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COST-EFFECTIVENESS OF CHAGAS DISEASE INTERVENTIONS IN LATIN AMERICA AND THE CARIBBEAN: MARKOV MODELS

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Abstract. Chagas disease is a parasitic disease in Latin America. Despite vector control programs that have reduced incidence by 70%, there are at least 12–14 million prevalent cases. We used a Markov model to examine strategies for control and treatment of Chagas disease that compared annual costs, life expectancies, and cost-effectiveness of three vector control and drug treatment strategies. Vector control programs alone and vector control plus drug treatment are dominant over no vector control (i.e., less costly and save more lives), and vector control plus drug is highly cost-effective compared with vector control alone. We demonstrated expected changes in deaths over time resulting from various prevention approaches. Vector control affects primarily incidence, not decreasing deaths and prevalence for 30 years, while drug treatment affects prevalence and deaths immediately. The best strategy to combat Chagas disease is combinations of vector control and a potential new drug.

INTRODUCTION

Chagas disease is a parasitic disease found primarily in Latin America and the Caribbean. It is caused by the flagellate protozoan *Trypanosoma cruzi*, which is transmitted to humans by triatomine bugs primarily through posterior transmission in fecal material, by blood transfusion, and by maternal transmission.[1,2] There are many strains of *T. cruzi*, and antigenic differences in these strains cause geographic differences in disease pathology. Chagas disease is one of the most serious public health problems and a major cause of death in Latin America.

Cross-sectional studies in the 1980s indicated that the prevalence of *T. cruzi* infection in the 18 disease-endemic countries of Latin America was 4.72% (16–18 million) of the population,[3] with an incidence of 700,000–800,000 new cases per year and approximately 45,000 deaths per year due cardiac disease caused by this parasite.[4] The current prevalence is not well documented, but is probably 3% (10–14 million cases) of the Latin American population.[5,6] However, it may be higher and is still frequently reported as 16–18 million. Infection incidence now is estimated to be as high as 1.5 million/year[7] and the World Health Organization (WHO) estimates that 23,000 deaths from Chagas disease occur annually.[8]

The initiation of several regional vector programs has been very successful in decreasing the incidence of Chagas disease in these regions from the 1980s to the present time. The Southern Cone initiative, which began in 1991 and accounts for almost 50% of the Latin American region, has been especially successful. The Andean and Central American initiatives begun in 1997, but have been less successful. The vector control programs in Latin America have focused on spraying of insecticides on houses and their outbuildings (usually 2 sprayings 6–12 months apart, and further evaluation and spraying of re-infested houses), combined with surveillance and education programs. These programs must be sustained and not have their priorities lowered, especially while *T. cruzi* infection rates are low.

Chagas disease is characterized by three major stages. The first is an acute stage that has clinically recognized symptoms in only approximately 1–2% of patients and is sometimes identified with a swelling around the eye known as Romana's sign or by a swelling on other parts of the body after being bitten by a triatomine. The second is an indeterminate stage in which there are no clinical symptoms and which lasts 10–30 years. The third is a chronic stage in which approximately 30–40% of those infected are characterized by a non-ischemic type of cardiomyopathy with or without congestive heart failure (CHF). In addition, approximately 18–30% of patients with chronic disease have megaviscera, either megaesophagus (11–18%) or megacolon (7–22%), which results in significant morbidity and mortality.[9] Unfortunately, a large number of patients with no clinical symptoms also die suddenly primarily due to ventricular tachyarrythmias.[10]

The cardiac form of Chagas disease is the main feature of chronic disease due to "antigenic components of the parasite in cardiac tissue and an abnormal immune response that fails to control the infection which then leads to cellular damage and diffuse or focal chronic myocarditis with evolution of fibrosis".[11] Chagas disease cardiomyopathy is characterized by segmental wall motion abnormality. Patients with cardiomyopathy with overt CHF have mortality rates between 50% and 80% after three years.[12,13]

The digestive form of Chagas disease in the chronic stage is due to "denervation of the enteric nervous system that regulates the motor functions of the digestive tube, causing motility disorders primarily of the esophagus (achalasia and loss of peristalsis resulting in dysphagia) and the sigmoid colon (hypomotility resulting in constipation)". Treatment is symptomatic rather than curative because the neuronal destruction is irreversible.[14]

Successful regional vector control programs have been responsible for reductions of 60–99% in incidence rates of Chagas disease in parts of Latin America.[1,15] However, there are still many prevalent cases of this disease in this region and a considerable disease burden.

Recent research has demonstrated that parasitic load plays a primary role in the disease, and all individuals with this disease should be treated with available drugs.[16] Current treatment is 60–70% effective only in the acute stage of this disease (defined as the disappearance of antibodies to *T. cruzi*).[16] However, few patients are diagnosed and treated in

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this stage. Treatment success in the chronic stage is only 8–26% with benznidazole and the same or slightly less effective with nifurtimox. Therefore, the need for additional treatments is a priority.[17]

In addition, new drug treatments are needed because although vector control programs have an immediate effect on incidence of acute disease, it takes approximately 20–30 years for these drugs to begin reducing the prevalence of the chronic stage, in which disease morbidity is seen and major medical treatment costs are accrued. Drugs for treatment of the large numbers of prevalent cases would be ideal and several are under early stage development. However, there is little accurate data on the costs and benefits of the various vector control and drug treatment options and none on the costs and effects of combination options such as potential new drug treatments and vector control programs. The purpose of this study was to use a Markov model to examine the costs and benefits of several current and potential strategies for the eradication and treatment of Chagas disease in Latin America and the Caribbean.

METHODS

We developed two types of models (Figure 1).

Incidence model. We compared the costs, quality-adjusted life years (QALYs), and cost-effectiveness of a cohort of healthy newborns in 1990, assuming first that regional vector control programs had not taken place and then that regional vector control programs had been initiated in 1991 in the Southern Cone region and in 1997 in the Andean countries and in Central America.[3,4] Although there were vector control programs operational in some parts of the Southern Cone and in Venezuela in the Andean region, there was no widespread regional program until the 1991 and 1997 initiatives. Therefore, when we say no vector control in this model, we are referring to this baseline level of vector control before the regional initiatives. We compared the costs and life expectancies annually of the two cohort groups going through the Markov model and the cost-effectiveness of three potential treatment/prevention strategies: 1) vector control program alone versus no vector control program; 2) no vector control

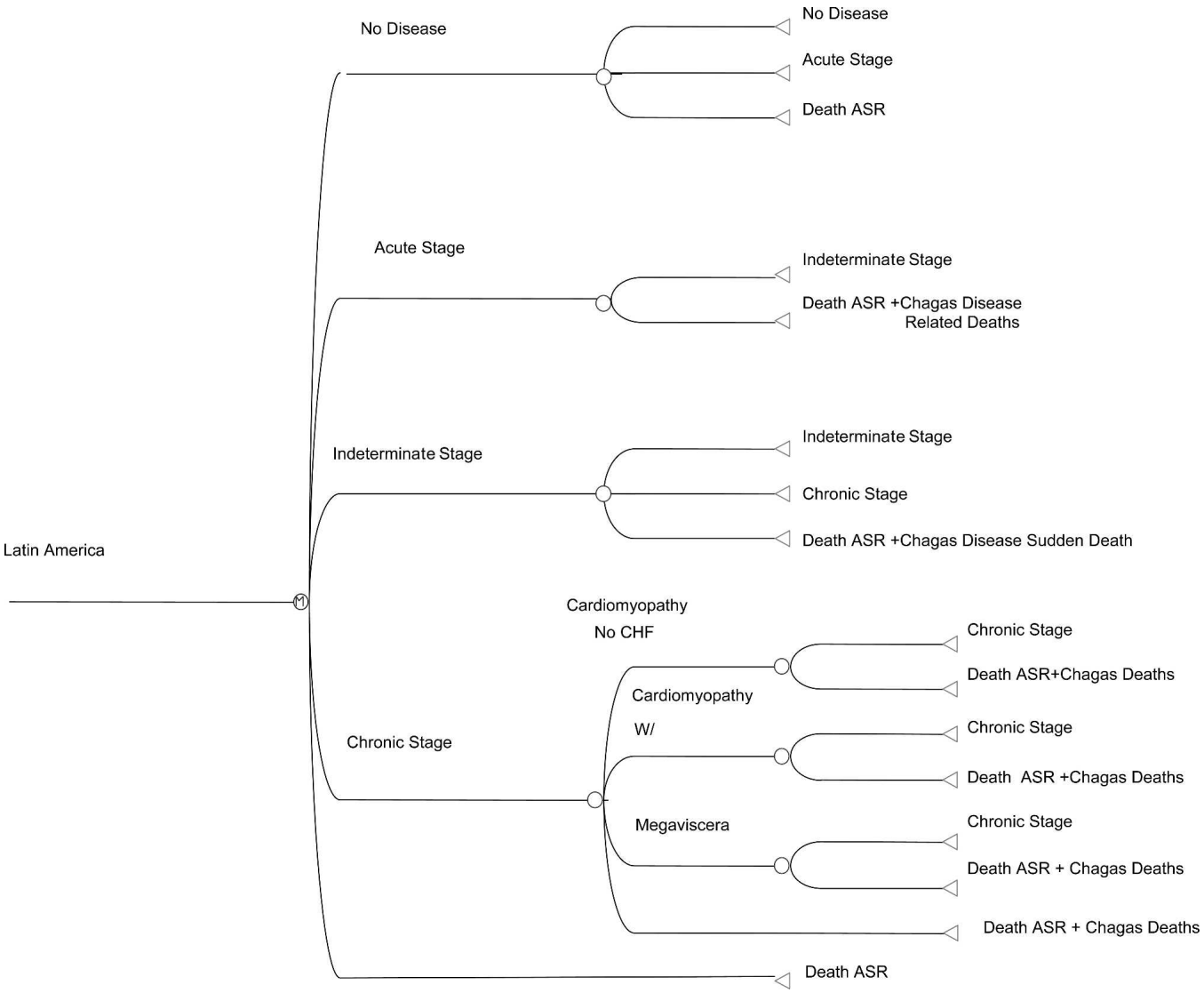

FIGURE 1. Markov model of Chagas disease. ASR = age-, sex-, and race-adjusted deaths from the life tables of Latin American countries; W/ = with.

program versus a vector control program plus a potential new drug treatment for Chagas disease given after the acute disease phase and having various cure rates; and 3) vector control programs alone versus vector control programs plus a potential new drug treatment given after the acute disease phase and having various cure rates.

Population prevalence model. We determined the costs, QALYs, and cost-effectiveness of a prevalent Chagas disease population (adding a defined probability distribution among the starting states corresponding to Chagas disease stages) for the same three potential treatment/prevention strategies.

Design. We used a steady-state Markov cohort simulation model and available literature on costs and benefits to model Chagas disease in Latin American countries with and without the benefits and costs of the vector control programs and with and without the benefits and costs of a potential new drug treatment for Chagas disease. We compared the cost and effectiveness of these different options. We discounted costs and effects by 3% to account for time preference and used 2003 US dollars. Data were analyzed with DATA™ Professional Software (TREEAGE Software, Inc., Williamstown, MA). We conducted sensitivity analysis to vary the cost and effect parameters in the model to see which variables were most sensitive within the model. We changed all rates to probabilities for use as transition probabilities in the model and used half-cycle corrections.

Markov models consider a patient to be in one of a finite number of discrete health states. All clinically important events are modeled as transitions from one state to another using transition probabilities of moving from one state to another.[18] These models are particularly useful when determining prognosis for a medical problem that involves a risk that is ongoing over time. Each state is assigned a utility (year of life expectancy in this case), and this utility contributes to the overall prognosis by adding up the length of time spent in each state. These utilities can also be adjusted downward for losses of quality during that state. The time horizon of the analysis is divided into equal cycle lengths (one year in this case) and a transition can be made from one state to another during each cycle. Patients are absorbed into the dead state, where they remain, not being allowed to transition to another state. We analyzed using a Markov cohort simulation that considers a hypothetical cohort of patients beginning the process with some probability distribution among the starting health states. For each cycle, the patients are newly distributed among the health states according to the transition probabilities specified. At the same time, a utility (quality-adjusted life expectancy [QALE) in this case) is summed for all the states for each cycle to arrive at a cumulative utility. The simulation is run until the entire cohort is in the dead state. We have seven health states in our model: no disease, acute stage, indeterminate stage, general chronic stage, cardiomyopathy with CHF, cardiomyopathy without CHF, and two death states, one for death due to Chagas disease and one for death due to all other causes.

Models. We used two types of steady-state Markov models: incidence and population prevalence. For all incidence models, we forced everyone to enter the model at the no disease state. The incidence model allows only a new born population to enter the model and run for 100 years. For the prevalence models we allowed entry into the model at all health states except death, using current prevalence figures on stage of disease and allowing incidence of disease at any age from the no disease state (prevalence models). The incidence models allow determination of disease progression alone, from well to death, including how the disease prevalence of each disease stage develops. The prevalence model allows one to see a static model of the period from 1990 to the present time and modeled into the next 100 years (excluding only migration effects and new births). This allows a more realistic estimate of Chagas disease prevalence by stage and the effects of drug treatment and vector control on them.

Population. We used the WHO life tables for 191 countries to determine the population and normal population mortality by age and sex in 2000 for each of 19 countries of Latin America and the Caribbean.[19] The total population of Latin America and the Caribbean from these life tables is 480.5 million (480,503,705). We allowed deaths from natural causes using the mortality from these life tables for our Markov model. Normal life expectancy in Latin America from mortality tables is 68.27 years when run alone in our model.

Incidence and prevalence. Disease incidence by age group, sex, and country where data was available was obtained from the report by Murray and Lopez.[20] As previously reported, the prevalence, incidence, and mortality of Chagas disease are constantly changing as a consequence of the impact of vector control programs, migration into and out of the areas, and changes in the economic conditions of the population.[1] We used the 1990 age-specific incidence estimates for the no vector control approach and estimated from the literature[1] a 70% decrease in incidence from these numbers beginning one year after the initiation date of each of the three regional vector control programs for that proportion of the total population affected by each program for our annual estimates of incidence for the with vector control approach. The age-specific incidence of Chagas disease we used in our model is shown in Table 1. The mean incidence estimates over a 100-year life time are 0.000932837, assuming no vector control in 1990.[1] When we decreased these estimates by 70% at various yearly intervals starting with one year after initiation of various regional vector control programs, we used an average incidence over all ages and years of 0.0002322 assuming vector control.

We used disease and stage prevalence to determine the probability distributions of who enters each stage at the start of the prevalence models. The estimates of Moncayo[1] that we used were based on a total prevalence of 15.6 million in 1990 with no vector control, an average age at onset of 13 years, and an average disease duration of 33.7 years. His incidence estimates were 728,000 for Latin American Countries and an incidence rate overall of 0.00164 in 1990 with no vector control.

TABLE 1
Chagas disease age-specific incidence with and without vector control

Age group (years)	Annual incidence with vector control	Annual incidence no vector control	Annual incidence high literature estimate
0–4	0.000816126	0.0054737	0.01257
5–6	0.000337284	0.0022621	0.01257
7–14	0.000678641	0.0022621	0.01257
15–44	0.000223558	0.0007452	0.01257
45–59	0.00012	0.0004	0.01257
60–100	0.000116129	0.0003871	0.01257

Disease stages: transition probabilities. *Acute disease.* We allowed patients to stay only a maximum of one year in the acute stage, including both symptomatic or apparent (only 1–2% of cases) and not symptomatic or inapparent cases, and allowed a 2.5% death rate (range = 0–5%) in this stage.[21] No one was allowed to return to the no disease state after having acute disease.

Indeterminate stage. All cases were then forced to go into the indeterminate stage. Patients stayed a minimum of 10 years in the indeterminate stage before being allowed to progress to the chronic stage. They were also allowed to die of other causes during this stage. Some patients (40%) may remain in the indeterminate stage for life, and our model assumes that eventually everyone will move to the chronic phase with either mild or severe symptoms, and/or eventually die either of Chagas related or other causes.[22] We did not allow deaths in the indeterminate stage except from normal life table deaths from other non-Chagas disease causes. Since deaths from sudden death that might occur in the indeterminate stage are often not attributed to Chagas disease, there is no data to document these deaths. The single study that tracked deaths from asymptomatic heart disease was used to account for deaths in the indeterminate stage, but they were attributed to the chronic stage (as asymptomatic heart disease; electrocardiographic [ECG] changes) because it followed the data better to model it in this way and was easier to account the exact probability of occurrence.[23]

General chronic disease. As soon as symptoms or any heart changes without symptoms occur, it was assumed that a transition into the general chronic stage had occurred. Beginning at year 10 (age 10) after contracting the disease, patients entered the chronic stage at approximately 1% per year.[24]

Cardiac disease. Depending on the type of symptoms, we then model increasing heart symptoms from a normal electrocardiogram and early segmental myocardial damage to some ECG changes and cardiomyopathy but no CHF, and finally to cardiomyopathy with CHF and death. The movement through the heart disease stages was based on a report by Espinosa and others.[23] Sudden deaths were assumed to occur during the asymptomatic chronic disease stage either before ECG changes or after early ECG changes.

Megaviscera. Those with gastrointestinal/esophageal symptoms were moved from the general chronic disease stage to the megaviscera stage, where we assumed that approximately 20% would have palliative surgery at some point and either improve or die. Death from megaviscera was assumed to occur as a surgical or post-surgical death only (Table 2).[25]

Chagas disease mortality. Patients were allowed to die of Chagas disease first in the acute stage at a rate of 2.5% (range = 0–5%) and then in the chronic stage from either cardiomyopathy with or without CHF, or megaviscera. Patients were allowed to die in the sudden death cardiomyopathy without CHF stages, and also to die either suddenly or not suddenly from the cardiomyopathy with CHF stage (Table 2). Sudden death is one of the major ways of dying from Chagas disease. It is unexpected cardiac death not preceded by any apparent clinical symptoms or by symptoms less than one hour in duration. It is most often precipitated by ventricular fibrillation preceded by a few beats of tachycardia and is sometimes associated with abnormal left ventricular function resulting from cardiomyopathy.[10,26] Patients were also allowed to die in the megaviscera stage, but primarily as a result of surgical procedures to treat these diseases. Most literature seems to indicate that there are few deaths from megaviscera with the exception of a death rate of approximately 1–5% due to surgery and its sequella.[25,27–31] People were also allowed to die of non-Chagas disease causes at each health state in the model using the age-specific mortality from life tables across the countries of Latin America as described earlier in this

TABLE 2
Model probabilities*

Probability variables	Age-specific	Probabilities	Reference	Range
Annual Chagas incidence: no vector control	Yes	0.000932837	20	0.0009–0.01257
Annual Chagas incidence with vector control	Yes	0.0002322	1, 20	
Decrease in incidence due to vector control programs	Yes	70%	1	70% and 90%
Normal mortality	Yes	Per life table	19	
Annual probability of general chronic Chagas disease	No	1%	24	
Annual probability of early segmental myocardial damage with no CHF if one has chronic disease	No	0.0365	23	
Annual probability of ECG changes and cardiomyopathy (no CHF) if one has segmental myocardial damage	No	0.068	23	
Annual probability of CHF if one has cardiomyopathy	No	0.042	23	
Annual probability of megaviscera if one has generalized chronic disease	No	0.0225	39	
Annual probability of death in acute disease stage	No	0.025	16, 21, 22	
Annual probability of death due to CHF	No	0.30	23	
Annual probability of death due to cardiomyopathy without CHF	No	0.042	23	
Annual probability of death due to megaviscera surgery and procedures	No	0.20 × 0.0225	Assume that 20%/year have surgical procedures and death rate (from 25)	
Prevalence model: 1991				
Prevalence of acute Chagas disease	No	0.00001	Author estimate	
Prevalence of indeterminate Chagas disease	No	0.024876	20	
Prevalence of generalized chronic Chagas disease (no heart disease)		0.00247	20	
Prevalence of CHF	No	0.001289	20	
Prevalence of no CHF chronic heart	No	0.006905	20	

* CHF = congestive heart failure; ECG = electrocardiogram.

report. Table 2 shows a summary of the probability variables used in the analysis.

Quality adjustment of life years. We adjusted life years using disability weights averaged from two sources, and used the QALY calculations to apply them to our model. A study by Akhavan[32] in Brazil obtained disability weights that included the infected indeterminate stage as well as both mild and severe states of both cardiomyopathy and megaviscera. We averaged these rates with those provided by Murray and Lopez,[20] which gave no disability to those in the indeterminate stage and provided different rates for those who are treated (35% of the Latin American population) for their cardiomyopathy and those who are not treated. We also reversed the disability weights so that 0 = death and 1 = perfect health for use in adjusting life years (life expectancy [LE]) downward (LE × quality adjustment) rather than for disability-adjusted life years (DALYs) (LE plus disability weighted years). This resulted in disability weights of 0.9625 for indeterminant stage, 0.769 for those with cardiomyopathy without CHF, 0.6651 for those with cardiomyopathy with CHF, and 0.8 for those with megaviscera (including both mild and severe). These numbers were used as utility weights to adjust for the loss of quality of life due to time with disease when in these disease states. We did not use the additional weighting of disability for loss of life during the productive years used by Murray and Lopez in the reporting of global burden of disease because we believed that it was more equitable to weight all life years equally.[20]

Disease stage prevalence. We estimated the distribution of cases among the different disease states for the prevalence Markov models by calculations using the data of Murray and Lopez.[20] (Table 2). The disease stage prevalence numbers were calculated for the whole population rather than for the Chagas disease population, unlike most of the published literature, to fit this Markov model, which is population based. We allowed these prevalent cases for each disease stage to enter the model at that stage and progress through the rest of the model. We still allowed acute cases to enter the model as new births (i.e., new acute cases beginning at age 0) as in the incidence model and also allowed an arbitrarily small number of prevalent acute cases to enter in the acute phase to complete the model. Individuals were allowed to get Chagas disease from the no disease state at any age.

Direct costs. There is very little data on the use of health care and their costs for Chagas disease and most is country specific. However, the estimates of Bosombrio and others[33] from Argentina were selected for the model and are shown in Table 3. His intervention costs primarily were obtained directly from the Chagas control program of the Salta Ministry of Public Health, with some additional costs from commercial providers of certain goods and services. The value of medical services for diagnosis and supportive treatment was the average of prices charged by different clinics and hospitals in Salta, Argentina.[33] The costs were divided by disease stage. The acute phase included initial medical consultation, general laboratory tests, parasitologic and conventional serologic tests for *T. cruzi* infection, drug treatment with benznidazole, electrocardiograms, chest radiographs, and hepatograms. The indeterminate stage included periodic medical visits, laboratory testing, radiographs, and electrocardiograms. The chronic phase included diagnosis and supportive treatment weighted according to the prevalence of the type and severity of symptoms. For mild cardiopathy medical consultation, electrocardiograms, chest radiographs, and intermittent antiarrhythmic drugs (such as amiodarone) were included. For severe cardiopathy a hospital admission, electrocardiograms, chest radiographs, digitalis, diuretics, vasodilators, and for some a pacemaker were included in treatment costs. For patients with megaviscera syndrome, requirements included medical visits, serologic tests, abdominal and chest radiographs, electrocardiograms, and heptograms, and for the 5% who have a surgical intervention, costs of a hemicolonectomy.[33] We excluded some costs of work days lost because we included these work losses as part of the quality of life adjustments according to the usual practice in cost-effectiveness analyses.[34] We inflated the 1992 costs of Bosombrio and others[33] for Argentina to 2003 constant currency in U.S. dollars, using an average gross domestic product (GDP) implicit price deflator of all Latin American countries for U.S. dollars to account for some of the variability in monetary movement across countries.[33,35] The GDP deflator takes into account all the various price components such as fluctuating exchange rates, different purchasing power of currencies, and rate of inflation, that must be considered when converting local currencies into constant currencies.[36]

TABLE 3
Direct (diagnosis and treatment) and indirect (work days lost) Chagas disease costs

Cost variables Costs: contains both direct cost of treatment and costs of work days lost	Estimated US$	Reference
Annual cost of acute treatment/person	$486.48	33
Annual cost of indeterminate treatment/person	$90.41	33
Annual cost of chronic treatment/person	$250	33
Annual cost of vector programs/person	$0.1126	Calculation from 22
Six month cost of drug treatment/person	$100	Estimate from costs of other drugs in the market
Annual cost of heart treatment/person (averaged across prevalence and cost by disease severity)	$350.42	33

Costs of vector programs. Preliminary cost estimates for the vector control programs initiated in the Southern Cone region of Latin America are $US200 million over 10 years.[22] Another study estimated that $US300 million was spent from 1991 to 2001 by the Southern Cone initiative (www.trypanosome.org). Although the Southern Cone region accounts for almost 50% of the entire Latin American region, the other two regions (Andean and Central American) have more areas that require vector treatment. Therefore, although we are aware that both the method and the target across countries varies, for this estimation, we assumed that the costs of vector control would be an average of those estimates ($20 and $30 million) or $US25 million per year for each year to keep up the current vector control rates used in our model. In addition, we assumed that the other two regions would also incur a cost of $US25 million per year to continue their vector programs. This resulted in a $US 50million per year cost for complete vector control at today's success rate of

a 70% decrease in incidence. When we divide this by the Latin American population, which was approximately 444 million, we get an average per person cost over the next 100 years of $0.11 per person per year with a range of $0.09 to $0.14.

The vector program costs vary greatly from country to country. For example, the average cost of spraying a house in the Southern Cone region is $US4.00.[37] In Guatemala, however, the total cost per house for spraying, labor, and transport is US$9.12, or US$48,225.7 for 5,286 houses. This is higher than in Brazil, mainly because of the higher cost of the insecticide in Guatemala.

Cost of potential new drug treatment. Because the details of a new drug treatment are as yet undefined, it is difficult to assess cost. Therefore, we chose a baseline cost assuming a six-month course of treatment given one time per infected person. We determined a cost for course of treatment based on currently available treatments for Chagas disease in that region and estimates of what the market will likely be willing to pay ($100) to have a regionally acceptable cost for our base case estimates. We assumed that all patients in the indeterminate and early chronic stages would receive drug treatment. Since we also assumed that the development of tests for Chagas disease and to assess outcomes of treatment would be developed along with the development of the drug, costs and success of testing are assumed to be included in the cost of treatment and rate of cure. We did not include case detection in the model because with no accurate data we did not want the model to appear more exact than it is.

RESULTS

Incidence models: life expectancy and life years saved: vector control versus no vector control programs. Using the quality-adjusted base-case incidence model, we compared the current vector control program with no vector control program. We entered all patients in year 1990 at the no disease state. This allows one to see what would happen to an incident (new) population if living in a vector-controlled population, which kept vector control for the next 100 years compared with a situation without vector control over this period (Table 4). The life expectancy determined from this model was 68.19 years with the vector control program. This was compared with the alternative no vector control program situation modeled with incidence rates in Latin America prior to the vector programs. Again, we allowed only those with no disease to enter the model. The model indicated that these individuals had a life expectancy of 67.91 years. Therefore, the current vector control initiatives save an additional 0.28 life years per person or an average of 3.4 months for each individual born in a Latin American country and entering the model in the no disease state. If there was no Chagas disease, the life expectancy using the incidence model was estimated to be 68.28 years.

Changes in disease incidence. Life expectancy will vary depending on the annual incidence of Chagas disease used in the model. Table 4 shows the changes in life expectancy when disease incidence varies. If the disease incidence was as high as 5% per year, life expectancy for the birth cohort would decrease to 63.73 years. Compared with the life expectancy using the current base case vector controlled incidence rate (68.19), this would mean a decrease in life expectancy of 4.46 years.

Cost-effectiveness of incidence models. Using the incidence model, we also compared the cost-effectiveness of both the vector control program with no vector control program and also a vector control program alone versus a vector control program plus a hypothetical new drug treatment. Tables 5, 6, and 7 show that the vector control program and the vector control program plus new drug treatment both dominate a situation with no vector control program, and that a vector control program plus drug treatment is cost-effective compared with a vector control program alone ($699/quality-adjusted life years saved [QALYS]). This cost-effectiveness of the addition of a new drug treatment is found despite that in these models we only use new incident cases and ignore the additional prevalent population that could also be treated with a new drug.

Incidence models and deaths. Table 8 shows for the incidence models the changes in proportion of deaths over time with and without vector control programs and with the addition of a potential new drug that cures 50% of the cases in the indeterminate stage. Using incidence models that only track new cases of the disease, the decreases in the number of deaths after the implementation of a combination of vector control and a new drug begin after 30 years when the first Chagas disease deaths occur in the chronic stage, and then increase over time. Over a life time, the decrease in probability of deaths due to vector control and drug compared with no vector control is approximately 0.328%, with a 0.31 increase in the QALE for a single new birth going through the model (Table 8).

TABLE 4

Base case incidence model: life expectancy estimation with vector control and varying chagas disease incidence estimates*

Annual incidence of Chagas disease	Life expectancy with vector control, years
0.40	62.16
0.30	62.21
0.25	62.25
0.20	62.33
0.10	62.80
0.05	63.73
0.025	65.02
0.0125	66.25
0.01	66.58
0.0015	67.97
0.001	68.07
No Chagas	68.28
No vector control (base case)	67.91
With vector control (base case)	68.19

* Base case contains the most likely estimates of probabilities.

TABLE 5

Incidence model: vector control program versus no vector control program*

Strategy	Cost (US$)	Incremental cost (US$)	Life expectancy (years)	Incremental effect	Incremental CE (QALYS)
Vector control program	$39.7		68.192		
No vector control program	$165.6	$125.9	67.907	–0.285	Dominated

* CE = cost effectiveness; QALYS = quality-adjusted life years saved.

TABLE 6

Incidence model: vector control program plus new drug with 50% cure rate versus no vector control program*

Strategy	Cost (US$)	Incremental cost (US$)	Life expectancy (years)	Incremental effect	Incremental CE (QALYS)
Vector control program plus drug	$58.4		68.223		
No vector control program	$165.6	$107.3	67.907	–0.316	Dominated

* CE = cost effectiveness; QALYS = quality-adjusted life years saved.

TABLE 7

Incidence model: vector control program alone versus vector control program plus new drug with 50% cure rate*

Strategy	Cost (US$)	Incremental cost (US$)	Life expectancy (years)	Incremental effect	Incremental CE (QALYS)
Vector control program alone	$36.7		68.1924		
Vector control program plus drug	$58.4	$21.6	68.2234	0.0310	$698.63

* CE = cost effectiveness; QALYS = quality-adjusted life years saved.

TABLE 8

Proportion (%) of deaths due to Chagas disease over time by type of treatment and control measures (incidence models)*

	Incidence models: no new drug		Incidence models with new drug	
	No vector control	Vector control	No vector control plus drug: cure 50%	Vector control plus drug: cure 50%
Age or years passed	Prob. of death due to Chagas	Prob. of death due to Chagas	Prob. of death due to Chagas	Prob. of death due to Chagas
5	0.053	0.008	0.053	0.008
10	0.088	0.015	0.088	0.015
20	0.127	0.027	0.127	0.027
30	0.149	0.033	0.147	0.033
40	0.179	0.041	0.171	0.039
50	0.216	0.051	0.196	0.046
60	0.257	0.060	0.221	0.052
Lifetime (100)	0.399	0.094	0.300	0.071
QALE	67.91	68.19	68.04	68.22

* Baseline incidence is age adjusted but the average annual incidence is 0.000933.
Discount rate is 3% per year. Prob. = probability; QALE = quality-adjusted life expectancy.

TABLE 9

Prevalence model: cost-effectiveness (CE) vector control program versus no vector control program*

Strategy	Cost	Incremental cost	Effect (QALY)	Incremental effect	Incremental CE (US$/QALYS)
Vector control program	$153.5		67.551		
Vector control program plus drug	$275	$121.3	67.276	–0.276	Dominated

* QALY = quality-adjusted life years; QALYS = quality-adjusted life years saved.

TABLE 10

Prevalence model: cost-effectiveness (CE) vector control program plus new drug versus no vector control program*

Strategy	Cost (US$)	Incremental cost	Effect (QALY)	Incremental effect	Incremental CE (US$/QALYS)
Vector control program plus new drug curing 50%	$229		67.812		
No vector control program	$275	$46	67.276	–0.537	Dominated

* QALY = quality-adjusted life years; QALYS = quality-adjusted life years saved.

Cost-effectiveness of population prevalence models. Tables 9, 10, and 11 show the cost-effectiveness of alternatives of three treatment strategies using the population prevalence models that allow the whole population of Latin American Countries to enter the model, including existing cases of Chagas disease at each stage.

Strategy 1: vector control compared with no vector control. Here, we compare situations with and without vector control using a prevalence approach, i.e., allowing entrance into the model to mimic what is seen in a cross-section of the Latin American population. Our results demonstrate that the vector control program is both less costly, saves more QALYs, and dominated the no vector control program alternative (Table 9).

Strategy 2: no vector control compared with vector control plus drug treatment. When we compared no vector control program with a vector control program strategy reducing incidence by 70% plus a new drug treatment program costing $100/person treated, and curing 50% at the indeterminate stage of Chagas disease, vector control plus drug also dominated the no vector control program (Table 10).

Strategy 3: vector control alone compared with vector control plus new drug treatment. When we compared vector control plus the addition of a new drug that cures 50% of those with Chagas disease at the indeterminate and mild chronic stage to the current vector control strategy alone, we also had a very efficient incremental quality adjusted cost-effectiveness ratio of US$289 per each additional QALYS (Table 11).

The cost-effectiveness of alternative health programs or treatments internationally is determined by the gross national income (GNI) of a country and its health expenditure per

TABLE 11

Prevalence model: cost-effectiveness (CE) vector control program versus vector control program plus new drug*

Strategy	Cost (US$)	Incremental cost	Effect (QALY)	Incremental effect	Incremental CE (US$/QALYS)
Vector control program alone	$153.5		67.551		
Vector control program plus new drug curing 50%	$229	$75	67.812	0.261	$288.78

* QALY = quality-adjusted life years; QALYS = quality-adjusted life years saved.

capita. Given the very conservative figures used in this model for incidence, mortality, effects of both the vector control programs and the potential new drug, a GNI per capita for Latin American countries of US$3,260, and a health expenditure per capita of US$255.6 (7.0% of the GDP), all strategies are cost-effective.[38]

We then further assessed the cost-effectiveness of our strategies by varying different parameter assumptions in our model using one-way and two-way sensitivity analyses for all variables, some of which are now discussed.

Sensitivity analysis on cost of drug, percent cure from drug, and death rates, serologic testing, and vector control costs. We varied the additional cost of a hypothetical new drug treatment of Chagas disease to determine the break even points using the prevalence model and comparing vector control alone with vector control plus drug at the baseline incidence and for both a 50% drug cure rate and an 80% drug cure rate (Figure 2). At an additional new drug cost of up to US$100 with the prevalence model and assuming that the new drug treatment gives an 80% cure rate, the vector control plus drug strategy dominates vector control alone (being less costly and curing more lives). At US$100 the vector control plus drug treatment strategy is still cost-effective but no longer dominates, costing less than US$100/QALYS, until a drug cost of $145. Even at a new drug cost of US$300, the additional treatment is cost-effective at US$442/QALYS. If one uses the baseline case model, which assumes only a 50% cure with the new drug, the sensitivity analysis on drug cost per case (base drug cost = US$100) shows that the vector control plus new drug treatment strategy dominates until a drug cost of US$45, and then has an incremental cost effectiveness ratio (ICER) less than US$100/QALYS until a drug cost of US$65, and an ICER less than US$500/QALYS until a drug cost of US$145. The ICER is still cost-effective until the US$400 maximum drug cost assessed (US$1,767/QALYS).

We also conducted a sensitivity analysis on the success of the vector control program. Our base case model assumed a continued 70% decrease in incidence with the program, and we varied that to a 90% decrease in incidence. With this assumption and a prevalence model with base line new drug costs (US$100) and a 50% drug cure rate, and comparing vector control alone with vector control plus new drug treatment, the vector control plus new drug strategy no longer dominates the vector control program alone strategy but continues to be very cost-effective, costing only US$112/QALYS. When varying the cost of vector control programs from US$ 0.11 to US$1.00 per person, the vector control plus drug strategy still dominated the no vector control strategy in the prevalence model.

Cases would need identification for drug treatment in the indeterminate and chronic stages of the disease and this would add additional cost to the drug treatment. Although we already tested a full range of drug costs that could include the cost of testing, we also conducted a sensitivity analysis that tested all cases that entered the prevalence model at a test cost of $3.00 per person to account for the need to test the entire population. The drug treatment plus vector control strategy still dominated the no vector control strategy in this case and up to a maximum cost of US$46 per person testing costs, where the two strategies break even for costs.

We varied death rates for non-CHF Chagas disease and megaviscera (both from 0 to 0.20) and for Chagas disease with CHF (0–0.80) and found that vector control programs still dominated no vector control at all probability levels. Varying the death rates similarly for the vector control alone compared with vector control plus drug strategy did not affect the outcome, varying the ICER very little and remaining cost-effective.

Aggregate deaths due to Chagas disease. We also calculated the proportion of the total deaths due to Chagas disease from our prevalence model (Table 12). We found that when using the prevalence model and assuming current vector control, by the age of 10 there is a 0.493% chance of death due to Chagas disease that increases to 0.938% by age 60 and to 1.04% over a life time. Both vector control alone and vector control plus drug treatment strategies showed a decreased probability of death at all ages compared with no vector control. Comparison of deaths in the incidence models (Table 8) with those in the prevalence models (Table 12) shows the variable effect as the cohort ages of the additional deaths avoided due to the addition of a potential new drug treatment when accounting for current prevalent cases compared with accounting for only new incident cases. Many deaths were avoided earlier. These comparisons demonstrate the importance of combining a drug treatment with a vector control program for the best outcomes.

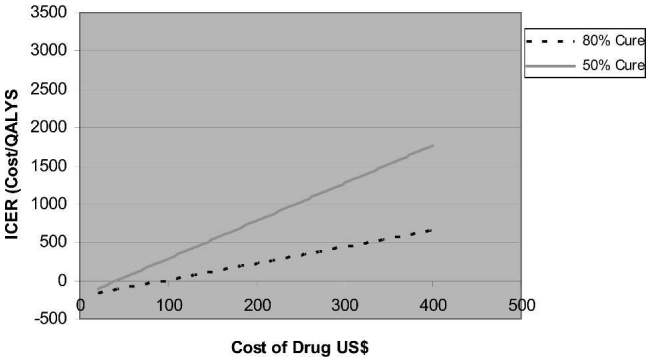

FIGURE 2. Effect on cost-effectiveness with variation in cost of drug treatment with estimated 50% and 80% cure rates (base case drug cost = US$100, comparison is vector control alone versus vector control plus new drug treatment). ICER = incremental cost-effectiveness ratio; QALYS = quality-adjusted life years saved.

TABLE 12

Proportion (%) of deaths due to Chagas disease over time by type of treatment and control measures*

	Prevalence model		Prevalence models: new drug cure 50%	
	Vector control alone	No vector control	Vector control plus drug	No vector control plus drug
Years passed	Prob. of death due to Chagas	Prob. of death due to Chagas	Prob. of death due to Chagas	Prob. of death due to Chagas
5	0.297	0.34	0.21	0.28
10	0.493	0.56	0.328	0.46
20	0.709	0.80	0.456	0.64
30	0.807	0.92	0.513	0.73
40	0.863	1.00	0.550	0.80
50	0.903	1.06	0.578	0.86
60	0.938	1.13	0.603	0.92
Lifetime	1.039	1.34	0.673	1.10
QALE	67.55	67.28	67.81	67.47

* Prob. = probability; QALE = quality-adjusted life expectancy.

DISCUSSION

This modeling study demonstrates the impact of vector control and the addition of a new drug treatment to vector control on the progression of Chagas disease over time. The models demonstrate that continued vector control in Latin American countries is highly cost-effective and that a new drug treatment alone, but preferably in addition to vector control programs, is also highly cost-effective. All cost-effectiveness ratios of the comparisons in this study for either a vector control program alone or vector control plus a new drug treatment fell below the per capita GDP in Latin America and the Caribbean (US$3,194 in 2002) and thus can be classified as very cost-effective. According to the recent report of the Commission on Macroeconomics and Health, interventions that cost less than the GDP per capita are classified as very cost-effective and those whose cost per DALY saved is less than three times the GDP per capita are classified as cost-effective. Interventions valued at these levels of GDP represent good value, and it is suggested that if countries cannot afford these interventions using their own resources, that the international community should find ways of supporting them.

In this report, it is suggested that by the most conservative estimates that each DALY is valued at one year of average per capita income, and at three times the current annual income with more conventional assumptions. None of our interventions reached the per capita GDP in Latin American countries. Therefore, our major conclusion is that for Latin American countries, both vector control and a new drug treatment of Chagas disease are very cost-effective interventions and worthy of investment. In addition, these interventions have the potential to save many millions of life years, avoiding morbidity and mortality for the whole population of Latin American countries when aggregated.

The pattern of impact of interventions differs for vector control and a new drug treatment with the drug treatment that has a more immediate impact in reducing deaths than a vector control program alone. Both interventions show more of a delay before mortality is affected because of the 20–30-year delay in Chagas disease from the onset of disease to death. These longitudinal data by stage demonstrate the value of supporting both vector control programs and a potential new drug treatment that could impact the disease in the indeterminate and mild chronic stages.

This model has several limitations because of various assumptions made. First, as mentioned previously, there is uncertainty about many of the variables used such as prevalence, mortality, incidence, and treatment costs. We used the best available estimates and then tested these with sensitivity analyses. In the base case, entry into our prevalence model was not age adjusted because of lack of data on this for those in the indeterminate and chronic stage of the disease. However, using rough estimates, we did run a prevalence model that was adjusted for age and this did not change our results significantly. Finally, our specifications for the new drug treatment are somewhat speculative and meant to supply information to those currently developing new drug treatments about the effects if given once over a six-month period at a cost of US$100 and curing 50% at the indeterminate or mild chronic stage. Many factors are undefined: e.g., accurate ability to identify and treat the disease at an early stage, the possibility that re-treatment may be needed, that cure may be partial or for fewer people, and that other treatments would continue to be needed, thus inflating costs. Differences in case detection could also change our results. However, our estimates seem plausible and conservative, despite lacking these known details. It seems clear that with our current assumptions, both vector control programs and a potential new drug treatment are highly cost-effective strategies. As drug treatments and methods of case detection become better defined, this model can be used with more accurate drug variables.

Finally, we demonstrated that the best strategies for the control and treatment of Chagas disease in Latin American Countries are a combined vector control plus new drug treatment approach. Such strategies result in earlier beneficial effects on morbidity and mortality and are highly cost-effective.

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