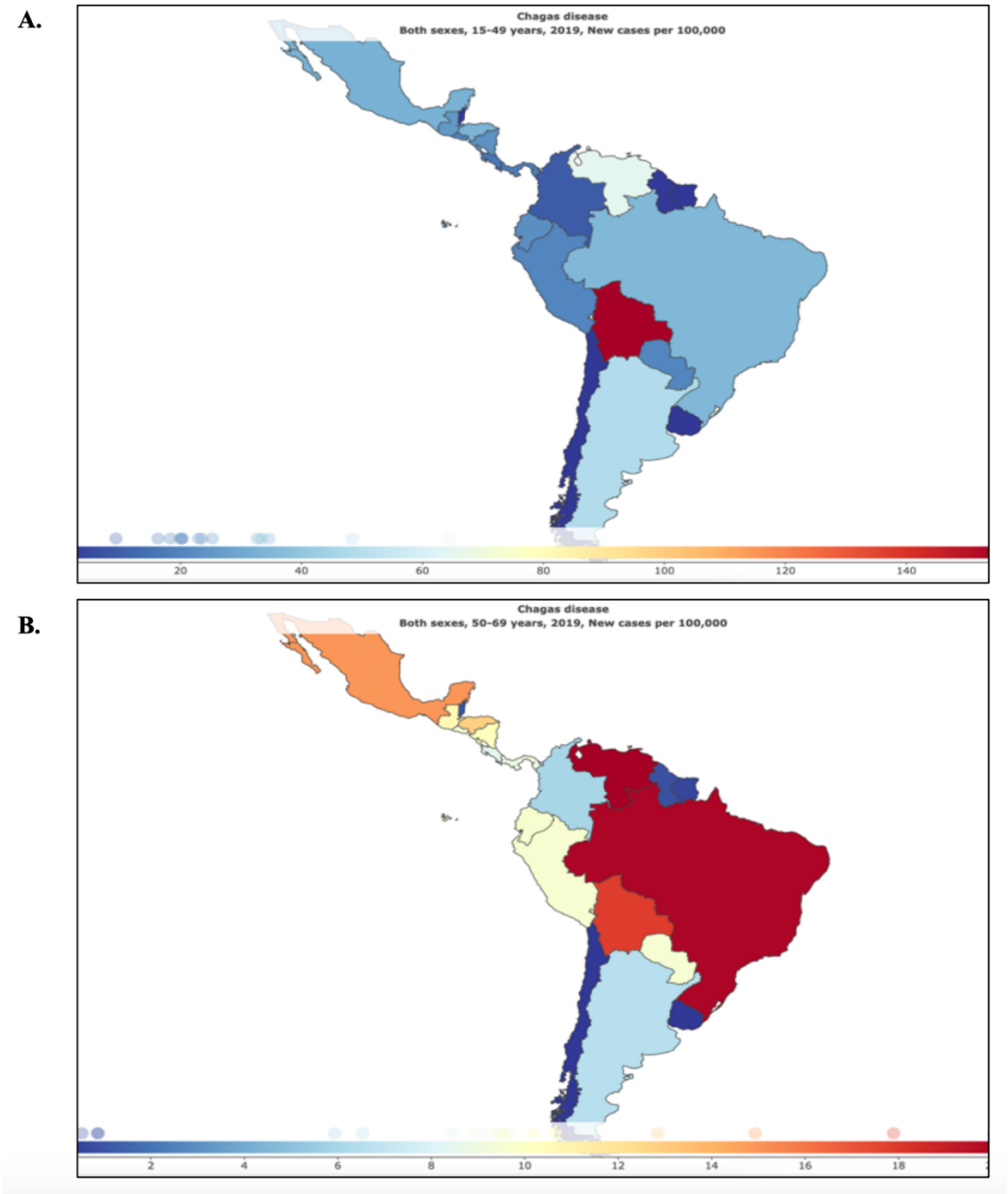
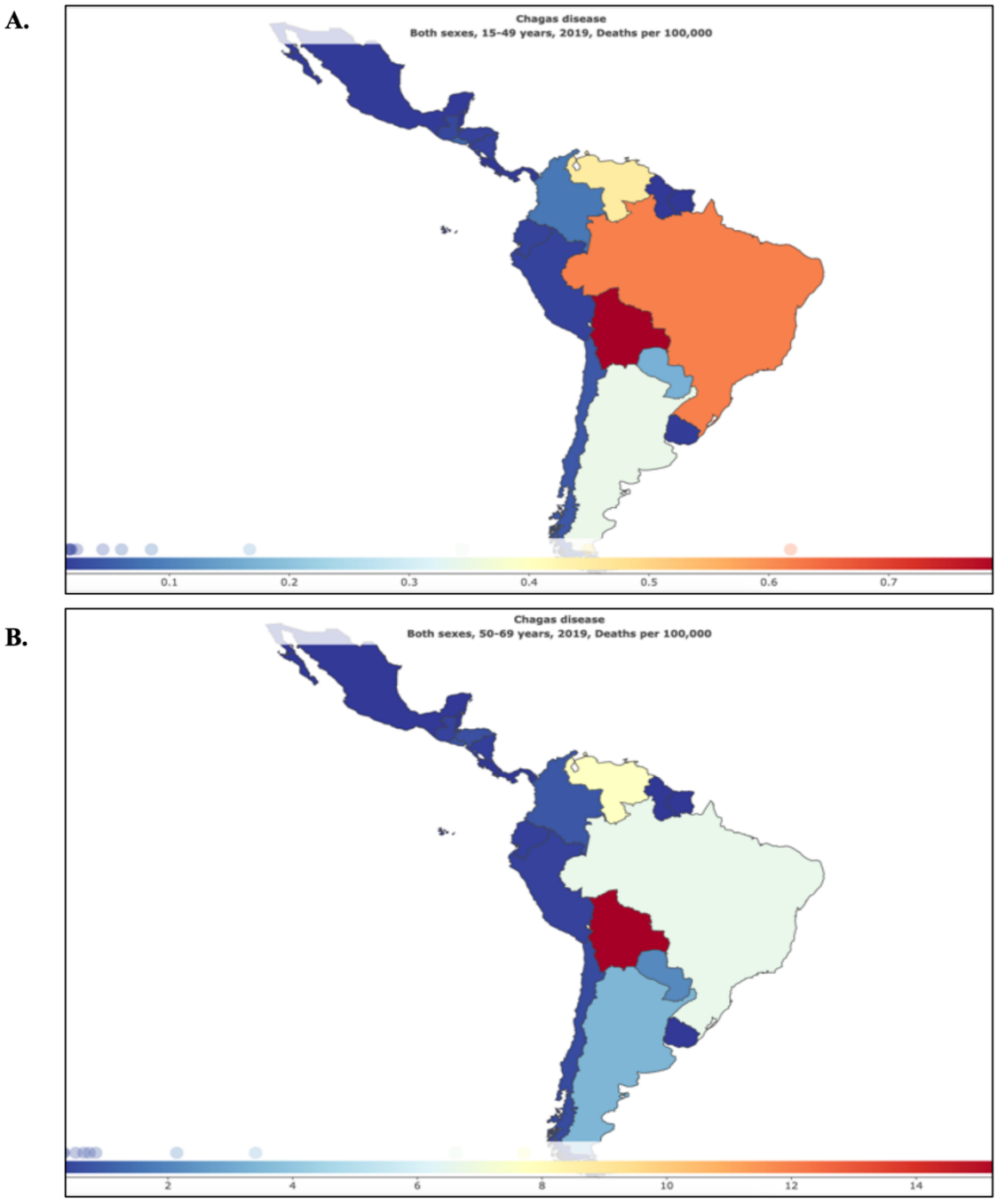


FIGURE 3. MORTALITY RATES OF CHAGAS DISEASE AMONG 15-49-YEAR-OLDS (A) AND AMONG 50-69-YEAR-OLDS (B) IN TWENTY ENDEMIC COUNTRIES, 2019, ACCORDING TO DATA PROVIDED BY THE INSTITUTE FOR HEALTH METRICS AND EVALUATION[16].



While many countries in Central and South America experienced declines in incidence of and mortality resulting from Chagas disease since 1990, the current rates, potential for sustained morbidity, complex ecology and global spread through population movement renders this disease a global health concern. With the adoption of the 2015 Sustainable Development Goals, the World Health Organization has directed global attention to Chagas disease. The objective of this study was to review recently published outbreak investigations of Chagas disease in South America and to assess the investigative methods used across outbreaks in hope of providing crucial insight on Chagas disease' epidemiology, thereby supporting the global health movement towards improved management and control measures of Chagas disease.

SYSTEMATIC LITERATURE REVIEW

Data Source

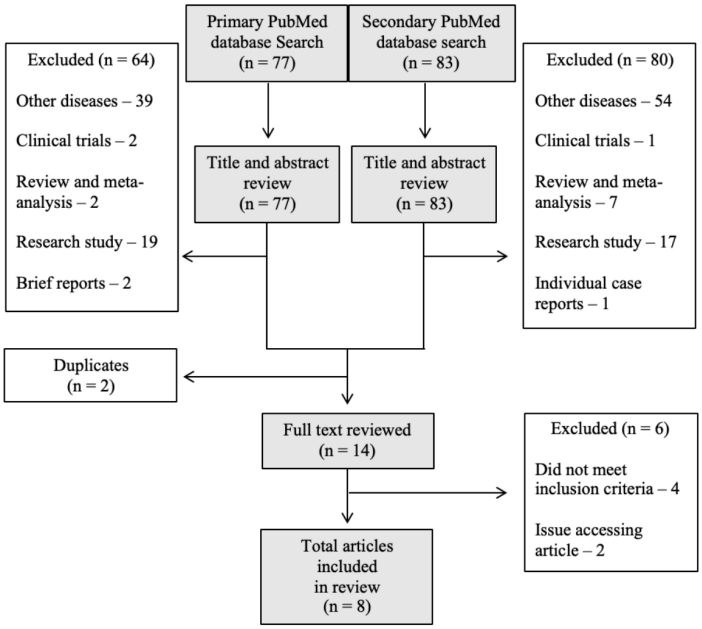
The PubMed database was searched for articles published between 2000 and 2022, describing outbreaks of Chagas disease (American trypanosomiasis) in humans in South America. Articles were filtered to include those published in English. The date range was selected to produce a sample of recent outbreaks. South America was chosen as the focus region for this review because of the endemicity of Chagas disease in the region and high potential for disease outbreak. Acute Chagas disease was the focus of this report as this is the initial phase of the disease that occurs immediately after infection.

Primary and secondary searches were conducted in PubMed. The primary search contained terms "acute" and "Chagas" with "disease outbreak" as Medical Subject Heading Terms (MeSH Terms) with filters for year of publication (2000-2022), human and English, resulting in 77 articles retrieved. A secondary search was conducted with search terms "acute," "Chagas," "outbreak" and "investigation" with filters for year of publication (2000-2022), human and English, resulting in 83 articles retrieved.

Report Selection

Articles were initially included if related to an outbreak of Chagas disease in South America based on the title and abstract. Articles focused on diseases other than Chagas disease, clinical trials, review articles and meta-analyses, research studies and brief reports including individual case reports were excluded. Following initial exclusion, two articles were found to be duplicated between the two searches and duplicates were removed. References of review articles and research studies related to an outbreak were also searched to ensure all relevant outbreak investigations were included in this systematic review. There were no additional articles found through the reference review that met inclusion criteria. Outbreak reports were the only articles of interest for this review. Fourteen articles underwent full text review. Articles were selected if they provided an extensive description of the outbreak investigation and the use of appropriate epidemiological methods. Articles included in the review contained epidemiological information including the identification of the population at risk, case definition, study design and statistical methods used. Figure 4 provides a flow diagram of this systematic literature review.

FIGURE 4. SYSTEMATIC LITERATURE REVIEW FLOW DIAGRAM OF CHAGAS DISEASE OUTBREAKS INFECTING HUMANS IN SOUTH AMERICA PUBLISHED FROM 2000 TO 2022 IN ENGLISH.



CHAGAS DISEASE OUTBREAKS IN SOUTH AMERICA

Research Methods

The PubMed database was searched twice to identify recent articles on Chagas disease outbreaks in humans in South America. The primary and secondary searches resulted in 77 and 83 articles, respectively. Titles and abstracts were reviewed to determine relevance of the article for this review. There were 64 articles excluded from the primary search and 80 articles excluded from the secondary search. Two articles were duplicated between the two searches and the duplicates were removed resulting in fourteen articles that underwent full text review. There were six articles removed, as four did not provide an extensive description of the outbreak investigation and the use of appropriate epidemiological methods while two articles were unavailable. A total of eight articles were included in this review. This literature process is summarized in Figure 4.

Impact

There were eight outbreaks between 1996 and 2021 reviewed, three in Venezuela[17,18,19] and five in Brazil.[14,20–22,23] Outbreaks primarily occurred in urban areas[14,17–19,21,22] with potential risk factors related to food production and handling in rural areas.[20,21] There were 186 cases in total, ranging from 4[17] to 119[19] cases. A total of five deaths resulted from outbreaks of acute Chagas disease,[17–19,22] one of which attributed to fetal death at 24 weeks gestation as the result of vertical transmission of acute Chagas disease.[17] The maximum number of deaths resulting from a single outbreak was two.[22] An organized description of the results of this review is provided in Table 1.

TABLE 1. SUMMARY OF SELECTIVE COMPONENTS OF THE ARTICLES IN THE REVIEW OF RECENT CHAGAS DIEASE OUTBREAKS IN BRAZIL AND VENEZUELA

Lead author	Year ↑	Location state, country	Investigative methods	Cases (death)	Measures of association /Risk factors	Mode of transmission	Vector	Reservoir	Control Measures
Andreza Karoline Souza Barros de Brito	2021	Amazonas, Brazil×	Descriptive study and vector identification and testing	5(0)	Ingestion of açaí	Oral	*R. pictipes*	NI	NI (Treatment only)
Belkisyolé Alarcón de Noya	2015	Miranda, Venezuela•	Cohort study	4(1)+	Common gathering	Oral* and vertical	NI	NI	NI (Treatment only)
Jesús A. Benítez	2010	Táchira, Venezuela•	Descriptive study, vector identification	6(1)	Single household	Oral*	*P. geniculatus*	NI	Pyrethroids sprayed (Treatment and education)
Rita de Cássia de Souza-Lima	2010	Amazonas, Brazil•×	Cohort study	17(0)	Contact with or ingestion of açaí with manioc flour AR = 85%	Oral	NI	NI	NI (Treatment only)

Belkisyolé Alarcón de Noya	2007	Caracas, Venezuela•	Case-control cohort nested study, vector and reservoir identification and testing	119(1)	Guava juice OR 3.5 [95% CI, 1.85–6.7]	Oral	*P. geniculatus*	Domestic rats	NI (Treatment only)
Aglaêr A. Nóbrega	2006	Pará, Brazil•	Retrospective cohort study, case-control study	11(0)	Ingesting açaí thick paste RR 4.5 [95% CI, 1.30-15.3]^^, ingesting açaí juice OR 4.5 [95% CI, 1.30-15.3]^^^	Oral	NI	NI	NI (Treatment only)
Juarez Pereira Dias	2006	Bahia, Brazil•	Descriptive study, vector and reservoir identification and testing	7(2)	Common gathering	Oral	*T. sordida*	Opossum	NI (Treatment only)
Sebastião Aldo da Silva Valente	1996	Amapá, Brazil×	Descriptive study, vector and reservoir identification and testing	17(0)	Single Community	Oral	*R. pictipes* and *P. geniculatus*	*Didelphis marsupialis* and *Marmosa* spp.	NI (Treatment only)

RR = relative risk; OR = odds ratio; AR = attack rate; NI = not identified

↑year of the outbreak

•urban

×rural

^ the attack rate was based on the 14 cases initially identified in the outbreak

^^measure of association included 5 cases linked by occupation and attendance at a common gathering.

^^^measure of association included 11 cases

+fetal death at 24 weeks gestation, infection via vertical transmission

*highly suggestive evidence of oral transmission

Outbreak Identification

Outbreaks of acute Chagas disease were identified by the presence of one to five individuals, usually presenting with non-specific symptoms including fever of unknown origin or the death of multiple individuals with similar symptoms including acute febrile disease and cardiorespiratory conditions[22] and confirmed with the identification of *T. cruzi* trypomastigotes in the patient's blood.[14,17–22,23] The most common symptoms noted across outbreaks were fever,[14,17–22,23] facial edema[14,17–21,22] and headache.[14,19,20,22,23] Cases were epidemiologically linked by school[19], community[23], occupation[14], or a common gathering typically of family and close friends.[17,18,20,21,22]

Case Findings

Once an outbreak of acute Chagas disease was identified, additional cases were found through hematological testing to identify the presence of *T. cruzi* parasites and serological testing to identify anti- *T. cruzi* antibodies in patients.[14,17–22,23] Patients epidemiologically linked to the index case or suspected source of oral transmission were voluntarily tested regardless of the presence of symptoms.

Investigative Methods

Epidemiological study designs used across outbreaks included descriptive,[18,20,22,23] cohort,[14,17,21] case-control[14] and case-control cohort nested studies.[19] Four outbreaks used a descriptive study design, including vector identification.[18,20,22,23] Three of the four included vector testing for the presences of *T. cruzi*[20,22,23] and two included reservoir identification and testing for *T. cruzi* infection.[22,23] Three cohort studies, one case-control, and one case-control nested cohort study were conducted. The case-control nested cohort study also included identification and testing of vectors and animal reservoirs.[19] Two studies provided measures of associations, including relative risk (RR) and odds ratio (OR). Another measure included in studies was the attack rate (AR). Risk factors identified included the ingestion of açaí in various forms and guava juice, as well as common gatherings, presiding in a single community or belonging to a single household. In one outbreak, ingestion of açaí thick paste had a RR of 4.5 [95% CI, 1.30-15.3] and ingestion of açaí juice had an OR of 4.5 [95% CI, 1.30-15.3].[14] In another outbreak, guava juice had an OR of 3.5 [95% CI, 1.85-6.7].[19] Oral transmission was either confirmed or highly suspected in all outbreaks and one outbreak identified a case of vertical transmission that resulted in fetal death.[17] Clinical and laboratory testing included hematological and serological testing conducted during each outbreak investigation.[14,17–22,23] Laboratory tests commonly used were a thick blood smear, enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence and indirect hemagglutination.

Environmental investigations included identification of vectors and animal reservoirs. Vectors identified in these outbreaks included *R. pictipes,*[20,23] *P. geniculatus*[18,19,23] and *T. sordida.*[22] Animal reservoirs included domestic rats,[19] opossum,[22] *Didelphis marsupialis* and *Marmosa* spp.[23]

Control Measures

Control measures were not discussed in most of the outbreaks. One outbreak mentioned pyrethroids spraying around homes following the environmental investigation.[18] Spraying was optional and 9.8% of household refused this control measure. Treatment was provided to patients in each outbreak as needed.[14,17–22,23] Benznidazole was the primary medication prescribed to patients, but Nifurtimox was also used specifically in the case of allergic reaction to Benznidazole. There was one patient denied treatment due to pregnancy; however, treatment was later provided following a change in their pregnancy condition.[17]

Limitations

Cases often initially present with non-specific symptoms such as fever leading to misinterpretation of disease etiology. Six outbreaks mentioned misdiagnosis initially in at least one case.[17–21,23] Misdiagnosis of dengue fever,[17,19] malaria,[20,21,23] cytomegalovirus infection,[17] atypical pneumonia,[18] mononucleosis, hepatitis and intoxication[19] were noted in the outbreak investigations. Furthermore, outbreaks originating in rural communities were difficult to access and investigate, sometimes taking up to 22 days to reach the community.[20] There were also limitations in laboratory testing as testing technologies are neither specific nor sensitive and no investigations were able to collect food samples and isolate the parasite from suspected food sources.

DISCUSSION

Oral Transmission and Shift in Disease Distribution

Oral transmission of Chagas disease in Brazil was recorded as early as 1965. In the broader region of Southern America, it remained a prevalent mode of transmission for over six decades.[14] The study explored this further, identifying oral transmission as the primary mode of transmission for Chagas disease in Brazil and Venezuela, noting that all outbreaks identify oral transmission as the route of infection.[14,17–22,23] Alarcón de Noya et al. (2017), is a notable example of vertical transmission of infection where the mother contracted Chagas disease through oral transmission, resulting in fetal death.[17]

Public health programs to combat Chagas disease, specifically in the last 30 years, have focused heavily on vector and blood transmission routes and met wide success. Endemic countries implemented widespread blood donor screening for Chagas disease and 80% were successful in interrupting vector transmission, some resulting in the elimination of multiple vector species in certain areas. Similar attention does not seem to have been dedicated to oral transmission routes, potentially due to the complexity and uncertainty regarding the point of contamination and infection. The oral associated infection typically results from the ingestion of contaminated foods and beverages. [4] Nóbrega and colleagues (2009) note that identifying the point of contamination during the food handling process may be difficult.

Clinical diagnosis of orally transmitted Chagas disease also faces difficulties. Symptoms for acute Chagas disease are generally non-specific including fever of unknown origin.[2,10] Fever was a primary symptom of Chagas disease infection and often was among the first symptoms recognized by patients.[14,17–22,23] Dengue fever and malaria are diseases that share regional endemicity with Chagas disease and present with overlapping symptoms including fever. [24,25] Misdiagnosis or suspicion of infection other than Chagas disease was common[17–21,23], with malaria or dengue fever suspected most often. [17,19–21,23]

Incorrect determination of disease etiology after initial patient assessment did not often negatively impact the timing of correct diagnosis and treatment of patients with Chagas disease. Brito et al., Souza-Lima et al., and Valente et al., reported diagnosis of *T. cruzi* infection during an investigation of malaria infection thought initially to be the cause of illness[20,21,23] While the ability to identify Chagas disease when other endemic diseases are suspected was common across outbreaks and prevented a considerable delay in diagnosis and treatment, the misdiagnosis of cytomegalovirus infection in a patient delayed care by two months potentially resulting in chronic Chagas disease infection.[17] The threat of lifetime infection and associated morbidity pressures the need for additional training provided to scientists investigating cases with indeterminate symptoms. As Brito et al. mentions, this training may support the ability of scientists to simultaneously evaluate the presence of *T. cruzi* while investigating diseases such as malari.[20]

The Centers for Disease Control and Prevention (CDC) and the Pan America Health Organization (PAHO) recommend parasitology and serology lab testing to diagnose Chagas disease.[2,7] Serological testing is especially recommended for the chronic phase of disease as parasitemia may be significantly lower during the phase, preventing parasitic detection. Positive results of *T. cruzi* on two of the following three serological tests is suggested for diagnosis (ELISA, hemagglutination inhibition assay, or indirect immunofluorescence).[26] Laboratory techniques were standard across all outbreaks and included both parasitology and serology in accordance with the above recommendations.[14,17–22,23] Thick blood smears were examined for the presence of *T. cruzi* parasites and serologic testing was conducted to detect anti-*T. cruzi* antibodies.[14,17–22,23]

The study designs used to investigate the outbreaks included descriptive studies[18,20,22,23], cohort studie[4,17,21], case-control[14] ,and case-control nested cohort study.[19] Descriptive studies were most often used and were conducted along with vector and reservoir identification and testing.[18,20,22,23] Vectors identified were *R. pictipes*[20,2], *P. geniculate*[8,19,23], *and T. sordida.*[22] *P. geniculatus* was identified in two of the three Venezuelan outbreaks, but Benítez et al. (2013) and Alarcón de Noya et al. (2010) noted no apparent exposure in index cases to a Chagas disease vector.[18,19] Both outbreaks were in urban areas, an uncommon location for Chagas disease infection. Chagas disease typically impacts rural communities of lower socioeconomic status.[10,11] However, population movement and migration has shifted the geographic distribution of disease[15] potentially increasing the likelihood of urban outbreaks. With five of the eight outbreaks occurring in urban areas, this review highlights the changing distribution of Chagas diseases.

Nóbrega et al., Souza-Lima et al., and Alarcón de Noya et al., (2010) identified a single exposure resulting in human infection.[14,19,2] Exposure to açaí in various forms, and guava juice were associated with illness.[14,19,21] The Preparation of these foods, particularly juices and açaí, may carry higher risk of infection due to food preparation practices and locations. The guava juice was prepared and then left unprotected overnight, during which time triatomine bugs are known to be more active. The outbreak reported by Alarcón de Noya et al. (2010) was the largest included in this review and the only that occurred in a school population.[19] The increased population at risk likely impacted the case count, as other outbreaks were related to smaller gatherings or single households. The oral transmission route may have also impacted the spread of disease in comparison to vector transmission more traditionally associated with Chagas disease.

Outbreak control measures were briefly discussed by Benítez and colleagues and only involved the spraying of pyrethroids around homes and provision of educational information to communities impacted by the outbreak.[8]All other outbreaks exclusively discussed treatment.[14,17,19–22,23] Control measures recommended for Chagas disease include educating the public on prevention methods and transmission routes, vector control using insecticides, eliminating risk factors related to poor home construction, using bed nets, and screening blood and organ donors.[3] While one study incorporated two of the recommended control measures, it was unclear if other outbreaks provided such measures, indicating a potential lack of prioritization of control measures during an outbreak of orally transmitted Chagas disease.

Strengths

Articles for this review were identified using two separate PubMed searches and a review of all article references to support a comprehensive list of relevant published outbreaks of Chagas disease in South America between 2000 and 2022. The search methods resulted exclusively in outbreaks related to oral transmission of Chagas disease in Brazil and Venezuela indicating oral transmission as an important mode of disease transmission in these countries. This study also captured the rural to urban shift in the epidemiology of disease. It has been discussed that Chagas disease, influenced by human movement and migration, is shifting from a primarily rural disease to one impacting semiurban and urban environments. This was clearly supported by the proportion of identified outbreaks occurring in urban areas.

Limitations

A primary limitation of this review is the language restriction used in the methods. Articles were restricted to those published in English, eliminating five potentially relevant publications. Secondary, oral transmission was not the primary focus of this review; however, it was the primary mode of transmission discussed in the resulting outbreaks. It is possible that the unique nature of oral transmission of Chagas disease and the urban location of many of the outbreaks encouraged publication of these outbreaks. Tertiary outbreaks belonging to only two countries out of the twenty-one endemic countries were found in this review potentially impacted by the language restrictions.

Recommendations

As mentioned by Brito et al., the clinical manifestations of Chagas disease relating to other endemic infections warrants increased surveillance and training to identify multiple infections when one is suspected.[20] Currently, the available Chagas disease diagnostic testing is neither sensitive nor specific.[22] Funding is needed specifically for the development of improved testing to allow for better diagnostics. Increasing surveillance for Chagas disease would allow for improved knowledge of the spread of disease and location and characteristics of impacted communities. The known rural to urban shift of the disease highlights the importance of surveillance as emergence and re-emergence of disease are occurring throughout Central and South America. Along with surveillance comes a need for training in the health sector. Health care workers trained to identify *T. cruzi* during diagnostic testing for other zoonotic diseases supported quick diagnosis and treatment for Chagas disease. Misdiagnosis may be common in an area where multiple zoonotic, vector-borne diseases are endemic. This step towards health care education could prevent fatalities and progression to chronic phases of disease. Valente and colleagues suggested using the current malaria infrastructure as a backbone for Chagas disease surveillance.[23] This could be highly efficient and effective in scaling up Chagas disease surveillance. But movement in this direction should consider the potential impact to malaria surveillance.

Finally, education of the public is an important step to take, particularly in regions and communities where the disease has recently emerged. Preventative measures such as quality housing construction, the use of bed nets, and proper storage of food and beverages is needed to empower communities to protect their health and wellbeing.

CONCLUSION

Chagas disease has remained a health issue throughout Central and South America and only recently has entered the global health agenda. Previous control measures were focused on vector control and blood and donor screening. Oral transmission of Chagas disease emerging in urban areas warrants considerable public health attention. Acute Chagas disease has the potential to become a lifelong health issue when diagnosis and treatment are delayed. Health personnel lack vital training to identify and diagnose Chagas disease infection particularly in regions burdened by multiple zoonotic diseases. Future research should focus on technological advancement in disease diagnostics while public health practice must emphasize improved surveillance, training, and education to lower the global and regional burden of disease attributed to Chagas disease.

REFERENCES

1. *Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030*. (2021, January 28). World Health Organization (WHO). Retrieved December 7, 2025, from https://www.who.int/publications-detail-redirect/9789240010352
2. Coura, J. R. (2015). The main sceneries of Chagas disease transmission. The vectors, blood and oral transmissions--a comprehensivereview. *Memorias do Instituto Oswaldo Cruz*, *110*(3), 277–282. https://doi.org/10.1590/0074-0276140362
3. *Neglected tropical diseases -- GLOBAL*. (n.d.). World Health Organization (WHO). Retrieved December 7, 2025, from https://www.who.int/health-topics/neglected-tropical-diseases
4. Coura, J. R. (2015). The main sceneries of Chagas disease transmission. The vectors, blood and oral transmissions--a comprehensive review. *Memorias do Instituto Oswaldo Cruz*, *110*(3), 277–282. https://doi.org/10.1590/0074-0276140362
5. Filigheddu, M. T., Górgolas, M., & Ramos, J. M. (2017). Orally-transmitted Chagas disease. *Medicina Clínica (English Edition)*, *148*(3), 125-131. doi:10.1016/j.medcle.2017.02.007
6. Justi, S. A., Russo, C. A., Mallet, J. R., Obara, M. T., & Galvão, C. (2014). Molecular phylogeny of Triatomini (Hemiptera: Reduviidae: Triatominae). *Parasites & vectors*, *7*, 149. https://doi.org/10.1186/1756-3305-7-149
7. *DPDx - American Trypanosomiasis*. (n.d.). CDC. Retrieved December 7, 2025, from https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html
8. Factsheet: Chagas Disease in the Americas for public health workers - PAHO/WHO | Pan American Health Organization. (n.d.-b). https://www.paho.org/en/documents/factsheet-chagas-disease-americas-public-health-workers
9. Lidani, K. C. F., Andrade, F. A., Bavia, L., Damasceno, F. S., Beltrame, M. H., Messias-Reason, I. J., & Sandri, T. L. (2019). Chagas Disease: From Discovery to a Worldwide Health Problem. *Frontiers in public health*, *7*, 166. https://doi.org/10.3389/fpubh.2019.00166
10. Centers for Disease Control and Prevention (CDC). (2012, August). *Chagas disease: What U.S. clinicians need to know - Table of contents*. Retrieved December 1, 2022, from https://www.cdc.gov/parasites/cme/chagas/start.html#skipmenu
11. Centers for Disease Control and Prevention (CDC). (2022, April 11). *Epidemiology & risk factors*. Retrieved December 1, 2022, from https://www.cdc.gov/parasites/chagas/epi.html
12. Buckner, F. S., Moore, A. C., & Cetron, M. S. (2017). Chagas disease. In C. A. Sanford, P. S. Pottinger, & E. C. Jong (Eds.), *The travel and tropical medicine manual* (5th ed., pp. 371–381). Elsevier. doi:10.1016/B978-0-323-37506-1.00026-X
13. Heymann, D. L. (Ed.). (2008). *Control of communicable diseases manual* (19th ed.). American Public Health Association.
14. Nóbrega, A. A., Garcia, M. H., Tatto, E., et al. (2009). Oral transmission of Chagas disease by consumption of açaí palm fruit, Brazil. *Emerging Infectious Diseases*, *15*(4), 653–655. doi:10.3201/eid1504.081450
15. World Health Organization. (n.d.). *Chagas disease (American trypanosomiasis)*. Retrieved December 1, 2022, from https://www.who.int/health-topics/chagas-disease
16. Institute for Health Metrics and Evaluation. (2015). *GBD Compare*. Retrieved November 28, 2022, from http://vizhub.healthdata.org/gbd-compare
17. Noya, B.A. de, Pérez-Chacón G., Díaz-Bello Z., et al. (2017). Description of an oral Chagas disease outbreak in Venezuela, including a vertically transmitted case. *Memórias do Instituto Oswaldo Cruz*, *112*(8), 569–571. doi:10.1590/0074-02760170009
18. Benitez, J.A., Araujo, B., Contreras, K., et al. (2013). Urban outbreak of acute orally acquired Chagas disease in Táchira, Venezuela. *The Journal of Infection in Developing Countries*, *7*(8), 638–641. doi:10.3855/jidc.3620
19. Alarcón de Noya, B., Díaz-Bello, Z., Colmenares, C., Ruiz-Guevara, R., Mauriello, L., Zavala-Jaspe, R., Suarez, J. A., Abate, T., Naranjo, L., Paiva, M., Rivas, L., Castro, J., Márques, J., Mendoza, I., Acquatella, H., Torres, J., & Noya, O. (2010). Large urban outbreak of orally acquired acute Chagas disease at a school in Caracas, Venezuela. *The Journal of Infectious Diseases*, *201*(9), 1308–1315. https://doi.org/10.1086/651608
20. Brito, A. K. S. B., Sousa, D. R. T., Silva Junior, E. F. D., Ruiz, H. J. D. S., Arcanjo, A. R. L., Ortiz, J. V., Brito, S. S., Jesus, D. V., Lima, J. R. C., Couceiro, K. D. N., Silva, M. R. H. D. S. E., Ferreira, J. M. B. B., Guerra, J. A. O., & Guerra, M. D. G. V. B. (2022). Acute micro-outbreak of Chagas disease in the southeastern Amazon: a report of five cases. Revista da Sociedade Brasileira de Medicina Tropical, 55, e0687. https://doi.org/10.1590/0037-8682-0687-2021
21. Souza-Lima, R.deC., Barbosa, M.d, Coura, J. R., Arcanjo, A. R., Nascimento, A.daS., Ferreira, J. M., Magalhães, L. K., Albuquerque, B. C., Araújo, G. A., & Guerra, J. A. (2013). Outbreak of acute Chagas disease associated with oral transmission in the Rio Negro region, Brazilian Amazon. *Revista da Sociedade Brasileira de Medicina Tropical*, *46*(4), 510–514. https://doi.org/10.1590/0037-8682-1367-2013
22. Dias, J. P., Bastos, C., Araújo, E., Mascarenhas, A. V., Martins Netto, E., Grassi, F., Silva, M., Tatto, E., Mendonça, J., Araújo, R. F., Shikanai-Yasuda, M. A., & Aras, R. (2008). Acute Chagas disease outbreak associated with oral transmission. *Revista da Sociedade Brasileira de Medicina Tropical*, *41*(3), 296–300. https://doi.org/10.1590/s0037-86822008000300014
23. Valente, S. A., da Costa Valente, V., das Neves Pinto, A. Y., de Jesus Barbosa César, M., dos Santos, M. P., Miranda, C. O., Cuervo, P., & Fernandes, O. (2009). Analysis of an acute Chagas disease outbreak in the Brazilian Amazon: human cases, triatomines, reservoir mammals and parasites. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *103*(3), 291–297. https://doi.org/10.1016/j.trstmh.2008.10.047
24. Centers for Disease Control and Prevention. (n.d.-a). *Areas with risk of Dengue*. Centers for Disease Control and Prevention. https://www.cdc.gov/dengue/areas-with-risk/index.html
25. Centers for Disease Control and Prevention. (n.d.-a). *About malaria*. Centers for Disease Control and Prevention. https://www.cdc.gov/malaria/about/index.html
26. Pan American Health Organization. (2019). *Guidelines for the Diagnosis and Treatment of Chagas Disease*. https://iris.paho.org/bitstream/handle/10665.2/49653/9789275120439_eng.pdf