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**Treating the Children of Bolivia
Infected with Chagas Disease**
– A Cost-Benefit Analysis

A Thesis Submitted to the
Yale University School of Medicine
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

by
Gregory A. Magee
2006

Abstract:**TREATING THE CHILDREN OF BOLIVIA INFECTED WITH CHAGAS DISEASE – A COST-BENEFIT ANALYSIS.**

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(Sponsored by Michael Cappello, Department of Pediatrics, Yale University School of Medicine).

The purpose of this study was to perform a cost-benefit analysis of an intervention to treat all the children in Bolivia (under 15 years of age) who are infected with Chagas disease. This research was carried out in La Paz, Bolivia where the author lived for a year collecting data in collaboration with the National Chagas Control Program, Bolivian Ministry of Health. Operational costs were based on current prices for laboratory testing and pharmaceuticals, average hourly wages for health care workers, and the number of children who would be treated. The benefit of the program was estimated as the sum of direct and indirect costs associated with chronic cardiac disease caused by Chagas infection. Direct costs were calculated as the minimum amount needed for adequate medical treatment summed over the patients' life span. Indirect costs were measured in Disability-Adjusted Life Years (DALYs) multiplied by average yearly salary to more fully account for the true burden of disease. Implementation cost was estimated to be approximately \$35 million. This intervention would prevent over 279,000 DALYs and alleviate \$123 million in direct and \$632 million in indirect costs. Clearly, such a program would be extremely cost-effective. Thus, with an initial investment of less than \$135 per infected child, approximately \$2,900 worth of future costs would be prevented, in addition to improvements in quality of life not captured by DALYs. A sensitivity analysis showed that even while assuming a high variability of the data, the cost and benefit of this intervention were significantly different (p -value < 0.001).

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1 Introduction

1.1 Epidemiology

Chagas disease, also known as American Trypanosomiasis, is caused by the parasite *Trypanosoma cruzi*, and it is found only in the American continents from Mexico to Argentina where it infects 16-18 million people [1, 2]. In 1985 an estimated 100 million people were living at risk in endemic areas, which constituted 25% of the population of Latin America [1, 2, 3]. The WHO has ranked Chagas as fourth in infectious disease burden in this region after diarrheal diseases, HIV, and tuberculosis. It far outweighs the burden of all other parasitic diseases in the region (e.g. malaria, leishmaniasis, schistosomiasis, etc.) combined [3]. The disease can be transmitted by transfusion of infected blood, and transplacentally, but the majority of new cases are vector-borne, transmitted by the reduviid bug (*Triatomina infestans*) [3]. *T. infestans* has adapted to the habitat of humans so well over the centuries that it is seldom found elsewhere. This adaptation and their slow gene migration rate have made them especially susceptible to eradication and over the past ten years several eradication programs have had tremendous success [3, 4].

Bolivia is the most highly endemic country with approximately 40% of its population living in the endemic area [3] and has a national prevalence of Chagas infected persons of approximately 25% (unpublished data from National Chagas Control Program, Ministry of Health, Bolivia). Within the endemic area, however, the prevalence rate is estimated as 50% or higher. In the past few years significant progress has been made (as a result of the Southern Cone Initiative [4]) in eradicating the vector from homes and currently 150 of 168 municipalities (89%) in the endemic area have a less

than three percent infestation rate (data from Ministry of Health, Bolivia). While these great strides have virtually eliminated the vector-borne transmission of Chagas disease in these areas, there is still a large portion of the population currently infected and susceptible of developing severe forms of chronic Chagas disease, which remains a pressing public health problem.

1.2 Clinical Forms

Chagas disease is a chronic infection with three stages. The acute phase lasts up to two months and is characterized often by non-specific systems such as fatigue, general malaise, fever, polylymphadenopathy, hepatomegaly, splenomegaly, vomiting, diarrhea, and anorexia [3]. Because it is usually contracted in the first 15 years of life and is first manifested by symptoms similar to other childhood illnesses it is rarely recognized as a Chagas infection. During this stage three percent will die (mainly in those under the age of three), but the remaining will recover without immediate sequelae [3]. In the indeterminate stage (so named because at this point what future symptoms will occur, if any, is unknown) there are generally no symptoms and, unless tested, the patient has no idea that he or she has a potentially life-threatening disease. The level of parasitemia falls after the acute stage and the parasite then forms pseudocysts in tissues that act as reservoirs [5]. This stage can last 10 to 20 years or, in the case of those that don't develop chronic symptoms, indefinitely. Thirty to fifty percent of those infected, however, will develop chronic symptoms, which typically begin in the late twenties to early thirties [3]. This represents the chronic stage, which lasts for the rest of the individual's life.

The chronic manifestations of Chagas disease come in two categories, cardiac and gastrointestinal. Ten to thirty percent of those infected will develop cardiac abnormalities and approximately 20 percent will develop gastrointestinal abnormalities, although the relative percentages of these vary by region [3]. For example, in Bolivia it is estimated that 25 percent of those infected will develop cardiac disease, while less than ten percent will develop gastrointestinal symptoms [6]. However, because gastrointestinal symptoms are less severe, these estimates may be under-reported.

Cardiac symptoms affect the conductive system, and cardiopathies include left and right ventricular hypertrophy, ventricular dilation, and apical aneurysms [7]. The gastrointestinal symptoms are mega-colon and mega-esophagus eventually resulting in severe constipation and dysphasia, respectively. Generally, a patient will not exhibit both of these symptoms, and chronic patients will have either gastrointestinal or cardiac manifestations, but not both. Additionally, patients who develop mega-colon generally do not develop mega-esophagus, and vice-versa. Approximately ten percent of those with cardiac symptoms will die as a direct result of their cardiac disease, and the others will often have a significant disability [8].

There is an increased risk of parasite reactivation when the host is immunosuppressed, for example from immunosuppressive drugs used after organ transplantation or AIDS, but at present this is not a major concern in Bolivia where there are very few transplantations and the prevalence of HIV infection is only 0.1 percent [9].

1.3 Pathology

1.3.1 Cardiac form

Clinical manifestations of Chagas cardiomyopathy can vary from only mild symptoms to heart failure and often sudden death. Also, cerebral embolism resulting from dilated cardiomyopathy is a leading cause of brain ischemia in the endemic area [3, 7].

The inflammation and fibrosis that are present throughout the myocardium result in severe cardiac lesions. There are several types of arrhythmias caused by these myocardial lesions – both tachyarrhythmias and bradyarrhythmias – with ventricular extra-systoles being the most common, and physical effort increases their frequency [7]. Sustained ventricular tachycardia is also common and often produces decompensation. Tachycardia can degenerate into ventricular fibrillation, which is the main cause of sudden death in these patients [7].

As for bradyarrhythmias, sinus bradycardia and sinoatrial block are the most common. Atrioventricular block also causes slow ventricular rhythms and often require an implanted pacemaker [7]. The most typical EKG changes seen in these patients are right bundle branch block, left anterior hemiblock, prolonged atrioventricular conduction, T-wave changes, and abnormal Q waves [3, 7].

1.3.2 Gastrointestinal form

The pathology of the gastrointestinal form of Chagas lies in the insidious destruction of parasympathetic ganglion cells connected to the muscular layers of affected organs (e.g. esophagus and colon) [10]. The exact method of nerve destruction is unknown.

1.4 Pathogenesis

Traditionally, there have been two leading theories to explain the pathogenesis of Chagas disease. The first is called the “autoimmunity hypothesis”, which states that the parasite induces an immune response which targets self tissues. This response is independent of the persistence of the parasite, and is hence, an autoimmune reaction [11, 12, 13, 14, 15, 16].

The second theory is called the “parasite persistence hypothesis”. It asserts that the cause of the chronic inflammatory reaction in specific tissues is actually the persistence of the parasite in those tissues of the host. This theory is now largely accepted as the more accurate one and several studies have evidence to support that claim [17, 18, 19, 20, 21].

Both theories, however, maintain that the immune response results in a cumulative, focal destruction of tissues, which ultimately cause the signs and symptoms of Chagas disease.

1.5 Diagnosis

There are a large number of parasites circulating in the host’s blood during the acute phase of Chagas disease. These parasites can easily be detected by direct observation of peripheral blood under a microscope because of their motility [22]. However, direct parasitological tests are not of much use during the chronic phase because the number of circulating parasites decreases dramatically. Serological tests, on the other hand, are highly effective because individuals infected with *T. cruzi* develop antibodies against parasite antigens, and these antibodies persist throughout the infection.

Indeed, the titer of these antibodies remains relatively constant during the chronic phase [3, 22]. The presence of these antibodies can be detected by a variety of serologic tests.

The three most commonly used tests are indirect hemagglutination (IHA), indirect immunofluorescence (IIF), and enzyme-linked immunosorbant assay (ELISA). The sensitivity of IIF and ELISA are approximately 99% [3, 22], so a positive result in either is sufficient to make the diagnosis. However, the specificity is not that high, as there can be cross reactions between *T. cruzi* and *Leishmania* species or *T. rangeli*. Thus, because no test yet exists with a sensitivity and specificity near 100%, often a screening test is used which has a high sensitivity, and then positive results are retested using a different test with a high specificity. Individuals that test positive to both are then considered to have the disease [22, 23, 24].

Other important practical features of serological tests that need to be considered are how fast and expensive they are, how much equipment is needed, and how much expertise is needed to carry them out. IHA results take about two hours, requires little equipment and no specialized technical skills, but its sensitivity is about 96%, which is lower than the other two standard tests [3]. IIF, on the other hand, while its sensitivity is 99%, requires several steps by a skilled technician and the use of a UV microscope [3]. This makes it undesirable for field use, but suitable for a small laboratory with a UV microscope. ELISA also requires a skilled technician and takes several hours, but can be automated and is, thus, suitable for testing many samples simultaneously. It has an excellent sensitivity (99%) and a good specificity (98.2%) [22, 25].

There are also several so-called 'non-conventional' tests now available [26, 27, 28]. One of these is called immunochromatography, which is an assay that detects IgG

antibodies directed against a combination of recombinant antigens of *T. cruzi*. Its major advantages to the aforementioned tests are that it is cheap (kit costs only \$1.60), requires only one step and minimal training to execute, and results are obtained quickly (in about 15 minutes) [26, 29]. Its sensitivity is 95.5% and specificity is 100% [29]. Tests such as these are most desirable for field use, and for mass screening.

1.6 Treatment

The only available drugs used to treat Chagas disease are benznidazole and nifurtimox. Benznidazole is a 2-nitroimidazole derivative which inhibits protein synthesis and ribonucleic acid synthesis in *T. cruzi* cells [30]. Nifurtimox is a 5-nitrofuran derivative that appears to be toxic to *T. cruzi* due to its production of free radicals [31, 32]. The recommended dose of benznidazole is 5-7mg/kg per day divided into two or three doses every 8 to 12 hours [3, 30]. Nifurtimox is administered every 8 hours for a total dose of 8-10mg/kg per day [3, 31, 32]. Both are best given after meals for a period of 60 days.

Until recently it was believed that treatment of Chagas disease after the acute phase was ineffective. This is because until recently it was thought that chronic Chagas disease had an auto-immune etiology [11]. However, this theory has been largely disproved, and in the past 10 years several studies have shown that treatment can be effective in the indeterminate stage, with earlier treatment providing better results. In a double-blind, randomized placebo-controlled trial with 129 children (ages 7-12) in Brazil, Andrade found that 58% of those treated became seronegative (indicating parasitologic cure), while five percent of those treated with placebo became seronegative (p-value < 0.05) [33]. Additionally, and surprisingly, those that were not cured benefited from

treatment by experiencing a five-fold decrease in *T. cruzi* antibody titers (196 vs. 1068, p-value < 0.00001), which is linearly correlated with severity of pathology [33].

Similar results were found by Sosa Estani in a study of 106 schoolchildren in Argentina using the same protocol as Andrade. They found that 62% of children under the age of 13 became seronegative, while none of the non-treated group became seronegative (p-value < 0.001) [34].

Another long term follow-up study of 201 patients of all ages (mean age 46 years) with chronic cardiomyopathy showed that there was significantly less clinical and electrocardiographic progress toward cardiomyopathy in the treatment group when examined 8 years after treatment. They found that benznidazole-treated patients were 7 times less likely to experience changes in EKGs – 4.2% vs. 30.0% (p-value < 0.01). Again clinical outcome was directly correlated with decreased titers of anti-*T. cruzi* antibodies [35].

Both benznidazole and nifurtimox produce side effects in most adult patients, but these subside after treatment is terminated. Side effects include headache, anorexia, vomiting, nausea, diarrhea, dizziness, intestinal colic, cutaneous maculopapular rash, and paresthesia. Children, however, have a much higher tolerance to treatment with only five to twenty percent experiencing minor side effects, none of which required cessation of therapy [33, 34]. Despite side effects, the benefits of treatment mentioned above warrant their use in all individuals with Chagas disease. Indeed, based on the observations that those treated have a significantly lower prevalence of heart complications and a better clinical outcome the Pan American Health Organization (PAHO) has concluded that

patients with chronic Chagas disease should receive treatment with either drug for a minimum of thirty, but preferably, sixty days [36].

1.7 Assessment of Cure

An individual is considered cured when the originally positive serological test turns negative. If the individual is treated during the chronic phase this can take up to 10 years or more [3]. This is the reason that those treated need to be followed with yearly serologic tests to assess the treatment's effectiveness and whether or not the patient has reverted to seronegative status. Whatever type of serological assay is chosen initially, the same test should be used every following year for consistency.

2 Methods

2.1 Study Objectives

The purpose of this study was to perform a cost-benefit analysis of a proposed intervention to treat the children of Bolivia who are infected with Chagas disease. The entirety of this research was carried out in Bolivia where the author lived for a year collecting data in collaboration with the National Chagas Control Program, Bolivian Ministry of Health. While vector eradication programs have been shown to be extremely cost-effective [37], there have been no previously published cost-benefit analyses of treatment programs for children with Chagas disease.

The proposed intervention is to send health care workers to the different localities in the endemic zone and (after receiving informed consent from the parents) screen all the children living there under 15 years of age for Chagas disease. Children that test positive for Chagas will be treated as described below.

All children that meet criteria will first be screened using an immunochromatography test. The rationale for choosing this test is that it is fast, cheap, can be performed without much training, and has a very high sensitivity of 95.5% [29]. Subsequently, those with a positive result will be confirmed by ELISA, with a positive ELISA result making the diagnosis. ELISA was chosen as the confirmatory test because it is also relatively cheap, is performed regularly by laboratories in Bolivia, can be automated to test many samples simultaneously, and has a high specificity of 98.2% [3, 22, 25]. These tests will be carried out in the local schools when possible, or otherwise the children will be brought to the local clinic. Children who test positive for Chagas disease will receive a counseling session with their parents by a medical doctor who will

explain the course of the disease, how it is contracted, and why treatment is important. Informed consent for treatment will be received at this time, and the doctor will administer the first treatment to demonstrate how it should be administered.

Treatment will be benznidazole 7mg/kg (to the nearest 25mg) spread out in three doses per day for 60 days [3, 30]. The additional treatments will be at home and parents will be given a week or two weeks supply of the drug at a time. Then every 7-14 days the family must visit a nurse at the local clinic to receive the next supply of drugs and to check that everything is going well. Additionally, they will receive a calendar to check off each time a treatment was given as a reminder and means to check adherence.

The inclusion criteria for screening and treating communities are: 1) the municipality *and* the locality have a less than 3% infestation rate of reduviid bugs in households, 2) the child lives in a non-infested home, and 3) the child is younger than 15 years of age. These requirements ensure that after treatment the child will not be re-exposed to the risk of infection – as there will be no vector transmission and presumably no blood transfusions. It therefore allows the treatment to have a meaningful and lifelong effect. The age restriction is due to the fact that children in this age group are more responsive to chemotherapy, and tolerate treatment better [3, 33, 34, 35, 36]. The treated group will receive a follow-up ELISA test every year for eight years to measure their titers and assess the efficacy of the treatment.

The goal of this intervention coincides with the WHO recommendations that national efforts be made to treat individuals in the early chronic phase where vector transmission has been eliminated [2, 3].

2.2 Source of Data

The data used in this study were gathered from many sources, with the majority coming from unpublished data gathered by the National Chagas Control Program – a division of the Bolivian Ministry of Health. However, because Bolivia is one of the poorest countries in the Western Hemisphere and has been undergoing major political turmoil for several years, the availability of accurate and current data on population demographics is somewhat scarce. Therefore, estimates had to be made at times; however, care was taken to estimate costs as accurately as possible given these constraints. Additionally, some demographic information came from published analyses of the United States Central Intelligence Agency and United States Embassy to Bolivia [9]. When appropriate previous studies of Chagas disease in Bolivia were cited, and when no data on prevalence statistics were available for Bolivia, estimates were made from studies in neighboring countries. Computations in most cases were simple arithmetic and are explained in the text. They were calculated using Microsoft Excel and then checked by hand.

2.3 Calculation of Implementation Costs

The intervention's costs are calculated as the costs of diagnostic tests (including lab, personnel & disposables costs), treatment (drug and administration costs), and medical consultation costs. Few changes in infrastructure will be necessary because for the most part basic health outposts already exist in the endemic area, often as a result of the vector eradication program. Additional costs for yearly follow-up serological tests are calculated separately because, while important for surveillance and to measure efficacy, they are not likely to have an effect on ameliorating future illness. Because

Bolivia is a developing country lacking stability, administrative and unforeseen costs could increase the total cost by up to 50 percent.

2.4 Calculation of Benefits

2.4.1 Direct Costs of Chagas cardiomyopathy

Direct costs are measured as the minimum costs that would be required for adequate treatment and follow-up in Bolivia. These costs are then adjusted for those that actually *seek* such interventions. Although with the presently available data we can only estimate the percentage that will seek treatment, it is assumed that it will be low because very few Bolivians can afford medical attention. The percentage of those infected that will seek treatment was estimated to be only 20% based on analyses of the percentage of people in other developing countries that seek treatment for chronic diseases [38]. However, it can be assumed that if interventions are not attained (i.e. direct costs are lower) the indirect costs will increase, as the disease will not be mitigated.

2.4.2 Indirect Costs of Chagas cardiomyopathy

Indirect costs are measured as the loss of society's productivity from disability and death due to Chagas disease as calculated by Disability-adjusted Life Years (see below).

2.5 Definition of Disability-Adjusted Life Years

For years the measure for the burden of a disease has been based on mortality statistics – that is, the number of deaths caused by each disease. However, recently there has been consensus that mortality statistics along are not an adequate measure because they do neither capture the average age of death caused by the disease, nor the number of

years lived with the disease [39]. Therefore, several attempts have been made to better capture the combined impact of premature death and disability caused by a disease in a single variable. Most researchers have agreed that the best variable to accomplish this task is time lost due to the disease – both time lost due to disability and time lost from premature death.

Many measures have been developed and used over the years, most of which are variations on the Quality-Adjusted Life Year (QALY) model. However, measuring the quality of life with a disease has proved to be a difficult task with many differing opinions and critics claiming such measures to be arbitrary. Therefore, in 1996 when the World Health Organization project on Global Burden of Disease was charged with the task of determining the total burden of the world's most significant diseases they decided that the currently used variables were unsatisfactory and inconsistent with each other. To solve this problem they developed an internationally standardized variable based on the QALY model, which they called the Disability-Adjusted Life Year, or DALY. One DALY is defined to be one lost year of healthy life. Premature death is defined as the number of years a person would have expected to live in his country if he did not have a given disease. In order to calculate total DALYs the number of years of life lost due to premature death (YLL) need to be estimated and added to the number of years lived with disability (YLD).

At first glance one may think that such a variable is self-evident and free of value choices, but upon closer inspection it can be seen that, in fact, society's values are built into this measure. Because disease burden measures the gap between actual health status

and a non-existent reference (or ideal) health status, there are five value choices that must be made to determine what this reference health status should be.

The first of these choices is, how long should people live? What is the reference age that people should live to? For the purpose of this study the reference age is chosen to be the average life expectancy in Bolivia. This is likely an underestimate of the burden because it is skewed downward due to the pervasiveness of the disease in question. However, it is more accurate than using the life expectancy of a western country, because even people without Chagas disease would not be expected to live as long as people in, for example, Japan. Also, since this study does not attempt to compare the disease burden of Chagas disease in Bolivia with that of other countries, it is the most appropriate estimate for a reference age.

Secondly, and equally important, is the question of equality. Should all people be considered equal, or should a certain socioeconomic group be worth more than another? The Global Burden of Disease (GBD) project decided that their variable should be as egalitarian as possible and, as such, all people should be regarded equally, regardless of socioeconomic status, race, and education. They do, however, consider men and women differently. This is largely because the life expectancies for women are longer than for men throughout the world. Because of the lack of exact data and because the difference in life expectancies between sexes in Bolivia is minimal (about five years), this study does not consider the sexes individually.

The third value choice is whether healthy life is more valuable during early adulthood than it is during childhood or late in life? Saying yes would amount to discriminating against the young and the old, and some would claim this violates the

principle of equality, but because every person will be expected to live through all stages of life, every individual life is treated equally. This is a controversial question, but several studies have shown that most cultures actually do value life more during young adulthood, and for the purpose of this study when also incorporate this judgment [39, 40, 41, 42, 43]. This is because young adults are a more necessary part of the family structure, are more economically productive, and play a more important role in the community and government.

The fourth value judgment is whether a year of healthy life in the future should be equivalent to a year of healthy life lived now. In economics the concept of interest and discounting of future money is well accepted, but valuing future health less than current health is much more controversial. The Global Burden of Disease project decided to use a discount rate of 3 percent per year, because they believed that most people would prefer to have a year of healthy life now than a year of healthy life in the future [39, 40]. Although using a discount factor has an impact on measures of disease burden, and estimates of cost-effectiveness of interventions, this study also utilizes a 3% rate for the same principle as stated above.

The final question is how to compare years of life lost to premature death with those spent living with disabilities of various severities. Defining disability and how it should be compared to death is a difficult task. To be useful relative severities of disability must accurately reflect society's preferences. To achieve a set of relative disabilities the Global Burden of Disease project surveyed health workers from around the world using a person trade-off method, where people are asked how many years of life with a given disability they would trade for one year of healthy life. For example if

people would trade five years of life with a given disability for one year of healthy life that would receive a disability weight of 0.8. Disabilities weights are thus a number between zero (representing perfect health) and one (equivalent to death). In spite of their different backgrounds they were able to agree on a set of disability weights for a wide variety of conditions and these weights were close to several additional surveys of other groups [39, 40]. The disability weight for Chagas cardiomyopathy is 0.25 (similar to that for angina pectoris), meaning that people would trade four years of this disability for 3 years of healthy life. The choices for age-weighting, discount rate, and disability weight used in this study were selected so as to best approximate the current cost of future illness.

The formulas for years of life lost due to premature death (YLL) and years of life lost to disability (YLD) are shown below [39, 40, 41, 42, 43]. Total DALYs are equal to the sum of YLL and YLD.

$$YLL = \frac{KCe^{ra}}{(r + \beta)^2} [e^{-(r + \beta)(L + a)} [-(r + \beta)(L + a) - 1] - e^{-(r + \beta)a} [-(r + \beta)a - 1]] + (1 - K)(1 - e^{-rL})/r$$

$$YLD = DW \left\{ \frac{KCe^{ra}}{(r + \beta)^2} [e^{-(r + \beta)(L + a)} [-(r + \beta)(L + a) - 1] - e^{-(r + \beta)a} [-(r + \beta)a - 1]] + (1 - K)(1 - e^{-rL})/r \right\}$$

where:

a = age of death (years).

r = discount rate (r = 3%).

β = age weighting constant ($\beta = 0.04$).

K = age-weighting modulation constant (e.g. K=1).

C = adjustment constant for age-weights (C = 0.1658).

L = standard life expectancy at age of death (years).

DW = disability weight (DW for Chagas cardiomyopathy = 0.25)

2.6 Purpose of Disability-Adjusted Life Years

Like every variable of disease burden, there are many opponents to DALYs who claim that a better measure can be reached [44]. However, despite its critics, it has revolutionized the study of disease burden and has become the overwhelmingly most common measure in studies of this type.

Some argue that the choices for age-weighting function, discount rate, and/or disability weights are somewhat arbitrary and can have a profound impact on the final results. However, when the authors of the Global Burden of Disease project tested it, they found that different choices for the age-weighting function had little impact on the relative ranking of diseases in terms of disease burden. Changing the disability weights also had a small effect, but different choices for the discount do significantly affect rankings. Increasing the discount rate puts more weight on older age groups, and hence, diseases that primarily affect older populations will be ranked relatively higher than if the discount rate were lower. The most important factor, however, is the accuracy of the basic epidemiological data [39, 40].

There have been several studies to evaluate the impact of using different health related quality of life measures on estimates of disease burden, and most of them have found that changing the measure causes little, if any, variation in rank order for disease burden. One study compared the effect of using Disability-Adjusted Life Years, Quality-Adjusted Life Years, and Years of Healthy Life measures on the burden of disease estimates of five common diseases. They found that rank order was only very slightly effected by the different measures, with only one disease changing order with DALY score, but otherwise the same [45].

This study does not compare burdens among diseases, but rather estimates the burden of a single disease, so preservation of rank order is of less importance than accuracy for Chagas disease in particular. For this reason the most important factors are the accuracy of the data for number of people with the disease, number of people that die prematurely, and the value of the disability weight. The limitations of using this variable to calculate the disease burden are that it only takes into account the disability for individuals that develop cardiac symptoms, and does not account for the psychological effects of having a potentially debilitating and life-threatening disease. For this reason the true burden of Chagas disease would most likely be higher than what is calculated here.

3 Results

3.1 Cost of Intervention

In order to estimate the cost of the proposed intervention to treat the children of Bolivia who have Chagas disease, it is necessary to know how many children live in the endemic area, and what percentage of them is likely to be infected. Through their efforts with vector eradication the National Chagas Control Program in Bolivia is constantly updating their estimates for the number of inhabitants in the endemic area, and these numbers are the most up-to-date available (see Table 1). While these estimates are not broken down into age groups, an estimate for the number of children under 15 years of age can be made using the population structure for the entire country. Bolivian population demographics are shown in Table 2 [9].

Table 1: Number of people living in endemic areas of Bolivia (latest data from National Chagas Control Program, Bolivian Ministry of Health, unpublished)

Departments	Population in Endemic Area
Chuquisaca	531,522
Cochabamba	1,335,280
La Paz	282,348
Potosi	403,856
Santa Cruz	1,983,392
Tarija	357,916
Total	4,894,314

Table 2: Population structure of Bolivia [9]

Age Groups	Population	Percentage
0-14	3,177,833	36.4%
15-64	5,154,030	59.1%
65 +	392,293	4.5%
Total	8,724,156	100%

The age groups are broken down into 0-14, 15-64, and 65+, with the youngest category making up 36.4% of the population. This is the age group of interest to the current study. Multiplying the total population in the endemic area by the fraction that is under 15 years of age ($4,894,314 \times 0.364$), an estimated 1,781,530 children are at risk of having Chagas disease.

While, the prevalence of Chagas disease can be as high as 50% in the endemic area of Bolivia, the prevalence amongst children will be significantly lower. This because the vector eradication program has been steadily decreased the number of houses infested and hence the risk of Chagas infection. Because the interventions inclusion criteria require that the locality have a fewer than a three percent infestation rate, the only way that newborn children (less than a year old) could be infected is through congenital transmission, which happens at a rate of about 5% in live births from women with Chagas disease [8, 46]. It is safe to assume that the prevalence amongst women of child-bearing age is approximately equal to the total prevalence in this area, which is about 40%. Therefore, it is expected that about two percent (0.40×0.05) of newborns will be infected.

Most people that become infected by *T. infestans* are infected during childhood, and because the risk of infection is relatively constant throughout childhood, the percentage of children infected at each age increases linearly from 2% at birth [8, 46] to

about 40% by 14 years of age. This linear relationship leads to the conclusion that the average number of children in this age group that are expected to be infected is 21% (see Appendix 1 for calculation of average number of children infected). Thus, 374,086 children, or 21% of the children at risk ($1,781,530 \times 0.21$), will be expected to be infected with Chagas disease

Currently only 70% of the localities have an infestation rate low enough to meet the inclusion criteria for this intervention, so the expected number of children at risk and infected that will be included in the study will be 1,247,071 ($1,781,530 \times 0.7$) and 261,860 ($374,086 \times 0.7$), respectively.

3.1.1 Cost of Screening

The cost of screening all the children at risk with the immunochromatography test will be about \$5 per child. This value includes the cost of the test kit itself (approximately \$1.60 each), the cost of paying and training the technician who will administer the test, as well as other materials such as gloves and needles. This dollar estimate is based on the average charge for this test at public laboratories in Bolivia. This test is very useful for screening because it only requires minimal training, provides rapid results, and is highly sensitive (95.5%) [29].

The total cost of screening will therefore be \$5 per test multiplied by 1,247,071 children, or \$6,235,356 (see Table 3).

3.1.2 Cost of Confirmatory Testing

Confirmatory testing of positive results will be done by ELISA at a larger laboratory and will also cost approximately \$5 per positive children from screening.

Again, five dollars was arrived at because it is the average charge for an ELISA test at public laboratories in Bolivia. This includes the cost of the kit (about \$0.80), reagents, technicians, gloves, needles, and all other costs. Although this test requires a trained biotechnician and takes several hours, the samples will be brought en masse to a larger laboratory that is accustomed to this type of test, and they can be run together to reduce costs. Two blood samples will be taken during screening so that no additional blood draws will be needed at this time. This test is appropriate for confirmatory testing because, as stated earlier, it has a specificity of 98.2%.

Because we estimate that 21% of the children screened will be positive for Chagas, the total costs of confirmatory testing will be \$5 per test multiplied by 261,860, or \$1,309,300 (see Table 3).

3.1.3 Medical Consultation Costs

Each child that has a positive ELISA test will be considered to be infected and the patient's parents will have an hour consultation with a medical doctor to discuss the nature of the disease and how it will be treated (as described previously). After informed consent is received the doctor will administer the first treatment of benznidazole and distribute a one or two weeks supply of the drug to the parents. Doctors familiarized with the program will be brought to each locality for only a few days to oversee testing and provide counseling. After this, a local nurse will provide the additional care, except in the case of an emergency.

The average charge of a medical consultation by a primary care physician in Bolivia is \$5 per hour. It may seem that the stated charges are extremely low, but it must be understood that the cost of labor in Bolivia is extremely low, even for trained

physicians. Thus, the estimate for the cost of medical consultations will be \$5 per positive child multiplied by 261,860, or another \$1,309,300 (see Table 3).

3.1.4 Pharmaceutical Costs

The cost of benznidazole when purchased in bulk directly from the WHO or the distributor is \$15 for 100 pills of 100mg each. This is an average cost of \$0.15 per 100mg, and the dose to be administered will be 7mg/kg per day for 60 days.

To calculate the total amount of benznidazole needed a standard growth chart was used to estimate the average weights for children at each age (see Appendix 1). These average weights were multiplied by the dose of 7mg/kg to calculate how many milligrams would be needed per person per day in each age group. These numbers were then rounded that to the nearest 25mg because each tablet can only be cut into four pieces. Multiplying this by 60 days and by the estimated number of children with Chagas in each age group provides an estimate of the total amount of benznidazole per group. By summing over all age groups and multiplying by \$0.15 per 100mg it is estimated that the total cost of pharmaceuticals will be \$5,369,188 (see Table 3 and Appendix 1 for further details on these calculations).

3.1.5 Cost of Follow-Up Testing

The effectiveness of treatment will be assessed by measuring the children's titers for anti-*T. cruzi* antibodies with ELISA every year for 8 years after treatment is completed. This is important not only to evaluate the success of the program but also to inform individuals if they have been cured or not.

The cost of follow-up ELISA tests will be the same as the initial confirmatory ELISA – \$5 per person per year. In order to calculate the cost of these tests in present day dollars it is necessary to apply the discount rate of 3% to future costs. This discount rate shows that the cost of one test per person for the next eight years is equivalent to 7 tests per person this year (present value = $1/(1-\exp(-r))^*[1 - \exp(-ar)]$, where r = discount rate and a = years of the annuity) [47, 48]. Thus, the total cost of follow-up testing will be \$5 per test per person multiplied by 7 tests multiplied by 261,860 people, which is \$9,173,286.

3.1.6 Administrative/Unforeseen Costs

Additional administrative and unforeseen costs could increase the total costs by up to fifty percent. If all follow-up testing is completed that would mean these extra costs could be up to \$11,698,215. If none of the follow-up testing is performed these additional costs would be about \$7,111,572. These additional costs relate to the relative unpredictability of future turmoil or changes in administrations as well as the relative inefficiency of poor developing nations.

Table 3: Intervention's Costs for Testing and Treating

Activity	Cost
Screening	\$6,235,356
Confirmatory testing	\$1,309,300
Medical consultation	\$1,309,300
Pharmaceuticals	\$5,369,188
Follow-up testing	\$9,173,286
Administrative/Unforeseen	\$11,698,215
Total	\$35,094,645

Thus, the total cost for the intervention would be \$35,094,645 – or only \$134.02 per infected child. Or if follow-up testing is not performed, the cost would be \$21,334,716 – only \$81.47 per infected child.

3.2 Benefits

3.2.1 Direct Costs of Chagas cardiomyopathy

The direct costs associated with Chagas cardiomyopathy are defined here as the minimal medical costs needed by those individuals that develop chronic cardiac symptoms as a result of Chagas disease. In order to determine this it is necessary to know how many people will develop cardiac symptoms, what medical procedures they will need, and how much those procedures will cost. Additionally, it is important to know the average age of onset of these symptoms, and the average life expectancy for this group.

As previously stated, approximately 25% of people with Chagas disease in Bolivia will develop chronic cardiac symptoms [6]. The onset of symptoms usually starts around 28 years of age. Ten percent of these patients will die prematurely as a direct result of their cardiac symptoms, at an average age of 47 years [49]. The rest have a life expectancy equal to that of the general population, which is 65 years [9].

The medical procedures necessary for individuals with cardiac symptoms include electrocardiogram, echocardiography, Holter monitor, chest X-ray, stress test, anti-arrhythmic medications, medical consultations, and for some, pacemaker implantation, and intensive care. Studies in Argentina and Chile estimated the average yearly cost per cardiac patient to be \$1,085 and \$1,000 respectively [49, 50]. However, medical costs are significantly lower in Bolivia and one previous study of the cost of congenital Chagas

in Bolivia estimated the yearly cost of cardiac symptoms to be \$800 per patient (submitted manuscript by Billot C. & Torrico F. 2004). This number is based on an average of \$125 for consultations, and an average of \$675 for tests, procedures, and when appropriate, anti-arrhythmic medications and/or permanent pacemaker implantation.

Using the above data the estimated number of people that will develop cardiac symptoms is 65,465 (25% of 261,860). Multiplying this number by \$800 arrives at a total direct cost per year of \$52,372,002 (assuming everyone got their ideal treatment). The ten percent of patients that die prematurely will live an average of 19 years after the onset of symptoms (from 28 to 47), which is equivalent to 14.7 years when the discount rate of three percent is applied. Those that don't die prematurely will live an average of 37 years (from 28 to 65) – equivalent to 22.68 years of when discounted by 3% per year.

To calculate the direct costs for those that will die prematurely it is necessary to multiply the number of people in this group ($6,547 = 0.1 * 65,465$) by \$800 per year, and then multiply again by the average number of years lived with symptoms (14.7 years discounted) to arrive at \$76,991,080. The same is done for those that will not die prematurely by simply changing the number of people to 88,098 and the average number of years lived with symptoms to 22.68 to arrive at a cost of \$1,146,240,825.

These are the costs at the age 28 when symptoms first occur, and to convert them into present-day dollars we discount by 18.6 years, because the current average age is 9.4 (see Appendix 1). We find that \$1 in 18.6 years is worth \$0.57 in current dollars. Thus, the sum total of direct costs in present-day dollars is \$656,303,442 (if everyone sought treatment) (see Appendix 2 for further explanation of calculations).

The estimate of \$800 per patient per year reflects the ideal minimum treatment that patients should receive if they were able to afford it, but in reality very few people in Bolivia can afford even basic medical care, let alone the care necessary for the treatment of Chagas cardiomyopathy. For the sake of this study it presumed that only 20 percent of those with symptoms will actually seek professional treatment, which is an estimate that has been quoted by some experts, of the percentage of people in developing countries who seek medical attention for their chronic health problems [38]. Even 20 percent may actually be an overestimate of the amount of medical assistance that will be consumed in Bolivia, where little specialized care of Chagas exists and people are not accustomed to seeking professional support. However, when direct costs are diminished it can be expected that there will be an accompanying increase in indirect costs from additional disability. Assuming that only 20 percent will seek treatment, the total direct cost of Chagas in present-day dollars is reduced to the more realistic value of \$131,260,688 (see Table 5).

3.2.1 Indirect Costs of Chagas cardiomyopathy

Calculation of indirect costs is an attempt to gauge the economic and social weight of disease. They usually outweigh direct costs by far, and this study is no exception. In this study indirect costs are measured solely by the lack of productivity from disability and premature death due to chronic cardiac manifestations of Chagas disease. There was neither an attempt to include psychological and other difficult to quantify costs, nor to include disability attributable to gastrointestinal manifestations of the disease due to the lack of available data. As such, it is likely an underestimate of the true social impact of Chagas disease.

Indirect costs are measured here by the use of Disability-adjusted Life-Years (DALYs), as previously described, and translated into monetary units by using the average per capita income in Bolivia – \$2,400 per year [9]. To measure the total DALYs the number of years lost due to premature death (YLL) must be measured, as well as the number of years lost due to disability (YLD). It is important not to forget, however, that those who die prematurely also suffer disability prior to death.

The first calculation is the number of years lived with disability for each group – those that die prematurely and those that do not. The disability weight used for chronic Chagas cardiomyopathy is 0.25, which is similar to the number determined by the Global Burden of Disease project for angina pectoris. To put this in perspective, it means that four years lived with this disability is equivalent to three years of healthy life. Again, the average onset of symptoms is 28 years of age, the life expectancy for those that will not die as a result of these symptoms is 65 years, and the life expectancy of those that will die prematurely is 47 years. Therefore, those that will not die as a result of their cardiac symptoms (90%) will live an average of 37 years with symptoms (from age 28 to 65). Inputting this information into the equation for YLD in section 2.5 this group will lose 6.878 years due to disability. Multiplying by the number of people in this group (58,919) the YLD for this group is 405,236.

The individuals that will die prematurely as a consequence of their cardiac symptoms will live an average of 19 years with disability (from age 28 to 47). Applying the formula for YLD it is determined that they will lose 4.936 years to disability; and multiplying by the group population (6,547) that is 32,312 YLD. Thus, the total number of years lost to disability (at the age of onset of symptoms) is 437,548. As with direct

costs, these numbers must again be discounted by 18.6 years (average age of onset minus average age now) to obtain the YLD at the present. Thus, multiplying by 0.57 the total years lost to disability at present is 250,527 (see Table 4).

Secondly, the number of years lost to premature death must be calculated. The average life expectancy for those that die early is 47, which is 18 years less than the average population, but applying the formula for YLL arrives at 13.74 years. Multiplying by the 6,547 people that will die prematurely the total YLL at the age of death is 89,927. To adjust the YLL at the age of death to those at present they must be discounted for 37.6 years (difference between average age of premature death and average age at present). This discount factor is 0.32, and thus, we find the total years of life lost due to premature death to be 29,119 (see Table 4).

Table 4: Total DALYs (discounted to present day)

YLD	250,527
YLL	29,119
Total DALYs	279,646

DALYs are the sum of years of life lost due to disability and premature death; consequently summing these two values the total DALYs due to chronic Chagas disease are 279,646 (see Table 4). To convert DALYs into a monetary value they are multiplied by \$2,400, which is the average yearly per capita income in Bolivia. Consequently, the total indirect cost in present-day dollars is \$671,149,125 (see Table 5).

3.3 Cost vs. Benefit

To compare the costs and benefits of the intervention the amount of future costs that would be alleviated by the program must be estimated. The total future costs (sum of direct and indirect costs) would be \$802,409,813 in present dollars (see Table 5).

Assuming a cure rate of 60 percent (as found in previous studies) [33, 34], then a minimum of 60 percent of the total cost of chronic Chagas can be prevented by the intervention. That would be a savings of \$481,445,888 ($0.6 * \$802,409,813$) from cure of the disease alone (see Table 6).

Table 5: Direct and Indirect Costs of Chronic Chagas

Direct Costs	\$131,260,688
Indirect Costs	\$671,149,125
Total Costs	\$802,409,813

However, in reality more will be saved because, previous studies showed that even those who are not cured will have about seven times less pathology than if they were not treated at all [35]. Therefore, it can be presumed that the remaining 40 percent of future costs of disease will be decreased seven-fold. That would be a savings of \$275,111,936 [$(\$802,409,814 - \$481,445,888) * 6/7$] due to decreased pathology for those that are not cured, bringing the total savings alleviated by the intervention to \$756,557,824 (see Table 6). These savings can be broken down into more than \$132 million in direct costs and \$632 in indirect costs prevented. The total savings per infected patient would be \$2,889 (equal to \$756,557,824 divided by 261,860).

Comparing the cost of the program to its benefits, it would cost only about \$35 million now to prevent \$757 million in the future (both in present dollars). That is a ratio of 22 to 1, meaning that it would be twenty-two times more expensive not to institute this intervention.

Table 6: Cost-Benefit Analysis

Interventional cost	\$35,094,645
Cost alleviated by cure	\$481,445,888
Cost alleviated by decreased pathology	\$27,511,936
Total cost alleviated by the program	\$756,557,824
Ratio of costs alleviated to program cost	22:1

The ratio of benefits to cost can be made even more dramatic if one considers that follow-up testing could be eliminated from the program (if sufficient funds were not available) without having any effect on the intervention's benefits. As previously discussed follow-up testing is only important to allow subjects and investigators to evaluate the treatment's effectiveness, but does not actually add to the treatment effect. If follow-up testing were eliminated it would bring the cost of the program down to \$21,334,716 increasing the benefit to cost ratio to 35 to 1.

3.4 Sensitivity Analysis

Due to the nature of imprecise data and unpredictability of the future, the values calculated here for costs and benefits may vary somewhat from their true values in the future. For this reason the cost and benefit can be treated as stochastic variables. If they are normally distributed with a means equal to their calculated values and standard deviations equal to twenty-five percent of their calculated values, then the 95%

confidence interval (CI) for the intervention's cost would be [\$17.5 million, \$52.6 million], and the 95% confidence interval for the intervention's benefit would be [\$378 million, \$1.1 billion]. With these assumptions the intervals clearly do not overlap, meaning that the cost and benefit are statistically different (p -value < 0.001). In fact, the standard deviations for these variables would have to be higher than 45.6% of their mean for them not to be significantly different (95% CI for cost = [\$3.1 million, \$66.9 million] and 95% CI for benefit = [\$66.9 million, \$1.45 billion], p -value = 0.05). However, because there has been no precedent for this intervention, it is more difficult to accurately estimate the cost to implement it; whereas the benefits of treatment have already been proven in several other studies [33, 34, 35]. For this reason there is apt to be more variability in the cost of the intervention than in its benefit. If this is the case, the calculated cost of the intervention would have to be off by more than an order of magnitude to bring it even close to the calculated value of the benefits.

4 Discussion

Based on the results of this study it can be concluded that with an initial investment of less than \$135 per infected person, it would be possible to prevent approximately \$2,900 worth of future costs, and relieve over 279,000 DALYs from the economic weight of illness in Bolivia. This is clearly a profitable investment. In fact, the magnitude of this profit margin is so astronomical that it is an opportunity Bolivia's struggling economy can ill afford to pass up.

This study has yet to consider the additional effects of Chagas disease on society. This intervention would additionally have a positive impact on patients' quality of life not captured in Disability-adjusted Life Years, prevent psychological damage and stress, as well as decrease social stigma and discrimination; not to mention eliminating the gastrointestinal symptoms of the disease. All governments have a responsibility protect their citizens whenever possible, and the public gratitude that could be engendered toward the government for undertaking such an intervention should not be underestimated. This is especially true because Chagas disease strikes people down during young adulthood after society has invested resources in their education and upbringing, and limits their ability to become fully productive members of society.

Another indirect benefit of the program would be to increase support for the vector control program by increasing public awareness of the risks of Chagas disease and thereby increasing demand for eradication of reduviid bugs from homes. Localities that did not initially fulfill the requirement of a less than three percent infestation rate would see the benefits of treatment that other communities are receiving and have a strong motivation to work towards eradication in their own community so that they could enjoy

these benefits themselves. The larger the incentives the more public support will be available for such programs.

This intervention would work best in conjunction with a program to test and treat congenital infections, because in these areas congenital infection would be the last remaining possible mode of transmission. Through the use of such a program it would be possible to eliminate Chagas disease entirely from the population in approximately 30 years. This would require continued vigilance, but the rewards are immense for a society that is already stricken with poverty. Indeed, if congenital infection is not effectively controlled it can cause Chagas disease to persist for generations after the vector has been eliminated. The yearly cost of a program to control congenital infection has been calculated to be approximately \$450,000 per year (submitted manuscript by Billot C. & Torrico F. 2004). This can be seen as a yearly supplement to the intervention proposed in this study.

Not only is it ethically responsible to provide the internationally recognized minimum standard of care, it is economically profitable. This study provides a means whereby both health care managers and health economists can agree that such a health intervention is feasible and imperative for the people *and* the economy of Bolivia.

While health studies based on DALYs such as this cannot substitute for other social and political factors necessary for decision making, they can provide invaluable insight to the hidden costs of a disease that primarily affects the most indigent of poor, developing nations, and consequently, does not often receive the attention it warrants. Perhaps when decision makers realize that this disease has a large direct impact on gross

domestic product (GDP), in spite of the population it effects, they will consider increasing spending to moderate its consequences.

4.1 Study Limitations

One of the limitations of this study is that some of the data were best estimates, but these estimations are as close as possible under the current circumstances. When estimations were necessary they are stated in the text. However, due to the magnitude of the difference between costs and benefits it is very unlikely that changes in the initial variables would lead to a different conclusion. This is shown mathematically through the sensitivity analysis.

Additionally, it is assumed that every individual will make the average income for Bolivia, but this may not be the case. In a country where unemployment and under-employment is the rule, the economy does not operate to its potential and the loss of an employee can be fairly easily substituted for another. However, for the sake of equality this limitation is acceptable because it is generally agreed upon that the value of life should not be based on socio-economic status, ethnic group, or any other discriminating factor. Furthermore, if Bolivia's economy develops further, and wages increase, this will reduce the effect of the above limitation.

The concept of "human capital" allows for the assignment of a monetary value to human life based on the productivity of that life, however, this should be an absolute minimum estimate, as human life is far more valuable to society than simply through its economic productivity. All ethical doctrines hold this truth to be self-evident.

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6 Appendices

6.1 Calculation of Drug Costs

age	average weights (kgs)	mgs drug/day	Amt. drug/day to nearest 25mg	total mgs of drug/person for 60 days	kids in each age group	% of kids with Chagas	kids with Chagas	total mgs of drug for 60 days	total cost for drugs	total cost of drugs per infected	average age calculation
0	5	35	50	3,000	83,138	2.0%	1,663	4,988,285	\$7,482	\$4.50	0
1	10	70	75	4,500	83,138	4.7%	3,919	17,636,081	\$26,454	\$6.75	3,919
2	13	91	100	6,000	83,138	7.4%	6,175	37,052,980	\$55,579	\$9.00	12,351
3	15	105	100	6,000	83,138	10.1%	8,432	50,591,185	\$75,887	\$9.00	25,296
4	16	112	125	7,500	83,138	12.9%	10,688	80,161,737	\$120,243	\$11.25	42,753
5	18	126	125	7,500	83,138	15.6%	12,945	97,084,493	\$145,627	\$11.25	64,723
6	21	147	150	9,000	83,138	18.3%	15,201	136,808,700	\$205,213	\$13.50	91,206
7	23	161	175	10,500	83,138	21.0%	17,457	183,302,008	\$274,953	\$15.75	122,201
8	25	175	175	10,500	83,138	23.7%	19,714	206,993,867	\$310,491	\$15.75	157,710
9	29	203	200	12,000	83,138	26.4%	21,970	263,640,830	\$395,461	\$18.00	197,731
10	32	224	225	13,500	83,138	29.1%	24,226	327,056,895	\$490,585	\$20.25	242,264
11	36	252	250	15,000	83,138	31.9%	26,483	397,242,062	\$595,863	\$22.50	291,311
12	40	280	275	16,500	83,138	34.6%	28,739	474,196,332	\$711,294	\$24.75	344,870
13	45	315	325	19,500	83,138	37.3%	30,996	604,413,014	\$906,620	\$29.25	402,942
14	51	357	350	21,000	83,138	40.0%	33,252	698,290,040	\$1,047,435	\$31.50	465,527
Totals:					1,248,459	21.0%	261,860	3,579,458,509	\$5,369,188	\$20.50	avg. age: 9.41

\$15 for 100 pills of 100mg
 cost per mg of drug \$0.0015
 Dose: 7 mg/kg

6.2 Calculation of Direct Costs due to chronic Chagas Disease

Direct costs of chronic Chagas disease

percentage of total cases with cardiac manifestations	25%
number of cardiac cases	65,465
direct costs per cardiac case/year	\$800
direct costs per year	\$52,372,002
percentage of cardiac cases that die early	10%
number of cardiac cases that die early	6,547
percentage of cardiac cases that don't die early	90%
number of cardiac cases that don't die early (90%)	58,919
discounted years of direct costs for those that die prematurely (from age of disability onset)	14.70
discounted years of direct costs for those that <i>don't</i> die prematurely (from age of disability onset)	22.68
sum of direct costs for those that die prematurely (at age of disability onset)	\$76,991,080
sum of direct costs for those that <i>don't</i> die prematurely (at age of disability onset)	\$1,069,249,746
total direct costs (at age of disability onset)	\$1,146,240,825
discount factor from age of disability onset to average age now	0.57
total direct cost now (if everyone sought treatment)	\$656,303,442
percentage that actually seek treatment	20%
total direct cost (now) if only a percentage seek treatment	\$131,260,688
total direct cost (now) (per infected patient)	\$501

6.3 Calculation of Indirect Costs due to chronic Chagas Disease

Indirect costs of chronic Chagas disease

cardiac Chagas disability weight	0.25
average years lost to disability for those that <i>don't</i> die early	6.878
Total years lost to disability for those that <i>don't</i> die early (at age of disability onset)	405,236
average years lost to disability for those that die early	4.936
average years lost to mortality for those that die early	13.74
Total years lost to disability for those that die early (at age of disability onset)	32,312
Total years lost to mortality for those that die early (at age of death)	89,927
Total years lost to mortality for those that die early (at age of disability onset)	50,856
Total YLDs (at age of onset)	437,548
Total YLDs (at present)	250,527
discount factor from age of premature death to average age now	0.32
Total YLLs (at present)	29,119
Total DALYs (at age of disability onset)	488,404
Average age of infected child (now) (see calculation to right)	9.41
Total DALYs (now)	279,645
Total indirect cost (now)	\$671,149,125
total indirect cost (now) (per infected patient)	\$2,563