Unveiling Chagas Disease: An In-Depth Analysis Of Epidemiological Patterns In High Burden Latin American Nations

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Unveiling Chagas Disease: An In-Depth Analysis of Epidemiological Patterns in High Burden Latin American Nations

Thesis in Candidacy for the Yale School of Public Health
Degree of Master of Public Health, Epidemiology of Microbial Diseases
Nicole Del Castillo

May 2024
Primary Adviser: Dr. Michael Cappello
Secondary Adviser: Dr. Bernardo Lombo
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I would like to dedicate my thesis to my hermanita Nu, Ma, and Pa. Their unwavering love and support throughout all of this helped me stay afloat when my spirit was shattered, most especially when I felt like giving up while going through serious illness and injury. I accomplished this work under my Pa’s most treasured saying, “Si te caes 1000 veces, te levantas 1001.”

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And finally, I would like to dedicate this to all future and current Latine graduate public health students, especially to the ones who are the first in their family to make the journey through higher education – Adelante hasta la victoria.
ABSTRACT

Background: Chagas Disease, endemic to 21 countries in Latin America, is transmitted by triatominae insects infected with parasites known as Trypanosoma cruzi.\textsuperscript{1–3} It is the most prevalent tropical disease in Latin America, affecting about 6 million individuals across the Americas.\textsuperscript{1} This literature review aims to summarize unique epidemiological patterns over a 9-year time period from 2010 to 2019 across three nations in South America that experienced the highest Chagas Disease burden in 2019: Bolivia, Venezuela, and Argentina.\textsuperscript{4}

Methods: For this rapid literature review, one independent reviewer extracted all data for publications reviewed within a 9-year time period: 2010 to 2019. The Population, Concept, and Context Framework was used to identify key Chagas Disease concepts. Two major databases were utilized, MEDLINE and EMBASE, as recommended by the Cochrane Review Guidelines.\textsuperscript{5} The use of a 3rd database was omitted as there was only one reviewer. Literature available in both English and Spanish language translations were reviewed. Inclusion criteria incorporated all study designs, unique infection patterns, and disease control measures while excluding case studies and certain specialized topics.

Results: In total, 1068 research articles were obtained from both the EMBASE and MEDLINE databases. Of these, 267 duplicates were removed, and 801 proceeded to title and abstract screening. Among the 238 articles that were assessed for full-text review, 30 were included in the full data extraction that demonstrated unique epidemiological patterns and characteristics across Bolivia, Venezuela, Argentina, and selected continents.

Conclusions: This rapid literature review demonstrates unique changes in epidemiological trends across the 3 nations over a 9-year time frame. Important future considerations to control and prevent Chagas Disease include strengthening Chagas Disease surveillance systems and delivering educational interventions to patients and providers.
INTRODUCTION

Chagas Disease (CD) is transmitted by Triatominae insects infected with parasites known as Trypanosoma cruzi or T. cruzi. These insects bite at night, and they acquired the name “kissing bug” for their tendency to feed on people’s faces. After they feed, they leave droppings—humans acquire CD when the feces infected with T. cruzi enter the body via broken skin or mucous membranes. CD is curable under treatment with Benznidazole and Nifurtimox if it’s treated during the beginning of the acute phase.

Approximately 70% of CD cases are asymptomatic. As a result, people can live with an asymptomatic infection for years and develop severe conditions such as cardiomyopathy. This is why CD screening is imperative, as detecting it early not only ensures timely and effective treatment but also helps prevent progression to severe cases of CD sequelae. As of 2019, the CD-endemic countries in Latin America that experienced the highest prevalence of CD per 100,000 population were Bolivia, followed by Venezuela and then Argentina. Outside of Latin America, non-endemic countries such as Spain saw the most significant increase in CD cases, followed by the United States and then Italy. With CD cases becoming increasingly prevalent across non-endemic locations, it is imperative for healthcare systems to prioritize immigrant health efforts so that high-quality CD care is made more accessible. This must be done in a way that does not perpetuate disease stigma nor induce xenophobia upon immigrant communities.

This review aims to describe the development of unique epidemiological patterns across Bolivia, Venezuela, and Argentina over a 9-year period from 2010 to 2019 and provide insights into the public health implications of CD. A similar study published in 2009 brought attention to CD epidemiology trends by highlighting changes in incidence and prevalence rates, disease control progress, and provided recommendations for surveillance and health policy. It is imperative, now more than ever, for global public health leaders to gain a comprehensive understanding of CD epidemiological development in Latin America. This review serves as a call to action to inform timely and effective community-centered CD public health interventions.
METHODS

**Literature Search:** In this rapid literature review, the Population, Concept, and Context framework was used to identify key CD epidemiology concepts across Venezuela, Bolivia, and Argentina, encompassing all age groups to highlight how these countries developed the highest burden of CD in 2019. The Cochrane Rapid Review method was utilized, focusing on MEDLINE and EMBASE database searches performed under one independent reviewer. Covidence was used to identify research articles most relevant to the review.

In EMBASE, the term “epidemiology” was exploded to explore its more comprehensive database. The inclusion criteria covered publications from 2010 to 2020 available in English or Spanish translations, encompassing all study designs, with a focus on CD patterns, control measures and general disease sequelae.

![PRISMA Flow Diagram](image)

Exclusion criteria encompassed studies outside of the 10-year time frame, studies not specific to the three chosen countries with the exception of some continental regions, case studies, and a range of other specialized studies. In Figure 1, the Preferred
Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram highlights the literature review process. Medical Subject Headings (MeSH) terms used in both searches included: “epidemiology, Chagas Disease, South and Central America, mortality, morbidity, incidence, prevalence, Trypanosoma Cruzi, Bolivia, Venezuela, and Argentina.”

The final **EMBASE search** attempt included the following search lines:

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| 6 | (mortality or morbidity or incidence or prevalence or control or prevention or surveillance).tw. |
| 7 | (1 or 2) and (3 or 4) and (5 or 6)                                                                  |
| 8 | limit 7 to yr="2010 - 2020"                                                                          |

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<td>(Bolivia* or Venezuela* or Argentin*).tw.</td>
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| 4 | Latin America/                                        
| 5 | (chagas or "Kissing bug" or "Trypanosoma cruzi" or triatomine*).tw.                               |
| 6 | (5 or 2) and (3 or 4)                                                                               |
| 7 | limit 6 to yr="2010 - 2020"                                                                          |

**Geographical and Global Burden of Disease Data**: Geographical Information Systems (GIS) software was utilized to provide the geographical distribution of incidence and age-standardized death rates of CD in Latin America. Data was acquired through published ArcGIS Online data from Bucknell University. In addition, the
Global Burden of Disease (GBD) Study from the Institute for Health Metrics and Evaluation (IHME) was used to provide data visualization of key health indicators related to CD, including but not limited to disease incidence, prevalence, and mortality data under the Cause of Death or Injury category.\textsuperscript{10}

RESULTS

Chagas Disease (CD) research articles focused on the three nations of interest were primarily community-based studies. Studies in other continents were included to highlight unique global CD distribution patterns. Each country’s cultural and social context was highlighted to gain a unique and thorough understanding of factors influencing CD epidemiology.

BOLIVIA EPIDEMIOLOGY PATTERNS

\textit{Bolivia is located in the heart of South America. Its territory includes part of the Gran Chaco, the second largest forest in the continent, an area known for its diverse ecological systems and hyperendemicity to CD. In 2019, Bolivia held the highest burden of CD.}

Parisi et al., in a 2018 cross-sectional survey, captured CD knowledge, perceptions, and practices for approximately 10\% (n = 669) of randomly selected households from Monteagudo in the Bolivian Chaco.\textsuperscript{11} Most of the population did not have health insurance, and 60\% lived in Monteagudo central, while 40\% lived in remote areas, with some in difficult-to-access areas.\textsuperscript{11} In 2016, Monteagudo had 2,261 individuals, or 17\% of the population greater than 15 years old, tested for CD, resulting in a total prevalence of 51.8\%.\textsuperscript{11} In addition, Parisi et al. found that participants valued individual CD experiences over information delivered by health care services.\textsuperscript{11}

Knowledge gaps were also noted across CD symptoms and disease transmission. About 90\% of participants knew CD was transmitted from triatomines (more commonly known as \textit{vinchucas} in Bolivia). Still, only 36.9\% knew about vertical (mother-to-child) transmission, 26\% knew of transmission from blood or organ
donations, and 6.1% knew of oral transmission. The majority of participants knew that CD could cause death and impact cardiac and intestinal health. Knowledge of acute symptoms was almost nonexistent, and 25.9% of participants were aware that chronic sequelae occurred 10 years post-infection. These knowledge gaps could explain why the prevalence of CD is high in the Monteagudo region.

Similarly, knowledge of primary prevention methods was common; however, practices that could potentially reduce the effectiveness of these methods included keeping animals close to home and the use of old houses (with the presence of vectors) instead of new ones.

Figure 2: Bolivia with Study Locations

Although not mentioned in the article, it is important to consider the reasoning behind using old houses, as it could be related to socio-cultural practices or norms. Finally, key social determinants of health highlighted among the region included
extreme poverty, difficulty accessing information and lack of access to care due to “lack of mobility” in rural areas.\textsuperscript{11}

As mentioned earlier, it is important to consider cultural factors that influence perception or attitudes towards CD to understand developments in CD epidemiological trends.

\textit{Figure 3: 2010 Geographical Distribution of CD Incidence Rates per 100,000}

In other words, it is imperative to center understanding around a population’s cultural context to gain a holistic understanding of why CD affects certain populations more than others. A cross-sectional survey conducted across two time periods, June 2014 – August 2014 and November 2014 – May 2015, in La Paz and Santa Cruz, as well as three rural areas, inter-Andean Valleys, Chaco, and Chiquitanía, focused on centering the cultural context of indigenous communities.\textsuperscript{13} Out of the 480 informants interviewed for a survey, about 480, or 79.8\% of informants knew what CD vectors looked like.\textsuperscript{13} Interestingly, informants from indigenous communities from rural areas knew what CD vectors looked like 80\% of the time, compared to La Paz (50.6\%) and Santa Cruz informants.\textsuperscript{13} These communities receive yearly insecticide treatment from government-led campaigns.\textsuperscript{13} However, these campaigns were not provided to every
village, and in addition, there existed mistrust, language barriers, and cultural misunderstanding between healthcare centers and indigenous communities.\textsuperscript{13}

When considering Chagas Disease epidemiology, its unique sequelae must also be taken into consideration – the most common CD sequelae is cardiomyopathy. At the time the 2012 Fernandez et al. study was conducted, the highest prevalence of CD occurred in the Gran Chaco area.\textsuperscript{14} In fact, of the 1,137 participants in the study who were 10 years or older, 66.2\% (n = 398) showed evidence of \textit{T. cruzi} infection.\textsuperscript{14}

\begin{figure}[h]
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\caption{2019 Geographical Distribution of CD Incidence Rates per 100,000}
\end{figure}

Through electrocardiogram (ECG) testing, the most common cardiac pathology found among participants were bundle branch blocks (n = 42).\textsuperscript{14} Interestingly, the presence of most CD cardiac issues in general became more common as individuals aged.\textsuperscript{14} In populations such as these that experience a high burden of CD cardiomyopathy, it is essential to establish equitable access to cardiac health services.

Chagas Disease also has an impact on maternal and infant health. For instance, in the findings across 2 major hospitals, Hospital Universitario Japonés in Santa Cruz and Hospital Municipal Camiri in Camiri, showed that women with high parasite loads transmitted \textit{T. cruzi} more frequently to their newborns compared to those without.\textsuperscript{15}
This was especially notable for women who delivered twins.\textsuperscript{15} Interestingly, vertical \textit{T. cruzi} transmission was more common among women who resided in houses not infested with triatomines compared to women who did, and pregnant women in Camiri had overall higher \textit{T. cruzi} infection prevalence across different age groups as seen in Figure 2.\textsuperscript{15} It is important to note that at the time the article was published, \textit{T. cruzi} infection prevalence was over 80\% in rural areas across the Bolivian Chaco.\textsuperscript{15}

This evidence parallels findings from an analysis on \textit{T. cruzi} seroprevalence data, which observed high rates of \textit{T. cruzi} seroprevalence among women aged 15-45 years (reproductive age) in rural areas of the Bolivian Chaco.\textsuperscript{16} Surprisingly, in 1986, \textit{T. cruzi} seroprevalence was 100\% compared to 74\%-79\% in 2013.\textsuperscript{16} However, another study had slightly different findings, stating that pregnant women living with \textit{T. cruzi} infections most likely resided in houses with triatomine infestation and were “slightly more likely” to reside in rural areas.\textsuperscript{17} These unique serological findings show that \textit{T. cruzi} infection patterns are highly variable and dynamic, potentially making managing CD control and prevention difficult.

\begin{figure}[h]
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\caption{Santa Cruz and Camiri \textit{T. cruzi} infection prevalence among pregnant women\textsuperscript{15}}
\end{figure}

Novel CD control tools have recently been developed and shown promising results. Saunders et al. in 2011, for instance, developed a risk score with 81\% sensitivity and 84\% specificity to predict the likelihood of vector infestation in houses.\textsuperscript{18} The five risk factors included in the risk score calculation were “cracks in the walls of houses; adobe walls; junk in the peri-domiciliary area; no insecticide spraying in the previous two years; and freely ranging animals.”\textsuperscript{18} Any home with four or more risk factors was considered at high risk for vector infestation, indicating a need for pesticide
treatment. Tools such as this risk score are crucial for developing future insecticide interventions and potentially eradicating *T. infestans*.

With hyperendemic CD trends across rural communities in Bolivia, mapping the geographical distribution of triatomines and their correlation with environmental factors is essential. Echeverria et al., from 2009 to 2014, mapped *T. infestans* infestation patterns with entomological surveys in the Toro Toto municipality in Potosi, Bolivia. Four environmental variables explained 57% of the variability of triatomine house infestation: “mean diurnal temperature range, temperature seasonality, minimum temperature of the coldest month, and precipitation of the coldest quarter.” These variables clearly demonstrate environmental factors’ role on influencing *T. infestans* house infestation, which is crucial for CD control efforts.

Insecticide use is another critical component for the control of triatomine infestation. Deltamethrin, is the main insecticide used for triatomine control. A 2014 study was conducted in 3 communities across the Charcas Province: Taqó Taqó, Julo Chico, Julo Grande, and Calahuta to assess wild and domestic *T. infestans* resistance to insecticide deltamethrin. Houses in these areas were built of adobe and stone, maintaining crops and domestic animals. The captured wild and domestic triatomines were all *T. infestans* species, which are the most common species in Latin America. Unfortunately, the triatomines collected before and after deltamethrin insecticide use were all found to be resistant to deltamethrin. These findings demonstrate that triatomine resistance is another key challenge to CD control, which could explain the high burden of CD in the Charcas, Bolivian region.

Certain large-scale interventions have proven successful in preventing and controlling CD. A 2017 study by Pinazo et al., assessed the effectiveness of a novel 2009 intervention: The Bolivian Platform for the Comprehensive Care of Adults with Chagas Disease, better known as the Bolivian Chagas Platform (BCP). The BCP’s success resulted from standardized medical attention and data management, coupled with health care worker training. Between 2010 and 2015, of the 26,227 patients who utilized the BCP, 69% had *T. cruzi* infections, 8,567 had started anti-parasitic treatment, and about 1,616 healthcare professionals received training, altogether which improved CD diagnostics, treatment, clinical practice, and health policy.
At the time the study was conducted, Bolivia had the highest global CD prevalence, standing at a rate of 6.1%, with CD endemic in about 60% of the nation.\textsuperscript{21} In addition, CD death rate stood at 13% for individuals between 15 and 75 years of age.\textsuperscript{21} Interestingly, patient care did not improve even though vector infestation had been low (below 3%).\textsuperscript{21} However, even the BCP has its limitations. Under the BCP, 6 medical centers provided free CD care across departments with high CD endemicity: Tarija, Chuquisaca, and Cochabamba.\textsuperscript{21} Although services were free and accessible in these areas, where providers received a 1-week long training upon starting, a shortage of benznidazole in 2012 delayed CD treatment efforts for patients.\textsuperscript{21} In addition, increased demand for services overwhelmed the administrative management of the BCP.\textsuperscript{21} Interestingly, delays in treatment can also be explained by the amount of people ineligible for etiological treatment of CD which includes the use of benznidazole and nifurtimox.\textsuperscript{21} The use of the BCP is a clear demonstration of the importance of large-scale interventions that carry forward holistic public health practice when addressing infectious disease issues.

**VENEZUELA EPIDEMIOLOGY PATTERNS**

*Venezuela, located to the north of South America held the second highest burden of CD in 2019.*

When considering CD epidemiology trends in Venezuela, it is important to first consider the impact of humanitarian crisis in the country.\textsuperscript{22} Unfortunately since 2014, Venezuela has been experiencing heightened levels of continuous political, economic, and social instability, all which have significantly contributed to the rapid decline of its public health system.\textsuperscript{22,23}
A 2019 systematic review by Grillet et al, highlights the impact of the humanitarian crisis on vector-borne disease trends. As of 2012, CD control and surveillance efforts have ended affecting epidemiological trends of CD across Venezuela. In the Portuguesa State, CD prevalence was reported to be an estimated 17.7%, Anzoátegui at 54.4%, Sucre at 8.3%, Nueva Esparta at 6.9%, and Guárico at 3%. In addition, clusters of oral CD outbreaks also occurred throughout the country as seen in Figure 3.

T. cruzi infections among newborns and post-partum women showed unique findings. In Anzoátegui, a cross-sectional study in 2016 screened 1200 women for T. cruzi infections, where 6.5% (n = 78) of women were found positive. Most importantly, the study found 11 newborns at 9 months of age tested negative for T.
cruzi infection, indicating that vertical transmission is not solely explained by presence of *T. cruzi* DNA at birth alone.\textsuperscript{26} Similar to Bolivia, post-partum women from rural communities in Venezuela also had high *T. cruzi* seroprevalence.\textsuperscript{26}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure7.png}
\caption{2019 geographical distribution of Chagas Disease in Venezuela\textsuperscript{25}}
\end{figure}

Moreover, ecoepidemiological factors contributing to CD infections in Venezuela are also important. A 2019 cross-sectional seroprevalence study in Sabana de Guacuco and Fuentidueño towns in the Nueva Esparta State, Venezuela reported an estimated 6.9\% *T. cruzi* prevalence mostly accounted by those >50 years and <30 years of age.\textsuperscript{27} 70\% of homes in both towns were made of materials such as coconut palm leaves which different species of triatomines such as *R. prolixus* like to reside in.\textsuperscript{27} Environmental factors such as these are important to consider when conducting a CD intervention in areas such as these.

Chagas Disease trends in Venezuela are unique across different populations. A 2019 review revealed confirmatory *T. cruzi* serologic findings for patients who were
referred by different health centers and from rural areas. Among both patient groups, active transmission was observed among children <10 years old. In addition, patients from rural areas were found to have 10.7% seroprevalence while 42.8% of patients referred from health centers had *T. cruzi* infections. The most distinct finding from this review was that CD clinical status was not influenced by *T. cruzi* mode of transmission nor by its genotype. However, the article does suggest CD clinical status could be influenced by “host susceptibility and/or parasite load.”

In addition to vector and vertical transmission of CD, orally transmitted CD is another route of transmission that requires more attention. A 2017 systematic review reported findings on orally-transmitted CD outbreaks in Venezuela – 6 of them occurred over 5 years from 2010 to 2015. The 2 categories of oral transmission that occurred were micro-epidemics and small group outbreaks. In comparison, Bolivia only experienced 1 outbreak in 2010 from consumption of raw majo juice.

**ARGENTINA EPIDEMIOLOGY PATTERNS**

*Finally, the focus falls on Argentina, located to the southernmost area of South America. Similar to Bolivia, Argentina also holds part of the Gran Chaco and was the country with the 3rd highest CD prevalence in 2019.*

A cross-sectional study done between 2010 and 2015 focused on finding CD seroprevalence among participants older than 14 years of age in rural Chaco areas through administration of surveys. This age range was chosen due to Argentina’s initiative of etiologic treatment provided to children up until 14 years of age. Out of 749 participants, 24.7% were positive for CD seroprevalence, and there was a positive correlation between socio-environmental variables and seroprevalence.
Another interesting study conducted in Argentina’s Chaco province focused on the association between maternal factors and congenital transmission, as it is the second most important route of transmission that contributes to endemicity of CD. Among the pregnant mothers surveyed, 83.4% were aware of their CD status, while an estimated 66% resided in rural areas during their childhood and 62.8% recalled seeing *vinchucas* at the time.

Figure 8: Argentina with Study Locations

In 2011, of 246 children born, approximately 6% of children showed positive CD serology. Interestingly, neonatal care was found to be a protective factor for developing *T. cruzi* infections after adjusting for other variables. The study also revealed that the number of children a mother has increases the risk of *T. cruzi* among siblings.
Similarly, an ecological-observational study utilizing data from the international collaboration known as the *Iniciativa del Cono Sur para controlar y eliminar la enfermedad de Chagas (INCOSUR)* or Southern Cone Initiative to Control and Eliminate Chagas Disease, to determine congenital CD burden in Argentina. The study confirmed that overall CD burden lies in northeast and central Argentina. At the end of 2014, CD control efforts were focused on about 271,776 pregnant women however, there was a notable decline in CD prevalence between 2010 to 2014 from an estimated 5.0% to 2.6%. Vertical transmission rates at the end of 2014 remained at 5.7%. There was also a correlation between the likelihood of acquiring a vector-borne CD infection and maternal infection prevalence across provinces.

With insecticide spraying used as a common tool for CD vector control, especially in remote areas, its effectiveness across different communities can potentially affect CD epidemiological trends, especially when certain triatomine species such as *T. infestans*, develop resistance. One 2015 study evaluated community-wide insecticide (deltamethrin) spraying effectiveness among indigenous communities in the Chaco, by assessing triatomine infestation in houses before and after spraying with positive results. At baseline, house infestation stood at 31.9% and fell to 0.7% in after 10 months post-spray. After 59 and 89 months, triatomines are no longer present.

Another 2013 cross-sectional study examined factors contributing to triatomine infestation in the Argentine Chaco, and found that infestation rates were high for both houses (59.7%) and peridomestic areas (58.3%) with the lowest being in domestic areas (4.3%). Similar to earlier findings, homes with chicken coops are have a greater risk of acquiring vector infestation. Furthermore, about 80% of the respondents were unaware of peridomestic structure use to control for triatomine infestation.

Other socio-ecological factors that increase *T.cruzi* infection rates in rural and indigenous communities in the Argentinian Chaco include living with a person who is seropositive, and social vulnerability (e.g. income level).
Moreover, the addition of new houses to replace old houses was thought to have the ability to control triatomine house infestation.

Figure 9: 2010 Geographical Distribution of CD Age-Standardized Death Rates per 100,000

A study in 2020 tested this theory and revealed no significant difference in triatomine infestation between new and old houses, even in areas where only new houses were built.\textsuperscript{38} However even when these factors are present, there continues to be evidence of successful insecticide interventions to control triatomine infestation, which is seen across other indigenous and creole communities.\textsuperscript{37} Effective spraying resulted in <1% triatomine infestation in houses, eventually leading to their eradication in houses by 2015.\textsuperscript{37}

On the other hand, educational interventions are another important tool for CD prevention and control. In 2012, an educational CD program was evaluated for its impact on CD knowledge.\textsuperscript{39} Through cross-sectional study methods during 2 time periods, findings showed an increase in correct questionnaire responses to questions on CD knowledge.\textsuperscript{39}
However, a decline in correct responses on congenital transmission was noted.\textsuperscript{39} Chagas Disease is not unique to rural areas in Argentina; in fact, recent evidence shows that urban areas are also at risk of triatomine infestation. In addition, the prevalence of triatomine infestation gradually increases across the urban, peri-urban, and rural areas as follows: 4.5\% for urban, 22.5\% for peri-urban, and 42.4\% for rural areas.\textsuperscript{40} Therefore, triatomine control efforts in urban and peri-urban settings cannot be ignored.

**GLOBAL EPIDEMIOLOGY TRENDS**

*From a global perspective, Chagas Disease has begun to manifest in non-endemic parts of the globe.*

To begin, in Japan, a study was conducted across 2 cohorts from different time periods, among individuals “at-risk” for CD which included those who migrated from Latin America or who had previously traveled to Latin America.\textsuperscript{41} Among both cohorts from 2 different time periods (January 2004 – October 2012 and January 2013 –
August 2016), those who did show positive serological results were individuals born or raised in Latin America.\textsuperscript{41} Across the second cohort, only 3 people out of 13,298 at-risk donors were found to be positive for \textit{T. cruzi} antibodies.\textsuperscript{41}

\textit{Figure 11: Deaths, Prevalence, and Incidence under Cause of Death or Injury Category - IHME Data}\textsuperscript{10}

To explore CD burden in Japan even further, another study focused on knowledge, behavior, and perceptions of CD of individuals from hyperendemic CD areas of Bolivia.\textsuperscript{42} Surprisingly, the majority of participants were not well-informed on foundational CD knowledge.\textsuperscript{42} In addition, <10% of participants were previously screened for CD.\textsuperscript{42} More notably, CD stigma was low across the cohort and barriers to care included health care and migration system navigation, along with language barriers.\textsuperscript{42}
In addition, Educational Activities were proven to be a successful tool to improve CD knowledge.\textsuperscript{42}

In addition, a 2017 systematic review also reported CD prevalence rates from Latin American individuals that resided in Canada, the United States, and several European countries; although these prevalence estimates were highly variable and are higher in comparison to prevalence rates from individual’s (living with CD) country of origin.\textsuperscript{43} A closer look into CD infection rates in Europe shows that those living with the highest burden of CD are individuals that have migrated from Bolivia.\textsuperscript{44} With the growing global distribution of CD infection, it is imperative to make care more accessible to address the needs of immigrant health across non-endemic countries.

Reporting on CD health indicators proves to be a challenging task, as noted by a 2015 CD data metrics review from the Institute for Health Metrics and Evaluation (IHME).\textsuperscript{45} Estimating prevalence rates of CD in general is challenging due to its delayed onset of symptoms, rapidly changing trends, weak surveillance systems, limited mortality-related data, and highly variable geographic distribution.\textsuperscript{45} Interestingly, the Global Burden of Disease (GBD) Study from the IHME, hold estimates on CD incidence, prevalence, and mortality data under the Cause of Death or Injury category that show a decline in overall CD prevalence, incidence, and mortality.\textsuperscript{10}

CONCLUSIONS

\textit{What was and what can be learned:} Chagas Disease epidemiological patterns across Bolivia, Venezuela, and Argentina changed over the course of 9 years. This literature review highlighted several unique trends of Chagas Disease and gaps in CD prevention, control, and treatment. Bolivia’s Chagas Platform – one of the most collaborative and innovative international CD interventions yet-still faces limitations when providing CD care due to the high demand for the platform. This should serve as a reminder that even the most comprehensive public health interventions need adequate staffing and resources in order to function properly.
It is also important to center a community’s cultural context when describing epidemiological trends. As seen in Venezuela, CD trends cannot be explained by seroprevalence studies alone; learning about the social, cultural, economic, and political context is critical to fully understanding why CD trends fluctuate over time. Most importantly, this review describes the CD burden before the onset of the global 2019 COVID-19 pandemic. It is necessary to understand the development of CD epidemiological trends pre-pandemic to assess how trends changed upon the onset of the pandemic, as many tropical diseases at the time gradually lost attention because public health demand shifted its focus on the pandemic. As such, it would be interesting to see how CD trends developed after the pandemic began.

**Limitations:** This literature review faced some limitations. Some articles did not have English or Spanish translations available. In addition, most studies included were from Argentina and were community-based. Global CD burden was limited to the US, Europe, and Asia; thus, there is a need to address CD burden across other continents. In addition, the lack of literature on Venezuela could be explained by its ongoing humanitarian crises. The rapid review was conducted over the course of 3 months by one reviewer, in addition to lacking a thorough search of a 3rd database as suggested by the Cochrane Review guidelines, thus was limited in its capacity for comprehensiveness. Finally, due to the variability of CD indicators, the literature findings in this rapid review serve as a descriptive overview and summary of epidemiology trends of Chagas Disease. They cannot serve as conclusive evidence for Chagas Disease trends.

**Public Health Implications:** As CD continues to reach other parts of the world, prevention and control efforts are needed now more than ever. One of the first strategies that can be used is development of educational interventions. As seen across many of the aforementioned studies, several gaps exist in awareness and knowledge of CD transmission routes, symptoms, and treatment among patients and communities. In order for an educational intervention to work, health educators must develop trust with the communities they serve by practicing cultural humility and speaking the applicable language. Health care centers in Bolivia, for instance, lack
trust and cultural understanding of indigenous communities, which could make it extremely difficult to deliver culturally sensitive and effective CD health education.\textsuperscript{13}

Healthcare providers are the second most important group in providing CD education. This is especially important as CD spreads to non-endemic countries. Many healthcare providers in the United States, for instance, are still unaware of CD and its epidemiology. Unfortunately, this is especially true among obstetricians and gynecologists.\textsuperscript{46} This is especially concerning as vertical CD transmission is one of the most common modes besides vector-borne transmission.

As the IHME noted, most CD prevalence data is challenging to obtain.\textsuperscript{10} Thus, stronger CD surveillance to track specific health indicators such as prevalence is imperative. This review is meant to serve as a swift call to action for global public health leaders searching for innovative and equitable ways to address Chagas Disease in Latin America and beyond for years to come.
REFERENCES


report/2021/country-chapters/venezuela


46. Stimpert KK, Montgomery SP. Physician Awareness of Chagas Disease, USA - Volume 16, Number 5—May 2010 - Emerging Infectious Diseases journal - CDC. doi:10.3201/eid1605.091440
## APPENDIX A

List of Included Studies

<table>
<thead>
<tr>
<th>ARTICLE TITLE</th>
<th>PUBLICATION DATE + [STUDY DATE]</th>
<th>COUNTRY (AREA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“We have already heard that the treatment doesn’t do anything, so why should we take it?”: A mixed method perspective on Chagas disease knowledge, attitudes, prevention, and treatment behaviour in the Bolivian Chaco</td>
<td>October 2022 [2018]</td>
<td>Bolivia (Bolivian Chaco)</td>
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<tr>
<td>A strategy for scaling up access to comprehensive care in adults with Chagas disease in endemic countries: The Bolivian Chagas Platform</td>
<td>August 2017 [2010 to 2015]</td>
<td>Bolivia (Nation Wide)</td>
</tr>
<tr>
<td>Resistance to deltamethrin by domestic and wild Triatoma infestans populations in the municipality of Toro Toro, Potosi, Bolivia</td>
<td>February 2018 [June and October 2014]</td>
<td>Bolivia (Taqó Taqó, Julo Chico, Julo Grande: Charcas Province in Potosi Department)</td>
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<tr>
<td>Electrocardiographic and echocardiographic abnormalities in Chagas disease: findings in residents of rural Bolivian communities hyperendemic for Chagas disease-</td>
<td>September 2015 [July 2012]</td>
<td>Bolivia (Santa Cruz Department)</td>
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<tr>
<td>Sustained Domestic Vector Exposure Is Associated With Increased Chagas Cardiomyopathy Risk but Decreased</td>
<td>September 2015 [2010 to 2013]</td>
<td>Bolivia (Santa Cruz Department)</td>
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<tr>
<td>Study Title</td>
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<tr>
<td>Parasitemia and Congenital Transmission Risk Among Young Women in Bolivia</td>
<td>September 2012</td>
<td>Bolivia (Cochabamba Department)</td>
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<tr>
<td>The development and validation of a risk score for household infestation by Triatoma infestans, a Bolivian vector of Chagas disease</td>
<td>September 2012 [January to March 2011]</td>
<td>Bolivia (Cochabamba Department)</td>
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<tr>
<td>“Trypanosoma cruzi-infected Pregnant Women without Vector Exposure Have Higher Parasitemia Levels: Implications for Congenital Transmission Risk”</td>
<td>March 2015 [June 2010 to October 2011]</td>
<td>Bolivia (Santa Cruz Department)</td>
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<tr>
<td>Ecoepidemiological Factors Related To Seroprevalence Of Anti-Trypanosoma (Schizotrypanum) Cruzi Antibodies In Autochthonous Inhabitants Of Communities From Margarita Island, Nueva Esparta State, Venezuela</td>
<td>June 2019 2015</td>
<td>Venezuela (Fuentidueño and Sabana de Guacuco, Nueva Esparta)</td>
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<td>Infección por Trypanosoma cruzi en mujeres puérperas y sus neonatos en Barcelona, estado Anzoátegui, Venezuela</td>
<td>June 2019 [May 2015 to August 2016]</td>
<td>Venezuela (Anzoátegui State)</td>
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<td>“Venezuela's Humanitarian Crisis, Resurgence of Vector-Borne Diseases, and Implications for Spillover in the Region”</td>
<td>May 2019 [19th and 20th Centuries]</td>
<td>Venezuela (Multiple Locations)</td>
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<td>[Impact of an educational program related to basic knowledge of Chagas disease in a population of the Argentine Northeast]</td>
<td>July 2018 [November 2012]</td>
<td>Argentina (Independencia Department)</td>
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<td>born and siblings in Chaco province, Argentina.&quot;</td>
<td>November 2018</td>
<td>Argentina</td>
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<tr>
<td>[Seroprevalence of Chagas Disease in those older than 14 years old in rural Chaco areas of Santa Fe Province.]</td>
<td>November 2018 [2010 to 2015]</td>
<td>Argentina (Santa Fe Province)</td>
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<td><strong>Beating the odds: Sustained Chagas disease vector control in remote indigenous communities of the Argentine Chaco over a seven-year period</strong></td>
<td>August 2018 [2008 to 2015]</td>
<td>Argentina (Chaco)</td>
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<td><strong>Factors associated with the presence of triatomines in rural areas of south Argentine Chaco</strong></td>
<td>September 2018 [December 2012 to November 2013]</td>
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<td><strong>Human Trypanosoma cruzi infection is driven by eco-social interactions in rural communities of the Argentine Chaco</strong></td>
<td>December 2019 [2006 to 2015]</td>
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<td><strong>Inequalities in the social determinants of health and Chagas disease transmission risk in indigenous and creole households in the Argentine Chaco</strong></td>
<td>December 2019 [2008 to 2015]</td>
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<td><strong>Rethinking the old hypothesis that new housing construction has an impact on the vector control of Triatoma infestans: A metapopulation analysis</strong></td>
<td>September 2020 [2014 to 2017]</td>
<td>Argentina (La Rioja Province)</td>
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<td><strong>Urbanization, Risk Stratification and House Infestation with a Major Vector of Chagas Disease in an Endemic Municipality of the Argentine Chaco</strong></td>
<td>June 2020 [October 2015 to March 2016]</td>
<td>Argentina (Chaco Province)</td>
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<td><strong>Seroprevalence of Trypanosoma cruzi infection among at-risk blood donors in Japan</strong></td>
<td>January 2019 [January 2004 to October 2012 and January 2013 to August 2016]</td>
<td>Japan</td>
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<td><strong>Knowledge, behavior and attitudes towards Chagas disease among the Bolivian migrant population living in Japan: a cross-sectional study</strong></td>
<td>May 2020 [March 2018 to June 2018]</td>
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<td>A global systematic review of Chagas disease</td>
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<td>prevalence among migrants</td>
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<td>The Burden of Chagas Disease Estimates and</td>
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