Published in final edited form as:
Lancet Infect Dis. 2013 April ; 13(4): 342–348. doi:10.1016/S1473-3099(13)70002-1.

Global economic burden of Chagas disease: a computational simulation model

Bruce Y Lee, MD, **Kristina M Bacon, MPH**, **Maria Elena Bottazzi, PhD**, and **Peter J Hotez, MD**
Public Health Computational and Operations Research, School of Medicine (B Y Lee MD, K M Bacon MPH), Department of Biomedical Informatics, School of Medicine (B Y Lee, K M Bacon), and Department of Epidemiology, Graduate School of Public Health (B Y Lee, K M Bacon), University of Pittsburgh, Pittsburgh, PA, USA; Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development, Houston, TX, USA (M E Bottazzi PhD, P J Hotez MD); and National School of Tropical Medicine, Baylor College of Medicine, Houston, TX, USA (M E Bottazzi, P J Hotez)

Summary

Background—As Chagas disease continues to expand beyond tropical and subtropical zones, a growing need exists to better understand its resulting economic burden to help guide stakeholders such as policy makers, funders, and product developers. We developed a Markov simulation model to estimate the global and regional health and economic burden of Chagas disease from the societal perspective.

Methods—Our Markov model structure had a 1 year cycle length and consisted of five states: acute disease, indeterminate disease, cardiomyopathy with or without congestive heart failure, megaviscera, and death. Major model parameter inputs, including the annual probabilities of transitioning from one state to another, and present case estimates for Chagas disease came from various sources, including WHO and other epidemiological and disease-surveillance-based reports. We calculated annual and lifetime health-care costs and disability-adjusted life-years (DALYs) for individuals, countries, and regions. We used a discount rate of 3% to adjust all costs and DALYs to present-day values.

Findings—On average, an infected individual incurs US$474 in health-care costs and 0·51 DALYs annually. Over his or her lifetime, an infected individual accrues an average net present value of $3456 and 3·57 DALYs. Globally, the annual burden is $627·46 million in health-care costs and 806 170 DALYs. The global net present value of currently infected individuals is $24·73 billion in health-care costs and 29 385 250 DALYs. Conversion of this burden into costs results in annual per-person costs of $4660 and lifetime per-person costs of $27 684. Global costs are $7·19 billion per year and $188·80 billion per lifetime. More than 10% of these costs emanate from the USA and Canada, where Chagas disease has not been traditionally endemic. A substantial proportion of the burden emerges from lost productivity from cardiovascular disease-induced early mortality.

Interpretation—The economic burden of Chagas disease is similar to or exceeds those of other prominent diseases globally (eg, rotavirus $2·0 billion, cervical cancer $4·7 billion) even in the

Correspondence to: Dr Bruce Y Lee, 200 Meyran Avenue, Suite 200, Pittsburgh, PA 15213, USA, byl1@pitt.edu.

Contributors
All authors have contributed substantially to the conceptualisation, design, analysis, interpretation, and drafting of the manuscript.

Conflicts of interest
We declare that we have no conflicts of interest.

See **Online** for appendix

USA (Lyme disease $2·5 billion), where Chagas disease has not been traditionally endemic, suggesting an economic argument for more attention and efforts towards control of Chagas disease.

Funding—Bill & Melinda Gates Foundation, the National Institute of General Medical Sciences Models of Infectious Disease Agent Study.

Introduction

As Chagas disease continues to expand beyond its traditional range of tropical and subtropical zones, including to regions of the southern USA and Europe, a growing need exists to better understand its resulting economic burden, which in turn could drive much decision making. Policy makers in affected countries must work out where Chagas disease should be placed on their lists of public health, medical, and scientific priorities. Without a comprehensive estimate of the costs associated with Chagas disease, many questions remain. For example, how should policy makers prioritise prevention, education, treatment, and control for Chagas disease? How much should be invested in development of new diagnostic, prevention, and treatment interventions?

Much of the true economic burden of Chagas disease can remain hidden for years. Although up to 10 million people might be currently infected with *Trypanosoma cruzi,* the causative agent for Chagas disease, many infected individuals can remain asymptomatic for more than a decade. Many such individuals will be unaware that they are infected if not tested—a procedure that is not routine in most locations. However, once clinical problems such as cardiomyopathy, heart failure, and megaviscera (ie, enlargement of the oesophagus or colon) occur, the accompanying health care, disability, and death can be very costly. Moreover, these clinical symptoms are chronic and progressive, accruing costs over many years. There is increasing awareness of widespread Chagas disease in pregnancy with vertical transmission and congenital infection.[1,2] Although a few studies have offered estimates of the annual disability-adjusted life-year (DALY) burden of Chagas disease,[3,4] capturing this hidden future effect will require computational modelling to forecast the downstream effects of currently asymptomatic infections. We aimed to develop a simulation model to estimate the global health and economic burden of Chagas disease from the societal perspective (a commonly used economic perspective that includes health-care costs plus cost related to work absenteeism).[5,6]

Methods

Model structure

We used TreeAge Pro (version 2009) and Microsoft Excel (version 2007) to develop a Markov computational simulation model, adapted from previously reported models.[5,6] Our Markov model structure had a 1 year cycle length (figure 1). Markov models are useful when a person has different time-dependent risks of undergoing different events or conditions over a long period, especially if the events or conditions can be easily separated into mutually exclusive states. A Markov model allows an individual to travel through many (hundreds) different paths, like a real person. Our major model parameter inputs, including the annual probabilities of transitioning from one state to another, came from various sources (appendix). The model consisted of five states: acute disease, indeterminate disease, cardiomyopathy with or without congestive heart failure, megaviscera, and death. Upon initial infection with *T cruzi*, up to 5% of individuals entered the symptomatic[7] state of acute disease, which can entail minor symptoms (eg, fever, rash, swelling at infection site, and nausea) or more severe outcomes (myocarditis or meningoencephalitis) that can lead to mortality.[7] For those surviving this acute state, symptoms resolved within the year (ie, one

cycle).[7] Treatment for this state included either benznidazole or nifurtimox. The remainder of initially infected individuals entered the asymptomatic indeterminate disease state, where they stayed for at least 9 years (ie, cycles) before having the possibility of transitioning to one of the symptomatic chronic disease states. Individuals treated while in this state accrued costs of drug treatment, diagnostics, and monitoring. Individuals in this state had a low risk of sudden death from asymptomatic cardiomyopathy (appendix). Individuals in the state of cardiomyopathy with or without congestive heart failure had probabilities of undergoing pacemaker implantation and a 4·0% annual probability of developing cardiomyopathy or congestive heart failure (appendix). Pacemaker implantation reduced mortality risk.[8] An individual could have a maximum of two pacemaker implantations, with the second being half as likely as the first.[9] Since therapeutics for Chagas disease are relatively ineffective in this state compared with the acute disease phase,[10] there was no possibility of cure. Megaviscera affected either the colon or oesophagus and could require surgery with an accompanying risk of mortality. Individuals could enter the absorptive state of death (ie, once an individual entered this state he or she left the model) from any of the above states. Death resulted from either Chagas-disease-related causes or other causes per age-based mortality.

We used a discount rate of 3% to adjust all costs and DALYs to present-day values.[11] Present case estimates for Chagas disease came from several sources[12–21] including WHO and other epidemiological and disease-surveillance-based reports. Compilation of countrywide infection data for Chagas disease resulted in an estimate of 7 968 094 (range 7 672 302–8 342 634) infections worldwide. On the basis of our extensive review of data sources from the scientific literature, 33 countries across four regions (Latin America, Europe, the USA and Canda, and Australia) reported Chagas disease cases within the past 15 years and were included in our analysis (appendix). We then grouped countries into quartiles on the basis of gross domestic product (GDP) per person: low income (GDP per person <US$5053), low middle income ($5053–11 171), high middle income ($11 172–39 615), and high income (>$39 615; appendix). We extrapolated available cost data to country quartiles for which no treatment-related costs were reported, assuming a linear relation between GDP per person and medical costs. We ran the model for each country quartile, generating the economic burden (in health-care costs, DALYs, and total costs, converting the DALYs into productivity losses) per case for each quartile group. Multiplying the cost per case—which was dependent upon which quartile the country was grouped in—by the number of cases yielded the economic burden (again in health-care costs, DALYs, and total costs) for each country. Our reported results include these numbers aggregated by region (Latin America, Europe, the USA and Canada, and Australia) and the world in addition to the highest country estimates for each region.

Each simulation run involved sending 1000 individuals through the model 1000 times for a total of 1 million realisations. Model validation involved comparison of generated model outputs—such as age at chronic disease onset, duration of chronic disease, and annual DALY burden estimates—to previously reported work.

Sensitivity analysis

Probabilistic sensitivity analyses simultaneously varied each input parameter (drawing from the distributions shown in the appendix). Additional one-way sensitivity analyses explored the effects of varying the parameters: treatment seeking probability (range ± 10% for non-surgical treatment; ±1% for surgical treatment), treatment costs (± 5%), disease-related work absenteeism durations (± 5%), and age at initial infection (0–50 years to account for all forms of transmission—eg, congenital, vector-borne, and transfusion-related). Annual cardiomyopathy risk was varied from values reported from endemic countries (2·0%) to

those reported from non-endemic countries (uniform distribution 0·47–0·7%) on the basis of a report that this risk might be lower in non-endemic countries.[20]

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

For an individual with chronic disease, our simulations generated an annual health-care cost of $383 (range $207–636) in Latin America, $1762 ($942–2971) in Europe, and $2162 ($1158–3628) in the USA, Canada, and Australia. The global weighted average was $474 ($222–914). Annual DALYs per individual with chronic disease were 0·51 (range 0·38–0·60). The discounted lifetime health-care cost for an individual with *T cruzi* infection was $2600 (range $1966–3034) in Latin America, $14 948 ($11 316–18 120) in Europe, and $19 514 ($14 980–23 378) in the USA, Canada, and Australia. The global weighted average was $3456 (range $2623–4060). Total lifetime DALYs lost per *T cruzi* infected individual was 3·57 (range 1·18–5·85).

The total annual cost to society (ie, health-care costs plus productivity losses) for an individual with chronic disease was $4059 (range $3569–4434) in Latin America, $13 580 ($11 340–15 003) in Europe, and $15 762 ($13 249–17 442) in the USA, Canada, and Australia. Globally, the weighted average of annual health-care and productivity cost for an individual with chronic disease was $4660 (range $3721–5649). As a result, the total discounted lifetime cost to society was $24 245 (range $11 425–34 868) in Latin America, $76 919 ($35 251–126 541) in Europe, and $91 531 (range: $42 992–149 333) in the USA, Canada, and Australia. This equates to a weighted average lifetime cost of $27 684 globally.

Figure 2 shows the effect of parameters varied in our sensitivity analysis on the annual health-care cost associated with each Chagas disease case. As expected, this cost was most sensitive to GDP per person followed by the likelihood of an affected individual seeking treatment. The level of endemicity (ie, endemic *vs* non-endemic) did not significantly affect the cost per case (data not shown).

The table shows the global and regional results from our simulations, for which the ranges shown are the variation resulting from our sensitivity analyses. Although the present annual burden is substantial, most of the Chagas disease burden remains to emerge in the future. Moreover, although most of the burden comes from Latin America, the portion from other regions is not insubstantial.

Burden varies substantially among different countries. In Latin America, the highest annual health-care costs were in Brazil (mean $129 211 209; range $48 983 985–253 405 222) followed by Argentina ($108 809 439; $41 249 671–213 393 871). In Europe, the greatest Chagas-disease-related health-care costs were in Spain, where an estimated $9 330 354 (range: $239 462–35 789 659) was spent annually, followed by the UK, which bore about a third of the cost of Spain (mean $3 018 583; range $547 341–7 678 066). In the USA, annual health-care costs equated to $118 179 806 (range $5 567 227–596 130 169), making it second only to Brazil in Chagas-disease-related health-care costs. Of the 33 countries included in our analysis, the highest annual DALY burden was in Brazil—196 206 (range 102 134–268 019)—which equated to nearly a quarter of the total morbidity burden globally. Brazil was followed by Argentina (mean 165 226; range 86 008–225 700) and Mexico (113 593; 59 130–155 169) in terms of DALY burden. *T cruzi* infections in the USA

resulted in an average of 27 590 (range 1798–99 210) DALYs accrued. This DALY burden was substantially greater than the most affected countries in Europe—Spain and the UK—which accrued a burden of 3488 (125–9349) and 1129 (287–2006) DALYs, respectively.

The net present value (NPV) of health-care costs attributable to Chagas disease occurring in the USA (mean $6 745 512 938; range $1 336 566 566–16 208 279 922) is greater than that of any other country, followed by Brazil ($4 543 280 792; $3 586 459 000–5 015 900 567) and Argentina ($3 825 920 667; $3 020 176 000–4 223 916 267). Spain bore the greatest burden in Europe, with a discounted mean of $449 270 628 ($46 871 060–839 386 990) in health-care costs over the lifetime of those infected. Latin America contained the three countries with the greatest DALY burden, which were Brazil (mean 7 215 856; range 2 444 838–11 336 192), Argentina (6 076 511; 2 058 811–9 546 267), and Mexico (4 177 602; 1 415 432–6 563 058). An average of 1 119 607 (range 82 517–4 462 907) DALYs were accrued in the USA. Spain had the greatest burden in Europe with an average of 137 569 (5455–415 066) DALYs.

When the entire burden was converted to monetary value ($US; table), in Latin America, the highest annual productivity costs were in Brazil (mean $1 760 332 111; range $1 108 725 750–2 271 608 055) followed by Argentina ($1 482 384 935; 933 663 789–1 912 933 099) and Mexico ($1 019 139 643; $641 893 855–1 315 141 506). In Europe, the greatest economic loss occurred in Spain ($78 012 486; $3 113 829–194 329 103) with the least burden in Austria ($398 864; $99 975–744 082). Once again, the USA had a greater burden than did Canada, with an average accrued cost of $861 727 155 (range $63 713 036–2 865 962 640). The highest lifetime economic losses (including productivity loss due to Chagas-disease-related mortality) in Latin America were in Brazil (mean $55 793 074 641; range $27 278 023 645–75 289 111 846) followed by Mexico ($32 301 253 739; $15 792 540 005–43 588 433 174). In North America, the USA had more than 99% of the burden ($31 639 839 055; $3 835 774 498–103 532 709 054), whereas Canada had less than 1% ($111 485 073; $52 364 055–181 887 315) of the overall health-care costs. In Europe, Spain and Italy had the greatest burden, with Chagas-disease-related costs of $2 696 250 914 (range $168 497 213–6 770 427 940) and $477 973 056 ($151 303 620–1 304 950 238), respectively.

Estimates generated by the model were much the same as those currently in the scientific literature in many ways. When individuals who entered the model were assumed to be 30 years of age (similar to 37·5 years [SD 13] reported by Espinosa and colleagues[22] as the average age of those with indeterminate disease), onset of cardiomyopathy occurred at 52 years (11) and congestive heart failure at 60 years (12), which is much the same as the 52 years (14) for cardiomyopathy and 55 years (11) for congestive heart failure identified by Espinosa and colleagues and in an additional study in which the age of patients with cardiomyopathy ranged from 49 to 85 years.[23] In our model, average duration of disease for those with cardiomyopathy was 11·6 years (10) and for those with congestive heart failure was 13·2 years (7·5), which is shorter than some other estimates (eg, 20–30 years for cardiomyopathy and 10–20 years for congestive heart failure[23]). An estimate of a lifetime cost of $14 718 for those with cardiomyopathy in Colombia[23] is somewhat higher than our estimate of $11 211 for the quartile in which Colombia falls in our analysis.

Discussion

Our results show that on average an infected individual incurs $474 in health-care costs and 0·51 DALYs annually. Over the course of his or her lifetime, an infected individual accrues an average net present value of $3456 and 3·57 DALYs. Globally, the annual burden is $627·5 million in health-care costs and 806 170 DALYs. The global net present value of

currently infected individuals is $24·73 billion in health-care costs and 29 385 250 DALYs. Conversion of the entire burden into US$ costs resulted in annual and lifetime per person costs of $4660 and $27 684, respectively, and global costs of $7·19 billion and $188·80 billion, respectively. The economic burden of Chagas disease extends beyond lower and middle income tropical and subtropical countries and exceeds those of other prominent diseases (panel).

The global burden of Chagas disease seems to be substantial. To put our calculated cost of Chagas disease in perspective, although annual costs do not approach those of the costliest cancers (lung cancer at $83 billion and breast cancer at $35 billion), they are similar to or greater than the global burden of some other cancers ($7·2 billion *vs* $6·7 billion for uterine cancer, $4·7 billion for cervical cancer, and $5·3 billion for oral cancer).[24] Our Chagas disease burden estimates exceed those of other infectious disease such as cholera ($5·43 billion)[25] and rotavirus ($2·0 billion).[26] The general methods for these disease burden studies were much the same as ours (ie, first identifying the number of cases and then associating potential unit costs to each case), but some variation existed in the specific cost components included. In addition to direct medical costs and productivity losses, the cancer estimates included non-medical costs such as transportation and complementary or alternative treatments, which our study did not incorporate. Inclusion of costs for alternative treatments would increase our estimates. Whereas vaccines for rotavirus and human papillomavirus (in large part to prevent cervical cancer) are being added to the WHO Expanded Program on Immunization for many countries, there has been substantially less attention on the development of a vaccine for Chagas disease, even though its burden is similar.

Existing global burden of disease estimates have been helpful, being the first attempt to quantify the global effect of Chagas disease. Our study results bring several key extensions to these initial estimates. The resulting annual DALY burden from our study is about 1·5 times higher than the calculated 2010 Global Burden of Disease estimate (806000 *vs* 546 000).[27] Moreover, focusing solely on DALYs neglects the substantial annual health-care costs associated with Chagas disease. Additionally, factoring in the net present value of the future burden of existing infections boosts the DALY burden more than 30 times.

Our findings suggest an economic argument for paying greater attention to Chagas disease since much of this disease's burden comes from productivity losses resulting from premature death. Currently, these productivity losses can go unrecognised. We do not know how many cardiovascular deaths might be attributable to unrecognised *T cruzi* infections and therefore are not counted towards the economic burden of Chagas disease. Although advocates of more resources to combat Chagas disease have used equity and justice as their main arguments, such large productivity losses sap many key parts of society, including the business sector, and bring a utilitarian argument for increased attention to this disease. In the past, the business sector has responded when realising the effects of certain diseases on their employee productivity and correspondingly their profits. For example, nearly a decade ago, employers in South Africa began sponsoring antiretroviral treatment programmes for their employees when presented with the substantial loss of productivity due to untreated HIV/AIDS.[28] This economic argument for offering HIV treatment via workplaces estimated that employers could save 9–38% of costs.[29] In general, generating more economic burden studies of various diseases can help decision makers and the research community better understand their relative effects and prioritise research, policy, and investment agendas.

Panel: Research in context

Systematic review

Before starting our study, we searched scientific literature listed in Medline, PubMed, and EconLit, using various search terms: "Chagas", "*Trypanosoma cruzi*", "cost", "economic", "burden", "congestive heart failure", "cardiomyopathy", and "megaviscera". We restricted the search to documents available in English; the last search was done on Aug 3, 2012. The search yielded no studies that aimed to quantify the global burden of Chagas disease.

Interpretation

As far as we are aware, this is the first reported attempt to quantify the economic burden of Chagas disease throughout the world. Our findings show that the economic burden of Chagas disease globally could exceed that of more well-known infectious and chronic diseases. Further studies quantifying Chagas-disease-related health-care costs on a regional or country level could further aid policy makers and other decision makers in establishing any necessary control measures.

Another important finding is that the Chagas disease problem is no longer restricted to lower and middle income countries in certain regions of the world. Whereas previous reports have shown that Chagas disease cases and transmission are occurring in higher income countries such as the USA,[30,31] there is a difference between reporting of increases in incidence or prevalence and quantification of the problem as a potential million or billion dollar issue. In the USA, our calculated annual burden of about $0·9 billion suggests that Chagas disease is in the league of other more publicised diseases such as Lyme disease (estimated $2·5 billion annual burden[32]), community-associated meticillin-resistant *Staphylococcus aureus* ($1·4–13·8 billion[33]), and *Clostridium difficile* (an estimated societal burden of $796 million or greater[34]).

Although computational modelling and simulation by no means should replace clinical and epidemiological studies, they can help overcome the limitations of cross-sectional or finite timeframe retrospective or prospective studies. Any study that does not extend over the entire lifetime of each study participant will miss a great proportion of burden. Moreover, since *T cruzi* infection is not a routine part of the cardiac disease differential diagnosis in non-endemic countries, much of the Chagas disease burden might occur outside the time windows of clinical or epidemiological studies (eg, confirmed *T cruzi* diagnoses might be delayed or never occur).

Since we endeavoured to be conservative, our findings might underestimate the Chagas disease burden for several reasons. First, our model did not account for the resulting burden on family members, friends, and co-workers. Second, cardiovascular treatment costs were conservative estimates and did not include all newer, more expensive treatment techniques and potential long distance travel for treatment (eg, medical tourism). Third, our study did not incorporate comorbidities (eg, pulmonary disease, immune disorders, or other infectious diseases) that can exacerbate disease outcomes. Fourth, many *T cruzi* infections remain undetected. Although under-reporting factors attempt to account for this underestimation, available incidence and prevalence figures might still not capture all activity. This disparity might be particularly prominent in countries in Europe, where currently no active screening occurs and diagnostic techniques are poor. Finally, our model focused on a finite set of major outcome categories rather than encompassing every possible outcome (eg, cardiomyopathy could lead to hepatic and renal failure). Our study also identified some important existing data gaps that can help guide future research and data collection. A vast amount of variation exists in the amount of screening and surveillance in different countries, probably leading to under-reporting of cases, particularly in high income countries. Furthermore, more attention should be focused on the types of treatments used and treatment regimens that are being implemented in different countries.

By definition, models are simplified representations of reality and cannot account for all nuances and uncertainties of the real world.[35,36] In real life, *T cruzi* infections do not progress through neatly divided mutually exclusive states as in our model (eg, instead a person gradually segues from being indeterminate to cardiomyopathy to congestive heart failure). Our model used fixed transition probabilities in some cases (eg, 4% annual risk of congestive heart failure) when these probabilities might actually change with time.

Model inputs came from various sources. Since few reports of treatment cost for Chagas disease by disease stage exist in the scientific literature, our study extrapolated existing cost estimates to countries for which no data were available. Extrapolation of data from locations within particular countries to apply to the entire country assumes that the data are truly representative and generalisable, overlooking potential heterogeneity within that country. The model used standard all-cause treatment costs for certain disorders and procedures such as cardiomyopathy and pacemaker implantation, rather than those particular to Chagas disease symptoms, for which subtle differences might exist. Although newborn babies infected via congenital transmission represented a portion of case estimates and resultant burden, since screening among newborn babies is not mandatory in all reporting countries, our results might not capture all congenital infections and therefore underestimate the true burden.

Acknowledgments

This work was funded by the Bill & Melinda Gates Foundation, and the National Institute of General Medical Sciences Models of Infectious Disease Agent Study (MIDAS) through grant 5U54GM088491-02.

References

1. Buekens P, Almendares O, Carlier Y, et al. Mother-to-child transmission of Chagas' disease in North America: why don't we do more? Matern Child Health J. 2008; 12:283–86. [PubMed: 17602289]
2. Barona-Vilar C, Gimenez-Marti MJ, Fraile T, et al. Prevalence of *Trypanosoma cruzi* infection in pregnant Latin American women and congenital transmission rate in a non-endemic area: the experience of the Valencian Health Programme (Spain). Epidemiol Infect. 2012; 140:1896–903. [PubMed: 22129521]
3. Lopez, A.; Mathers, C.; Ezzati, M.; Jamison, DT.; Murray, CJ. Global Burden of Disease and risk factors. Washington, DC, and New York City, NY: Oxford University Press, The World Bank; 2006.
4. World Health Organization. The Global Burden of Disease 2004 Update. Geneva: World Health Organization; 2008.
5. Lee BY, Bacon KM, Wateska AR, Bottazzi ME, Dumonteil E, Hotez PJ. Modeling the economic value of a Chagas' disease therapeutic vaccine. Hum Vaccin Immunother. 2012; 8:1293–301. [PubMed: 22894964]
6. Lee BY, Bacon KM, Connor DL, Willig AM, Bailey RR. The potential economic value of a *Trypanosoma cruzi* (Chagas disease) vaccine in Latin America. PLoS Negl Trop Dis. 2010; 4:e916. [PubMed: 21179503]
7. Teixeira AR, Nitz N, Guimaro MC, Gomes C, Santos-Buch CA. Chagas disease. Postgrad Med J. 2006; 82:78898.
8. Rassi A Jr, Rassi SG, Rassi A. Sudden death in Chagas' disease. Arq Bras Cardiol. 2001 Jan.76:75–96. [PubMed: 11175486]
9. Costa R, Rassi A, Leao M. Clinical and epidemiolgical characteristics of patients with Chagas' disease submitted to permanent cardiac pacemaker implantation. Rev Bras Cir Cardiovasc. 2004; 19:107–14.
10. Cancado JR. Long term evaluation of etiological treatment of Chagas disease with benznidazole. Rev Inst Med Trop Sao Paulo. 2002; 44:29–37. [PubMed: 11896410]

11. Gold, M.; Siegel, J.; Russell, L.; Weinstein, M. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
12. Bern C, Kjos S, Yabsley MJ, Montgomery SP. *Trypanosoma cruzi* and Chagas' disease in the United States. Clin Microbiol Rev. 2011; 24:655–81. [PubMed: 21976603]
13. Schmunis GA. Epidemiology of Chagas disease in non-endemic countries: the role of international migration. Mem Inst Oswaldo Cruz. 2007; 102 (suppl 1):75–85. [PubMed: 17891282]
14. Schmunis GA, Yadon ZE. Chagas disease: a Latin American health problem becoming a world health problem. Acta Trop. 2010; 115:14–21. [PubMed: 19932071]
15. Angheben A, Anselmi M, Gobbi F, et al. Chagas disease in Italy: breaking an epidemiological silence. Euro Surveill. 2011; 16:6–13.
16. Perez-Molina JA, Perez-Ayala A, Parola P, et al. EuroTravNet: imported Chagas disease in nine European countries: 2008 to 2009. Euro Surveill. 2011; 16:52–56.
17. Jackson Y, Chappuis F. Chagas disease in Switzerland: history and challenges. Euro Surveill. 2011; 16:pii 19963.
18. Navarro M, Perez-Ayala A, Guionnet A, et al. Targeted screening and health education for Chagas disease tailored to at-risk migrants in Spain, 2007 to 2010. Euro Surveill. 2011; 16:41–45.
19. Basile L, Janso JM, Carlier Y, et al. Chagas disease in European countries: the challenge of a surveillance system. Euro Surveill. 2011; 16:pii 19968.
20. Guerri-Guttenberg RA, Grana DR, Ambrosio G, Milei J. Chagas cardiomyopathy: Europe is not spared! Eur Heart J. 2008; 29:2587–91. [PubMed: 18840880]
21. WHO. Control and prevention of Chagas disease in Europe. Geneva: World Health Organization; 2009.
22. Espinosa R, Carrasco HA, Belandria F, et al. Life expectancy analysis in patients with Chagas' disease: prognosis after one decade (1973–1983). Int J Cardiol. 1985; 8:45–56. [PubMed: 3997291]
23. Castillo-Riquelme M, Guhl F, Turriago B, et al. The costs of preventing and treating Chagas disease in Colombia. PLoS Negl Trop Dis. 2008; 2:e336. [PubMed: 19015725]
24. Bloom, DE.; Cafiero, ET.; Jane-Llopis, E., et al. The global economic burden of non-communicable diseases. Geneva: World Economic Forum, Harvard School of Public Health; 2011.
25. Center for Biosecurity of UPMC. [accessed July 10, 2012] Infectious disease cost calculator. 2011. http://www.idcostcalc.org/Hold_May2012/about/cost-of-ID.html
26. Grimwood K, Lambert SB, Milne RJ. Rotavirus infections and vaccines: burden of illness and potential impact of vaccination. Paediatr Drugs. 2010; 12:235–56. [PubMed: 20593908]
27. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380:2197–223. [PubMed: 23245608]
28. Greener R. Why companies should intervene: a case study of the costs of HIV/AIDs to employers. Economic impact: Southern Africa. AIDS Anal Afr. 1998; 8:3–4. [PubMed: 12293622]
29. Rosen S, Simon JL, Thea DM, Vincent JR. Care and treatment to extend the working lives of HIV-positive employees: calculating the benefits to business. South Afr J Sci. 2000; 96:3000–04.
30. Gascon J, Bern C, Pinazo MJ. Chagas disease in Spain, the United States and other non-endemic countries. Acta Trop. 2010; 115:22–27. [PubMed: 19646412]
31. Cantey PT, Stramer SL, Townsend RL, et al. The United States *Trypanosoma cruzi* infection study: evidence for vector-borne transmission of the parasite that causes Chagas disease among United States blood donors. Transfusion. 2012; 52:1922–30. [PubMed: 22404755]
32. Maes E, Lecomte P, Ray N. A cost-of-illness study of Lyme disease in the United States. Clin Ther. 1998; 20:993–1008. [PubMed: 9829450]
33. Lee BY, Singh A, David MZ, et al. The economic burden of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA). Clin Microbiol Infect. 2012 published online May 21. 10.1111/j.1469-0691.2012.03914.x
34. McGlone SM, Bailey RR, Zimmer SM, et al. The economic burden of *Clostridium difficile*. Clin Microbiol Infect. 2012; 18:282–89. [PubMed: 21668576]

35. Lee BY, Biggerstaff BJ. Screening the United States blood supply for West Nile virus: a question of blood, dollars, and sense. PLoS Med. 2006; 3:e99. [PubMed: 16420099]

36. Lee BY. Digital decision making: computer models and antibiotic prescribing in the twenty-first century. Clin Infect Dis. 2008; 46:1139–41. [PubMed: 18444847]

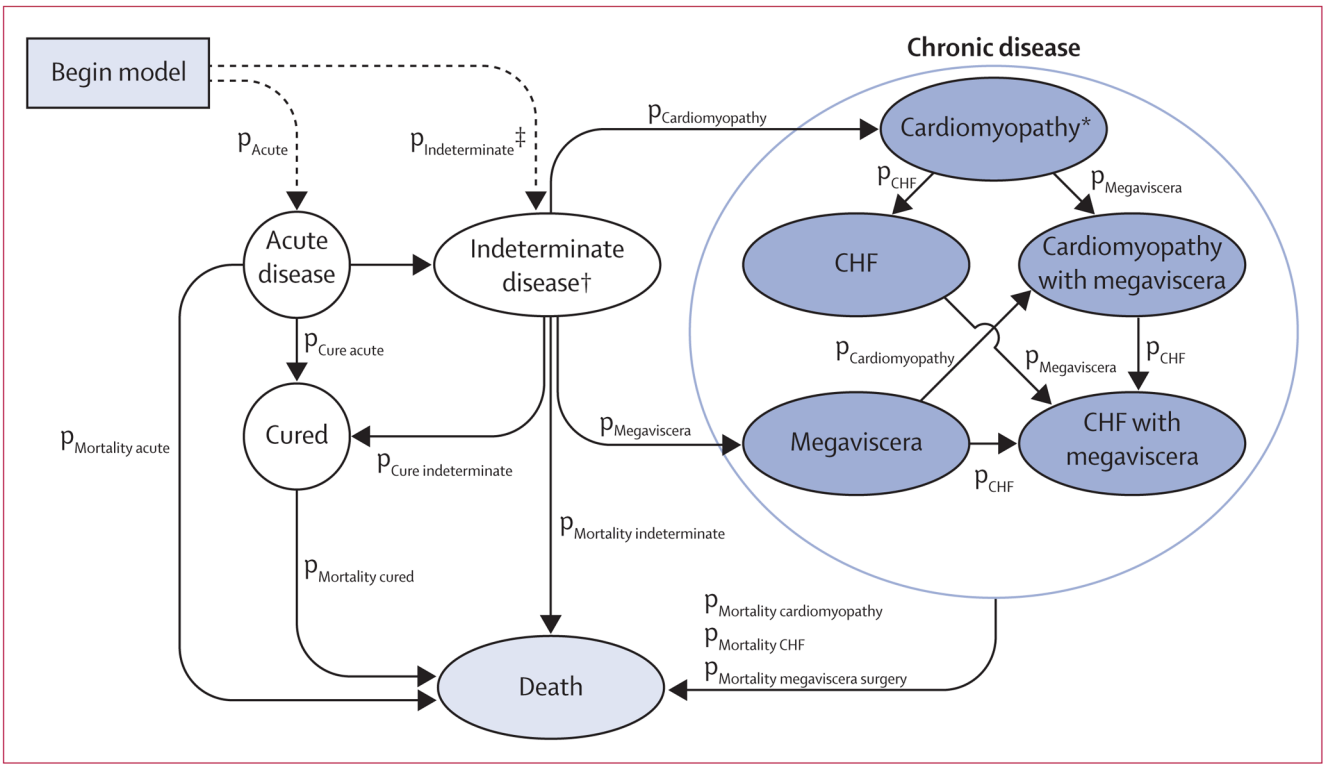

Figure 1. Individual-based Chagas disease model structure

Generated per-person disease cost and disability-adjusted life-year estimates. p=probability. CHF=congestive heart failure. *For annual burden estimates, all individuals began model in this state. †Individuals who survived acute disease transitioned to the indeterminate disease state. ‡$p_{Indeterminate}=1-p_{Acute}$.

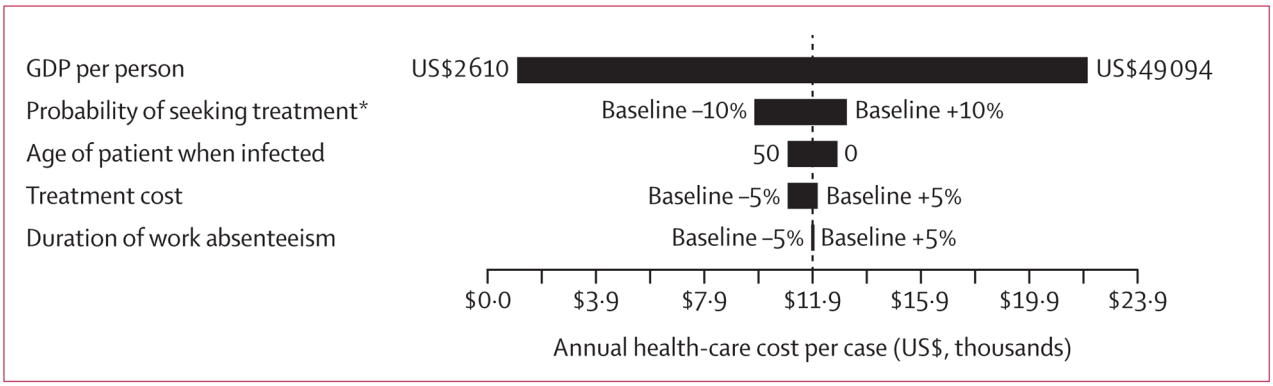

Figure 2. Effect of varying model parameters on the annual health-care cost per case of Chagas disease

Chagas disease endemicity had no effect on the cost of a case. GDP=gross domestic product. *±1% for surgeries.

Table

global burden of Chagas disease

	Latin America	USA and Canada	Europe	Australia	Total
Annual burden					
Health-care costs (range)	$491 598 884 ($179 045 694–983 010 464)	$118 596 220 ($5 643 228– 597 177 457)	$16 898 393 ($1 527 493– 57 702 251)	$364 790 ($66 579–917 451)	$627 458 287 ($186 282 994– 1 638 807 623)
DALYs (range)	772 304 (396 255– 1 063 932)	27 687 (1 823–99 384)	6093 (742–14 690)	85 (22–153)	806 170 (398 840–1 178 159)
Percentage of global estimate					
Cost	78·35%	18·90%	2·69%	0·06%	100·00%
DALYs	95·80%	3·43%	0·76%	0·01%	100·00%
Net present value (of currently infected cases)					
Health-care costs (range)	$17 115 793 558 ($13 301 489 929– 19 212 916 548)	$6 769 281 200 ($1 354 812 697– 16 236 754 793)	$827 951 048 ($311 863 935– 1 368 391 804)	$20 821 623 ($15 984 090–24 944 735)	$24 733 847 429 ($14 984 150 652– 36 843 007 880)
DALYs (range)	28 017 511 (9 392 622–44 266 305)	1 123 552 (83 643–4 470 747)	240 731 (32 485–652 598)	3456 (987–6868)	29 385 250 (9 509 737–49 396 520)
Percentage of global estimate					
Cost	69·20%	27·37%	3·35%	0·08%	100·00%
DALYs	95·35%	3·82%	0·82%	0·01%	100·00%
Annual burden with Chagas-disease-related mortality converted into lost productivity					
Total cost (range)	$6 182 398 476 ($3 781 925 482– 8 095 029 998)	$864 763 508 ($64 582 815– 2 870 997 592)	$139 580 628 ($19 409 810–310 797 558)	$2 659 925 ($761 949– 4 410 750)	$7 189 402 537 ($3 866 680 055– 11 281 235 899)
Percentage of global estimate (range)	85·99%	12·03%	1·94%	0·04%	100·00%
Net present value with Chagas-disease-related mortality converted into lost productivity					
Total cost (range)	$152 098 442 980 ($94 480 524 778– 267 361 914 617)	$31 751 324 128 ($3 888 138 553– 103 714 596 370)	$4 849 270 774 ($1 070 562 963– 10 853 128 069)	$97 663 853 ($45 872 288–159 338 067)	$188 796 701 735 ($99 485 098 582– 382 088 977 122)
Percentage of global estimate (range)	80·56%	16·82%	2·57%	0·05%	100·00%

All costs are US$. DALY=disability-adjusted life-year.