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THE ECONOMICS OF CARING FOR CHILDREN WITH PEDIATRIC GASTROENTERITIS IN BOLIVIA: A CAREGIVER'S PERSPECTIVE

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Hubert Department of Global Health
2011

Abstract

THE ECONOMICS OF CARING FOR CHILDREN WITH PEDIATRIC GASTROENTERITIS IN BOLIVIA: A CAREGIVER'S PERSPECTIVE

By Rebecca E. Moritz

BACKGROUND Globally, diarrheal disease is responsible for approximately 1.3 millions deaths annually for children under the age of five and rotaviruses are the primary agent for 40% of all acute diarrheal cases. In Bolivia, rotaviruses are the primary cause for almost half of all diarrheal related hospitalizations and a mortality rate of 66 per 100,000 children. Therefore, it is important to understand the conditions that perpetuate the country's diarrheal morbidity and mortality rates by exploring the role of the caregiver and the relationship between the caregiver's socio-economic factors and a diarrheal event.

GOALS To quantify the financial impact an episode of diarrhea has on a Bolivian caregiver and to determine which characteristics of a Bolivian caregiver for a child suffering from a diarrheal episode are associated with a catastrophic cost of 1% or greater to the caregiver's household.

METHODS This cross-sectional study took place during the summer months of 2007-2009. The study population consisted of 1,109 Bolivian caregivers of children who presented with diarrhea to various pediatric wards, emergency rooms and outpatient clinics in four Bolivian cities: El Alto, La Paz, Cochabamba and Santa Cruz. The caregivers were asked questions related to treatment habits, access to care, perceptions of health care costs and cost estimates attributed to the diarrheal event. A logistic regression was conducted modeling the probability that a caregiver's behavioral characteristics were associated with a catastrophic cost of 1% or greater.

RESULTS The median total direct costs for a diarrheal episode in a Bolivian household were approximately 23 bolivianos and the median indirect costs were 60 bolivianos. The presence of a working spouse had a "protective" effect whereas a caregiver who took the child to any place prior to the current site of treatment proved to be a significant risk factor for experience catastrophic cost at the 1% or greater level.

CONCLUSION Bolivia should work towards improving the economic conditions of Bolivian caregivers' and their households by providing support to mitigate the financial ramifications of a diarrheal episode and thereby reducing the probability that a household will experience catastrophic cost as a result of the diarrheal event.

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ACKNOWLEDGEMENTS

I would like to thank everyone who supported me during the thesis process with special thanks to my thesis advisor, Dr. Juan Leon. Working with Dr. Leon was one of the best experiences I have had at Emory and would welcome the opportunity again. I would also like to thank my friends and family for their continual encouragement and support. Finally, I would like to extend my gratitude to the participants of this study - without their participation this research would not have taken place.

TABLE OF CONTENTS

REVIEW OF THE LITERATURE

Rotaviruses and Diarrheal Diseases

Diarrheal disease is responsible for approximately 1.3 millions deaths annually for children under the age of five with particular virulence in developing countries, especially sub-Saharan Africa and southeast Asia [1] where rates of mortality are greater than 600,000 childhood deaths annually [2]. While rates of morbidity and mortality due to diarrhea are lower in Latin America as compared with Africa and Asia, diarrheal diseases are still considered endemic in many Latin American countries with WHO estimates of childhood mortalities due to diarrheal causes around 20% [3]. While there are a number of bacterial and non-bacterial agents attributed to diarrheal disease, rotaviruses have been identified as the primary agent for approximately 40% of all acute diarrheal cases worldwide for children under the age of five [4].

Epidemiology and Pathology

Rotavirus infections are most common among children between the ages of 3 and 24 months, however current data suggests that most children worldwide by the age of five have been infected [5, 6]. The burden of disease is particularly virulent in areas where access to clean water and/or proper sanitation measures is inadequate as rotaviruses are transmitted primarily via fecal-oral contamination. They can also be transmitted through contaminated water or food, contact with contaminated surfaces or person-to-person contact [5, 7]. There is also a relationship between risk of infection and climatic changes with seasonal-dependent differences occurring in temperate regions where spikes in incidence coincide with the winter season. The rates of infection in tropical regions are less varied than temperate climates, though rotavirus infections have been found to be

more common during the cooler dry months. One study estimated that for every incremental increase in temperature Celsius, mean monthly rainfall and relative humidity, the incidence of rotavirus decreased by a range of 3% to 10% [8, 9]. While rotaviruses are commonly acquired within the community or outbreaks reported after a natural environmental disaster [10], they are also frequently attributed to nosocomial infections.

The impact of diarrhea as related to rotaviruses in Latin America is not well understood as quality surveillance data is sparse due to insufficient diagnostic capabilities and inconsistent case definitions. In order to improve the understanding of diarrhea in Latin America, the Pan-American Health Organization (PAHO) established a rotavirus surveillance network in 2006 in 11 Latin American and Caribbean countries, including Bolivia [11]. Over the course of a 2-year period, 8,141 positive rotavirus cases with a 31.5% median rate were identified out of a total of 19,817 participating children under the age of 5 from one of 11 Latin American or Caribbean countries who participated in national surveillance networks. According to the surveillance networks, Bolivia was found to have a 39% rotavirus-positive stool sample rate for children under five which is a comparable rate to similar Latin America countries, such as Chile with a 30% positive-stool sample rate and 42% in Honduras [11]. Other literature suggests that Latin America's rotavirus rate for children under-five varies between 16 and 52% [12] with approximately 15,000 deaths and 75,000 hospitalizations attributed to rotaviruses [13]. Globally, the incidence rate of rotaviruses are similar irrespective of location and socioeconomic status [14]. Yet despite similar rates of incidence when comparing developed and developing nations, mortality rates due to rotaviruses are drastically higher

in developing countries. Mortality estimates of rotavirus-attributed diarrhea is around approximately 527,000 childhood deaths annually with an estimated 90% of all diarrheal deaths due to rotaviruses occurring in children under five from low-income countries [15-17].

The exact pathogenesis of rotavirus is not completely understood. However, one theory is that the rotavirus virus interrupts the gastrointestinal process by releasing a viral enterotoxin, NSP4, which interacts with the gut mucosa by weakening the cell junctions. This affects the cytoskeleton of the infected mature enterocytes, which are intestinal absorptive cells, in the mid and upper portions of the villi of the small intestine [18, 19]. This triggers an increase in chlorine ions, which in turns activates the gut motility in the enteric nervous system. This excessive fluid in the intestinal cavity combined with a loss in cell absorption results in severe diarrhea attributed to rotaviruses [20].

Classification of Rotaviruses

Rotaviruses are a genus belonging to the *Reoviridae* family composing of an 11 segmented double-stranded RNA genome [21]. They consist of seven serogroups (A-G) with each group containing various serological types. Groups A, is the most common serogroup identified in human pathogens though Group B and G have also been linked with human-rotavirus infections (HRV) [9]. Groups A-G are capable of infecting animals. As group A is the most understood and virulent serogroup, it is the primary target of the available rotavirus vaccines [20].

Rotaviruses are medium-sized non-enveloped viruses consisting of three layers: outer, intermediate and inner. Each of the 11 genome segments provides the coding for a viral protein - either structural (VP1, VP2, VP3, VP4, VP6, VP7) or non-structural (NSP1-NSP6) [22]. The outer capsid houses two proteins: VP4 and VP7, the intermediate layer is made of protein VP6 – an antigen that determines group and subgroup specificities [23], and the inner layer or core consists of protein VP2 which also encloses proteins VP1 and VP3 [9, 24]. Sequencing for the VP4 and VP7 genes are also used to classify these genes into different genotypes that correspond with the virus serotype [20]. While the G serotypes and genotypes correlate completely, the P serotypes and genotypes do not [25]. Therefore, in order to distinguish between the P serotypes and genotypes, the genotypes are written separately with the genotype number included in square brackets [25]. Additionally, understanding the role of the outer layer proteins VP4 (serotype P - protease-cleaved protein) and VP7 (serotype G - glycosylated protein) is vital for vaccine development because these proteins not only determine serotype classification but are also the first proteins that initially interact with the host cell. This initial interaction situates the proteins as targets for neutralizing antibodies and contribute to protective immunity [9].

Globally, there are an estimated 10 serotype G and 11 serotype P strains associated with HRV. The most common serotypes are G1-G4, which represent over 90% of all rotavirus strains in circulation [23]. Vaccine development has largely focused on these four G serotypes though recent serotype surveillance efforts have discovered that there is greater strain-type diversity than originally believed with a now estimated 42 P-G combinations

in circulation [23]. This discovery has important implications for ongoing research in rotavirus vaccine development and vaccine effectiveness, as it will demand greater heterotypic coverage beyond the four serotypes currently addressed.

Rotavirus Vaccinations

Types of Rotavirus Vaccines

While not conclusive, studies have shown that rotaviruses may provide some natural defenses against future re-infections, or 'infection induced protective immunity' [26], in particular, in severe cases of diarrhea among children [27, 28]. In one study that followed a cohort of Mexican children from birth to two years of age, the authors found that two rotavirus infections – asymptomatic or symptomatic – provided protection comparable to the rotavirus vaccine against more severe illnesses. Following a rotavirus infection, the immune system creates a natural immunity towards future rotavirus infections. However the duration of the natural immunity was unclear [29].

Given the widespread recognition of both the virulence and prevalence of rotavirus infections, the World Health Organization placed great importance on the development of rotavirus vaccines that would be effective in reducing both morbidity and mortality associated with rotaviruses. Beginning in 1983, there have been five primary candidates for rotavirus vaccines with primary methods adopted from animal strains that were comparable to naturally occurring strains in humans. Later strategies included creating a hybrid strain by crossing human and animal strains. However, these were found to be limited in scope [2]. Eventually in 1998, Rotashield, a rhesus-human quadrivalent

vaccine, was introduced to the market. However, the vaccine was pulled one year later as it was found to be associated with a higher risk of intestinal intussusception [30].

Following the withdrawal of the Rotashield vaccine from the market, efforts to find a new vaccine were accelerated. RotaTeq by Merck and Rotarix by GlaxoSmithKline (GSK) are currently the only two vaccines available on the global market with varying levels of distribution. There is also a monovalent Lanzhou Lamb Rotavirus (LLR) vaccine which is available only in China and little data exists on the efficacy of the Chinese vaccine, though reports from a case-control study estimate an effectiveness of 73% [31]. There are also four vaccines in varying stages of development including RV3 a live rotavirus vaccine developed in Melbourne, Australia, RV-UK, an attenuated tetravalent human-bovine vaccine and two naturally occurring bovine-human vaccines 116E and 1321 originating in India [32].

The two primary rotavirus vaccines available for widespread distribution differ in their approaches and protection development against the rotavirus. RotaTeq is a pentavalent vaccine comprising of bovine-human reassortant strains that are highly efficacious against severe cases of rotavirus-attributed gastroenteritis. It is available in over 90 countries [33] and estimates indicate that RotaTeq demonstrates an 85% efficacy in middle to high-income countries [30] and 98% against severe disease [33]. The vaccine is administered in three doses at the ages of 2, 4 and 6 months.

The other commercially available vaccine is Rotarix developed by Glaxo Smith Kline (GSK). It is a monovalent vaccine and is administered in two doses at the ages of 2 and 4 months. It is available in over 100 countries and similarly to the RotaTeq vaccine, the World Health Organization recommends Rotarix for routine immunizations. Rotarix provides protection against the most common strain of the rotavirus via a single-strain vaccine that is effective against multiple rotavirus serotypes. Neither RotaTeq nor Rotarix have been linked to an associated risk of intussusception [34].

Efficacy and Effectiveness

Both RotaTeq and the Rotarix vaccine have been found to have an efficacy of 85-95% protection against the most severe forms of rotavirus-induced hospitalizations and diarrhea in large-scale studies in Europe and the Americas [31]. Both RotaTeq and Rotarix have relatively high rates of efficacy when comparing responses in middle to high-income countries. A recent study conducted by GAVI Alliance comparing Rotarix response rates found that upper-middle income countries had a mean efficacy of 72% compared to a mean of 86% in high-income countries [35]. However, there was a varied range in overall mean response rates in the upper-middle income countries when assessing the efficacy rates by on a country-level. On the upper end, Brazil responded with an efficacy of 85.7% and Mexico responded with an efficacy of 89.6% while in the lower range Venezuela had 62.5% efficacy and South Africa had 44.3% efficacy [35]. This suggests that even amongst 'successful' countries the impact of the rotavirus vaccine is mixed with large variation in results when comparing across regions.

Recently implemented RotaTeq efficacy trials found similar trends to the Rotarix trials with preliminary results indicating greater success in the higher income countries when

compared to the lower income countries. The trials reported a 64% efficacy in Africa (Kenya, Ghana and Mali), and a 51% efficacy in Asia (Bangladesh and Vietnam) [18]. However, promising studies show an increasing efficacy rates in other countries. While still in the nascent stages of its recently introduced immunization program, Nicaragua is expected to show favorable results towards reducing the number of severe morbidity and mortality for children less than 2 years of age [36]. Mexico, who was one of the first countries to introduce the rotavirus vaccine, has reported a 41% decrease in mortality for children under the age of 11 months who had received at least one dose of the vaccine [37]. However, when comparing the success rate of Rotarix and RotaTeq in lower income countries, there was a notable decrease in efficacy rates with the Rotarix vaccine resulting in an overall mean efficacy of only 63% to 75%. Country-level mean efficacy rates of Rotarix include 58.3% in India to 66.7% in Peru [35]. While many hypotheses exist to explain the differing reported efficacy rates when comparing high to low-income countries, further research is still needed to be understand why these discrepancies exist especially if current immunization programs are to be effective in reducing the morbidity and mortality rates in developing countries [35].

Caregivers of Children with Diarrhea

The role of caregivers for children with diarrhea is a very influential position that often impacts not only the probability of a diarrheal event but also the very nature of the outcome. Socioeconomic status as characterized by financial status, level of education and living conditions is often believed to be the greatest significant predictor of diarrheal events in young children. A study conducted in Kingston, Jamaica found that caregivers with poor access to clean water and refrigerators were more likely to have children with

gastrointestinal problems than homes where the socioeconomic status provided for a higher quality of living [38]. Socioeconomic status also influences the likelihood of seeking treatment. In the Amazonian region of Peru, a study found that the poorest quintile of caregivers were significantly less likely to use antibiotics and seek professional care in the event of a cold plus diarrheal infection as compared to other higher economic quintiles [39]. Similarly, in India households of lower socioeconomic levels were also less likely to seek hospitalization due to health reasons including tuberculosis and diarrhea as compared to households with higher socioeconomic statuses [40].

Education level is often associated with the extent to which an individual understands behavioral practices that are related to the prevention or care of diarrhea episodes. The level of education of the caretaker, typically the mother, is a correlating factor with the presence and type of treatment seeking behavior for diarrhea. In Prague, Czech Republic, a study found that maternal knowledge of treatment of diarrheal episodes, in particular the use of oral rehydration salts (ORS), was significantly associated with the level of maternal education [41]. In Hanoi, Vietnam households with a high prevalence of diarrhea among the children was significantly associated with mothers who had a comparatively low level of education [42]. The higher the education level, especially maternal education, the more likely it is that the caretaker will know how to address or seek information regarding proper treatment behavior or preventative care, such as breastfeeding [43].

The perception of a diarrheal-attributed illness is also shaped largely by the role of the caregiver and often linked with the beliefs surrounding the underlying causes of the infection itself. In some situations, the severity of the illness is not well understood by the caregiver and treatment is only sought in the direst of conditions. A longitudinal study conducted in Brazil found that as the duration of the diarrheal illness increased, the level of care decreased [44] implying that caregivers did not understand the correlation between chronic diarrhea and severity of the illness. In other instances, a caregiver's lack of knowledge about the causes for diarrheal episodes in young children is reflected in nature of the treatment sought. In India, Hindu communities define and therefore treat a diarrheal episode differently from their Muslim counterpoints. Hindus see diarrhea as a 'self-resolving' illness and are more likely to self-treat diarrhea whereas Muslims tend to view an episode in a more serious context with far greater consequences. As a result, Muslims in India are more likely to see professional health care for diarrheal disease as compared to Hindus [45].

The impact of diarrhea on the caregiver has financial ramifications due to costs that occur directly and/or indirectly or on a catastrophic level, which may influence the nature and level of care for a child suffering from a diarrheal episode. Direct medical costs are the accumulated expenditures related to the total medical treatment of the patient and can include expenses related to a hospital visit, facilities, treatment procedures and medication supplies [46]. While little data exists on evaluating the direct financial impact of rotaviruses on the caregiver, studies indicate that hospitalizations due to diarrhea are quite severe and place a heavy burden on the caregiver. In Taiwan, on average, 294

USD, or approximately 40%, of the monthly salary of an unskilled work may go towards the cost of child's hospitalization due to a rotavirus infection [47]. In Latin America direct costs associated with inpatient hospitalizations costs (excluding transportation and indirect costs) range from 72.49 USD in the Dominican Republic to 190.12 USD in Panama [46]. While direct hospitalization costs are approximately 15% of the average monthly wage in the Dominican Republic in Panama, the cost of hospitalization carries a higher burden: 26% of the monthly wage [48, 49]. In Bolivia, a recent study estimated that the high costs of diarrheal care and treatment were a primary reason for at least 20% of Bolivian caregivers to withhold appropriate diarrheal treatments for their children [50].

Indirect costs are quantified economic consequences as a result of lost productive (i.e. lost wages or time) by caregivers or parents of children suffering from rotavirus-attributed diarrhea. A study in Brazil found that approximately 50% of caregivers lost time from work while treating a child suffering from gastroenteritis. These lost hours impacted the financial welfare of the household translating into a total indirect cost of 41.90 USD for hospitalized patients and 28.88 USD for outpatients. For the average Brazilian household this was a loss was 15% of their monthly salary to indirect costs alone [51, 52], Similarly in Colombia, lost wages due to rotavirus-attributed diarrheal events were around 44 USD on average roughly equal to 11% of their average monthly salary lost to indirect costs [52, 53]. Other studies in the US and Western Europe report that nonmedical costs associated with rotaviruses have been previously underreported and represent a considerable financial burden on households [54, 55].

Little is known about the nature of catastrophic costs specific to an episode of diarrhea. The information that is available varies depending on location and mean income level of the area. A household suffers catastrophic costs when their available income is reallocated to cover health care expenses thereby forcing the household to reduce everyday expenditures which places them at risk for poverty [56]. In one study catastrophic cost was defined as costs related to a health event that exceed 40% of a household's income after the basic needs have been covered. The out-of pocket payments correlate with catastrophic cost with an increase in the amount of payments associated with an increase in the range of catastrophic cost [57]. Other estimates indicate that in households suffering from poverty the threshold value of catastrophic cost is closer to 6-15% of a household's income [58].

Cost-Effective Models

A number of studies have demonstrated the high costs – direct and indirect - accrued due to an episode of diarrhea. However, what is unclear are the characteristics attributed to the caregiver that are associated with these high costs. Currently, due to limited models available in the literature, little is known about the impact of the caregiver's behavioral choices on the financial outcomes of an event. A recent study does suggest that the Bolivian caregiver's treatment seeking behavior was significantly associated with a catastrophic cost greater than 1% of the annual household income [50].

Correspondingly, while little information is available on the cost-effectiveness of the rotavirus vaccines on a micro-level (i.e. caregivers, individual household), there are a number of studies that focus on the cost-effectiveness from either a national or healthcare

system level. While the macro approach is not useful for the purposes of my analysis, understanding the overall effect a national rotavirus immunization program has on a country does provide some value. For instance, a study by A. Valencia-Mendoza *et al*. measured the impact the vaccine has on cost per saved life in Mexico from a healthcare perspective [15]. The study found that a national vaccine program with each dose costing 15 USD or less would prevent 59% of hospital visits and 70% of deaths attributed rotavirus-gastroenteritis. A Mexican national rotavirus immunization program would ultimately be most cost-effective in poorer areas with less access to medical care where the likelihood of diarrheal mortality is greater [15]. A cost-analysis study in Columbia sought to determine the difference in diarrheal frequency in three child cohorts: children receiving Rotarix, RotaTeq, or no vaccine. The study found that when both vaccines were available for less than 7 USD the cost-effectiveness was around 1063 USD per DALY [53]. While both the Mexico and Columbia studies takes a macro approach to understand the cost benefits of a rotavirus immunization program, the information is useful in identifying key areas and populations where the impact will be the greatest (i.e. rural and poorer region).

In Bolivia

Based on the UNDP human development scale which measures a country's progress in three primary areas: longevity and health of life, educational advancement, and quality of life, Bolivia ranks 113th out of 182 countries placing it as one of the poorest Latin American countries [52, 59]. The Bolivian GNI per capita, PPP, is approximately 4,260 international dollars with an estimated 60% of Bolivians living in poverty and 37.7% living in extreme poverty (i.e. below the international poverty line of 1.25 USD per day).

Rural poverty is estimated around 77.3% [52, 60]. Although access to clean water and proper sanitation systems has seen noted advancements, access to basic amenities continues to plague the country, in particular among Bolivia's rural population. In 2010, approximately 95% of all urban dwellers had access to clean water while only 60% of all urban dwellers had access to clean water in the rural population. Progress has been less remarkable when measured by access to proper sanitation facilities with only 30% of the urban population documented as having access and 10% in the rural population as having access [61]. Lack of clean water and adequate sanitary conditions are primary contributors to the relatively high rates of diarrheal morbidity and mortality. Diarrhea, a leading cause of mortality for children under-five in developing nations, accounts for 15-37% of childhood deaths in Bolivia with vast differences noted between the urban and rural populations with 55 deaths per 1000 live births in urban populations compared to 99 deaths per 1000 live births in rural Bolivian areas [61, 62].

The impact of rotavirus infections on Bolivia is less understood but it is believed that rotaviruses are the primary cause for almost half of all diarrheal related hospitalizations [63] and a mortality rate of 66 per 100,000 children in children under 5 [64]. However with the introduction of a universal rotavirus vaccination program through a subsidy of the Global Alliance for Vaccine and Immunization (GAVI) to the Bolivian government in 2008, the number of rotavirus attributed diarrheal cases has dropped by 10% with coverage rates exceeding 80% for the first dose and 64% for the second dose [63].

Given the important role that caregivers have in the treatment and outcome of diarrheal events, it's important that their place in the line of defense against diarrheal diseases be understood and evaluated. While little data exists on the impact of caregivers on diarrheal outcomes in Bolivia, a study conducted by USAID and the Environmental Health Project (EHP) in conjunction with the Bolivian Ministry of Health found a high correlation between poor hygiene behavior among mothers and caretakers and the presence of diarrhea in their children [65]. A study in Bolivia examining the role of mothers in the presence of childhood diarrheal morbidity, suggests the two primary factors that were associated with a reported presence of diarrhea were level of maternal income and education. The higher the income level the more protective the variable was against reported diarrheal episodes. Education levels also influenced the likelihood of reporting an event with mothers who had at least a primary school education more likely to report diarrheal events as compared to mothers with no education [66]. These results suggest that the role of caregivers needs to be addressed and any prevention treatment programs cannot solely focus on issues of water sanitation but must also examine the influential role of caregivers in determining the outcome of childhood diarrheal morbidity and mortality.

Goals

The goal of this study is to focus on the long-term financial and socio-economic effects on caretakers of children suffering from rotavirus attributed diarrheal diseases. Specifically, the study will seek to determine whether diarrheal diseases and the presence of the rotavirus vaccine may be associated with future socioeconomic status. To answer this question, two aims have been identified:

1. To quantify the financial impact one episode of diarrhea has on a Bolivian caregiver's economic status, and
2. To determine whether behavioral traits of a Bolivian caregiver, diarrhea and the absence of the rotavirus vaccine in infants are significantly associated with current conditions of poverty as measured by catastrophic cost to the caregiver.

Significance

As described previously, socioeconomic status has been shown to be a risk factor for diarrheal diseases. Living conditions, maternal education and access to clean water, among others, are all indicators of a community's susceptibility to endemic diarrhea. The study will provide information that is relevant to programs focusing on developing future strategies for reducing the negative impact of diarrheal diseases on a community's socioeconomic status. This information will allow Bolivia to understand the cost-effectiveness of immunization programs and will ultimately work towards improving the quality of life for caregiver's and their children. Although the use of rotavirus vaccines as prophylaxis for infants is available, it is unclear as to the long-term socioeconomic effects the usage of the vaccine has on a Bolivian caregiver's socioeconomic status. The study will seek to understand the impact that a vaccine might have a on caregiver's current socioeconomic status in order to hypothesize whether the presence of endemic diarrhea in a community with available rotavirus vaccines can be used as a predictor of poverty [67]. If a universal vaccine program is implemented in Bolivia, the influence of outside confounders including the role of the caregiver may be minimized simply by the presence and utilization of a universal vaccine program. Ultimately, the study will aim to

determine what are the behavioral traits of a Bolivian caregiver that are significantly associated with financial ramifications of one episode of diarrhea. By identifying the primary predictors correlated with experiencing financial hardship in the event of a diarrheal event, this information can be useful to mitigate the effects of a diarrheal case on a household. Given that there is little data currently available on the relationship between a caregiver's behavioral choices as related to a diarrheal event and the financial implications, this study will seek to provide new information on a micro level that can be useful in community outreach programs with a focusing on education caregivers of children with diarrhea.

AUTHOR CONTRIBUTION

For this manuscript, the author is responsible for the data analysis, writing of all sections and the development of the tables and figure.

MANUSCRIPT

ABSTRACT

BACKGROUND Globally, diarrheal disease is responsible for approximately 1.3 millions deaths annually for children under the age of five and rotaviruses are the primary agent for 40% of all acute diarrheal cases. In Bolivia, rotaviruses are the primary cause for almost half of all diarrheal related hospitalizations and a mortality rate of 66 per 100,000 children. Therefore, it is important to understand the conditions that perpetuate the country's diarrheal morbidity and mortality rates by exploring the role of the caregiver and the relationship between the caregiver's socio-economic factors and a diarrheal event.

GOALS To quantify the financial impact an episode of diarrhea has on a Bolivian caregiver and to determine which characteristics of a Bolivian caregiver for a child suffering from a diarrheal episode are associated with a catastrophic cost of 1% or greater to the caregiver's household.

METHODS This cross-sectional study took place during the summer months of 2007-2009. The study population consisted of 1,109 Bolivian caregivers of children who presented with diarrhea to various pediatric wards, emergency rooms and outpatient clinics in four Bolivian cities: El Alto, La Paz, Cochabamba and Santa Cruz. The caregivers were asked questions related to treatment habits, access to care, perceptions of health care costs and cost estimates attributed to the diarrheal event. A logistic regression was conducted modeling the probability that a caregiver's behavioral characteristics were associated with a catastrophic cost of 1% or greater.

RESULTS The median total direct costs for a diarrheal episode in a Bolivian household were approximately 23 bolivianos and the median indirect costs were 60 bolivianos. The presence of a working spouse had a "protective" effect whereas a caregiver who took the child to any place prior to the current site of treatment proved to be a significant risk factor for experience catastrophic cost at the 1% or greater level.

CONCLUSION Bolivia should work towards improving the economic conditions of Bolivian caregivers' and their households by providing support to mitigate the financial ramifications of a diarrheal episode and thereby reducing the probability that a household will experience catastrophic cost as a result of the diarrheal event.

INTRODUCTION

Diarrheal disease is responsible for approximately 1.3 millions deaths annually for children under the age of five with particular virulence in developing countries, especially sub-Saharan Africa and southeast Asia [1]. While rates of morbidity and mortality due to diarrhea are lower in Latin America as compared with Africa and Asia, diarrheal diseases are still considered endemic in many Latin American countries with WHO estimates of childhood mortalities due to diarrheal causes around 20% [3]. Though there are a number of bacterial and non-bacterial agents attributed to diarrheal disease, rotaviruses have been identified as the primary agent for approximately 40% of all acute diarrheal cases worldwide for children under the age of five [4]. In Bolivia, diarrhea accounts for 15-37% of childhood deaths with vast differences noted between the urban and rural populations [61, 62]. The impact of rotavirus infections on Bolivia is less understood but it is believed that rotaviruses are the primary cause for almost half of all diarrheal related hospitalizations [63] and a mortality rate of 66 per 100,000 children in children under 5 [64].

Understanding the various elements that predispose a child to diarrhea is complex. However, one element that is crucial and often overlooked is that of the caregiver. Caregivers are in a very influential position that often impacts not only the probability of a diarrheal event but also the very nature of the outcome. Socioeconomics factors, beliefs surrounding the nature of the health event and health care costs are all defining determinants of a caregiver. Studies on the impact of socioeconomic factors, in particular living conditions, economic status and level of education have been significantly

associated with diarrheal events in young children [38-43]. Other studies have explored how a caregiver's perception of diarrheal illnesses or of perceived health care costs attributed to diarrhea shape their treatment decisions. For example, caregivers who understood the severity and nature of diarrhea were more likely to seek treatment for diarrhea as compared to caregivers who did not grasp the magnitude of the event [44, 45]. Treatment decision can also be influenced by perceived health care cost with one study finding a relationship between caregivers who believed that treating diarrhea is too costly and the withholding of treatment [50]. Ultimately, identifying the complex factors that shape a caregiver's decision-making process during a diarrheal episode is vital to comprehending the possible economic ramifications attributed to the event.

A review of published literature indicates that a diarrheal event has both direct and indirect financial consequences that may result in a household experiencing a cost burden beyond that of a secure financial position. Direct medical costs are the accumulated expenditures related to the total medical treatment of the patient and can include expenses related to a hospital visit, facilities, treatment procedures and medication supplies [46]. Indirect costs are quantified economic consequences as a result of lost productive (i.e. lost wages or time) by caregivers or parents of children suffering from rotavirus-attributed diarrhea.

Studies indicate that hospitalizations due to diarrhea are quite severe and place a heavy burden on the caregiver. In Taiwan, approximately 40% of the monthly salary of an unskilled work may go towards the cost of hospitalization due to a rotavirus infection

[47]. In Latin America direct costs associated with inpatient hospitalizations costs (excluding transportation and indirect costs) range from approximately 15% to 26% of the average monthly wage. Studies evaluating the impact of indirect costs on a household have found that indirect costs are often underreported yet represent a considerable financial burden on households. Depending on geographical location, indirect costs constituted a loss of wages approximate to 11% to 15% of a caregiver's monthly salary [51, 52]. These studies demonstrate that both direct and indirect costs accrued from a diarrheal event place a heavy cost burden on households threatening the socio-economic welfare of the household. By quantifying the direct and indirect costs of a diarrheal event, we will be able to better comprehend the economic burdens confronting the caregivers.

An additional assessment of economic consequences of a diarrheal event is to measure the level at which a household experiences catastrophic cost as a result of the health event. A household suffers from catastrophic costs when their expendable income is reallocated to cover health care expenses thereby forcing the household to reduce everyday expenditures placing them at risk of falling below the poverty line [56]. It is pertinent to understand at what point health care costs become catastrophic, especially in developing countries, like Bolivia, where at the outset the average household has very little expendable income. Determining the level at which health care costs become catastrophic to the household varies depending on location, mean income and context of the health event. Some studies estimate the level at which health care costs become catastrophic as high as 40% while others assess catastrophic cost at a 10% level [57, 58].

Currently, there is no published literature assessing catastrophic cost due to a diarrhea. Though, a recent thesis study did measure catastrophic cost assessment in Bolivia at the 1% level given the impoverished setting and limited expendable income [50]. Whereas data are available on the high costs accrued during an episode of diarrhea, what is unclear is at what level those diarrheal-attributed costs can be considered catastrophic to the household.

To address these needs, the goals of this analysis are to quantify the financial impact one episode of diarrhea has on a Bolivian caregiver's economic status and to determine which defining factors of a Bolivian caregiver for a child suffering from a diarrheal episode are significantly associated with their current conditions of poverty as measured by a catastrophic cost of 1% or greater to the caregiver's household. By understanding the various factors that influence a caregiver's treatment process in relation to their demographic and socio-economic characteristics, we can ultimately identify the traits that may place Bolivian caregivers of children suffering from diarrhea at risk for poverty. This information can be useful in establishing community outreach programs with a focus on educating Bolivian caregivers on proper diarrhea prevention and treatment.

MATERIALS AND METHODS

Study Population

The study population consists of Bolivian caregivers of children who presented with diarrhea to various pediatric wards, emergency rooms and outpatient clinics in four Bolivian cities: El Alto, La Paz, Cochabamba and Santa Cruz. Caregivers were surveyed from seven different health facilities selected based on geographic region and facility type. Further details about the study population, subject recruitment, inclusion criteria, data collection process, and data entry and database management were previously discussed in E. Smith's study of the same population [50].

Health Care Cost Determination

The health care costs determinations have been previously described in E. Smith's thesis [50].

Definitions

Direct Medical Costs to the Caregiver were defined as the total fees associated with consultations, medicines and analyses for this diarrheal treatment as well as direct medical costs associated with previous methods of treatment for the same diarrheal event.

Direct Non-Medical Costs to the Caregiver were defined as all non-medical costs incurred as a result of treatment for the pediatric diarrheal episode. The types of non-medical costs included the roundtrip cost of transportation to all health facilities where treatment was sought for the diarrheal event, daily food costs while hospitalized, the cost of childcare for other children while the caregiver sought medical treatment for the child suffering from the diarrheal event and the excess cost of diapers for the diarrheal episode.

Indirect Costs to the Caregiver were defined as financial losses due to a decrease in work productive for the caregiver and their spouse as a result of the diarrheal episode. The loss in productivity costs were calculated based on the self-reported number of workdays missed for the current diarrheal episode multiplied by the estimated daily salary.

Household Income was measured as a function of the number of days worked each week or weeks per month as well as the daily and monthly reported pay earned for work. Household income assessed both the caregiver and spouse's household income, as reported by the caregiver. If the caregiver did not report an income, the caregiver was asked about monthly expenditures and sources of income for those costs.

Cost Burden of Treatment was defined as the healthcare and opportunity costs associated with one episode of pediatric diarrhea as a proportion of the annual household income. This study assessed cost burden of treatment using direct medical and direct non-medical costs. Indirect medical costs were not included in the analysis due to a low sample size. Initially in order to calculate totals for the direct medical and non-medical cost variables all observations that had missing values were set to zero. However in order to find the cost burden of treatment for the direct, indirect and combined costs, observations with zero values in the variable annual household income were excluded from the analysis. The catastrophic level – the level at which the proportion of healthcare costs per annual household income becomes a burden – is commonly cited at a 10% threshold [68]. However, the threshold level is subjective as it is dependent upon the context and setting of the study. Previous studies of the same population assessed catastrophic cost at the 1% level given Bolivia's impoverished setting and the limited expendable income available to most citizens [50, 69]. This study also chose to assess burden at a catastrophic level of

1% of the annual household income because it provided a more sensitive analysis of the cost burden experienced by the study population as compared to the sensitivity of an analysis that used a greater percentage of catastrophic cost.

Statistical Methods

The descriptive statistics included parametric and non-parametric measurements. The mean, frequency, percentage, standard deviation, median, mode and inter-quintile range were computed for the socio-demographic characteristics of the sample population, all treatment costs, cost burden and cost burdens set at levels 1-10%.

Initial stages of the logistic regression model included categorizing all 230 variables into the following categories: direct and indirect costs, demographics, income, previous treatment seeking behavior, access to care, perception of health costs and disease severity. Within each category, variables were then selected based on the exposures identified in the study aims and biological plausibility. Variables with sample sizes less than or equal to thirty were automatically excluded. Three new variables were created. They included combining number of transports taken to all relevant diarrheal appointments, any place that medical attention was sought prior to the current surveyed site and different persons who the caregiver borrowed money from to help pay for treatment. The variables *numtrans*, *numtrans1*, and *numtrans2* were combined to create *numtrans_any*. The variables *b4dispen*, *b4emergency, b4extcons, b4family, b4friend, b4pharm, b4privcons, b4yatiri* were combined to create *b4_any*. The variables *bwrfamily* and *bwfriends* were combined to create *bwr_any*. New variables were coded based on like values for the source variables. For example if *numtrans*, *numtrans1* or *numtrans2*

contained a one value, then *numtrans_any* took on a one value. If any of the *b4* or *bwr* variables indicate a 'yes' value, then the new variable took on the 'yes' value. In total, 18 variables were included in the initial gold standard model.

Using a univariate logistic regression, significant associations between all initial independent variables and the outcome *poverty* were determined based on point estimates and corresponding p-values. *Poverty w*as defined as a cost burden of 10% or greater. A statistically significant association was defined as a p-value <0.05.

Following the univariate analysis, a multivariate logistic regression was conducted modeling the probability that a caregiver's behavioral characteristics were associated with their current state of poverty. The logistic regression was conducted using a backward elimination method beginning with the independent variables and any relevant dummy variables found to be significantly associated with the outcome during the univariate analysis. At each step, a variable with a point estimate with the highest associated p-value was eliminated. If an ordinal variable contained at least one dummy variable with a significant p-value, it was not eliminated irrespective of the significance of the other dummy variables. The final model included all variables or ordinal series that were significantly associated with the outcome *poverty* based on a p-value <0.05.

RESULTS

The goals of this analysis are to quantify the financial impact one episode of diarrhea has on a Bolivian caregiver's economic status and to determine which characteristics of a Bolivian caregiver for a child suffering from a diarrheal episode are significantly associated with their current conditions of poverty as measured by a catastrophic cost of 1% or greater to the caregiver's household. By understanding the various factors that influence a caregiver's treatment process in relation to their demographic and socio-economic characteristics, we can ultimately identify the traits that may place Bolivian caregivers of children suffering from diarrhea at risk for poverty.

Characteristics of the Population

Throughout the four survey sites - Santa Cruz, Cochabamba, El Alto and La Paz - the majority of the 1,109 caregivers surveyed were mothers with more than half identifying as housewives (Table 1). Of those who described living in an urban or rural environment, most respondents reported residing in an urban environment. Slightly more than half of the diarrheal cases presenting with the caregivers were male children under two years of age. Of those surveyed, approximately 40% of presenting children had received the rotavirus vaccine. Financially, there was a wide range of reported annual combined household income with the median value approximately 16,320 bolivianos (2,345 USD).

Median costs for treatment of a pediatric diarrheal episode

To understand the financial impact that one pediatric diarrheal episode has on a Bolivian caregiver's household, we assessed the direct and indirect costs accrued as a result of the

diarrheal episode. Respondents were asked questions related to costs of direct medical treatments, direct non-medical costs including transportation and food expenses and indirect costs such as number of days missed of work (Table 2). The median value, 5th and 95th quintiles for each cost attributed to a diarrheal episode were reported. The distribution of the cost totals was left skewed due to using zero value for the unreported cost estimates with the direct cost values in the specified quintiles primarily containing zero values. The median total direct costs for a diarrheal episode in a Bolivian household were approximately 23 bolivianos. After excluding the zero values, the median value for direct costs was 46 bolivianos (data not shown). The median indirect costs were 60 bolivianos though data were collected on only 15% of the respondents. Overall a caregiver's indirect costs accrued during an episode of a diarrheal event represented a greater financial obligation than the direct costs suggesting that direct financial payments did not constitute the greatest economic strain on a caregiver but rather lost wages due missed work opportunities.

Catastrophic Cost of a Diarrheal Episode

To understand the cost burden that a pediatric diarrheal episode has on a Bolivian household, the percentage of costs attributed to the diarrheal episode given the caregiver's household's annual income, were calculated (Table 2). The median direct cost burden was approximately 0.3% and the median combined cost burden was 2.0%. When comparing the inter-quintile range between the two cost burdens, the combined cost burden had a slightly larger distribution with a range from 0.1% - 10.5% compared to the direct cost burden which ranged from 0.02% -7.2%.

Following the assessment of median cost burden, a sensitivity analysis was performed to determine the frequency of households affected by the diarrheal episode given a range of catastrophic cost levels (Table 3). Of the 462 respondents with data on direct cost burden, 28.1% reported spending more than 1% of their combined annual household income while only 2.4% of household's experienced catastrophic costs at the 10% level. Generally, catastrophic costs for the caregiver were greater when cost burdens were based solely on indirect costs versus direct costs. However, the sample population supplying indirect cost information represented only a third of the population supply direct cost information. Given the low sample size for data collected on indirect costs, the cost burden of a diarrheal episode was based on direct costs alone. Based on these figures it is evident that a high percentage of families experience catastrophic costs at the 1% level representing a traumatic financial consequence for the caregiver's household. These estimates illustrate the financial strain due to treating an episode of diarrhea that is placed upon Bolivian caregivers and their households.

Behavioral Characteristics and Catastrophic Costs Greater than 1%

A number of factors were considered in order to understand the association between a Bolivian caregiver's behavioral characteristics and the probability of experiencing a cost burden of treatment at a catastrophic level of 1% or greater of the combined household income. The study assessed the relationship between intermediate factors such as a caregiver's access to care, treatment seeking behavior and perceptions of health care costs on the severity of a diarrheal episode and how those influenced the overall outcome as measured by catastrophic cost (Figure 1). The caregivers responded to questions that explored each of these factors from a number of perspectives, including number and type

of transportation efforts undertaken, previous treatment appointments and means of obtaining money in order to pay for treatment expenses. Relevant questions were analyzed univariately using the outcome *poverty* as defined by total direct costs of a diarrheal episode that amounted to a catastrophic cost of 1% or greater of a household's combined annual income (Table 4).

Of the 18 relevant variables within the categories, *demographics, perceptions of health care costs, treatment seeking behavior* and *access to care*, seven variables were significantly associated with the outcome (p-value <0.05). All categories were probable predictors of a catastrophic cost greater than 1% of the combined household income. The variables that were significantly associated with the outcome *poverty* were the occupation of the caregiver, the presence of a working spouse, the sex of the child, the location of the hospital, withholding of treatment due to the perceived costliness of the health care treatment, whether ORS had been administered to the child and if the caregiver took the child to any place prior to the current site of treatment. The type of insurance program and the presence of the rotavirus vaccine were not significantly associated with the outcome. The magnitude, and direction, of effect for each variable differed. The caregiver's occupation, a working spouse and a male child had a "protective" effect on the likelihood of *poverty* whereas the location of the hospital, withholding of treatment due to the perceived costliness of the health care treatment, administering ORS to the child and taking the child to any place prior to the current site of treatment placed the caregiver's household at risk for experiencing catastrophic cost at the 1% level.

Following the univariate analysis, a multivariate logistic regression was computed with the aim of determining which variables, once adjusted, could be used as predictors of the outcome, *poverty*. The backward elimination method based on highest p-value was used to determine which of the significant variables from the univariate analysis were associated with the outcome once adjusted for by the other independent variables in the model (Table 5). When comparing the p-values from the "Individual Model" obtained from the univariate analysis to those from the "Full Model", only the variable *took child to any place before current treatment site* was significantly associated with the outcome. Using the backward elimination process, two variables, *working spouse,* and *took child to any place before current treatment site* were significantly associated with the outcome in the final model (Table 6). The presence of a working spouse had a "protective" effect and was significant in preventing the likelihood of a caregiver suffering from poverty as defined by catastrophic cost at the 1% level. In contrast, a caregiver who took the child to any place prior to the current site of treatment proved to be a significant risk factor for *poverty*. The wide 95% confidence interval for the variable *took child to any place before current treatment site* (95% CI (4.27, 254.87) suggests that our parameters estimates are imprecise. Cell counts for the outcome and significant exposure variables were less than five indicating that the imprecision is likely explained by the limited data. Ultimately, the categories *Demographics* and *Treatment Seeking Behavior* were the only categories found to be to linked with the outcome suggesting that caregivers' socio-economic traits have a far greater impact on the outcome *poverty* than other treatment-related decisions and options.

DISCUSSION

The goals of this study were two-fold: (1) to quantify the financial impact of one episode of diarrhea on a Bolivian caregiver's economic status and (2) to determine which factors are significantly associated with current conditions of poverty for a Bolivian caregiver of a child suffering from a diarrheal episode. A caregiver's household suffered from poverty if the household experienced catastrophic cost (ratio of caregivers' reported cost estimates by household income) of 1% or greater. The study found that the median cost of total direct (medical and non-medical) costs for treating a diarrheal episode were 23 bolivianos (US$3.30) and the median total indirect costs for care were 60 bolivianos (US$8.62) (Table 2). Given a 1% or greater catastrophic level, the presence of the rotavirus vaccine did not appear to impact the socio-economic stability of caregiver's household (Table 4). Two caregiver traits that were significantly associated with catastrophic cost: presence of a working spouse and whether any previous sites of treatment were attempted prior to presenting at the treating hospital (Table 6).

Though limited, there are a few published studies that assess the costs accrued per diarrheal episode for families residing in similar geographical areas. Our study found that the median cost of total direct (medical and non-medical) costs for treating a diarrheal episode were 23 bolivianos (US$3.30) (Table 2). However, the direct cost estimates for other studies with similar methodologies do vary. In Peru, the average cost of an outpatient visit was approximately US$7.49, with hospitalization costs estimated at US$63.93 [70]. A Columbian study reported outpatient visits to cost an estimated US$12.50 per visit with the cost of hospitalization at US$97.20 [53]. In a study assessing

the economic burden of rotaviruses in developing countries, the cost burden in the Americas ranged from US$4.92 – US$20.44 for an outpatient visit while hospitalization estimates ranged from US$57.12 – US$201.67 [71].

In our analysis of accrued direct (medical and nonmedical) costs, the costs were low when compared to estimates from other studies. While other national estimates of published direct costs were much higher than our study's estimate (US$3.30, Table 2), variations in study designs and cost perspectives (e.g. health care versus the caregiver) could account for the discrepancies in the direct cost estimates. Our study methodology set all missing values to zero, which resulted in a negatively skewed distribution and a lower median value of the reported estimates. Additionally, the direct costs used in this analysis were the caregiver's reported costs rather than total direct health care costs for the entire diarrheal episode. Median estimates based on total direct health care costs are likely to be higher as compared to estimates based on a caregiver's actual out-of pocket expenses. Although in a Brazilian study measuring caregivers' out-of-pocket expenses, the study found a higher median direct cost than our results. They reported median costs approximate to US$12.89 compared to US$3.30 found in our study [72].

One additional explanation for these relatively low median cost estimates could be that SUMI—the Bolivian universal insurance program for mothers and children—is assuming a large portion of the direct medical costs (direct medical median costs US$0, see Table 2). SUMI is a publicly funded, free insurance program that provides extensive coverage for maternal and child health care. In recent years, participation in SUMI has risen

steadily, especially in the lower economic quintiles (73, 74]. Therefore, the country has seen an increase in the number of individuals accessing health care services who would not have ordinarily received health care services, thereby offsetting the likelihood of poverty due to adverse health events [75]. In our own sample population, over 90% of respondents reported SUMI as their primary insurance program (data not shown). The impact of SUMI may be evident by the low reported direct medical costs in comparison to the direct nonmedical costs. Through SUMI, all direct medical costs are covered whereas the caregiver is responsible for all of the nonmedical costs. Among caregivers who used SUMI, the median direct costs were US$2.57. Whereas among uninsured caregivers or those who reported using an insurance source other than SUMI, the median direct medical costs were US$4.57 (data not shown). Therefore even though, the direct medical costs are likely to be higher than the nonmedical costs, the caregiver is likely to pay more for nonmedical expenses, as the caregiver is responsible for paying the full amount.

The study's low total direct medical and nonmedical costs could be explained by inconsistencies in cost reporting. As values are derived from caregiver-reported costs as opposed to those obtained from medical invoices, there may be a reporting bias with non-medical costs, such as diapers and food more likely to be reported than other less tangible cost [55]. In this study, direct costs could also be lower than expected given that all missing values were set to zero. As the median and 5th quintile values were largely zero, the total cost values may be lower than anticipated. The true median cost estimates would likely be higher if that value was derived from only the respondents that did

supply cost information. Overall, there is very little information in the literature on the reported values of costs that the caregiver is directly responsible. Most data on the direct costs due to a diarrheal event are from a macro perspective, such as the health care provider or health system.

In our analysis of the indirect costs of a diarrheal episode for Bolivian caregivers, we found the median total indirect costs for care were 60 bolivianos (US$8.62) (Table 2). Our indirect costs results were more consistent with the literature's findings than our direct costs results but there were still discrepancies in the reported indirect costs estimates when compared to countries in the same geographical region. In a study on Colombian caregivers, the study reported a caregiver's indirect costs to be US$44.80 [53] due to lost wages. Whereas in that same study that explored economic cost burdens in developing countries, indirect costs in the Americas ranged from US$2.47 – US$10.87 [71]. While both the Colombian study and the analysis of cost burdens in developing countries included transportation costs, our study defined indirect costs as the loss of wages only. While our study's indirect cost estimate is drastically lower than that the Columbian study perhaps due to the exclusion of transportations costs, our indirect costs estimates are inline with the range indicated in Rheingans *et al.*'s 2009 cost-analysis study.

Access to universal health insurance is also important in lower health costs when considering the impact of the indirect costs or lost wages as a result of treating a diarrheal episode. In our study, the indirect costs assumed by the caregiver were much higher across all measurements when compared to the total direct costs. Since compensation is

not provided towards lost wages, indirect costs reflect a higher cost burden than the direct costs. While SUMI covers all direct medical costs, there is not an infrastructure in place to support the burden of the indirect costs. Therefore, the caregivers are held completely accountable for those indirect expenses culminating in a higher cost burden.

The gender of the participants is also important when interpreting the indirect costs. As over 90% of the study's respondents were mothers (Table 1), there may be inflation in the estimation of lost spousal wages, thereby driving up the overall estimated indirect costs. Consequently, bias in gender reporting may represent another explanation for the higher reported indirect costs.

There is support in the literature on the effectiveness of the rotavirus vaccine in reducing health care costs both to the caregiver and the health care system [72, 31]. Research has also show the importance of the rotavirus vaccine in reducing a country's diarrheal-attributed DALYs. Studies have found that investment in national rotavirus vaccine programs will reduce the overall economic burden created by the high diarrheal morbidity and mortality rates [64]. However, our study did not find the presence of the rotavirus vaccine as having a protective effect in defense of a household experiencing catastrophic costs (Table 4). The lack of significance of the rotavirus vaccine in preventing catastrophic costs could be due to a number of explanations. In this study, the presence of the rotavirus vaccine may not have been protective if the cause of the diarrheal episode was not due to a rotavirus infection. Study participants were selected if they presented with children suffering from a diarrheal illness and were not specifically

screened on confirmed rotavirus-attributed diarrheal episodes. Consequently it may be difficult to understand the actual impact of the rotavirus vaccine within this sample population.

However, given the widespread published literature on the cost-effectiveness of the rotavirus vaccine, it is likely that our study's methodology and design reduced the influence that the presence of a rotavirus vaccine has on the outcome. As the question regarding vaccination history was only asked in later studies to a small portion of the total sample population, it is likely that the limited response rate reduced the power of the study. In future cost-analysis studies with a larger sample size, the presence of the rotavirus vaccine may be more likely to be associated with the outcome.

The quantification of the financial burden of diarrheal episodes is only one component of addressing the long-term socio-economic effects of diarrhea on Bolivian caregivers. Understanding which characteristics of a caregiver are associated with their current socio-economic condition is equally of importance. Ultimately, demographics and access to care were the only categories that were associated with poverty as defined by a living in a household that experiences a catastrophic cost of 1% or greater due to one diarrheal episode (Table 6). While socio-economic factors have been clearly established as predictors of diarrhea, the literature provides little insight beyond predictors of this relationship and does not explore the likelihood of catastrophic cost due to diarrhea. The existing research indicates an association between certain demographics, such as sex, hospital location and a household's risk of catastrophic cost [76]. Despite the limited

available literature, the presence of a working spouse is clearly a protective feature for ensuring the stability of household's economic status in the event of a diarrheal episode. A working spouse provides financial stability and is likely to mitigate the time losses experienced by households with single caregivers. Though little research on the cost burden experienced by caregivers of children with diarrhea exists, studies on the cost burden of caring for young children show that the burden is often greater for single-parent families as opposed to married families [77]. In our own study, it is evident the heavy influence that loss in wages (indirect costs) has on a family's cost burden. Therefore households with a stable support system, such as a working spouse, are more likely to avoid accruing high indirect costs and are least likely to experience a negative shift in financial stability.

Studies have also explored the relationship between poverty and low economic status as a barrier to accessing care for adverse health events [39]. However, there is a paucity of research on the reverse relationship between demographics, access to care and the impact on financial outcomes of care during a health event, particularly diarrhea. A study from the health care system perspective found that access to health care options reduces treatment burden while those with limited to no health care options were associated with increasing cost of treatment [78]. Choosing to seek alternative health care options prior to the current site of treatment poses a risk to a household's financial stability. If the caregiver does not understand the scope of the diarrheal episode, he or she may delay seeking proper health care treatment, thereby increasing the severity of the diarrheal episode. Alternatively, access to proper care facilities may be limited, forcing the

caregiver to seek less desirable alternatives that ultimately lead to an increased severity in the diarrheal episode. Another plausible explanation is that as a caregiver continues to seek treatment for the affected child, more expenses accumulate during the overall treatment of the diarrheal episode.

Strengths and Limitations

There are a number of strengths for this study that encompass all phases of the analysis. In our study design, we collected reported cost values directly from caregivers instead of compiling cost values from various published sources. Using caregiver reported costs allowed for a more accurate representation of the caregiver's true cost burden as opposed to the total cost burden of a diarrheal episode. The study sample was also quite large and represented a wide portion of Bolivia's caregiver population. Additionally, as diverse selection methods were used to enroll study participants, the results can be extrapolated to the population at large. Another strength of the study is the unchartered perspective of the analysis. Traditional cost-analysis studies on the financial impacts of diarrhea primarily focused on the impact from the health care provider or health system standpoint. However we chose to focus on the costs from the individual Bolivian caregivers perspective.

While there are a number of strengths for our study, there were a few limitations that affect the overall analysis. A major limitation for this study is the accuracy of the reported cost values. As the caregivers were responsible for reporting their own cost obligations, recall bias may hinder the accuracy of our results. In the literature, studies have found that patients typically underestimate the cost value of treatment when

compared to hospital records [79]. The gender of the reporting participant may also lead to imprecise value reporting, particular with indirect costs, which rely on accurate estimates of spousal salary. Studies have also shown that there is an association between gender and cost burden reporting with women more likely to report higher cost burdens than males [80]. Given the majority of participants in our study are female, there may be inflation in the cost burden estimation, especially indirect costs where spousal wages are estimated.

In addition to issues with reported cost values, another limitation in our study is the dearth of supplied information on specific cost values. Due to limitations in reported cost estimates for various medical and non-medical expenses, we replaced any missing variables with zero values in order to obtain meaningful results. By assigning missing data a cost value, we generated a bias in both the cost analysis component and the predictive modeling phase, which could ultimately skew the studies results.

A final limitation is how the study chose to define poverty. The study defined poverty as a household that experienced catastrophic health care costs, which were equal to or greater than 1% of the combined household income. Given the reporting biases surrounding income and other indicators of economic stability, using reported salary as a proxy for economic livelihood may be shortsighted. Future studies may want to consider additional indicators such as household assets and “other” cost-earning opportunities in addition to reported income when determining a household’s economic status.

With the introduction of SUMI, Bolivia is in an excellent position to address the major health issues affecting children, especially those under the age of five suffering from diarrhea. From a financial perspective, the low direct medical costs obligated to the caregiver illustrate the benefits that a universal healthcare system has on reducing the financial strain that a diarrheal episode has on a Bolivian household. However, what isn't addressed is the strain that non-medical and indirect costs have on the household. Therefore, it is important to understand the impact of the direct costs – medical and non-medical– and indirect costs on a household. These unavoidable costs accrued during a diarrheal episode can have lasting ramifications on a household thrusting it into a potentially unstable economic condition.

Equally of importance is the context with which these costs are derived from, in particular, the socio-economic setting of the country, itself. Bolivia is one of the poorest Latin American countries with an estimated 60% of Bolivians living in poverty and 37.7% living in extreme poverty [59, 61]. Any financial considerations beyond the daily household expenses pose a financial challenge for a large portion of the society. Bolivia must find a way to support all components of the cost burden associated with a diarrheal episode, especially those that are often underreported and underestimated. Further cost analysis studies measuring the various costs accrued are necessary in order to comprehend the true scope of a caregiver's financial obligations and shortfalls.

Additionally, Bolivia must recognize and address the underlying socio-factors that are associated with the economic status of a Bolivian caregiver's. It is important that health

care professionals and diarrheal education program address all factors that contribute to catastrophic cost conditions for a household. In particular the protective effect that a working spouse has on reducing the likelihood of poverty for caregivers of children suffering from diarrhea should be noted and supported by institutional policy. Bolivia must guarantee greater job stability for its citizens thereby protecting the financial ramifications that one adverse health event can cause on a household.

In conjunction with addressing the importance of job stability in prevent poverty due to catastrophic health care costs; deficits and misunderstandings in access to care options should also be addressed. Bolivian caregiver's should be encouraged to seek proper health professionals in the event of a serious diarrheal condition as opposed to seeking other alternative methods that may increase the severity of the episode. With that said, the appropriate health services should be conveniently located for all Bolivian's to access thereby reducing the likelihood of caregiver's seeking alternative options for treatment. Ultimately, attention should be given to each of these factors in order to further improve the conditions of Bolivian caregiver's and their households thereby reducing the burden that child diarrheal episodes place a household.

Table 1. Socio-demographic characteristics of the caregivers surveyed (n=1109)

Individual Characteristics	n	Frequency (%)		
Caregiver (% mother)	802	731 (91.2)		
Caregiver employment status (% housewife)	801	450 (56.2)		
Urban residence	707	602 (85.2)		
Gender of child (% male)	1,067	608 (57.0)		
Child received rotavirus vaccine (% yes)	267	106 (39.7)		
	n	Median	5th Quintile	95th Quintile
Caregiver age, years	92	28	19	40
Child age, months	997	11	2	32
Annual household income*	462	16,320	7,200	43,200
Number of persons in household	770	4	2	8

* *In Bolivianos*

Table 2. Median costs for treatment to the caregiver of an episode of a pediatric diarrheal event* (n=1,109)

	n	Median	5th Quintile	95th Quintile
Direct medical costs				
Diagnostic	1,109	0	0	15
Medicines	1,109	0	0	108
Fees	1,109	0	0	250
Total	*1,109*	*0*	*0*	*395*
Direct non-medical costs				
Transportation	1,109	3	0	49
Food during visit	1,109	0	0	30
Diapers	1,109	0	0	45
Child care	1,109	0	0	0
Total	*1,109*	*15*	*0*	*113*
Total Direct Costs	1,109	23	0	474
Cost burden of Direct Costs	462	0.3%	0.02%	7.2%
Indirect costs	163	60	0	500
Total (direct and indirect) cost per episode	163	181.7	3	1,118
Cost burden of Direct and Indirect Costs	148	2.0%	0.1%	10.5%

* *In Bolivianos*

Table 3. Catastrophic Cost: the frequency of households spending more than the indicated percentage of their annual combined household income on one pediatric diarrheal episode

	Direct Costs (n=462) Frequency (%)	Indirect Costs (n=148) Frequency (%)	Indirect and Direct Costs (n=148) Frequency (%)
Total Treatment Costs >= 1%	130 (28.1)	58 (39.2)	97 (65.5)
Total Treatment Costs >= 2%	81 (17.5)	34 (23.0)	74 (50.0)
Total Treatment Costs >= 3%	53 (11.5)	16 (10.8)	50 (33.8)
Total Treatment Costs >= 4%	40 (8.7)	13 (8.8)	36 (24.3)
Total Treatment Costs >= 5%	33 (7.1)	6 (4.1)	31 (21.0)
Total Treatment Costs >= 6%	26 (5.6)	3 (2.0)	25 (16.9)
Total Treatment Costs >= 7%	25 (5.4)	3 (2.0)	22 (14.7)
Total Treatment Costs >= 8%	18 (3.9)	2 (1.4)	15 (10.1)
Total Treatment Costs >= 9%	14 (3.0)	0 (0)	12 (8.1)
Total Treatment Costs >= 10%	11 (2.4)	0 (0)	9 (6.1)

Table 4. Univariate analysis of variables associated with a caregiver suffering from poverty as defined by catastrophic cost of 1% or greater of the annual combined household income (n=462)

Category	Variable	Univariate Analysis		
		n	OR	95% CI
Demographics	Occupation of caregiver	460		
			Works - referent	
	Housewife		0.16	0.09, 0.29*
	Student		0.50	0.13, 1.87
	Other		0.10	0.01, 0.76*
	Number of members in household	439	1.07	0.97, 1.17
	Working spouse	237	0.25	0.06, 1.00†
	Male child	461	0.63	0.42, 0.96*
	Hospital location	458		
			Santa Cruz – referent	
	Cochabamba		2.31	1.35, 3.95*
	El Alto		0.68	0.35, 1.30
	La Paz		4.83	2.12, 11.04*
	Reside in a rural area	408	1.67	0.93, 2.97
	Age of Caregiver	47	0.92	0.83, 1.03
	Type of insurance	269		
			SUMI‡ - referent	
	"HMI"		1.94	0.67, 5.66
Perceptions of Health Care Costs	To pay for treatment will borrow from family or friends	411	1.24	0.78, 1.97
	To pay for treatment will not eat	411	1.50	0.71, 3.20
	To pay for treatment will sell something	411	2.08	0.72, 6.00
	Will withhold treatment if perceived costs too great	405	1.79	1.05, 3.05*
Treatment Seeking Behavior	Child received a rotavirus vaccine	233	2.21	0.96, 5.11
	Administered ORS to child	256	2.86	1.26, 6.51*
	Number of days child was ill	438	1.02	0.99, 1.06
	Number of transports taken for any treatment attempt	387	1.34	0.80, 2.24
Access to Care	Location of previous treatment	125		
			Hospital – referent	
	Clinic		2.80	0.84, 9.32
	Consultation		7.00	0.86, 56.90
	Home		1.59	0.47, 5.40
	Pharmacy		2.00	0.35, 11.36
	Took child to any place before current site of treatment	462	3.86	2.39, 6.24*

* Significant at p-value <0.05

† Significant p-value, despite 95% CI containing the null value

‡ Bolivian universal insurance program for mothers and children

Table 5. Parameter estimate p-values used during backward elimination to select a logistic regression model predicting the caregiver behavioral traits were associated with a poverty status as defined by catastrophic cost of 1% of annual income for treatment of a pediatric diarrheal episode

	N*	Individual Model	Full Model	Reduced Model 1	Reduced Model 2	Reduced Model 3	Reduced Model 4	Reduced Model 5
Variable								
Working spouse	237	0.0500	0.0841	0.0829	0.0445	0.0463	0.0645	0.0425
Took child to any place before current site of treatment	462	0.0001	0.0028	0.0029	0.0031	0.0030	0.0016	0.0008
Hospital location	458							
Santa Cruz		referent	referent	referent	referent	referent	referent	‡
Cochabamba		0.0488	0.1778	0.1169	0.1178	0.0892	0.0611	‡
El Alto		0.0001	0.2922	0.2791	0.2362	0.2316	0.1659	‡
La Paz		0.0002	†	†	†	†	†	
Administered ORS to child	256	0.0120	0.0966	0.0879	0.1057	0.1173	‡	
Male child	461	0.0315	0.3469	0.3736	0.3682	‡		
Occupation of caregiver	460							
Works		referent	referent	referent	‡			
Mother		0.0001	0.8411	0.8174	‡			
Student		0.3003	0.5271	0.5224	‡			
Other		0.0263	0.8550	0.8578	‡			
Will withhold treatment if perceived costs too great	405	0.0320	0.9220	‡	‡			

* N value for “Individual Model”

† Excluded due to the number of missing observations

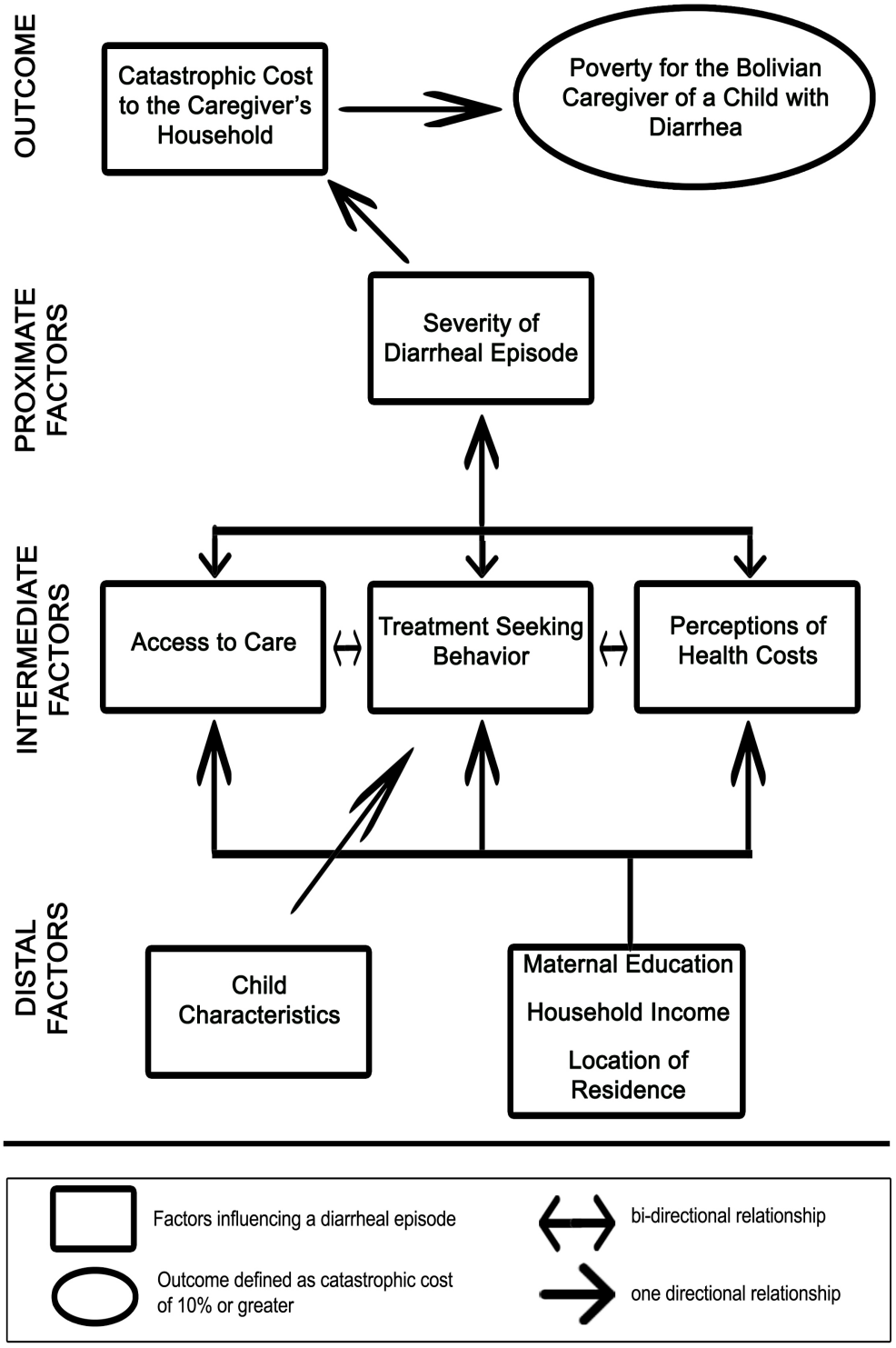
‡ Eliminated in this step due to highest p-value

Table 6. Logistic regression model predicting the caregiver behavioral traits were associated with a poverty status as defined by catastrophic cost of 1% of annual income for treatment of a pediatric diarrheal episode (n=237)

Parameter		Model Estimates		
		Beta Coefficient	Standard Error	Odds Ratio (95% Confidence Intervals)
	Intercept	-3.27	1.22	
Demographics	Working spouse *	-1.78	0.88	0.17 (0.03, 0.94)
Access to Care	Took child to any place before current site of treatment *	3.50	1.04	32.97 (4.27, 254.87)

* Indicates a dichotomous variable where "yes" is being modeled

Figure 1. Conceptual Framework illustrating the various socio-factors that influence the cost burden of treating a diarrheal episode and its impact on a Bolivian household's economic status.



PUBLIC HEALTH IMPLICATIONS

With the introduction of SUMI, Bolivia is in an excellent position to address the major health issues affecting children, especially those under the age of five suffering from diarrhea. From a financial perspective, the low direct medical costs obligated to the caregiver illustrate the benefits that a universal healthcare system has on reducing the financial strain that a diarrheal episode has on a Bolivian household. However, what isn't addressed is the strain that non-medical and indirect costs have on the household. These unavoidable costs accrued during a diarrheal episode can have lasting ramifications on a household thrusting it into a potentially unstable economic condition.

Equally of importance is the context with which these costs are derived from, in particular, the socio-economic setting of the country, itself. Bolivia is one of the poorest Latin American countries with an estimated 60% of Bolivians living in poverty and 37.7% living in extreme poverty [59, 61]. Any financial considerations beyond the daily household expenses pose a financial challenge for a large portion of the society. Additionally, Bolivia must recognize and address the underlying socio-factors that are associated with the economic status of a Bolivian caregiver's. It is important that health care professionals and diarrheal education program address all factors that contribute to catastrophic cost conditions for a household. In particular the protective effect that a working spouse has on reducing the likelihood of poverty for caregivers of children suffering from diarrhea should be noted and supported by institutional policy.

In conjunction with addressing the importance of job stability in prevent poverty due to catastrophic health care costs; deficits and misunderstandings in access to care options should also be addressed. Bolivian caregiver's should be encouraged to seek proper health professionals in the event of a serious diarrheal condition as opposed to seeking other alternative methods that may increase the severity of the episode. With that said, the appropriate health services should be conveniently located for all Bolivian's to access thereby reducing the likelihood of caregiver's seeking alternative options for treatment. Ultimately, attention should be given to each of these factors in order to further improve the conditions of Bolivian caregiver's and their households thereby reducing the burden that child diarrheal episodes place a household.

Therefore, it is important to:

- Understand the impact of the direct costs – medical and non-medical– and indirect costs on a household as they place a heavy financial burden on the population
- Support all components of the cost burden associated with a diarrheal episode, especially those that are often underreported and underestimated,
- Provide more reliable and quality health care professionals for a population that has little access to health care services

Given the results, our study suggests the following courses of action from a variety of levels. Ultimately, the goal of these suggestions is to further improve the conditions of Bolivian caregiver's and their households thereby reducing the burden that child diarrheal episodes place a household.

- Mandate ‘sick leave’ policies thus protecting employees from undue financial hardships as a result of caring for an ill child
- Institute sliding-scale reimbursement policies that cover direct non-medical expenses accrued while treating a diarrheal episode
- Educate caregivers on the importance of seeking proper health care services immediately in the event of a diarrheal episode
- Ensure that proper quality health care services are readily available to all Bolivians

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APPENDIX

Appendix 1. Signature form for Non-Research Projects and Project Description

HUBERT DEPARTMENT OF GLOBAL HEALTH

Signature form for Non-Research Projects

This form is to be used for students who have chosen to write a Literature Review or Special Project and are not required to apply for IRB approval.

Attach a one to two page description of the project including general subject, hypothesis to be tested or question(s) to be answered, and lay summary.

I have read the attached information and verify that this project is not research and therefore <u>does not</u> need to be submitted to the Emory University Institutional Review Board.

_____ _____

Signature of Thesis Advisor **Date**

Project Description

BACKGROUND Globally, diarrheal disease is responsible for approximately 1.3 millions deaths annually for children under the age of five and rotaviruses are the primary agent for 40% of all acute diarrheal cases. In Bolivia, rotaviruses are the primary cause for almost half of all diarrheal related hospitalizations and a mortality rate of 66 per 100,000 children. Therefore, it is important to understand the conditions that perpetuate the country's diarrheal morbidity and mortality rates by exploring the role of the caregiver and the relationship between the caregiver's socio-economic factors and a diarrheal event.

GOALS To quantify the financial impact an episode of diarrhea has on a Bolivian caregiver and to determine which characteristics of a Bolivian caregiver for a child suffering from a diarrheal episode are associated with a catastrophic cost of 1% or greater to the caregiver's household.

METHODS This cross-sectional study took place during the summer months of 2007-2009. The study population consisted of 1,109 Bolivian caregivers of children who presented with diarrhea to various pediatric wards, emergency rooms and outpatient clinics in four Bolivian cities: El Alto, La Paz, Cochabamba and Santa Cruz. The caregivers were asked questions related to treatment habits, access to care, perceptions of health care costs and cost estimates attributed to the diarrheal event. A logistic regression was conducted modeling the probability that a caregiver's behavioral characteristics were associated with a catastrophic cost of 1% or greater.

RESULTS The median total direct costs for a diarrheal episode in a Bolivian household were approximately 23 bolivianos and the median indirect costs were 60 bolivianos. The presence of a working spouse had a "protective" effect whereas a caregiver who took the child to any place prior to the current site of treatment proved to be a significant risk factor for experience catastrophic cost at the 1% or greater level.

CONCLUSION Bolivia should work towards improving the economic conditions of Bolivian caregivers' and their households by providing support to mitigate the financial ramifications of a diarrheal episode and thereby reducing the probability that a household will experience catastrophic cost as a result of the diarrheal event.