

Contents lists available at ScienceDirect

# Parasite Epidemiology and Control



journal homepage: www.elsevier.com/locate/parepi

## Trends and associated characteristics for Chagas disease among women of reproductive age in the United States, 2002 to 2017



Chioma Ikedionwu<sup>a</sup>, Deepa Dongarwar<sup>a,\*</sup>, Manvir Kaur<sup>b</sup>, Lisa Nunez<sup>b</sup>, Annabella Awazi<sup>b</sup>, Jere' Mallet<sup>b</sup>, KaShena Kennedy<sup>b</sup>, Michelle Cano<sup>b</sup>, Chinwe Dike<sup>b</sup>, Jessica Okwudi<sup>b</sup>, Justice Stewart<sup>b</sup>, David Igwegbe<sup>b</sup>, Flora G. Estes<sup>b</sup>, Kiara K. Spooner<sup>c</sup>, Jason L. Salemi<sup>c</sup>, Hamisu M. Salihu<sup>a,c</sup>, Omonike A. Olaleye<sup>b</sup>

<sup>a</sup> Center of Excellence in Health Equity, Training, and Research, Baylor College of Medicine, Houston, TX, USA

<sup>b</sup> College of Pharmacy and Health Sciences, Texas Southern University, Houston, TX, USA

<sup>c</sup> Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX, USA

## ARTICLE INFO

Article history: Received 26 March 2020 Received in revised form 14 July 2020 Accepted 15 July 2020

Keywords: Neglected disease Chagas disease Ethnic/racial disparities United States Reproductive health HCUP

## ABSTRACT

*Background:* American trypanosomiasis, commonly referred to as Chagas disease, is caused by a single cell protozoan known as *Trypanosoma cruzi* (*T. cruzi*). Although those affected are mainly in Latin America, Chagas has been detected in the United States (US), Canada and in many European countries due to migration. Few studies have explored the epidemiology of Chagas within the US or changes in disease burden over the past decade. The objective of this study was to explore the trends and associated characteristics for Chagas disease among hospitalized women of reproductive age in the US.

*Methods:* We analyzed admissions data including socio-demographic and hospital characteristics for inpatient hospitalization for women of reproductive age (15–49 years) in the US from 2002 through 2017. We employed Joinpoint regression analysis to determine trends in the prevalence of Chagas disease over this period.

*Results*: A total of 487 hospitalizations of Chagas disease were identified, corresponding to 3.7 per million hospitalizations over the study period. The rate statistically increased from 1.6 per million in 2002 to 7.6 per million hospitalizations in 2017. Chagas was most prevalent among older women, Hispanics and those in the highest zip income bracket. The in-hospital mortality rate was about 10 times greater among women with Chagas compared to those without the condition (3.1% versus 0.3%), and the condition tended to be clustered in women treated at large, urban teaching hospitals in the Northeastern region of the US.

*Conclusion:* Chagas disease diagnosis appears to be increasing among hospitalized women of reproductive age in the US with a 10-fold elevated risk of mortality.

© 2020 Published by Elsevier Ltd on behalf of World Federation of Parasitologists. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

https://doi.org/10.1016/j.parepi.2020.e00167

<sup>\*</sup> Corresponding author at: Center of Excellence in Health Equity, Training, and Research, Baylor College of Medicine, 3701 Kirby Drive, Houston, TX 77098, USA. *E-mail address:* deepa.dongarwar@bcm.edu. (D. Dongarwar).

<sup>2405-6731/© 2020</sup> Published by Elsevier Ltd on behalf of World Federation of Parasitologists. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

## 1. Introduction

American trypanosomiasis, commonly referred to as Chagas disease, is a tropical infection caused by the protozoan, *Trypanosoma cruzi* (*T. cruzi*) (CDC - Chagas Disease - Epidemiology and Risk Factors, 2020). Its primary vectors are insects belonging to the *Reduviidae* family, or "kissing" bugs, and the disease is typically spread via insect bites. While Chagas disease is found almost exclusively in the Western Hemisphere within rural areas of South America, Central America, and Mexico, more than 8 million people are presumed to be affected worldwide resulting in more than 10,000 deaths annually (CDC - Chagas Disease - Epidemiology and Risk Factors, 2020; WHO, 2020a). Because of this, Chagas has been designated a neglected disease by the World Health Organization, and as a major public health concern (WHO, 2020b).

Within the United States, more than 230,000 individuals are diagnosed with Chagas disease (Manne-Goehler et al., 2016). This figure, however, is just an approximation and likely underestimates the true burden of the condition. Because American trypanosomiasis is not endemic within humans in the US, its incidence is most commonly linked to global migration and travel. This could lead to underestimation of the true disease prevalence as a result of the incomplete ascertainment of cases within the undocumented immigrant populations, many of whom arrive from areas where American trypanosomiasis is endemic. Additionally, due to low clinical suspicion of the disease by healthcare providers in the US, under-diagnosis in clinical settings could contribute to the overall prevalence estimates.

Among those infected in the US, approximately 10% are women of reproductive age (CDC - Chagas Disease - Congenital Chagas Disease, 2020). While Chagas disease is primarily a vector-borne illness and transmitted via insect bites, vertical transmission is possible and can result in congenital infection in newborns. This occurs in up to 5% of infants born to mothers with American trypanosomiasis, and the infection commonly persists with severe clinical symptoms presenting later in life (CDC - Chagas Disease - Congenital Chagas Disease, 2020). Focusing preventive measures on women of reproductive age presents an opportunity to reduce the prevalence of Chagas disease in the newborn.

Data on the prevalence and risk factors of Chagas disease among women of reproductive age in the United States are scanty. Literature shows that those from poorer regions of Latin America are most commonly affected (Moncayo and Silveira, 2017), but similar factors have been sparsely studied within North America. Further, there is limited epidemiologic data regarding the incidence and prevalence of American trypanosomiasis in general over time. The objective of this study is to fill these gaps and explore trends and associated characteristics of Chagas disease among women of reproductive age in the United States.

## 2. Methods

Our analysis covered the period from January 1, 2002 through December 31, 2017 using cross-sectional data from the Nationwide Inpatient Sample (NIS). The NIS, made available by the Healthcare Cost and Utilization Project (HCUP), currently constitutes the largest all-payer, publicly available inpatient database in the US (HCUP-US NIS Overview, 2020). Each year, to create the sample of inpatient hospitalizations, HCUP employs a two-stage cluster sampling design that first stratifies all nonfederal community hospitals from participating states by five major hospital characteristics: rural/urban location, number of beds, geographic region, teaching status, and ownership. Then, from each unique stratum, 20% of hospitals are selected using a systematic random sampling technique. NIS employed International Classification of Disease, Ninth revision, Clinical Modification (ICD-9-CM) till third quarter of 2015 and ICD 10-CM from October 1st 2015 till date to code the diagnoses and procedures associated with each hospitalization.

We restricted the analysis to women of reproductive age (i.e.15–49 years) and identified whether or not they had Chagas disease using ICD-9-CM codes '086.0', '086.1' and '086.2'; and ICD-10 codes beginning with 'B57'. Covariates included in the study were age, which was sub-grouped as follows: 15–24 years, 25–34 years, and 35–49 years. Race/ethnicity was available in the dataset as Non-Hispanic White (NH-White), Non-Hispanic Black (NH-Black), Hispanic and NH-Others. Discharge status was recategorized as routine, transfer, died, discharged against medical advice (DAMA) and others. Socio-economic level based on zip codes was categorized into quartiles. Primary Payer was designated as Medicare, Medicaid, private insurance, self-pay and others. Hospital regions included Northeast, Midwest, South, and West. Hospital location and type were available as rural, urban-teaching, urban non-teaching; while bed size was defined as small, medium, and large. HCUP publishing guidelines recommends suppressing the report of sample sizes less than or equal to 10, for privacy protections. Also, missing information was not reported to prevent inference based on small sample sizes.

We calculated the proportion and prevalence of Chagas across socio-demographic and hospitalization characteristics. Next, we used Joinpoint regression (Joinpoint Regression Program, 2019) to estimate and describe temporal changes in the rates of Chagas during the 16-year study period. Joinpoint regression is valuable in identifying key periods in time marking changes in the rate of events over time. The iterative model-building process was initiated by fitting the annual rate data to a straight line with no joinpoints, which assumed a single trend best described the data. Then a joinpoint – reflecting a change in the trend – was added to the model and a Monte Carlo permutation test assessed the improvement in model fit. The process continued until a final model with an optimal (best-fitting) number of joinpoints was selected, with each joinpoint indicating a change in the trend, and an average annual percent change (AAPC) was then estimated to describe how the rate changed over the entire study period. After removing the missing information from the covariates, survey logistic regression models were run to compute unadjusted and adjusted odds ratios for the association between our selected socio-demographic features, hospital characteristics, and Chagas. All tests of hypotheses were two-tailed with a type 1 error rate set at 5%. Data analyses were performed using R

(version 3·6·1) and RStudio (Version 1·1·423). The Institutional Review Board of Baylor College of Medicine designated our study as exempt since we utilized publicly available, de-identified data for the study.

## 3. Results

Our analysis included a total of 131,529,240 hospitalizations for women of reproductive age in the US from 2002 to 2017. Among these, a total of 487 admissions had an associated diagnosis of Chagas disease, yielding a prevalence of 3.7 cases per million hospitalizations over the study duration. Socio-demographic characteristics for women both with and without Chagas disease are shown in Table 1. The proportion of Chagas disease among hospitalized women increased with age as only 6.8% of cases were in women aged 15–24 years while 76.6% of women with Chagas disease were aged 35–49 years. The prevalence of Chagas also followed a dose-response curve with age and was more than 7 times greater among the oldest reproductive aged women (7.58 cases/million) than in the youngest (1.03 cases/million). Hispanic women comprised the greatest proportion of Chagas disease patients accounting for 75.8% of cases, while NH-White and NH-Black women accounted for 10.5% or less. About 84.2% of those with Chagas disease were discharged routinely. However, the prevalence of Chagas disease was highest among those who died during hospital admission (35.36 cases/million). We also noted a greater frequency of Chagas disease among women

Table 1

Socio-demographic characteristics of Chagas hospitalizations among women of reproductive age.

$ \frac{No}{n} \frac{Ves}{N} \frac{Ves}{n} \frac{Ves}{N} \frac{Ves}{N} error error million hospitalizations of the second seco$		Chagas				
$n$ $\chi$ $n$ $\chi$ Age15–24 years32,061,48224.4%336.8%1.0325–34 years50,228,08438.2%8116.6%1.6135–49 years40,228,28737.4%37.376.6%7.58Race19307,3681.47%Suppressed*1NH-White19.307,3681.47%Suppressed*1Hispanic19.307,3681.47%Suppressed*1Other9.31,40,247.1%4910.1%5.26Missing21,689,67916.5%Suppressed*1Discharge status120,703,76191.8%41084.2%3.40Transfer4,147,3703.2%Suppressed*1Didd424,1710.3%153.1%35.36Didd424,1710.3%153.1%35.36Didd424,1710.3%153.1%32.0Didd424,1710.3%153.1%3.20Didd424,1710.3%153.1%3.20Didd424,1710.3%153.1%3.20Didd424,1710.3%153.1%3.20Didd424,1710.3%153.1%3.20Didd424,1710.3%153.1%3.10Didd424,1710.3%153.1%3.10Didd424,1710.3%153.1%3.10Didd424,1710.3%15 <td< th=""><th></th><th>No</th><th colspan="2">No</th><th></th><th>Prevalence per million hospitalizations</th></td<>		No	No			Prevalence per million hospitalizations
Age15-24 years32.061,48224.42336.8%1.0325-34 years30.228,98438.2%811.66%1.6133-49 years49.238.20737.4%37.376.6%7.58Race1.93.54.115.2%36.9%7.58NiH-Black19.935,92.115.2%36.9%7.5%18.51Other9.314.0247.1%4910.1%5.26Discharge status1.65%Suppressed35.36Discharge status120.703,7619.18%4108.2%35.36Discharge status1.11%Suppressed35.36Discharge status1.474,3703.2%Suppressed35.36Discharge status3.6%5.310.9%1.1.12Discharge status3.6%5.31.0%3.2%Zip income quartile2.404,53.27018.3%7916.2%3.28Jord quartile2.443,5581.1%543.2%2.01Highest quartile9.206,6777.2%3.5%2.20Primary paver1.9%1.5%1.50Private insurance5.526,59043.0%851.5%4.32Other insurance5.526,59043.0%851.5%4.32Private insurance5.526,59043.0%851.5%4.32Missing1.198,7631.7%1.502.4%3.6%2.6%Midicard0.009,8110.5% <th></th> <th>n</th> <th>%</th> <th>n</th> <th>%</th> <th></th>		n	%	n	%	
1-5-24 years 2-3-4 years 3-49 years32,061,482 22,83,28733,36.8% 33,40 23,28,28716.6% 37,801.61 37,80Race <td< td=""><td>Age</td><td></td><td></td><td></td><td></td><td></td></td<>	Age					
25-34 years50.228,98438.2%8116.6%1.6135-49 years49.238,28737.4%37.07.68%7.58Rac19.230,29614.7%Suppressed*1NH-Mlack19.307,96814.7%Suppressed*1Hispanic19.935,42115.2%3697.5%18.51Other9.314.0247.1%4910.1%5.26Discharge status12.093,76191.8%4108.2%3.66Transfer12.0703,76191.8%4108.2%3.66Ded42.417.170.3%153.1%3.56DAMA4.147.3703.2%Suppressed*1Other4.765.7383.6%5310.9%11.12Jip income quartile24.435.8%17.1%459.2%2.01Zip income quartile24.435.8%17.1%459.2%2.01Hispest quartile9.30,705424.3%1102.6%3.28Yindicard9.526,6077.2%3.5%4.323.67Medicard0.069,81130.5%17.5%3.5%4.32Primary payer19.9%11.9%2.1%3.5%3.63Highest quartile9.526,60943.0%1515.5%4.32Private insurance56.26,99043.0%1515.6%3.31Other missing19.443,15012.8%1515.63.31Highest quartile region19.43,13110.2%12.2%	15–24 years	32,061,482	24.4%	33	6.8%	1.03
33-9 years49,23,28737.4%37.376.6%7.5.8RaceNH-White61,281,66046.6%5110.5%0.83NH-Black19,307,96814.7%Suppressed*1Hispanic19,307,96814.7%4910.1%5.26Other9,314,0247.1%4910.1%5.26Discharge status12,079,76115.8%Suppressed*1Routine10,073,76191.8%Suppressed*3.40Transfer12,079,7710.3%5310.1%3.53DAMA1,431,1171.1%Suppressed*1Other4,765,7383.6%5310.1%3.28Other56,5950.0%Suppressed*1Lowest quartile24,053,27018.3%7916.2%3.282nd quartile24,053,27018.3%7916.2%3.20Prinary payer19,406,67714.8%1543.1%794Highest quartile19,406,67714.8%1543.1%794Medicaré0,006,8110.5%17.33.5%4.32Prinary payer11,1871.1%1.503.2%1.61Medicaré9,526,4077.2%3.54.32Private insurance56,526,904.30%1521.50Self-pay0,11,987,2339.1%1.554.32Other/missing13,183,1171.1%1.2%1.94Medicaré9,26,4077.2%3	25–34 years	50,228,984	38.2%	81	16.6%	1.61
RaceNH-White[61,281,6604.64%Suppressed'NH-Black19.937,98014.7%Suppressed'Hispanic19.935,42115.2%3697.5%8.261Other9.314,0247.1%3697.8%8.261Discharge status15.2%Suppressed'-Routine120.703,7619.1%4108.42%3.636Discharge statusOther4.147,3703.2%Suppressed'-Died4.24,1710.3%153.1%35.36Other4.765,7383.6%5010.9%11.12Diado quartile4.765,7383.6%5310.9%11.12Other quartile2.443,5832.16%918.7%3.20Jard quartile19.406,67714.8%1543.1%3.20Indige quartile19.406,67714.8%1543.6%3.20Indige quartile9.526,4077.2%1543.6314.1%Missing3.72.09,7642.3%17.1%4.5%3.64Missing19.406,67714.8%1543.1%3.64PrimareMedicaid0.966,8113.05%17.5%4.32Primare1.5%3.64-Medicaid0.968,8110.05%17.5%4.53Other missing1.341,8171.1028.5%1.5%3.16Midwes	35-49 years	49,238,287	37.4%	373	76.6%	7.58
NH-White61,231,66046.6%5110.5%0.83NH-Black19,307,96814,2%36975.8%18.51Hispanic9,314,0247.1%4910.1%5.26Other9,14,0247.1%4910.1%5.26Discharge status21,689,67984714910.1%5.26Brown and an and and	Race					
NH-Black19.037.96814.7%Suppressed*Hispanic19.037.4011.1%4910.1%5.26Other9.314.0247.1%4910.1%5.26Discharge status21.69.07010.5%Suppressed*-Routine12.0703.76191.8%41084.2%3.40Transfer4.147.3703.2%Suppressed*-Died424.1710.3%153.1%3.536DAMA1.431.1171.1%Suppressed*-Other4.765.7383.6%5310.9%11.12Missing55.950.0%Suppressed*-Zip income quartile24.43.58311.6%918.7%3.202nd quartile24.43.35817.1%459.2%2.01Highest quartile19.406.67714.8%1543.16%7.94Missing7.209.702.8%1192.4.4%3.20Primar Insurance55.55.6943.0%153.67Medicaid40.09.8113.0.5%17.5%6.31Other/missing1.9.87.2339.1%1102.6%9.18Other/missing1.9.87.2339.1%1102.6%9.18Other/missing2.8.43.15071.7.8%1.3.6%3.1Hospital edi2.4.31.1071.7.8%3.13.1Other/missing3.0.9.1110.2%8.71.5.0South5.1.89.693.8.%1.521.5.6M	NH-White	61,281,660	46.6%	51	10.5%	0.83
Hispanic1935,42115.2%66975.8%18.51Other9.314.02771.1%4910.1%5.26Missing21.689,67916.5%Suppressed-Bicharge status120.703,76191.8%41084.2%3.40Transfer147.3703.2%Suppressed-Died424.1710.3%153.1%356DAMA1.431,1171.1%Suppressed-Other4.765,7383.6%5310.9%1.12Missing56.59suppressedZip income quartile28.415,68321.6%911.8.7%3.202nd quartile24.403,327018.3%7916.2%3.283rd quartile24.403,327018.3%7916.2%3.283rd quartile24.403,327018.3%7916.2%3.283rd quartile24.403,327018.3%7916.2%3.26Primary payer24.43,35817.1%459.2%2.01Mising37.209,7642.8.3%1543.167.94Mising19.406,6771.2%35.5%4.32Primary payerMedicare9.562,6077.2%35.5%4.32Medicare56.566,904.3%17.335.5%4.32Medicare9.341,831130.5%17.5%6.33Hospital regionNortheast <td< td=""><td>NH-Black</td><td>19,307,968</td><td>14.7%</td><td>Suppressed</td><td>a</td><td></td></td<>	NH-Black	19,307,968	14.7%	Suppressed	a	
Other         9314,024         7,1%         49         10.1%         5.26           Missing         21,689,679         16.5%         Suppressed*         -           Routine         120,703,761         91.8%         410         84.2%         3.40           Transfer         14147,370         03.8%         15         3.1%         35.36           Ded         424,171         0.3%         5         3         0.9%         11.12           Other         4,765,738         3.6%         5         10.9%         11.12           Missing         56.595         0.0%         Suppressed*         2.10           Missing         22,443,588         21.6%         91         18.7%         3.20           216 quartile         22,443,538         1.54         15.4         3.16         7.94           Highest quartile         22,443,538         1.54         31.6%         7.94         3.20           Primary payer         14.96,677         14.8%         154         31.6%         7.94           Medicaid         40.069,811         30.5%         17.5%         4.32           Primary payer         11.987,233         9.1%         110         2.26         9.16	Hispanic	19,935,421	15.2%	369	75.8%	18.51
Missing Discharge status18.89,67916.5%Suppressed"Discharge status120.703,76191.8%41084.2%3.40Transfer4147,3703.2%Suppressed"5.5Died424,1711.1%Suppressed"5.5DAMA1431,1171.1%Suppressed"1.12Other4.765,7383.6%5310.9%1.12Jincome quartile2.6,5320.0%Suppressed"2.2%Ilowest quartile2.4,633,27018.3%7916.2%3.282nd quartile2.4,633,27018.3%7916.2%3.203rd quartile1.9,406,67714.8%1543.16%7.94Missing7.29,7642.8.3%1192.4.4%3.20Primary payer19.406,67714.8%1543.16%7.94Medicare9.526,4077.2%357.2%3.67Medicare9.526,4077.2%351.503.16Self-pay1.3,817.311.102.2.6%9.183.16Other, missing1.3,418,11571.34.37%9.093.11Hospital region2.4.339.1%1.123.31Hospital region2.4.343.212.973.31West2.8.45,7662.1.8%59.13.31Hospital bed size3.515.513.513.51Midwest2.8.45,7569.633.376.2%4.25Jing Lange7.9.2%	Other	9,314,024	7.1%	49	10.1%	5.26
Discharge statusUU84.2%3.40Routine12.0703,76191.8%41084.2%3.40Transfer4.147.3703.2%Suppressed*UDied424.1710.3%153.1%3.56DAMA1.431.1171.1%Suppressed*UOther4.765.7383.6%5310.9%11.12Missing56.5950.0%Superssed*UUZip income quartile24.05.27018.3%7916.2%3.283rd quartile24.043.35817.1%459.2%2.01Highest quartile19.406.67714.8%1543.1.6%3.20Primary payer37.20.76428.3%1192.4.43.20Primary payerUS5.5%17.33.5.5%4.32Private insurance56.526.99043.0%8517.5%4.32Private insurance19.88/110.05%17.33.55%4.32Private insurance56.526.99043.0%8517.5%6.33Other/missing1.418.31110.2%8517.5%6.33Hospital region11.899693.89%1523.163.16West2.805.91021.3%9319.1%3.31Hospital bed size1523.1%3.13.1Midwest3.604.5262.6%9218.9%2.63Jontal bed size11.899.693.3769.2%4.25Missing <t< td=""><td>Missing</td><td>21,689,679</td><td>16.5%</td><td>Suppressed</td><td>a</td><td></td></t<>	Missing	21,689,679	16.5%	Suppressed	a	
Routine         120,703,761         91.8%         410         84.2%         3.40           Transfer         4,147,370         3.2%         Suppressed*           Died         424,171         0.3%         15         3.1%         35.36           DAMA         1,431,117         1.1%         Suppressed*	Discharge status					
Transfer4,147,3703,2%Suppressed*Died424,1710.3%153,1%3,5.36DAMA1,431,1171.1%Suppressed*Other4,765,7383,6%5,091.1.2Missing56,5950.0%Suppressed*Zip income quartile24,053,27018,3%7916,2%3,282nd quartile24,043,32817,1%459,2%2,01Highest quartile24,043,35817,1%459,2%2,01Highest quartile29,09,76428,3%11924,4%3,20Primary payer8,5%155,5%3,67Medicaid40,069,81130,5%17,3%3,5%4,32Private insurance5,526,90043,0%851,5%1,50Self-pay11,98,7239,1%1102,6%9,18Other/missing1,3418,31110,2%851,5%6,33Hospital region1,418,31110,2%8,1%1,04South51,89,90021,3%362,972,97West28,059,91021,3%376,922,97West51,089,6533,87521,2%2,97West51,089,6533,876,2%1,04South51,899,693,89%15231,2%2,97Medicaid51,989,693,89%15231,2%2,97Medicaid51,989,693,89%15231,2%	Routine	120,703,761	91.8%	410	84.2%	3.40
Died         424,171         0.3%         1.8         3.1%         35.36           DAMA         1,431,117         1.1%         Suppressed*         11.12           Missing         56,595         0.0%         Suppressed*         11.12           Zip income quartile         24,053,270         18.3%         91         18.7%         3.20           2nd quartile         24,4053,270         18.3%         79         16.2%         3.28           3nd quartile         24,403,358         17.1%         45         9.2%         2.01           Highest quartile         19,406,677         14.8%         154         3.16%         7.94           Missing         37,209,764         28.3%         110         2.4%         3.20           Primary payer	Transfer	4,147,370	3.2%	Suppressed	а	
DAMA1,431,1171.1%Suppressed"Other4,765,7383.6%531.0.%11.12Other4,765,7383.6%531.0.%11.12Missing55.050.0%Suppressed"21.0Zip income quartile2.4.053,27018.3%7916.2%3.283rd quartile24.053,27018.3%7916.2%3.283rd quartile24.43,35817.1%45.43.16%7.94Missing37209,76428.3%11924.4%3.20Primary payer55.26,4077.2%35.54.32Medicarid40.069,81130.5%17.33.5.%4.32Private insurance56.52,69043.0%8517.5%1.50Self-pay11,987,2339.1%1102.6%9.18Other/missing14.18,11110.2%8517.5%6.33Hospital region17.8%21.3%9.09Midwest28,437.36621.9%306.2%1.04South51.189,96938.9%15231.2%2.97West28,059,01021.3%551.2.1%3.51Medium35,024,5266.6%9.28.9%2.63Large9.252,55860.3%33769.2%4.25Medium45,78430.3%Suppressed"1.1%Hospital location and teaching status43,78,943.6%6.37Missing43,50,	Died	424,171	0.3%	15	3.1%	35.36
Other         4,765,738         3.6%         53         10.9%         11.12           Missing         0.0%         0.0%         Suppressed*         Suppressed*           Lowest quartile         28,415,683         21.6%         91         18.7%         3.20           Ind quartile         24,053,270         18.3%         79         16.2%         3.28           3rd quartile         24,43,358         17.1%         45         9.2%         2.01           Highest quartile         19,406,677         14.8%         154         31.6%         7.94           Missing         3.72,09,764         28.3%         119         24.4%         3.0           Primary payer	DAMA	1,431,117	1.1%	Suppressed	a	
Missing56,5950.0%Suppressed²Zip income quartile28,415,68321.6%9118.7%3.20Lowest quartile24,053,27018.3%7916.2%3.283rd quartile22,443,35817.1%459.2%2.01Highest quartile19,406,67714.8%15431.6%7.94Missing37,209,76428.3%11924.4%3.20Primary payer55.5%4.323.67Medicaid40,069,81130.5%17335.5%4.32Private insurance56,526,99043.0%8517.5%1.50Self-pay19,87,2339.1%1102.6%9.18Other/missing13,418,31110.2%8517.5%6.33Hospital region17.8%30.66.34Wortheast28,447,36621.9%306.2%1.04South51,189,96938.9%15231.2%2.97West28,647,36621.9%306.2%1.04South50,29,91021.3%5912.1%3.51Hospital bed size3376.2%2.63Hospital location and teaching statu43,78,430.3%Suppressed*2.63Hospital location and teaching statu43,50,3946.8%6.93.67Hospital location and teaching statu43,50,3946.8%6.96.9Hospital location and teaching statu43,50,394 <td>Other</td> <td>4,765,738</td> <td>3.6%</td> <td>53</td> <td>10.9%</td> <td>11.12</td>	Other	4,765,738	3.6%	53	10.9%	11.12
Zip income quartile         Normal Stress           Lowest quartile         28,415,683         21.6%         91         18.7%         3.20           2nd quartile         24,053,270         18.3%         79         16.2%         3.28           3rd quartile         22,443,358         17.1%         45         9.2%         2.01           Highest quartile         19,406,677         14.8%         154         31.6%         7.94           Missing         37.209,764         28.3%         119         24.4%         3.20           Primary payer           35.5%         4.32           Medicare         9,526,407         7.2%         35         7.2%         3.67           Medicare         9,526,407         7.2%         35         7.2%         3.67           Private insurance         56,526,990         30.5%         17.5%         1.50           Self-pay         11,987,233         9.1%         110         22.6%         9.18           Other/missing         13,418,311         10.2%         85         17.5%         1.50           South         51,89,969         38.9%         152         31.2         2.97           West         28,65	Missing	56,595	0.0%	Suppressed	a	
Lowest quartile28,415,68321.6%9118.7%3.202nd quartile24,053,27018.3%7916.2%3.283rd quartile24,043,35817.1%459.2%2.01Highest quartile19,406,67714.8%15431.6%7.94Missing37,209,76428.3%11924.4%3.20Primary payer557.2%3.67Medicaid40,069,81130.5%17.335.5%4.32Private insurance56,526,99043.0%8517.5%1.50Self-pay11,987,2339.1%1102.2.6%9.18Other/missing13,418,31110.2%851.7.5%6.33Hospital region23,431,50717.8%21343.7%9.09Midwest28,847,36621.9%306.2%1.04South21,89,991021.3%9319.1%3.31Hospital bed size12.8%5912.1%3.51Small16,793,82512.8%33769.2%4.25Missing43,503436.8%469.4%0.95Hospital location and teaching status14,315,38810.9%Suppressed*5Hospital location and teaching status14,315,38810.9%Suppressed*5Missing45,78430.3%Suppressed*553.7Missing68,05,12652.0%43685.5%6.37Missin	Zip income quartile					
2nd quartile         24,053,270         18.3%         79         16.2%         3.28           3rd quartile         22,443,358         17.1%         45         9.2%         2.01           Highest quartile         19,406,677         14.8%         154         31.6%         7.94           Missing         37,209,764         28.3%         119         24.4%         3.20           Primary payer           35.5%         4.32           Medicarid         40.069,811         30.5%         17.3         35.5%         4.32           Private insurance         56,526,990         43.0%         85         17.5%         6.63           Other/missing         11,987,233         9.1%         110         22.6%         9.18           Other/missing         13,418,311         10.2%         85         17.5%         6.33           Hospital region          23,431,507         17.8%         213         43.7%         9.09           Midwest         28,847,366         21.9%         30         6.2%         1.04           South         59,9010         21.3%         93         19.1%         3.31           Hospital region         16,793,825         26.6	Lowest quartile	28,415,683	21.6%	91	18.7%	3.20
3rd quartile         22,443,358         17.1%         45         9.2%         2.01           Highest quartile         19,406,677         14.8%         154         31.6%         7.94           Missing         37,009,764         28.3%         119         24.4%         3.20           Primary payer	2nd quartile	24,053,270	18.3%	79	16.2%	3.28
Highest quartile19,406,67714.8%15431.6%7.94Missing28.3%11924.4%3.20Primary payer	3rd quartile	22,443,358	17.1%	45	9.2%	2.01
Missing37,209,76428.3%11924.4%3.20Primary payer	Highest quartile	19,406,677	14.8%	154	31.6%	7.94
Primary payer         Verticate         Sold (AUT)         7.2%         Sold (AUT)         7.2%         Sold (AUT)	Missing	37,209,764	28.3%	119	24.4%	3.20
Medicare         9,526,407         7.2%         35         7.2%         3.67           Medicaid         40,069,811         30.5%         173         35.5%         4.32           Private insurance         56,526,990         43.0%         85         17.5%         1.50           Self-pay         11,987,233         9.1%         100         22.6%         9.18           Other/missing         13,418,311         10.2%         85         17.5%         6.33           Hospital region         23,431,507         17.8%         213         43.7%         9.09           Midwest         28,847,366         21.9%         30         6.2%         1.04           South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         93         19.1%         3.31           Hospital bed size	Primary payer					
Medicaid         40,069,811         30.5%         173         35.5%         4.32           Private insurance         56,526,990         43.0%         85         17.5%         1.50           Self-pay         11,987,233         9.1%         110         22.6%         9.18           Other/missing         13,418,311         10.2%         85         17.5%         6.33           Hospital region	Medicare	9,526,407	7.2%	35	7.2%	3.67
Private insurance         56,526,990         43.0%         85         17.5%         1.50           Self-pay         11,987,233         9,1%         110         22.6%         9,18           Other/missing         13,418,311         10.2%         85         1.75%         6.33           Hospital region	Medicaid	40,069,811	30.5%	173	35.5%	4.32
Self-pay         11,987,233         9.1%         110         22.6%         9.18           Other/missing         13,418,311         10.2%         85         17.5%         6.33           Hospital region           43.7%         213         43.7%         9.09           Midwest         28,847,366         21.9%         30         6.2%         1.04           South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         93         19.1%         3.31           Hospital bed size           59         12.1%         3.51           Medium         16,793,825         12.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> 4.25           Hospital location and teaching status          Suppressed <sup>3</sup> 4.25           Iurban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Iurban teaching         68,405,126         52.0%         436         89.5%<	Private insurance	56,526,990	43.0%	85	17.5%	1.50
Other/missing         13,418,311         10.2%         85         17.5%         6.33           Hospital region	Self-pay	11,987,233	9.1%	110	22.6%	9.18
Hospital region           Northeast         23,431,507         17.8%         213         43.7%         9.09           Midwest         28,847,366         21.9%         30         6.2%         1.04           South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         9.09         19.1%         3.01           Hospital bed size          31.1%         3.01         3.01           Medium         35,024,526         26.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> -           Rural         14,315,388         10.9%         Suppressed <sup>3</sup> -           Ivban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>3</sup> -         -	Other/missing	13,418,311	10.2%	85	17.5%	6.33
Northeast         23,431,507         17.8%         213         43.7%         9.09           Midwest         28,847,366         21.9%         30         6.2%         1.04           South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         9.09         3.31           Hospital bed size         5         59         12.1%         3.51           Medium         16,793,825         12.8%         59         12.1%         3.51           Medium         35,024,526         26.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> -           Hospital location and teaching status         -         -         -           Rural         14,315,388         10.9%         Suppressed <sup>3</sup> -           Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843	Hospital region					
Midwest         28,847,366         21.9%         30         6.2%         1.04           South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         93         19.1%         3.31           Hospital bed size	Northeast	23,431,507	17.8%	213	43.7%	9.09
South         51,189,969         38.9%         152         31.2%         2.97           West         28,059,910         21.3%         93         19.1%         3.31           Hospital bed size           3.51         3.51           Small         16,793,825         12.8%         59         12.1%         3.51           Medium         35,024,526         26.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> 4.25           Hospital location and teaching status           Y         Y           Rural         14,315,388         10.9%         Suppressed <sup>3</sup> Y           Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>3</sup> Y         Y	Midwest	28,847,366	21.9%	30	6.2%	1.04
West         28,059,910         21.3%         93         19.1%         3.31           Hospital bed size	South	51,189,969	38.9%	152	31.2%	2.97
Hospital bed size       5       12.8%       59       12.1%       3.51         Medium       35,024,526       26.6%       92       18.9%       2.63         Large       79,252,558       60.3%       337       69.2%       4.25         Missing       457,843       0.3%       Suppressed <sup>3</sup> 5         Hospital location and teaching status       5       5       5       5         Ivan non-teaching       48,350,394       36.8%       46       9.4%       0.95         Urban teaching       68,405,126       52.0%       436       89.5%       6.37         Missing       457,843       0.3%       Suppressed <sup>3</sup> 5       5	West	28,059,910	21.3%	93	19.1%	3.31
Small         16,793,825         12.8%         59         12.1%         3.51           Medium         35,024,526         26.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> 5           Hospital location and teaching status         14,315,388         10.9%         Suppressed <sup>3</sup> Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>3</sup> 5.37         5.37	Hospital bed size					
Medium         35,024,526         26.6%         92         18.9%         2.63           Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>a</sup> -           Hospital location and teaching status         -         -         -           Rural         14,315,388         10.9%         Suppressed <sup>a</sup> -           Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>a</sup> -	Small	16,793,825	12.8%	59	12.1%	3.51
Large         79,252,558         60.3%         337         69.2%         4.25           Missing         457,843         0.3%         Suppressed <sup>3</sup> -         -	Medium	35,024,526	26.6%	92	18.9%	2.63
Missing         457,843         0.3%         Suppressed <sup>a</sup> Hospital location and teaching status	Large	79,252,558	60.3%	337	69.2%	4.25
Hospital location and teaching status         I         Number of teaching         I <thi< th="">         I         <thi< th=""></thi<></thi<>	Missing	457,843	0.3%	Suppressed	a	
Rural         14,315,388         10.9%         Suppressed <sup>a</sup> Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>a</sup> 50.5%         50.5%	Hospital location and teaching status					
Urban non-teaching         48,350,394         36.8%         46         9.4%         0.95           Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>a</sup>	Rural	14,315,388	10.9%	Suppressed	a	
Urban teaching         68,405,126         52.0%         436         89.5%         6.37           Missing         457,843         0.3%         Suppressed <sup>a</sup> 6.37	Urban non-teaching	48,350,394	36.8%	46	9.4%	0.95
Missing 457,843 0.3% Suppressed <sup>a</sup>	Urban teaching	68,405,126	52.0%	436	89.5%	6.37
	Missing	457,843	0.3%	Suppressed	a	

<sup>a</sup> Per HCUP publishing guidelines for privacy protections, we have suppressed cells containing values less than or equal to 10 and omitted missing data to prevent inference of these values.

who self-paid for their medical care (9.18 per million), than among those utilizing private insurance (1.50/million), Medicare (3.67/million), or Medicaid (4.32/million). With respect to zip income quartiles, the greatest proportion and prevalence of Chagas was observed in women within the highest income quartile and accounted for almost one-third of all cases of Chagas disease. The majority of women with Chagas disease were treated in large, urban teaching hospitals. Hospitals in the Northeast had the fewest admissions overall, but had the greatest number of Chagas disease cases (n = 213) and highest prevalence (9.09/million).

Fig. 1 depicts an increasing trend in the rates of Chagas disease among hospitalized women of reproductive age in the US. The rate of diagnosis of Chagas increased from 1.60 per million hospitalizations in 2002 to 7.59 per million hospitalizations in 2017, yielding a positive average annual percent change (AAPC) of 6.8% [95% CI 1.9–12.0] over the study period, which was statistically significant.

Adjusted survey logistic regression revealed a significant association between age and diagnosis of Chagas disease in both unadjusted and adjusted models as seen in Table 2. Women aged 35–49 years had the greatest adjusted odds for Chagas disease (aOR 9.39 [4.18–21.07], p < .0001). Compared to NH-Whites, the likelihood of Chagas disease was more than 25-fold among Hispanic women (aOR 25.85 [5.64–118.5), p < .0001]. In-hospital death was strongly associated with Chagas disease as women who died in hospital were approximately seven times as likely to have been diagnosed with Chagas disease compared to women who were routinely discharged. Women in the lowest, second, and third zip income quartiles were protected and had lower adjusted odds for Chagas disease diagnosis compared to those in the highest zip income quartile. Region of residence was predictive of Chagas disease diagnosis, and women from the South and West regions experienced about 50% and 65% lower adjusted odds for Chagas disease diagnosis, respectively, than those in the Northeast. By contrast, there was no significant association between Chagas disease and primary payer for hospital visit, hospital size, location or teaching status in our adjusted models.

## 4. Discussion

Significant findings of our analysis include evidence of a dose-response relationship between age and prevalence of Chagas disease among hospitalized women of reproductive age. Hispanic women comprised the greatest proportion of hospitalized women with American trypanosomiasis and had exceedingly high odds of being diagnosed with the infection compared to their NH-White and NH- Black counterparts. Women of higher socioeconomic status were also more likely to have the disease despite making up the smallest proportion of the study group. While hospital location was associated with diagnosis of Chagas disease, hospital size did not exhibit significant correlation. We also ascertained that there had been an increasing prevalence of Chagas disease over the past two decades which is likely to continue with increasing globalization.

The association between Hispanic ethnicity and diagnosis of American trypanosomiasis is unsurprising as migration from Latin America, where Chagas disease is endemic, has been considered the fundamental cause for the presence of the disease in the US.



Fig. 1. Joinpoint trends of rates of Chagas hospitalizations 2002-2017.

#### Table 2

Unadjusted and adjusted association between various socio-demographic and hospital characteristics and Chagas disease.

	Chagas					
	Unadjusted		Adjusted			
	OR(95%) <sup>a</sup>	p-Value	OR(95%) <sup>a</sup>	p-Value		
Age						
15-24 years	Reference		Reference			
25-34 years	1.56(0.63-3.83)	0.34	1.76(0.7-4.38)	0.23		
35–49 years	6.29(3.25-9.34)	< 0.0001	9.39(4.18-21.07)	< 0.0001		
Race						
NH-White	Reference		Reference			
NH-Black	0.54(0.08-3.65)	0.53	0.45(0.06-3.43)	0.44		
Hispanic	49.05(15.75-138.65)	< 0.0001	25.85(5.64-118.5)	< 0.0001		
Other	6.21(1.43-10.02)	0.01	5.16(1.07-24.94)	0.04		
Discharge status						
Routine	Reference		Reference			
Transfer	0.71(0.17-2.89)	0.63	0.74(0.17-3.17)	< 0.0001		
Died	10.42(3.27-33.15)	< 0.0001	6.68(2.03-22.01)	< 0.0001		
Other	3.27(1.60-6.66)	< 0.0001	2.61(1.32-5.17)	0.01		
Zip income quartile						
Highest quartile	Reference		Reference			
Lowest quartile	0.41(0.20-0.84)	0.01	0.25(0.12-0.52)	< 0.0001		
2nd quartile	0.41(0.19-0.89)	0.02	0.37(0.18-0.78)	0.01		
3rd quartile	0.25(0.11-0.57)	< 0.0001	0.24(0.11-0.52)	< 0.0001		
Primary payer						
Medicare	Reference		Reference			
Medicaid	1.17(0.48-2.88)	0.73	1.2(0.47-3.11)	0.7		
Private Insurance	0.41(0.16-1.03)	0.06	0.5(0.19-1.33)	0.17		
Self-Pay	2.48(0.93-6.66)	0.07	2.36(0.86-6.49)	0.1		
Other	1.72(0.70-4.21)	0.23	1.49(0.59-3.76)	0.39		
Hospital region						
Northeast	Reference		Reference			
Midwest	0.11(0.04-0.29)	<0.0001	0.41(0.16-1.10)	0.08		
South	0.33(0.16-0.66)	<0.0001	0.49(0.24-0.98)	0.04		
West	0.36(0.18-0.75)	0.01	0.34(0.17-0.68)	< 0.0001		
Hospital bed size						
Small	Reference		Reference			
Medium	0.75(0.29-1.94)	0.55	0.73(0.28-1.94)	0.53		
Large	1.21(0.49-3.02)	0.68	1.32(0.52-3.37)	0.56		
Hospital location and teaching status						
Rural	Reference		Reference			
Urban non-teaching	2.74(0.35-8.45)	0.34	1.16(0.15-9.25)	0.89		
Urban teaching	8.26(2.51-13.29)	<0.0001	5.76(0.76-43.54)	0.09		

<sup>a</sup> OR: Odds Ratio, CI: Confidence Interval.

*Goehler* et al also reinforce this linkage, and did demonstrate that states with the greatest distribution of Latin American immigrants have higher rates of Chagas disease (Manne-Goehler et al., 2016; Bern and Montgomery, 2009). Chagas disease is a chronic illness and many who travel to the United States are long term carriers. The early exposure to the bite of a kissing bug compounded with migration from an endemic region may contribute to the association between age and race/ethnicity with Chagas disease observed in our study.

While our findings indicate that there has been an increase in Chagas disease within the US, others showed evidence of decreasing trypanosomiasis cases within Latin America. *Perez-Molina* et al reported that the prevalence of Chagas disease had decreased by more than 60% in endemic Latin American countries since 1980 (Pérez-Molina and Molina, 2018). Improvement in reducing the prevalence of Chagas was achieved through public awareness and health measures to try and minimize vector transmission, measures not yet established in the US (Coura et al., 2014; Coura, 2013). Instead, there have been few initiatives to assess for Chagas disease, and even then, the focus has been on transmission via blood donation (Bennett et al., 2018). Meta-analyses and prior studies also note that living in a rural area is a risk factor for Chagas disease, (Roca et al., 2011; Conners et al., 2016; Custer et al., 2012) whereas rural hospitals in our study population had the lowest prevalence of trypanosomiasis. These differences may be ascribed to mode of transmission in the US being through migration, especially to urban areas. Furthermore, the kissing bug thrives in palm thatched roofs and rural, adobe housing buildings that are common in endemic regions, but not in the US (Rozendaal and World Health Organization, 1997).

Strengths of our study include a large sample size and nationwide data both of which limit the amount of geographic or regional selection bias in our analysis. However, our study populations were derived from inpatient data and are thus inherently more sick or likely to have additional comorbidities compared to the general population. Additionally, we did take into account in our analysis the contribution of immigration status, duration of residence in the US, or recent travel to endemic regions since this information was not available in the NIS. Our study revealed that Chagas disease is an important chronic condition among women of reproductive age in the United States. The prevalence reported in the study might represent an underestimate because the condition is not routinely investigated in clinical settings among at-risk populations. The persistently increasing prevalence of Chagas disease among women of reproductive age calls for additional preventive measures and clinical initiatives in order to reduce the burden of this neglected tropical disease in the US.

## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgments

Research funding support was provided by the US Department of Health and Human Services, Health Resources and Services Administration for the Maternal and Child Health Pipeline Training Program: TSU-BCM Maternal and Child Health Student Training for Academic Readiness and Success (MCH STARS) Undergraduate Fellowship Program, Grant no. T16MC29831.

#### References

Bennett, C., Straily, A., Haselow, D., et al., 2018. Chagas disease surveillance activities – Seven States, 2017. MMWR Morb. Mortal. Wkly. Rep. 67 (26), 738–741. https://doi.org/10.15585/mmwr.mm6726a2.

Bern, C., Montgomery, S.P., 2009. An estimate of the burden of Chagas disease in the United States. Clin. Infect. Dis. 49 (5), e52–e54. https://doi.org/10.1086/605091. CDC - Chagas Disease - Congenital Chagas Disease. https://www.cdc.gov/parasites/chagas/health\_professionals/congenital\_chagas.html. Accessed February 27, 2020. CDC - Chagas Disease - Epidemiology & Risk Factors. https://www.cdc.gov/parasites/chagas/epi.html. Accessed February 27, 2020.

Conners, E.E., Vinetz, J.M., Weeks, J.R., Brouwer, K.C., 2016. A global systematic review of Chagas disease prevalence among migrants. Acta Trop. 156, 68–78. https://doi. org/10.1016/j.actatropica.2016.01.002.

Coura, J.R., 2013. Chagas disease: control, elimination and eradication. Is it possible? Mem. Inst. Oswaldo Cruz 108 (8), 962–967. https://doi.org/10.1590/0074-0276130565.

Coura, J.R., Viñas, P.A., Junqueira, A.C.V., 2014. Ecoepidemiology, short history and control of chagas disease in the endemic countries and the new challenge for nonendemic countries. Mem. Inst. Oswaldo Cruz 109 (7), 856–862. https://doi.org/10.1590/0074-0276140236.

Custer, B., Agapova, M., Bruhn, R., et al., 2012. Epidemiologic and laboratory findings from 3 years of testing United States blood donors for Trypanosoma cruzi. Transfusion 52 (9), 1901–1911. https://doi.org/10.1111/j.1537-2995.2012.03569.x.

HCUP-US NIS Overview. https://www.hcup-us.ahrq.gov/nisoverview.jsp#data. Accessed February 11, 2020, 2020.

Joinpoint Regression Program, 2019. https://surveillance.cancer.gov/joinpoint/.

Manne-Goehler, J., Umeh, C.A., Montgomery, S.P., Wirtz, V.J., 2016. Estimating the burden of Chagas disease in the United States. PLoS Negl. Trop. Dis. 10 (11). https://doi.org/10.1371/journal.pntd.0005033.

Moncayo, A., Silveira, A.C., 2017. Current epidemiological trends of Chagas disease in Latin America and future challenges: epidemiology, surveillance, and health policies. American Trypanosomiasis Chagas Disease: One Hundred Years of Research, Second edition Elsevier Inc, pp. 59–88 https://doi.org/10.1016/B978-0-12-801029-7.00004-6.

Pérez-Molina, J.A., Molina, I., 2018. Chagas disease. Lancet 391 (10115), 82-94. https://doi.org/10.1016/S0140-6736(17)31612-4.

Roca, C., Pinazo, M.J., López-Chejade, P., et al., 2011. Chagas disease among the latin american adult population attending in a primary care center in Barcelona, Spain. PLoS Negl. Trop. Dis. 5 (4). https://doi.org/10.1371/journal.pntd.0001135.

Rozendaal, J.A., 1997. Triatomine bugs. In: World Health Organization (Ed.), Vector Control: Methods for Use By Individuals and Communities. World Health Organization, Geneva https://www.who.int/water\_sanitation\_health/resources/vector210to222.pdf.

WHO | Epidemiology. https://www.who.int/chagas/epidemiology/en/. Accessed February 27, 2020a.

WHO | Neglected Tropical Diseases. https://www.who.int/neglected\_diseases/diseases/en/. Accessed February 27, 2020b.