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Travel as a Risk Factor for Diarrheal Disease: Analysis of a Case-Control Study in Ecuador

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B.S., University of Michigan, 2010

Thesis Committee Chair: Dr. Karen Levy, PhD

An abstract of
a thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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2015

Abstract

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Background: Enteric and diarrheal disease has long been, and continues to be, a major cause of morbidity and mortality across the world. While there is extensive research describing the individual risks of diarrheal disease, a systems-level approach and investigation of patterns of social interaction and pathogen movement is needed to fully understand the factors that contribute to diarrheal disease. Individual movement and the human population movement are essential to the understanding of disease dynamics. While research has related human movement to transmission of vector-borne diseases, sexually transmitted infections and respiratory illness, the majority of research relating human movement and enteric disease has focused on international travel and traveler's diarrhea.

Methods: This project is a case-control study carried out at four sites (Quito, Esmeraldas, Borbón and within the rural communities around Borbón) in Ecuador from April 2014 to February 2015. Cases were any patients that were seen for acute diarrheal disease or gastroenteritis and controls were recruited from the same facility and matched on age. All participants completed questionnaires that collected data related to demographic information, socio-economic status, water and sanitation practices and travel history. Multiple logistic regression models were fit to assess the effect travel in the past year, travel to urban areas and travel to specific destinations had on diarrheal disease.

Results: Across all four sites (N=673), 62% of participants reported traveling away from their home areas at least once in the past year. When controlling for sex and water treatment at home, cases were 1.4 times more likely to have traveled in the past year than controls (*aOR*=1.40, 95%*CI*: 1.02, 1.92). From the same model, treating water at home (*aOR*=0.67, 95%*CI*: 0.49, 0.91) was found to have a protective effect against diarrheal disease. Travel in the past week was not associated with diarrheal disease.

Conclusion: Travel is associated with diarrheal disease, but the degree of this association differs by study site and the length of the travel history recall period.

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Introduction

Global Burden of diarrheal disease

Enteric and diarrheal disease has long been, and continues to be, a major cause of morbidity and mortality across the world. The World Health Organization (WHO) estimates there are currently 1.7 billion cases of diarrheal disease every year, most of which are preventable or treatable [1]. Diarrhea can last for many days and deplete the body of necessary water and salts. If severe enough, it can result in death by causing severe fluid loss and dehydration. The Global Burden of Disease Study (GBD), which provides a framework to systematically assess trends in mortality around the world, estimates that there were 2.6 million deaths (47.4 per 100,000) caused by diarrheal diseases in 1990. However, in 2013, that estimate had been reduced to 1.4-1.9 million deaths per year[2, 3].

Diarrheal diseases are typically associated with overcrowding and lack of access to clean water and sanitation. WHO estimates that there are 780 million individuals who lack access to improved drinking water and 2.5 billion who lack access to improved sanitation [1].

Children who are malnourished or have compromised or under developed immune systems are most at risk for severe diarrheal disease. As a result, incidence and mortality rates of children under 5 years of age are of particular interest. Diarrheal disease is the leading cause of malnutrition in children under-5 years old worldwide [1] and can have lasting negative effects on growth and cognitive development [4]. Enteric infections are estimated to result in 43% of stunted growth. Diarrhea during the first two years of life can cause an average of 8 cm less growth and a 10 IQ point decrease by the time the child is 7-9 years old [5]. A pooled analysis that covered a 20-year period in five countries found that the 25% of stunting was attributed to 5 or more diarrheal episodes before age 2 [6]. As a result, diarrheal disease research often focuses on children under 5 or under 2 years of age.

The GBD Study estimates that there were 1.6 million deaths among children under-5 years old that were caused by diarrhea in 1990 [7]. At that time, diarrheal disease was still the third leading cause of mortality among children (behind preterm birth complications and pneumonia) [8]. Since 2000, under-5 deaths resulting from diarrhea have continued to decrease by about 6.5% per year [9]. In 2013, this total was estimated to be just under 600,000 [7, 9]. Because of the different analytic approaches used in each study, it is difficult to directly compare this estimate to the original GBD estimates from 1990. However, these studies together indicate that under-5 deaths caused by diarrhea have likely decreased. The introduction of Oral Rehydration Solution (ORS), the development of a rotavirus vaccine, and water, sanitation and hygiene interventions have all contributed to this decrease. Diarrheal disease is now the fourth leading cause of under-five deaths, behind preterm birth complications, pneumonia and intrapartum-related complications. However, roughly one in ten child deaths that occur during the first five years of life are still a result of diarrheal disease [9]. Most of these occur in sub-Saharan Africa and south Asia [10].

The global public health community has prioritized reducing the substantial disease burden caused by diarrhea and enteric diseases. Reducing diarrheal disease is essential to the progress on the Millennium Development Goals (MDGs) that were outlined in the United Nations Millennium Declaration of 2000. MDG-4 aims to reduce the under-five mortality rate by two-thirds from 1990 to 2015. There has been progress in reducing under-five mortality, but the goal has not yet been reached. Although the number of annual births has increased, the number of under-five deaths has decreased from 12.4 million in 1990 to 7.6 million in 2010 (a 40% reduction) [11].

As a result of this importance and scope, there is ongoing research to understand factors of diarrheal disease in children. The Global Enteric Multicenter Study (GEMS) was the largest and one of the most comprehensive studies of diarrheal disease among children in developing countries. The study aimed to overcome the differences in study design and methodology in previous research by applying consistent methods and studying 22,568 children at seven sites across two continents. The GEMS project involved a 3-year, prospective matched case-control study of children less than 5 years of age and looked at the cause, incidence and impact of moderate-to-severe diarrhea [12].

GEMS estimated that in children under 2 years of age in participating countries, there are about 30 diarrhea episodes per 100 children each year. Children that had a single episode of diarrheal disease had nearly an 8.5 times increased risk of death during the two-month follow up period. GEMS found that the majority of cases were due to four pathogens: Rotavirus, *Cryptosporidium, Shigella* and enterotoxigenic *E. coli*. Rotavirus was the leading cause of diarrhea under 2 years olds across all study sites. *Shigella* was the first or second leading cause among 2-5 year old children at most study sites [12].

Rotavirus infection is the most common cause of mortality resulting from severe diarrheal disease and the majority of these deaths occur in resource-limited countries. However, rotavirus disease incidence is similar worldwide. Rotaviruses that affect humans are extremely diverse and at least 42 different serotypes have been identified. RotaTeq, a vaccine recommended by the Advisory Committee on Immunization Practices (ACIP), has been found to effective against each of the common circulating rotavirus serotypes [13]. Another vaccine, Rotarix, was tested in Latin American countries and found to have an overall efficacy of 86% [14, 15]. Rotarix has also been recommended by ACIP and has recently been introduced in more than 90 countries [13].

E. coli is a part of the natural flora of the human gut, but also has the ability to be pathogenic and cause infection in the gastrointestinal tract, the urinary tract, bloodstream and central nervous system [16]. The site and mechanism of colonization and clinical symptoms displayed by *E. coli* can vary [17]. The six major diarrheagenic *E. coli* pathotypes are: enteropathogeic *E. coli* (EPEC), Shiga toxin-producing *E. coli* (STEC), enteroaggregative *E. coli* (EAEC), diffusely adherent *E. coli* (DAEC), entertoxigenic *E. coli* (ETEC) and adherent invasive *E. coli* (AIEC).

History of enteric disease research

Research and public health interventions aimed at reducing diarrheal disease has taken a variety of approaches over the years. Eisenberg et al. (2012) reviewed four decades of research in order to outline the progression of literature related to the transmission of diarrheal disease. The reviewers found that enteric disease research can be grouped into three periods classified by the type of research that was most prevalent: observational studies, intervention studies and meta-analyses.

The review found the majority of observational research related to enteric disease has focused on only a single transmission pathway (person to person, sanitation, food/food hygiene, domestic hygiene and water). A large number of the studies that focused on single transmission pathways looked at transmission through water, either by swimming pools and municipal water supplies in developed countries or as a function of water quantity and quality in developing countries. Studies that looked at hygiene focused more on the public domain (e.g. daycares, cruise ships) in developed countries but focused on the private domain (e.g. household hand washing, disposal of child feces) in developing countries. All studies that focused on sanitation-related pathways occurred in developing countries and looked at latrine use at the household level. Studies that investigated person-to-person transmission either looked at transmission in a household (without specific mechanisms of transmission) or sexual transmission [18].

Of the studies that have looked at multiple transmission pathways, most assumed that the multiple risk factors were independent. Eisenberg et al. also found that some observational studies described the socioeconomic status of their population or controlled for it as a confounder in the analysis, but few studies looked at socioeconomic status as an underlying cause of diarrheal disease.

Intervention trials originally focused on improving water quality at the source through improvements in source water treatment and community education in supporting these interventions. However, in the 1990s, trials that targeted individual hygiene through hand washing became more popular and water interventions began to focus on household level treatment [18]. During the 2000s, there was a dramatic increase in research related to point of use water treatment, primarily through chlorination, solar disinfection, filtration and flocculation [19]. Over time, more rigorous study designs and methods (e.g. randomization, blinding) have been implemented in an effort to better understand the effectiveness of these interventions.

There is now a focus on meta-analyses in order to comprehensively understand the large body of research related to diarrheal disease interventions. Many of these meta-analyses focus on one individual intervention (e.g. hang-washing or point-of-use water treatment) but some have looked at differences in effectiveness of individual study results or interventions. Eisenberg's review found that differences in diarrheal disease reduction among water treatment interventions have been found to result from differences in sanitation [20], hygiene practices [21], duration of study follow up [22] and presence of blinding [23]. These variations have led to questions about the ability to sustain or scale up individual interventions [24, 25].

Eisenberg et al. argue that the scope of enteric disease research should be expanded to include the interdependencies of multiple transmission pathways, socioeconomic status, gender, remoteness and ecosystem changes. They argue that a systems-level approach is needed to understand the interdependencies of all the factors that contribute to diarrheal disease. Recent systems-level research has focused on the effects of temporary weather events (e.g. heavy rainfall), climate change, seasonality, road construction and remoteness on the incidence of diarrheal disease [26-29].

However, some factors related to diarrheal disease have not been extensively studied. Since people live within households and communities, a person's risk is not only dependent upon their own behavior but also the behavior of any community surrounding members. Eisenberg et al. call for study designs that include patterns of social interaction and pathogen movement [18]. A major component of social interaction and pathogen movement is human travel.

Human Movement

Individual movement and the human population movement (HPM) have long been known to influence disease transmission and are essential to the understanding of disease dynamics [30]. Likewise, neglecting to factor in human movement has led to problems in program implementation. The failure to consider human population movement is often viewed as a reason for the failure of the Global Malaria Eradication Programme in the 1950s and 1960s [31, 32] and, as a result, HPM is often used to influence malaria control programs in present day [32]. However, human movement patterns vary between demographic groups, regions and countries [33] and can have varying influence on disease transmission.

Human population movement can alter the spread of pathogens in a variety of ways. Nathaniel grouped these mechanisms into four main categories: Ecological change and agricultural development that lead to a change in environmental conditions; providing a new means for dissemination of a pathogen and/or resistance; breakdown of public health systems;' and alterations in human behavior [34].

Human population movement can lead to a change in the physical environment in which potential hosts and natural pathogen reservoirs exist. Altering the proximity or frequency of contact between hosts and pathogen reservoirs can result in increased disease transmission. For example, the construction of new dams or irrigation systems can increase vector (i.e. mosquito) breading sites and lead to an increase of transmission of malaria or dengue [34].

The movement of populations or individuals can also bring susceptible hosts into contact with pathogens and/or drug resistance that they have not previously encountered. Individuals who move between populations and facilitate disease transmission can be thought of as active transmitters and/or passive acquirers. Active transmitters are infectious individuals who impact the health status of the naïve population into which they move and passive transmitters are susceptible individuals who have an increased exposure to health hazards when they move into endemic areas [30]. For example, multi-drug resistant tuberculosis has increased in the United States as a result of immigration [35].

Mass human population movement can lead to large populations in areas where the existing infrastructure and health systems are unable to meet the needs of the resulting population. An insufficient supply of water and sanitation resources, basic health centers or vaccinations can all lead to an increase in disease transmission [34]. One example is mass urbanization, which can quickly result in huge cities with crowded living conditions that are growing at a faster rate than the health infrastructure needed to support the new residents.

As people and populations move to new areas, they encounter new people and cultures that can result in alterations of human behavior. These changes in behavior may be the result of a breakdown in traditional values and cultural norms or change in mindset that occurs when traveling [34]. The spread of HIV and other sexually transmitted infections as a result of sex tourism or intercourse with sex workers is an example of altered behavior while traveling.

A collection of individual migratory movements can lead to HPM. Factors that trigger and drive HPM can be thought of as "push" (when the needs of a population can no longer be met by the current environment) and "pull" (when a different environment appears to offer better opportunity) forces [36]. These factors can be related to safety, politics, economical or social opportunities or improved living conditions. Armed conflicts, natural disasters, poverty, famine, drought and environmental degradation are examples of "push" factors that cause people to leave their area of residence. Examples of "pull" factors include better economic opportunities, protection and safety, social opportunities and political stability. Areas in which people are more likely to leave are known as "sources" while areas more likely to receive migrants are known as "sinks" [33].

In order to understand how these factors affect disease transmission, Prothero provided an original framework for studying human movement and it's influence on the spread of pathogens [30]. He classified human movement into 24 categories based on spatial and temporal characteristics. In the spatial dimension, he differentiated between rural and urban environments and categorized travel between all combinations of both types of environment. This established four spatial categories of travel: rural-urban, rural-rural, urban-rural and urban-urban.

The primary temporal categories differentiate between migratory (change of residence) and circulatory (leaving of residence with the eventual return) movements. Circulatory movements are further classified into four categories based on the amount time away from the residence. Daily circulation includes any movements away from residence for up to 24 hours. Periodic movement is away from the residence for more than 24 hours, but less than 12 months and seasonal movement is a periodic movement in which the time away from residence is related to a specific agricultural, employment or weather season. Long-term is any movement in which the resident is away from home for more than 12 months but still returns to their original residence [30]. Using these definitions and the spatial/temporal framework, movement can be classified into different categories suitable for research related to disease transmission.

Since Prothero's original framework in 1977, new methods have evolved for measuring, documenting and conceptualizing human movement. Stoddard et al built on the spatial scale framework to conceptualize human movement with an "activity space model" [37]. The concept is based on the assumption that organisms have habitual behavior and represents a 3-D conceptualization of where humans spend most of their time. Using dengue (vector-borne) as the pathogen of interest, they determined the amount of exposure to an infectious pathogen by quantifying and summing the exposure to the pathogen at different points inside a daily activity space. In order to quantify the exposure at each individual point, factors such as the number of infected, host seeking vectors at each site, their biting behavior and the amount of time the individual spent at that site were considered.

The researchers used the results to help determine what individuals or places contributed disproportionally to the transmission of disease.

In order to measure human movement, researchers must consider several factors in their study design process. These include the spatial scale, type of movement, measurement method, observation interval and data management [37]. In order to determine the spatial scale, researchers must understand the pathogen dynamics of interest. Human movement can contribute to the spread of a disease to a new area [38, 39] or sustain local transmission in a selected geographic area [40, 41]. Researchers may be interested in high spatial and temporal resolution (such as Stoddard's activity space model), may be concerned with movement outside of a specific geographic area [40] or may only be interested in the distance of travel on a normal day's commute [42]. When viewing human population movement on a large scale, sometimes the analysis of transit networks can describe the nature of a previous or potential outbreak [43-45].

Depending on the type of movement being measured and resources available, there are many methods used to measure individual human movement. Travel history interviews, questionnaires or other recall methods can be used to measure travel retroactively, but must be done within an appropriate cultural context and are subject to recall bias and memory decay [40, 42]. However, these methods of data collection can provide information on modes of transportation and activity as well as physical location and duration of travel.

National census data is typically available from international governments and can provide large HPM datasets indicative of migration data [33, 46]. Wesolowski et al. used de-identified mobile phone data to measure population movement and quantify it's impact on the spread of malaria [47]. Using call/sms records and tower locations, they were able to assign nearly 15 million mobile phone users a high-resolution daily location. Wesolowski et al. went on to compare the data generated from mobile phone records with national census migration data and found significant relationships between the patterns, indicating that national census data can be used to estimate movement on smaller temporal scales. If researchers are able to gain access to them, mobile phone records can be used to generate location data for a large number of people without any inconvenience to the individuals. However, there is opportunity for bias because this method is dependent on people owning and using mobile phones

Global Positioning System (GPS) devices are thought to have potential for tracking human movement in real time [37, 48]. GPS devices use a system of satellites to determine the latitude, longitude and altitude of any location in the world. Some devices can also record speed of movement and time. Cost, limited battery-life and technical limitations have presented challenges in using them to measure human movement [37] but as commercially available devices improve, they are proving to be a reliable way to measure mobility patterns and in relationship to risk of disease exposure [48]. Many mobile phones now have GPS capabilities built into them, but this presents similar opportunities for bias as mobile phone records because the use and coverage is inconsistent. GPS devices typically produce data in latitude and longitude coordinates that needs to be analyzed with Geographic Information Systems (GIS) software.

Along with the method of measuring human movement, researchers need to determine the length of time that data will be recorded or behavior will be observed [37]. In retrospective epidemiologic studies, this depends mainly on the characteristic of the pathogen of interest. Incubation and latent periods of the pathogen must be considered. For prospective studies, the behavior of interest is essential because the researchers want to design their observation interval to capture that behavior. Humans often repeat the same, simple patterns [49] and if the behavior of interest in common, a shorter observation interval may be sufficient.

Research related to the relationship between human movement and disease transmission has primarily focused on vector-borne diseases [37, 47], sexually transmitted infections [50] and respiratory illness [51]. The majority of research relating human movement to waterborne diseases has focused on traveler's diarrhea. Traveler's diarrhea occurs when an individual develops diarrhea after or during a trip to a foreign country. The incidence is usually defined within a two-week window of stay because the risk of developing traveler's diarrhea changes with time spent in the foreign country. Risk of traveler's disease is considered high if the incidence in greater than 20% during the first two weeks in a foreign country [52]. The overall two-week incidence of traveler's diarrhea is estimated to be between 10% to 40% (depending on the destination of travel) and is inversely related to the income level of the destination country [53, 54]. For many traveler's diarrhea studies, data is collected retrospectively or through surveillance systems and doesn't look at travel within an individual's own country.

Enteric disease in Ecuador

Although diarrheal disease is a major concern in Latin America, the GEMS study unfortunately did not include a site in the region. In Ecuador in 2012, the reported diarrheal disease incidence was 46/1,000 inhabitants [55]. A recent case-control study aimed to complement the GEMS results and provide the etiology of diarrheal disease in Ecuador. The study took place in a low income, urban neighborhood (Quito) and a low-income community in a rural setting (Borbón). Similar to the GEMS results, this study found that rotavirus was associated with diarrheal disease in both the urban and rural settings. However, Shigellae was only associated with diarrheal disease in the urban setting [56].

Goldstick et al. it looked at how the varying level of disease in a region of Ecuador affects transmission dynamics between villages within that area. The study found that water treatment was much less protective when the diarrheal prevalence in surrounding villages was high [57]. These results indicate there is another pathway, that doesn't involve water, which influences transmission of diarrheal diseases between villages. Research in the same area has found that greater social connectivity [58] and remoteness (from a major road) may inhibit diarrhea prevalence rates [29]. All of these results indicate that human movement likely contributes the diarrheal disease transmission on several spatial scales.

Methods

The data in this thesis come from a research project conducted by Dr. Karen Levy at Emory University titled *Impacts of Human Movement on Regional Strain Distribution of Diarrheagenic* E. coli. The project builds on the previous EcoDess (Ecología, Dearollo, Sociedad, y Salúd) research project carried out in the same region by Dr. Levy and Dr. Joseph Eisenberg at the University of Michigan.

Study Design and Participant Recruitment

The data come from a case-control study carried out in three locations in Ecuador. Data used in this analysis were collected from April 2014 to February 20th, 2015. A case-control design was chosen to allow for the evaluation of risk factors for diarrheal disease, a relatively rare outcome. This particular study design also allows the project to capture both symptomatic and asymptomatic strains of pathogenic *E. coli*.

Participants were recruited as part of one of four study sites in Quito, Esmeraldas, Borbón and within the rural communities around Borbón. Quito is the capital city of Ecuador and has a population of about 1.6 million (2010 census). Esmeraldas, a coastal city in the northwest of Ecuador, is the capital of Esmeraldas Province and has a population of 154,000 (2010 census). Borbón, a town in the Esmeraldas province, has approximately 5,000 people and is the main population center of 125 villages in the region. It is located about two hours by bus from the city of Esmeraldas. Esmeraldas has many cultural similarities and experiences a lot of human movement with the Borbón area.

In all sites, participants were recruited from Ministry of Health facilities (hospital or clinic) or activities. In Quito, patients were initially recruited from Hospital del Sur.

However, there were not enough cases presenting at the hospital of the appropriate age distribution for a study of diarrhea, so patient recruitment moved to a local clinic (Subcentro de Chilibulo). Participants in Esmeraldas were recruited from Hospital Delfina Torres de Concha. In Borbón, subjects were recruited from the Borbón Hospital, which sees an average of 1,000 patients per month. Participants in the rural communities were recruited in association with rural field visits carried out by the Ministry of Health, or through the Borbón Hospital.

Data Collection

Permission for the study was obtained from the Ministry of Health and the Emory Institutional Review Board (IRB) and the Universidad San Francisco de Quito (USFQ) Ethical Committee approved all contact with human subjects. Each study site initially aimed to recruit 200 cases and 200 controls. Eligible cases were any patients that were seen for acute diarrheal disease or gastroenteritis, which was defined as three or more loose stools within 24 hours. Controls were patients in the same facility that presented with any other illness or disorder. One control was selected for each case and matched on age by the following criteria: 0-24 months (+/- 6 months), 25-60 months (+/- 12 months), 61-180 months (+/- 24 months) and >181 months (>181 months). Potential controls were excluded if they reported having diarrhea in the past seven days. Both cases and controls were excluded if they reported using antibiotics before arriving at the health center or did not live within the specific study site area for at least six months. Case and control status was determined by reason for presenting at the health facility (as described above). All study participants also provided a stool sample to be processed and plated within hours.

All participants were administered a survey about travel in the past week and past year. If participants indicated that they traveled to a destination of interest, follow up questions about frequency, duration and reason for travel were asked. The list of destinations varied by site (e.g., a participant in Quito could not indicate that they traveled to Quito). Since the Borbón Hospital also sees patients from surrounding areas, "Borbón" was listed as a possible travel destination for patients from the Borbón site. Surveys also included questions about demographics, socioeconomic status, water and sanitation practices, rotavirus vaccination history and contact with animals. Definitions for "improved" sanitation and water sources were consistent with the widely used definitions created by the World Health Organization [59]. However, bottled water was reclassified as an improved water source. Surveys were administered on Android devices using Open Data Kit (ODK), a free open source software.

Data Analysis

Data cleaning and summary

Data from the four study sites were merged into one dataset for cleaning and analysis. In order to ensure a similar age distribution between sites, the observations from Quito were limited only to those collected at the local clinic. Categorical variables that allowed more than one answer were turned into indicator variables. All categorical variables of interest were summarized with frequencies and percentages.

Analysis dataset and bivariate analysis

All analysis was done in SAS 9.4 (SAS Institute, Cary, North Carolina, USA). The dataset used for analysis was restricted by the inclusion and exclusion criteria specified in the study design. Any subjects that reported using antibiotics in the past week or did not live in respective community for at least 6 months were excluded in the analysis. Any controls that reported having diarrhea in the past seven days were also excluded. To assess the similarities of each study site, bivariate analysis was conducted between all variables of interest and study site. Bivariate associations were also conducted between all variables of interest and case control status (as an aggregated dataset and stratified by study site). Bivariate associations were assessed at the alpha=0.05 level using *p*-values from Pearson's Chi Square Test. If any expected cell counts were less than five, *p*-values from Fisher's Exact Test were used.

Multivariate analysis

Several multivariate models were used to examine the data.

(1) Travel vs. Diarrheal Disease (for all study sites combined): An initial logistic regression model was fit to produce an adjusted measure of association between travel and diarrheal disease. The outcome was status as a case (diarrheal disease) and the primary exposure of interest was a dichotomous variable indicating travel within the past year. All variables that were significantly associated with diarrheal disease in the bivariate analysis were considered as potential confounders. Sex, race, study site, treating water at home, contact with chickens (both production and home chickens) and improved sanitation at home met this criteria. A log-likelihood ratio test was carried out to determine the presence of effect modification between the exposure of interest (travel within the past year) and any of the potential confounders.

After assessing effect modification, a change in effect estimate was used to assess confounding. An effect estimate adjusted for all potential confounders was obtained. This effect estimate was compared to the effect estimates produced by models controlling for all possible subsets of potential confounders. Only models that changed the effect estimate by less than 10% were considered. A final model that adequately controlled for confounding and contained the most precise effect estimate was selected. Collinearity was assessed by examining the condition indices (CNIs) and variance decomposition proportions (VDPs). A collinearity problem was diagnosed if the largest CNI was greater than 30 and at least two of the VDPs were greater than 0.5. Goodness of fit was assessed using the Hosmer-Lemeshow test (*alpha*=0.05). Any variables that were determined to confound the relationship between travel and diarrheal disease were retained in all subsequent models described below.

(2) Travel to Urban Areas vs. Diarrheal Disease (for all non-urban study sites combined): Next, two separate logistic regression models were run to assess the effect of traveling to Quito and Esmeraldas in the past year. In both models, the outcome of interest was diarrheal disease. One model contained all observations from Esmeraldas, Borbón and the rural communities and included a dichotomous variable indicating travel to Quito in the past year. The second model contained all observations from Quito, Borbón and the rural communities and a dichotomous variable indicating travel to Esmeraldas in the past year.

(3) Specific Destinations vs. Diarrheal Disease (by individual study site): To assess the effect of destination, four separate logistic regression models (one per site) were fit with case status (diarrheal disease) as the outcome. Each model contained indicator variables denoting travel to each possible destination, specific to that site.

To assess the effect of travel duration, a continuous variable was created for each destination to represent the number of days spent in each destination. For example, if a participant indicated that they spent “2-6 days” at a particular destination, the continuous value was set to 4 days. The rest of the duration categories were coded as follows: “1 day”=1, “7-14 days”=10, “2-4 weeks”=21, “1-2 months”=45, and “2+ months” = 60. Four logistic regression models (one per site) were run with case status as the outcome. Each model contained a term for the continuous variable for each possible travel destination, specific to that site.

To assess the effect of travel frequency within the past year, a continuous variable was created for each destination to represent the number of trips to that destination. The frequency categories were coded as follows: "once"=1, "twice"=2, "3 to 5 times"=4, "every other month"=6, "every month"=12, "every other week"=26. Four logistic regression models (one per site) were run with case status (diarrheal disease) as the outcome. Each model contained a term for the continuous variable indicating frequency of travel to each possible destination, specific to that site.

Results

Data Summary

The data collection led to a recruitment of 767 potential participants. Two people did not provide consent so there was no data collected for those individuals. There were 45 observations that came from the hospital in Quito that were dropped prior to any summarization or analysis. The demographic characteristics of the remaining observations (N=720) are summarized in Table 1. There were a total of 380 (52.8%) cases. There were 271 participants from Quito, 237 from Esmeraldas, 108 from Borbón and 104 from the rural communities surrounding Borbón.

Table 1: Demographic and socioeconomic characteristics of all participants, by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate *p*-values that are significant at the alpha=0.05 level.

	N 720	Rural communities n=104	Borbon n=108	Esmeraldas n=237	Quito n=271	p-value[a]
		n (%)	n (%)	n (%)	n (%)	
Cases	380	64 (61.5)	58 (53.7)	119 (50.2)	139 (51.3)	0.250
Demographics						
Age						0.002*
<2 years	268	29 (27.9)	49 (45.4)	90 (38.0)	100 (36.9)	
2-5 years	126	33 (31.7)	15 (13.9)	39 (16.5)	39 (14.4)	
5-15 years	136	18 (17.3)	23 (21.3)	49 (20.7)	46 (17.0)	
15+ years	190	24 (23.1)	21 (19.4)	59 (24.9)	86 (31.7)	
Male	386	52 (50.0)	67 (62.0)	133 (56.1)	134 (49.4)	0.110
Reported Race	697	104 (100)	108 (100)	222 (93.7)	263 (97.0)	
White	9	0 (0)	0 (0)	1 (0.5)	8 (3.0)	<0.001*
Indigenous	44	33 (31.7)	5 (4.6)	1 (0.5)	5 (1.9)	
Manaba	30	9 (8.7)	9 (8.3)	8 (3.6)	4 (1.5)	
Mixed	419	29 (27.9)	28 (25.9)	119 (53.6)	243 (92.4)	
Black	195	33 (31.7)	66 (61.1)	93 (41.9)	3 (1.1)	
Socioeconomic Status						
Reported SES Data	698	104 (100)	108 (100)	223 (94.1)	263 (97.0)	
Receives government assistance	135	46 (44.2)	30 (27.8)	44 (19.7)	15 (5.7)	<0.001*
Somebody in the house is employed	361	21 (20.2)	40 (37.0)	97 (43.5)	203 (77.2)	<0.001*
House ownership						<0.001*
Loaned	66	10 (9.6)	6 (5.6)	25 (11.2)	25 (9.5)	
Owned	418	88 (84.6)	84 (77.8)	160 (71.7)	86 (32.7)	
Rented	214	6 (5.8)	18 (16.7)	38 (17.0)	152 (57.8)	
Some level of education	690	102 (98.1)	107 (99.1)	219 (92.4)	262 (96.7)	0.012*
Highest level - Primary School	76	26 (25.0)	5 (4.6)	15 (6.3)	30 (11.1)	<0.001*
Highest level - Secondary School	399	67 (64.4)	85 (78.7)	117 (49.4)	130 (48.0)	
Highest level - University	215	9 (8.7)	17 (15.7)	87 (36.7)	102 (37.6)	
Reported nursery use data	340	52 (50.0)	59 (54.6)	107 (45.1)	122 (45.0)	
Attended a nursery in past month	70	17 (32.7)	19 (32.2)	19 (17.8)	15 (12.3)	0.002*
Contact with animals in the past week	340	41 (39.4)	51 (47.2)	101 (42.6)	147 (54.2)	0.02*

[a]*P values calculated using Pearson's Chi Square or Fisher's exact test*

Analysis by site

There was a significant difference (*p*-value=0.002) in the distribution of age categories across the collection sites, with Borbón having a high proportion (*n*=49, 45.4%) of subjects being under two years of age. The distribution of race also differed (*p*-value<0.001) across study sites, with Quito having a very high proportion of participants of mixed race (*n*=243, 92.4%). Borbón (61.1%), Esmeraldas (41.9%), and the rural communities around Borbón (31.7%) all had higher proportions of black participants.

As expected, there were many differences in variables related to socioeconomic status across the four study sites. The proportion of participants who receive financial support from the government was highest in the rural communities (44.2%), followed by Borbón (27.8%), Esmeraldas (19.7%) and Quito (5.7%) (*p*-value<0.001). Inversely, the highest proportion of participants to have employment was in Quito (77.2%), followed by Esmeraldas (43.5%), Borbón (37.0%) and the rural communities. (20.2%) (*p*-value<0.001). Home ownership was highest in rural communities (84.6%, *p*-value <0.001) but participants in the urban areas were more likely to have somebody in the household who completed high school or university (*p*-value <0.001).

Participants from Quito were most likely to report having contact with an animal in the past week (54.2%, p-value=0.020) and the majority of those people reported having contact with a dog (87.8%) (*Appendix*: Table 1.1). Participants were most likely to report having contact with a dog (*n*=257) or a cat (*n*=141) across all sites.

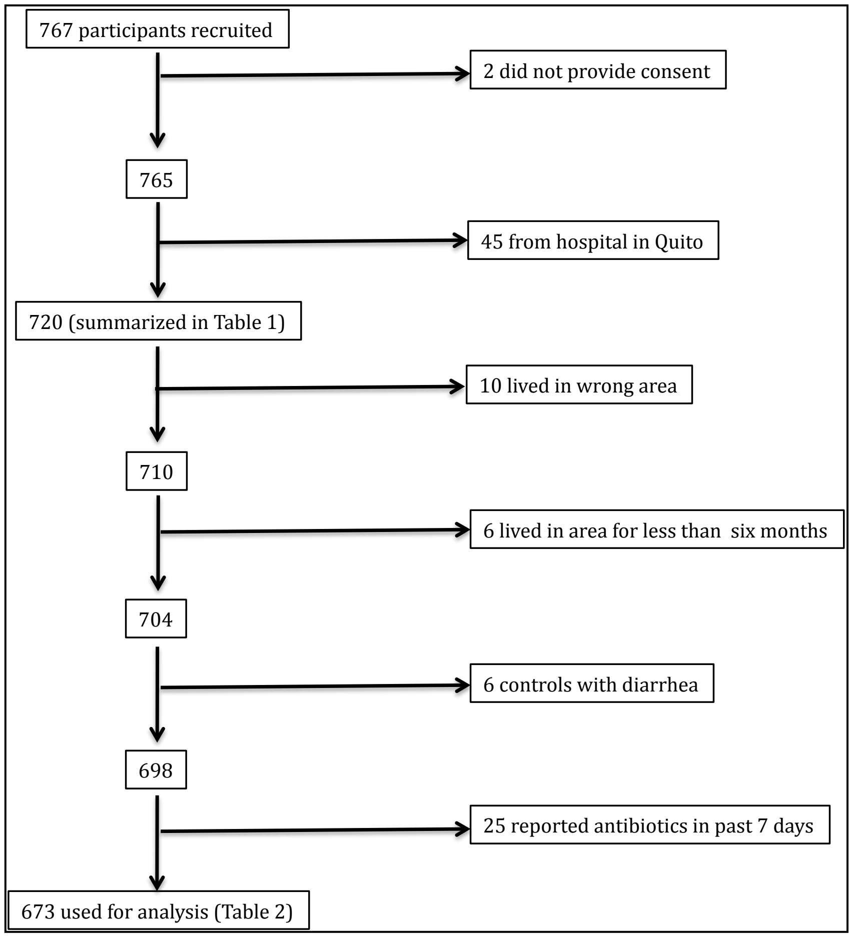
Of the participants that had rotavirus test results (*n*=574), the proportion of people who tested positive for rotavirus (*n*=44, 7.7%) did not differ significantly by site (*p*-value=0.80). Among people who reported the vaccine history (*n*=128), rotavirus vaccine coverage also did not differ by site (*p*-value=0.95), with 87.5% of people having received the first rotavirus vaccine and 76.6% of participants having both rotavirus vaccines. Participants from the urban areas (Esmeraldas: 36.6%, Quito: 41.1%) were more likely to report using medicine in the past week (*p*-value<0.001). The proportion of participants who were breastfeeding did not differ by site (*p*-value=0.34) but participants in Quito were most likely to report exclusive breastfeeding (23%).

Several characteristics related to water and sanitation differed by study site (*Appendix*: Table 1.2). Participants were most likely to report improved sanitation at home in Quito (99.6%) and Esmeraldas (99.5%) compared to Borbón (80.6%) and the rural communities (59.8%, *p*-value<0.001). Participants were more likely to have an improved water source in Quito (99.6%) and Esmeraldas (99.5%) compared to Borbón (88.0%) and the rural communities (89.4%, *p*-value<0.001). Participants were also more likely to report treating their water in Quito (64.3%, *p*-value<0.001). Only 55 people reported their sanitation practices while traveling, but 52 (94.5%) of those people reported using improved sanitation practices while traveling. Only 60 participants reported their water source while traveling, but 58 (96.7%) of those reported using an improved water source.

Analysis dataset

There were 47 observations that did not meet the inclusion criteria and were excluded from all analysis: 10 participants did not live in the study area, 6 lived in the study site for less than six months, 6 controls had diarrhea in the past week, and 25 participants reported using antibiotics in the past 7 days. Of these excluded participants, 18 were from Quito, 28 from Esmeraldas and 1 from Borbón.. All observations from the rural communities were included, leaving a total of 352 cases and 321 controls (N=673) in the final analysis (Figure 1).

Figure 1: Summary of exclusion criteria. The number of participants that were excluded for each reason is shown in the right column.



Travel results

A total of 417 (62%) people reported traveling away from their home areas at least once in the past year yet only 59 (8.8%) of participants reported traveling in the past week (*Appendix*: Table 1.3). Every participant from the rural communities (*n*=104) and Borbón (*n*=107) reported traveling at least once in the past year. Travel in the past year was much less common in Esmeraldas (34%) and Quito (54.2%). However, reporting traveling at least once in the past week was most common in Quito (11.5%) and least common in the rural communities (4.8%). These results are provided in detail in Table 2.

Table 2: Travel practices of cases and controls, stratified by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported *p* values test the null hypothesis that there is no difference between cases and controls at each site. Asterisks indicate *p*-values that are significant at the alpha=0.05 level. *P*-values that could not be calculated are marked (--).

		All Subjects			Rural Communities			Borbon			Esmeraldas			Quito		
		Controls 321	Cases 352		Controls 40	Cases 64		Controls 49	Cases 58		Controls 109	Cases 100		Controls 123	Cases 130	
	Total N	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**
Travel History																
Reported travel practices	673	321 (100)	352 (100)		40 (100)	64 (100)		49 (100)	58 (100)		109 (100)	100 (100)		123 (100)	130 (100)	
Traveled in the past week	59	28 (8.7)	31 (8.8)	0.970	2 (5.0)	3 (4.7)	>0.99	5 (10.2)	5 (8.6)	>0.99	5 (4.6)	10 (10.0)	0.130	16 (13)	13 (10.0)	0.450
Traveled in the past year	417	184 (57.3)	233 (66.2)	0.010 *	40 (100)	62 (100)	--	49 (100)	58 (100)	--	28 (25.7)	43 (43.0)	0.008 *	67 (54.5)	70 (53.8)	0.920

[a] *P values calculated using Pearson's Chi Square or Fisher's exact test*

The majority of participants from the rural communities reported short, frequent trips to Borbón. There were 57 (55.9%) participants who listed Borbón as a travel destination in the past year and those people took an average of 4.8 trips there with a median duration of one day (Table 3). The majority of these trips were for medical reasons (68.4%) or shopping (21.1%). Participants from the rural communities also frequently traveled to other rural communities (26.5%, average of 1.2 trips), and Esmeraldas (28.4%, average of 3.1 trips), typically to visit family members.

Table 3: Destination, frequency and duration of travel in the past year, by site, Ecuador, 2014-2015. Frequencies and percents of total participants from each specific site that traveled in the past year are shown for each destination. "Avg #" is the average number of trips that each person took to a specific destination. "Mdn D." is the median duration of total time spent during all trips to that destination. The symbol (--) denotes destinations that were not response options on the questionnaire for that site.

	Total N=417	Rural Communities n=102			Borbon n=107			Esmeraldas n=71			Quito n=137		
Destination	**N**	**n (%)**	**Avg #**	**Mdn D.[a]**	**n (%)**	**Avg #**	**Mdn D.[a]**	**n (%)**	**Avg #**	**Mdn D.[a]**	**n (%)**	**Avg #**	**Mdn D.[a]**
Borbon	76	57 (55.9)	4.8	1	18 (16.8)	9.6	1	1 (1.4)	1.0	21	0 (0.0)	0	0
Rural communities	58	27 (26.5)	1.2	2	21 (19.6)	1.5	2	5 (7.0)	--	--	5 (3.6)	--	--
Esmeraldas	72	29 (28.4)	3.1	4	43 (40.2)	4.0	4	--	--	--	0 (0.0)	0	0
Esmeraldas Province	20	--	--	--	--	--	--	--	--	--	20 (14.6)	--	--
Guayaquil	69	6 (5.9)	2.5	10	15 (14)	4.3	4	27 (38.0)	1.9	4	21 (15.3)	2.0	4
Quito	38	2 (2.0)	2.5	4	12 (11.2)	3.5	4	24 (33.8)	3.2	4	--	--	--
San Lorenzo	35	10 (9.8)	4.7	1	17 (15.9)	5.6	1	5 (7.0)	2.8	4	3 (2.2)	2.0	4
Santo Domingo	26	3 (2.9)	2.3	10	8 (7.5)	5.0	4	7 (9.9)	2.1	4	8 (5.8)	3.4	4
Other	205	62 (60.8)	--	--	51 (47.7)	--	--	7 (9.9)	--	--	85 (62.0)	--	--

[a] *Median duration*

-- destination not applicable for that site

Participants from Borbón were most likely to report traveling to Esmeraldas (*n*=43, 40.2%) within the past year. These trips were also frequent (average of 4 trips per traveler) and longer in duration (median=4 days). Most of these trips were to visit family (58.1%), to shop (20.9%) or for work (18.6%).

Participants from Esmeraldas were most likely to report traveling to Guayaquil (*n*=27, 38%) and Quito (*n*=24, 33.8%). These trips also tended to be longer in duration (median=4 days). Many of the trips to Guayaquil were to visit family (44.4%) or vacation (29.6%) whereas the trips to Quito were typically for medical reasons (25.0%), vacation (25.0%) or transit (20.8%).

Of the available destinations for participants in Quito, people who traveled in the past year were most likely to go to Esmeraldas Province (*n*=20, 14.6%) and Guayaquil (*n*=21, 15.3%). Most of the travel to Guayaquil was for vacation (61.9%) and had a median duration of 4 days. However, 85 (62.0%) of people who traveled from Quito selected "other" as their destination, indicating most people traveled to destinations that were not of primary focus for this analysis.

Bivariate results

The distribution of race differed by case and control status (*p*-value=0.029) (*Appendix:* Table 2.1). However, when the data was stratified by site, this association was not significant in any of the individual strata. None of the other demographic or social economic status variables were significantly associated with being a case. However, of all the participants that reported having contact with animals in the past week, being a case was significantly associated with contact with both home chickens (*n*=38, *p*-value=0.037) and production chickens (*n*=31, *p*-value=0.043).

Testing positive for rotavirus was strongly associated with being a case (*p*-value<0.001). All of the cases that tested positive for rotavirus and reported vaccination data (*n*=7) had the full rotavirus vaccine dosage. However, having received both doses of the rotavirus vaccine was not associated with case status. Cases were also much more likely to have used medicine in the past seven days (*p*-value<0.001).

While controls were more likely to use improved sanitation at home, this association was not significant (*p*-value=0.080) (*Appendix*: Table 2.2). A significantly larger proportion of controls reported having a tap inside their home as a water source (*p*-value=0.050) and treating their water (*p*-value=0.004). None of the other variables related to water and sanitation were significantly associated with being a case.

There was no difference is the proportion of cases who reported traveling in the past week (8.8%) compared to controls (8.7%, *p*-value=0.970) (Table 2). However, there was a significant difference in the proportion of cases that reported traveling the past year (66.2%) compared to controls (57.3%, *p*-value=0.010). Stratifying the data by site indicates that this difference is mainly present in participants from Esmeraldas. Since all participants from Borbón and the rural communities indicated that they have traveled in the past year, a measure of association or *p*-value cannot be calculated. In Quito, 53.8% of cases indicated they traveled in the past year, compared to 54.5% of controls (*p*-value=0.920). However, in Esmeraldas, 43.0% of cases reported traveling in the past year compared to 25.7% of controls (*p*-value=0.008).

Multivariate results

The initial model selection process found that adjusting for sex and water treatment at home sufficiently controlled for confounding in the relationship between traveling in the past year and diarrhea disease. None of the variables related to socio-economic status (government assistance, employment, education and home ownership) confounded the effect estimate. The resulting adjusted odds ratio indicated that cases were 1.4 times more likely to have traveled in the past year than controls (aOR=1.40, 95%CI: 1.02, 1.92) (Table 4).

Table 4: Adjusted odd ratios comparing cases to controls for all participants, Ecuador, 2014-2015. The adjusted odds ratios and accompanying 95% confidence intervals are from a logistic regression model with case status as the outcome. The sample size was 672 participants and there were no collinearity problems.

	aOR	95% Wald CI	
Traveled in Past Year	1.40	1.02	1.92
Male	1.26	0.93	1.71
Treat Water at Home	0.67	0.49	0.91

When the data was restricted to three sites to asses the risk of traveling to the larger cities, neither travelling to Quito (aOR=1.92, 95%CI: 0.94, 3.93, *Appendix:* Table 4.1) nor traveling to Esmeraldas (aOR=0.94, 95%CI=0.46, 1.59, *Appendix*: Table 4.2) were found to be significantly associated with diarrheal disease after adjusting for sex and water treatment at home.

When stratifying the data by site and including indicator variables for each possible destination, there were not any specific destinations that were associated with diarrheal disease (adjusting for sex and water treatment at home) among participants from the rural communities (*Appendix:* Table 4.3). However, an equivalent logistic regression model restricted to participants from Borbón Hospital indicated that cases were 4.5 times more likely to have traveled to Borbón in the past year (*aOR*=4.52, 95%*CI*: 1.21, 16.85). The Borbón Hospital serves people from surrounding communities so Borbón was included as a possible travel destination for these participants.

A similar model restricted to participants from Esmeraldas did not produce any destinations that were significantly associated with diarrhea disease, but Guayaquil (*aOR*=2.27, 95%*CI*: 0.96, 5.41) and Quito (*aOR*=2.51, 95%*CI*: 0.99, 6.39) were close to significant. When restricted to only participants from Quito, there were not any significant associations with individual travel destinations after controlling for sex and treating water at home (*Appendix:* Table 4.3).

Among participants from the rural communities, each trip to another rural community was found to have a protective effect on diarrheal disease, adjusted for sex and water treatment (*aOR*=0.47, 95%*CI*: 0.23, 0.97) (*Appendix:* Table 4.4). Participants from Borbón who traveled to San Lorenzo in the past year were found to have increased odds of being a case for each trip they took (*aOR*=1.40, 95%*CI*: 1.02, 1.93) when controlling for sex and water treatment. The models produced for participants from Esmeraldas and Quito did not find a significant association between number of trips to a specific destination and being a case.

When fitting four models that controlled for sex and water treatment at home and contained continuous variables for number of days spent at each travel destination, there were very few destinations that were found to have a significant association between the number of days spent in each destination and diarrheal disease (*Appendix:* Table 4.5). Among participants from Borbón Hospital, each day spent traveling in Borbón increased the odds of being a case nearly 3.5 times (*aOR*=3.48, 95%*CI*: 1.03, 11.74). Similarly, participants from Esmeraldas experienced an increase in odds of being a case for each day they spent in Quito (*aOR*=1.30, 95%*CI*: 1.06, 1.60). There were no significant associations from the rural communities or Quito.

Discussion

Key findings and plausibility

The most important finding from this analysis is that travel within the past year is associated with having diarrheal disease. Even after controlling for confounding variables (sex and treating water at home), the association remained significant (*aOR*=1.40, 95%*CI*: 1.02, 1.92) among all participants. None of the variables related to socio-economic status (receiving government assistance, employment, education and home ownership) confounded this association. When looking closer at this association, the association is most evident among participants from Esmeraldas. When the data was stratified by site, the association between traveling in the past year and diarrheal disease only remained significant in Esmeraldas. This association could not even be calculated among participants from Borbón and the rural communities because all of those participants indicated that they had traveled within the past year. Most of these trips by participants from Esmeraldas were to Quito and Guayaquil, for a variety of reasons including to visit family, medical reasons and vacation (*Appendix:* Figure 5).

This result is particularly of interest when compared to the null relationship between diarrheal disease and traveling within the past week. (*p*-value=0.970). One of the biggest challenges in analyzing the impact of travel on disease transmission is determining the appropriate observation or recall period necessary to capture the dynamics of interest. It is possible that the incubation periods of the most common pathogens are longer than a week and therefore people who contracted an enteric disease while traveling might not show symptoms and appear at a health facility within a week. These results together indicate that collecting travel histories that only capture the previous week may be too short to understand the influence of travel.

This analysis further provides insight into where, why, how often and for how long people in these four study sites travel. As expected, people typically take many frequent, but short, trips among the rural communities and between Borbón and the rural communities. Often, these trips into Borbón are for medical purposes (68.4%) or to shop (21.1%). However, almost all trips out to the rural communities (either from Borbón or other rural communities) are to visit family members. Also as expected, trips to further destinations tend to have longer durations.

Participants from the larger urban areas (Esmeraldas and Quito) were less likely to have traveled in the last year (34.0% in Esmeraldas and 54.2% in Quito vs. 100% in both Borbón and the rural communities). This is most likely characteristic of differences between urban and rural lifestyles. People who live in urban areas do not need to travel outside of their city to find medical care, places to shop or work and thus are less likely to travel long distances. Along those lines, when they did travel, people from the urban areas typically took longer trips and most of these were to visit family or vacation. Interestingly, participants from Quito were most likely to report that they had travelled in the past week (11.5%). This group might be a reflection of differences in employment opportunities and as a result, differences in ability to travel frequently. Understanding the differences in the travel patterns among participants from each site is essential for studying the relationship between travel and disease dynamics.

From a water and sanitation perspective, the major finding is that controls were significantly more likely to treat their water than cases (*p*-value=0.004). Water treatment at home remained in all the logistic regression models as a confounder of relationship between travel in the past year and diarrheal disease. When controlling for travel in the past year and sex, treating water at home had a protective effect on diarrheal disease (*aOR*=0.67, 95% *CI*: 0.49, 0.91). When the data is stratified by site, this effect is also most evident in Esmeraldas. This finding could suggest that a) public knowledge of the benefits of water treatment is more prevalent in Esmeraldas, b) water treatment methods are more effective in Esmeraldas or c) pathogens susceptible to water treatment exist at higher levels in Esmeraldas. Considering a higher proportion of participants in Quito reported treating their water (64.4%) than in Esmeraldas (40.7%), the first explanation is unlikely. Furthermore, a higher proportion of participants reported drinking tap water in Quito (84%) than in Esmeraldas (51%), indicating that treatment might be more important in Esmeraldas.

The bivariate analysis also indicated that contact with production chickens (*OR*=0.46, *p*-value=0.043) and/or backyard chickens (*OR*=0.58, *p*-value=0.037) is protective against diarrheal disease. Even though the number or participants who actually had contact with both groups is small (n=38 for backyard chickens and n=31 for production chickens), this could represent an underlying difference in socioeconomic status. Participants of higher socioeconomic status are probably more likely to come in contact with either type of chicken and also might be less likely to have diarrheal disease. Additionally, participants who report contact with chickens are more likely to be raising chickens in the home for consumption, which could have a positive impact on nutritional status. Neither contact with backyard chickens nor contact with production chickens confounded the relationship between travel and diarrheal disease.

Limitations

This research has several limitations that should be acknowledged and considered when developing future research directions. The most obvious limitation is that the travel history section of the questionnaire might not have captured the necessary information to determine the influence of travel on diarrheal disease transmission. While collecting data on travel within the past year produced a significant association, it was not able to produce distinguishable differences between rural and urban communities. All participants in Borbón and the rural communities indicated that they traveled in the past year, meaning the only way to relate that information to status as a case or control was to pool together the data from all sites. On the other hand, the proportion of cases who traveled in the past week was almost identical to the proportion of controls who traveled during the same time period, indicating that recall of one week is not long enough to capture differences in diarrheal disease dynamics. Future research should either include a recall interval between one week and one year in an attempt to capture the relevant differences.

Second, there is potential for bias in both the way participants were selected and classified. Since participants from the rural communities were not recruited in a health center like the other three sites, it is possible the degree of diarrheal disease severity is different across sites, making it difficult to compare results from the different sites. Also, the participants that came from the Borbón site were recruited from the Borbón Hospital, which not only serves people living in the town or Borbón but also surrounding communities. During the data analysis, there was an attempt to re-classify individuals that reside in neighboring communities as coming from the rural communities site. However, it is likely that some of these were missed and that is partially evident among the 18 observations from Borbón that also indicated Borbón as a travel destination. Further analysis should involve correctly classifying all of those individuals and re-producing the results.

Any type of retrospective study that involves questionnaires about previous travel practices is subject to recall bias. Participants might not be able to remember exactly how many times or for how many days they traveled over the course of an entire year. The survey response options were designed to absorb some of that potential bias (i.e. "every other month" or "2-4 weeks" as response options for frequency or duration of travel) but recall bias could still have influenced results.

Future directions and conclusions

Future directions should be focused on using these results as a starting point for better understanding travel patterns in the region. With respect to this dataset, further analysis on the data from Esmeraldas should be done to develop a better understanding of what causes such a strong association between travel in the past year and diarrheal disease at that site. Furthermore, the results from this analysis and future research can provide a better understanding of travel patterns in the region, which is essential to the development of research questions relating travel to disease transmission dynamics. One of the biggest challenges to collecting travel data is determining the appropriate observation or recall interval and the appropriate data points to collect. These decisions are unique to specific regions and pathogens.

Data collection for the larger research project is still ongoing in Borbón and the rural communities. Future plans for the project involve looking at corresponding fine scale genetic data to investigate parallels between genetic similarity of pathogenic *E. coli* strains and human movement patterns across the country. The overall conclusions of this paper indicate that travel is indeed associated with diarrheal disease, but the degree of this association differs by site and the length of the travel history recall period. These conclusions will be considered and factored into future data collection and analysis on this project.

Appendix

Supplemental Figures and Tables

Figure 2: Reason for travel within the past year to each destination by all participants, Ecuador, 2014-2015. Participants could indicate more than one reason for each destination. The sample size for each destination is: Borbón n=76, Esmeraldas n=72, Guayaquil n=69, Santo Domingo n=26, San Lorenzo n=35 and rural communities n=48.

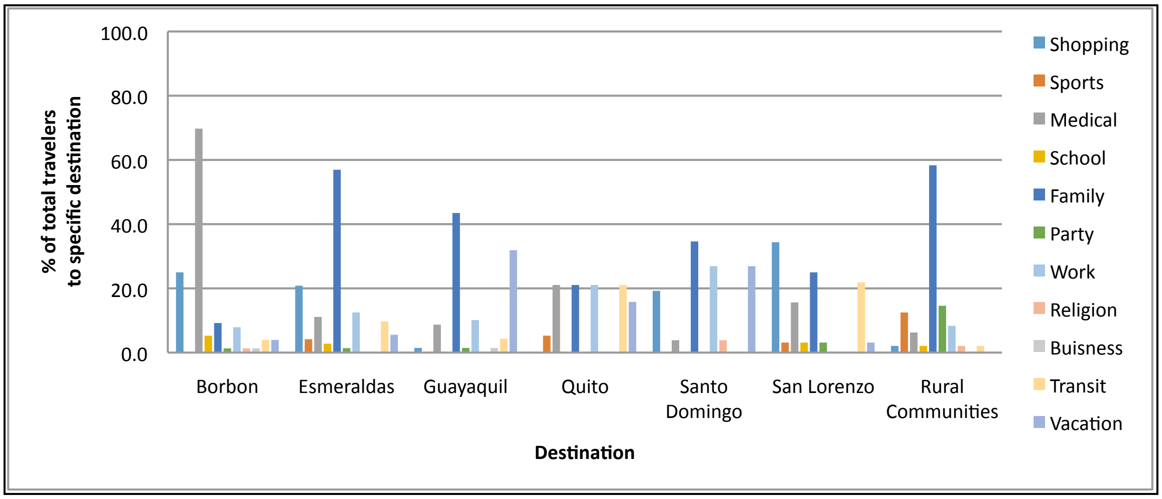


Figure 3: Reason for travel within the past year to each destination by participants from rural communities, Ecuador, 2014-2015. Participants could indicate more than one reason for each destination. The sample size for each destination is: Borbón n=57, Esmeraldas n=29, Guayaquil n=6, Quito n=2, Santo Domingo n=3, San Lorenzo n=10, and rural communities n=27.

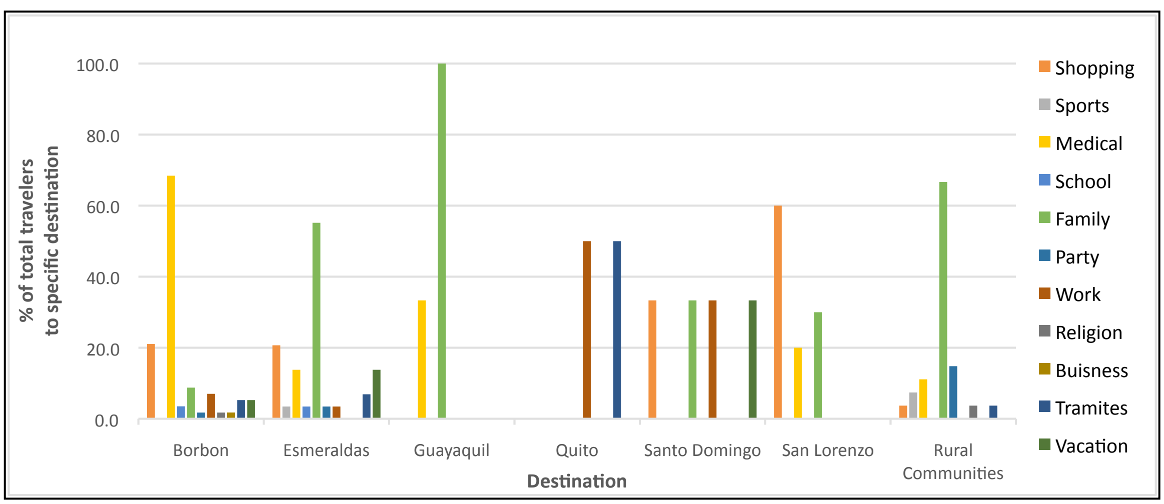


Figure 4: Reason for travel within the past year to each destination by participants from Borbón, Ecuador, 2014-2015. Participants could indicate more than one reason for each destination. The sample size for each destination is: Borbón n=18, Esmeraldas n=43, Guayaquil n=15, Quito n=12, Santo Domingo n=8, San Lorenzo n=16, and rural communities n=21.

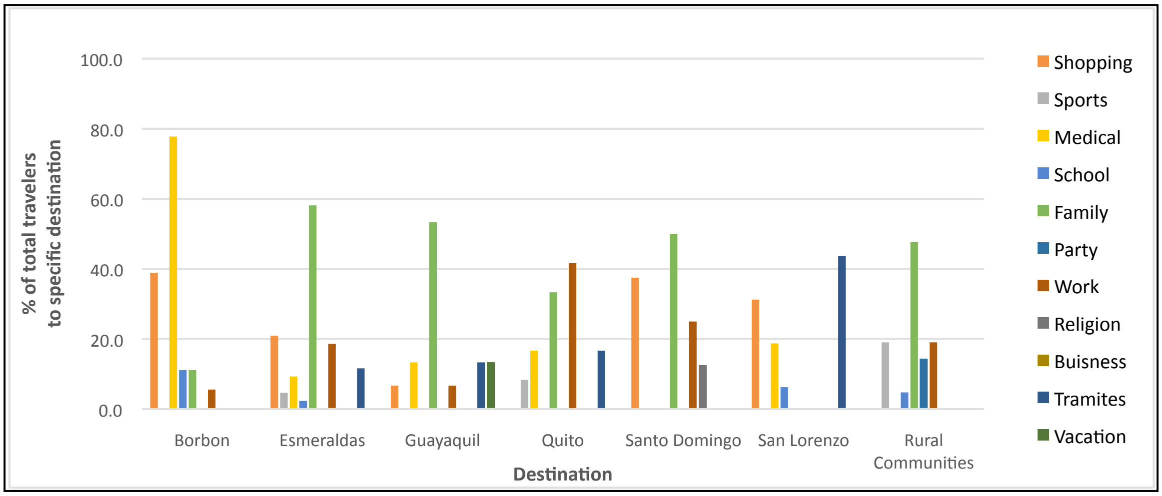


Figure 5: Reason for travel within the past year to each destination by participants from Esmeraldas, Ecuador, 2014-2015. Participants could indicate more than one reason for each destination. The sample size for each destination is: Borbón n=1, Guayaquil n=27, Quito n=24, Santo Domingo n=7 and San Lorenzo n=5.

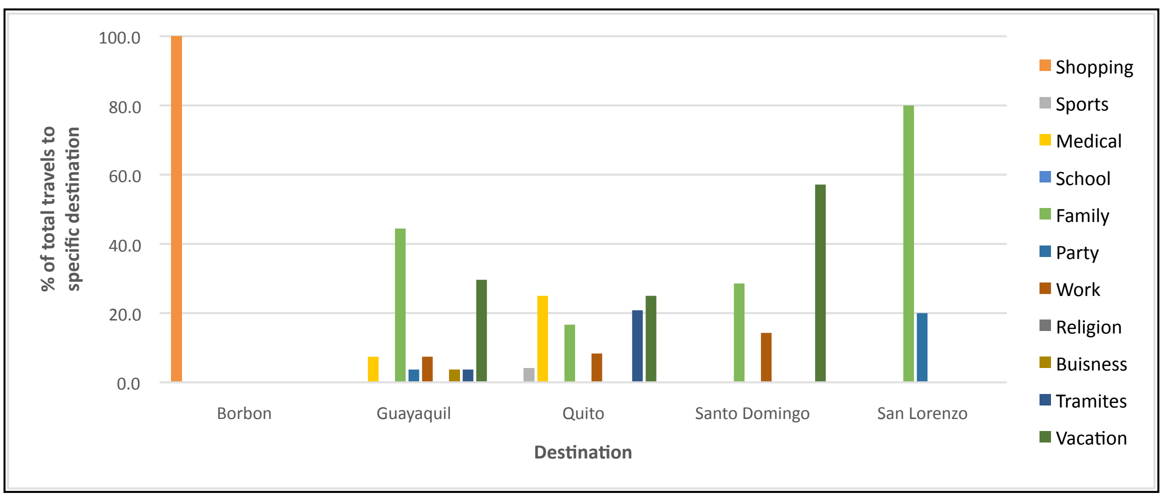


Figure 6: Reason for travel within the past year to each destination by participants from Quito, Ecuador, 2014-2015. Participants could indicate more than one reason for each destination. The sample size for each destination is: Guayaquil n=21, Santo Domingo n=8 and San Lorenzo n=3.

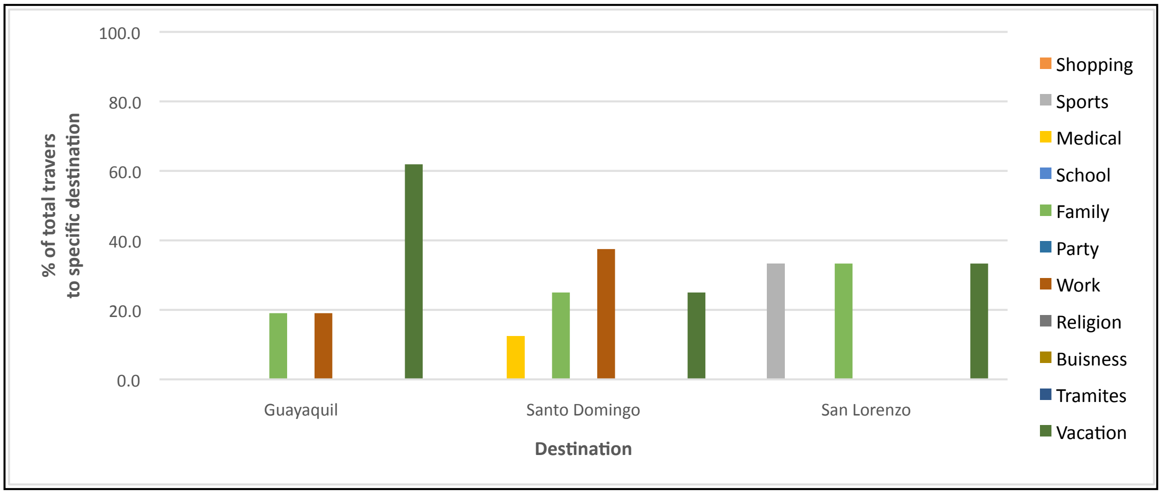


Table 1.1: Demographic, socioeconomic and medical characteristics of all participants, by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate p-values that are significant at the alpha=0.05 level.

	N	Rural communities	Borbon	Esmeraldas	Quito	p-value[a]
	720	n=104	n=108	n=237	n=271	
		n (%)	**n (%)**	**n (%)**	**n (%)**	
Cases	380	64 (61.5)	58 (53.7)	119 (50.2)	139 (51.3)	0.250
Demographics						
Age						0.002*
<2 years	268	29 (27.9)	49 (45.4)	90 (38.0)	100 (36.9)	
2-5 years	126	33 (31.7)	15 (13.9)	39 (16.5)	39 (14.4)	
5-15 years	136	18 (17.3)	23 (21.3)	49 (20.7)	46 (17.0)	
15+ years	190	24 (23.1)	21 (19.4)	59 (24.9)	86 (31.7)	
Male	386	52 (50.0)	67 (62.0)	133 (56.1)	134 (49.4)	0.110
Reported Race	697	104 (100)	108 (100)	222 (93.7)	263 (97.0)	
White	9	0 (0)	0 (0)	1 (0.5)	8 (3.0)	<0.001*
Indigenous	44	33 (31.7)	5 (4.6)	1 (0.5)	5 (1.9)	
Manaba	30	9 (8.7)	9 (8.3)	8 (3.6)	4 (1.5)	
Mixed	419	29 (27.9)	28 (25.9)	119 (53.6)	243 (92.4)	
Black	195	33 (31.7)	66 (61.1)	93 (41.9)	3 (1.1)	
Socioeconomic Status						
Reported SES Data	698	104 (100)	108 (100)	223 (94.1)	263 (97.0)	
Receives government assistance	135	46 (44.2)	30 (27.8)	44 (19.7)	15 (5.7)	<0.001*
Somebody in the house is employed	361	21 (20.2)	40 (37.0)	97 (43.5)	203 (77.2)	<0.001*
House ownership						<0.001*
Loaned	66	10 (9.6)	6 (5.6)	25 (11.2)	25 (9.5)	
Owned	418	88 (84.6)	84 (77.8)	160 (71.7)	86 (32.7)	
Rented	214	6 (5.8)	18 (16.7)	38 (17.0)	152 (57.8)	
Some level of education	690	102 (98.1)	107 (99.1)	219 (92.4)	262 (96.7)	0.012*
Highest level - Primary School	76	26 (25.0)	5 (4.6)	15 (6.3)	30 (11.1)	<0.001*
Highest level - Secondary School	399	67 (64.4)	85 (78.7)	117 (49.4)	130 (48.0)	
Highest level - University	215	9 (8.7)	17 (15.7)	87 (36.7)	102 (37.6)	
Reported nursery use data	340	52 (50.0)	59 (54.6)	107 (45.1)	122 (45.0)	
Attended a nursery in past month	70	17 (32.7)	19 (32.2)	19 (17.8)	15 (12.3)	0.002*
Contact with animals in the past week	340	41 (39.4)	51 (47.2)	101 (42.6)	147 (54.2)	0.02*
Pig	23	8 (19.5)	11 (21.6)	1 (1.0)	3 (2.0)	<.0001*
Cat	141	19 (46.3)	32 (62.8)	52 (51.5)	38 (25.9)	<.0001*
Dog	257	26 (63.4)	34 (66.7)	68 (67.3)	129 (87.8)	<.0001*
Backyard chicken	38	11 (26.8)	12 (23.5)	3 (2.97)	12 (8.2)	<.0001*
Rat	1	0 (0)	0 (0)	0 (0)	1 (0.7)	>0.99
Production chicken	31	11 (26.8)	10 (19.6)	3 (3.0)	7 (4.8)	<.0001*
Cow	5	1 (2.4)	2 (3.9)	1 (1.0)	1 (0.7)	0.254
Other	8	2 (4.9)	0 (0)	2 (2.0)	4 (2.7)	0.473
Medical						
Tested for rotavirus	574	91 (87.5)	85 (78.7)	198 (83.5)	200 (73.8)	
Positive rotavirus test	44	9 (9.9)	7 (8.2)	13 (6.6)	15 (7.5)	0.800
Had full rotavirus vaccine	7	1 (11.1)	1 (14.3)	1 (7.7)	4 (26.7)	0.695
Reported rotavirus vaccine history	128	12 (11.5)	15 (13.9)	34 (14.3)	67 (24.7)	
Received the first rotavirus vaccine	112	11 (91.7)	14 (93.3)	29 (85.3)	58 (86.6)	0.949
Received the second rotarirus vaccine	98	10 (90.9)	9 (64.3)	26 (89.7)	53 (91.4)	0.076
Tested for parasites	187	6 (5.8)	20 (18.5)	160 (67.5)	1 (0.4)	
Positive parasite test	40	0 (0)	7 (35)	33 (20.6)	0 (0)	0.289
Reported history of medicie use	687	104 (100)	107 (99.1)	213 (89.9)	263 (97)	
Used medicine in Past 7 Days	191	1 (1)	4 (3.7)	78 (36.6)	108 (41.1)	<.0001*
Reported breastfeeding practices	338	50 (48.1)	59 (54.6)	107 (45.1)	122 (45)	
None	4	0 (0)	0 (0)	1 (0.9)	3 (2.5)	<.0001*
Done breastfeeding	175	31 (62)	39 (66.1)	66 (61.7)	39 (32)	
Mixed	109	15 (30)	18 (30.5)	24 (22.4)	52 (42.6)	
Exclusive brestfeedng	50	4 (8)	2 (3.4)	16 (15)	28 (23)	
Under 1 year old	47	2 (50.0)	2 (100)	15 (93.8)	28 (100)	0.008*
Under 6 months old	36	1 (25.0)	1 (50.0)	10 (62.5)	24 (85.7)	0.025*

[a]*P values calculated using Pearson's Chi Square or Fisher's exact test*

Table 1.2: Water and sanitation characteristics of all participants, by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate p-values that are significant at the alpha=0.05 level.

	N	Rural communities	Borbon	Esmeraldas	Quito	p-value[a]
	720	n=104	n=108	n=237	n=271	
		n (%)	n (%)	n (%)	n (%)	
Water and Sanitation						
Reported sanitation practices at home	693	104 (100)	108 (100)	218 (92.0)	263 (97.0)	
Improved sanitation[b]	627	61 (59.8)	87 (80.6)	217 (99.5)	262 (99.6)	<.0001*
Flush toilet	294	0 (0)	1 (0.9)	98 (45.0)	195 (74.1)	<.0001*
Open defecation	14	11 (10.6)	2 (1.9)	0 (0)	1 (0.4)	<.0001*
Community latrine	9	7 (6.7)	1 (0.9)	1 (0.5)	0 (0)	<.0001*
Diaper	175	21 (20.2)	33 (30.6)	65 (29.8)	56 (21.3)	0.050*
Hole	51	31 (29.8)	19 (17.6)	1 (0.5)	0 (0)	<.0001*
Private latrine	33	9 (8.7)	5 (4.6)	9 (4.1)	10 (3.8)	0.240
Septic tank	117	24 (23.1)	47 (43.5)	45 (20.6)	1 (0.4)	<.0001*
River	2	2 (1.9)	0 (0)	0 (0)	0 (0)	0.022
Reported sanitation practices while traveling	55	2 (1.9)	8 (7.4)	16 (6.8)	29 (10.7)	
Improved sanitation[b]	52	1 (50.0)	8 (100)	14 (87.5)	29 (100)	0.154
Flush toilet	26	0 (0)	0 (0)	4 (25.0)	22 (75.9)	<.0001*
Open defecation	2	0 (0)	0 (0)	2 (12.5)	0 (0)	0.172
Community latrine	2	1 (50.0)	0 (0)	0 (0)	1 (3.4)	0.091
Diaper	14	0 (0)	4 (50.0)	6 (37.5)	4 (13.8)	0.077
Hole	1	1 (50.0)	0 (0)	0 (0)	0 (0)	0.036*
Own latrine	3	0 (0)	2 (25.0)	0 (0)	1 (3.4)	0.143
Septic tank	7	0 (0)	2 (25.0)	4 (25.0)	1 (3.4)	0.083
Reported water source at home	696	104 (100)	108 (100)	221 (93.2)	263 (97.0)	
Improved water source[c]	670	93 (89.4)	95 (88.0)	220 (99.5)	262 (99.6)	<.0001*
Purchased	212	22 (21.2)	49 (45.4)	79 (35.7)	62 (23.6)	<.0001*
Tap Inside	374	9 (8.7)	33 (30.6)	112 (50.7)	220 (83.7)	<.0001*
Tap outside	46	7 (6.7)	6 (5.6)	32 (14.5)	1 (0.4)	<.0001*
Neighbor's tap	5	4 (3.8)	1 (0.9)	0 (0)	0 (0)	<.0001*
Rain	57	51 (49.0)	6 (5.6)	0 (0)	0 (0)	<.0001*
Tank	15	5 (4.8)	10 (9.3)	0 (0)	0 (0)	<.0001*
River	13	8 (7.7)	3 (2.8)	1 (0.5)	1 (0.4)	<.0001*
Treat water	302	23 (22.1)	23 (21.3)	87 (39.4)	169 (64.3)	<.0001*
Reported water source while traveling	60	5 (4.8)	10 (9.3)	16 (6.8)	29 (10.7)	
Improved water source[c]	58	5 (100)	10 (100)	15 (93.8)	28 (96.6)	0.820
Purchased	40	5 (100)	10 (100)	11 (68.8)	14 (48.3)	0.005*
Tap Inside	14	0 (0)	0 (0)	2 (12.5)	12 (41.4)	0.016*
Tap outside	3	0 (0)	0 (0)	1 (6.3)	2 (6.9)	>0.99
Rain	1	0 (0)	0 (0)	1 (6.3)	0 (0)	0.517
River	2	0 (0)	0 (0)	1 (6.3)	1 (3.4)	>0.99
Treat water	15	0 (0)	0 (0)	4 (25.0)	11 (37.9)	0.059

[a]P values calculated using Pearson's Chi Square or Fisher's exact test
[b]Includes flush toilet, latrines, diaper and septic tank
[c]Includes purchased, taps and rain

Table 1.3: Travel history and exclusion criteria of all participants, by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate p-values that are significant at the alpha=0.05 level.

	N	Rural communities	Borbon	Esmeraldas	Quito	p-value[a]
	720	n=104	n=108	n=237	n=271	
		n (%)	n (%)	n (%)	n (%)	
Travel History						
Reported travel practices	698	104 (100)	108 (100)	223 (94.1)	263 (97.0)	
Traveled in the past week	61	5 (4.8)	10 (9.3)	16 (6.8)	30 (11.1)	0.160
Traveled in the past year	427	102 (100)	108 (100)	75 (33.6)	142 (54.0)	<.0001*
Exlcusion Criteria						
Lived in the wrong city or area	10	0 (0)	0 (0)	10 (4.2)	0 (0)	
Lived in the area for less than 6 months	6	0 (0)	0 (0)	1 (0.5)	5 (2.1)	
Control had diarrhea	6	0 (0)	0 (0)	3 (2.6)	3 (2.3)	
Took antibiotics in past 7 dyas	25	0 (0)	1 (0.9)	14 (6.2)	10 (3.8)	

[a]P values calculated using Pearson's Chi Square or Fisher's exact test

Table 2.1: Demographic, socio-economic status and medical characteristics of cases and controls, stratified by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate p-values that are significant at the alpha=0.05 level.

		All Subjects			Rural Communities			Borbon			Esmeraldas			Quito		
		Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
		321	352		40	64		49	58		109	100		123	130	
	Total N	n (%)	n (%)	p-value[a]	n (%)	n (%)	p-value[a]	n (%)	n (%)	p-value[a]	n (%)	n (%)	p-value[a]	n (%)	n (%)	p-value[a]
Demographics																
Age																
0-2	242	116 (36.1)	126 (35.8)		9 (22.5)	20 (31.3)		22 (44.9)	26 (44.8)		38 (34.9)	35 (35)		47 (38.2)	45 (34.6)	
2-5	121	56 (17.4)	65 (18.5)		13 (32.5)	20 (31.3)		6 (12.2)	9 (15.5)		20 (18.3)	16 (16)		17 (13.8)	20 (15.4)	
5-15	131	66 (20.6)	65 (18.5)		7 (17.5)	11 (17.2)		12 (24.5)	11 (19)		24 (22)	23 (23)		23 (18.7)	20 (15.4)	
>15	179	83 (25.9)	96 (27.3)	0.890	11 (27.5)	13 (20.3)	0.740	9 (18.4)	12 (20.7)	0.880	27 (24.8)	26 (26)	0.970	36 (29.3)	45 (34.6)	0.730
Male	355	158 (49.2)	197 (56)	0.080	19 (47.5)	33 (51.6)	0.690	29 (59.2)	37 (63.8)	0.630	54 (49.5)	59 (59)	0.170	56 (45.5)	68 (52.3)	0.280
Race Reported	672	320 (99.7)	352 (100)	0.477	40 (100)	64 (100)	0.340	49 (100)	58 (100)	0.290	108 (99.1)	100 (100)	>0.99	123 (100)	130 (100)	--
White	9	4 (1.3)	5 (1.4)		0(0)	0(0)		0 (0)	0 (0)		1 (0.9)	0 (0)		3 (2.4)	5 (3.8)	
Indigenous	44	11 (3.4)	33 (9.4)		8 (20.0)	25 (39.1)		1 (2)	4 (6.9)		0 (0)	1 (1)		2 (1.6)	3 (2.3)	
Manaba	29	15 (4.7)	14 (4)		4 (10)	5 (7.8)		4 (8.2)	5 (8.6)		5 (4.6)	2 (2)		2 (1.6)	2 (1.5)	
Mixed	402	192 (60.0)	210 (59.7)		12 (30)	17 (26.6)		12 (24.5)	16 (27.6)		53 (49.1)	59 (59)		115 (93.5)	118 (90.8)	
Black	188	98 (30.6)	90 (25.6)	0.029 *	16 (40)	17 (26.6)	0.216	32 (65.3)	33 (56.9)	0.691	49 (45.4)	38 (38)	0.276	1 (0.8)	2 (1.5)	0.951
Socioeconomic Status																
Receives government assistance	132	62 (19.3)	70 (19.9)	0.850	17 (42.5)	29 (45.3)	0.780	13 (26.5)	16 (27.6)	0.900	22 (20.2)	20 (20)	0.970	10 (8.1)	5 (3.8)	0.150
Somebody in the house is emplyed	351	166 (51.7)	185 (52.6)	0.830	6 (15)	15 (23.4)	0.300	20 (40.8)	20 (34.5)	0.500	48 (44)	46 (46)	0.780	92 (74.8)	104 (80)	0.320
House ownership																
Loaned	63	28 (8.7)	35 (9.9)		2 (5)	8 (12.5)		0 (0)	6 (10.3)		13 (11.9)	9 (9)		13 (10.6)	12 (9.2)	
Owned	408	200 (62.3)	208 (59.1)		36 (90)	52 (81.3)		41 (83.7)	42 (72.4)		82 (75.2)	70 (70)		41 (33.3)	44 (33.8)	
Rented	202	93 (29)	109 (31)	0.680	2 (5)	4 (6.3)	0.489	8 (16.3)	10 (17.2)	0.052	14 (12.8)	21 (21)	0.260	69 (56.1)	74 (56.9)	0.940
Some level of education	665	318 (99.1)	347 (98.6)	0.727	40 (100)	62 (96.9)	0.522	49 (100)	57 (98.3)	>0.99	106 (97.2)	99 (99)	0.623	123 (100)	129 (99.2)	>0.99
Highest level - Primary School	70	30 (9.3)	40 (11.4)		9 (22.5)	17 (26.6)		1 (2)	3 (5.2)		5 (4.6)	9 (9)		15 (12.2)	11 (8.5)	
Highest level - Secondary School	388	180 (56.1)	208 (59.1)		29 (72.5)	38 (59.4)		40 (81.6)	45 (77.6)		56 (51.4)	56 (56)		55 (44.7)	69 (53.1)	
Highest level - University	207	108 (33.6)	99 (28.1)	0.402	2 (5)	7 (10.9)	0.473	8 (16.3)	9 (15.5)	0.813	45 (41.3)	34 (34)	0.369	53 (43.1)	49 (37.7)	0.350
Reported nursery use data	326	154 (48)	172 (48.9)		16 (40)	36 (56.3)		26 (53.1)	32 (55.2)		53 (48.6)	45 (45)		59 (48)	59 (45.4)	
Attended a nursery in past month	63	31 (20.1)	32 (18.6)	0.730	7 (43.8)	10 (27.8)	0.260	11 (42.3)	8 (25)	0.160	7 (13.2)	7 (15.6)	0.740	6 (10.2)	7 (11.9)	0.770
Contact with animals in the past week	326	154 (48)	172 (48.9)	0.820	21 (52.5)	20 (31.3)	0.030 *	18 (36.7)	33 (56.9)	0.040 *	45 (41.3)	49 (49)	0.260	70 (56.9)	70 (53.8)	0.620
Pig	23	13 (8.4)	10 (5.81)	0.355	4 (19.1)	4 (20)	>0.99	7 (38.9)	4 (12.1)	0.037 *	1 (2.2)	0 (0)	0.479	1 (1.4)	2 (2.9)	>0.99
Cat	137	57 (37.0)	80 (46.5)	0.083	5 (23.8)	14 (70.0	0.003 *	10 (55.6)	22 (66.7)	0.433	23 (51.1)	27 (55.1)	0.699	19 (27.1)	17 (24.3	0.699
Dog	247	120 (77.9)	127 (73.8)	0.390	14 (66.7)	12 (60)	0.658	12 (66.7)	22 (66.7)	>0.99	30 (66.7)	33 (67.4)	0.944	64 (91.4)	60 (85.7)	0.438
Backyard chicken	38	24 (15.6)	14 (8.1)	0.037 *	5 (23.8)	6 (30.0)	0.655	8 (44.4)	4 (12.1)	0.015 *	3 (6.7)	0 (0)	0.106	8 (11.4)	4 (5.7)	0.227
Rat	1	0 (0)	1 (0.6)	0.058	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	1 (1.4)	>0.99
Production chicken	31	20 (13.0)	11 (6.4)	0.043 *	5 (23.8)	6 (30.0)	0.655	7 (38.9)	3 (9.1)	0.023 *	3 (6.7)	0 (0)	0.106	5 (7.1)	2 (2.9)	0.441
Cow	5	4 (2.6)	1 (0.6)	0.193	1 (4.8)	0 (0)	>0.99	1 (5.6)	1 (3.0)	>0.99	1 (2.2)	0 (0)	0.479	1 (1.4)	0 (0)	>0.99
Other	7	5 (3.3)	2 (1.2)	0.262	2 (9.5)	0 (0)	0.488	0 (0)	0 (0)	--	1 (2.2)	1 (2.0)	>0.99	2 (2.9)	1 (1.4)	>0.99
Medical																
Tested for rotavirus	553	282 (87.9)	271 (77)	<0.001 *	39 (97.5)	52 (81.3)	0.020	46 (93.9)	38 (65.5)	<0.001	98 (89.9)	88 (88)	0.660	99 (80.5)	93 (71.5)	0.100
Positive rotavirus test	42	1 (0.4)	41 (15.1)	<0.001 *	0 (0)	9 (17.3)	0.009	0 (0)	7 (18.4)	0.003 *	1 (1)	11 (12.5)	0.001 *	0 (0)	14 (15.1)	<0.001 *
Received full rotavirus vaccine	7	0 (0)	7 (17.07)	>0.99	0 (0)	1 (11.11)	--	0 (0)	1 (14.3)	--	0 (0)	1 (9.1)	>0.99	0 (0)	4 (28.6)	--
Reported rotavirus vaccine history	118	63 (19.6)	55 (15.6)		3 (7.5)	9 (14.1)		9 (18.4)	5 (8.6)		19 (17.4)	10 (10)		32 (26)	31 (23.8)	
Received first rotavirus vaccine	103	52 (82.5)	51 (92.7)	0.098	3 (100)	8 (88.9)	>0.99	8 (88.9)	5 (100)	>0.99	16 (84.2)	9 (90.0)	>0.99	25 (78.1)	29 (93.6)	0.148
Received full rotavirus vaccine	89	47 (90.4)	42 (82.4)	0.234	3 (100)	7 (87.5)	>0.99	5 (62.5)	3 (60.0)	>0.99	15 (93.8)	7 (77.8)	0.530	24 (96.0)	25 (86.2)	0.358
Tested for parasties	175	91 (28.3)	84 (23.9)	0.190	1 (2.5)	5 (7.8)	0.402	10 (20.4)	10 (17.2)	0.680	80 (73.4)	68 (68)	0.390	0 (0)	0 (0)	--
Positive parasite test	38	25 (27.5)	13 (15.5)	0.050 *	0 (0)	0 (0)	0.190	5 (50)	2 (20)	0.350	20 (25)	11 (16.2)	0.190	0 (0)	0 (0)	--
Reported hisotry of medicine use	662	314 (97.8)	348 (98.9)		40 (100)	64 (100)		48 (98)	58 (100)		103 (94.5)	96 (96)		123 (100)	130 (100)	
Used medicine in past 7 days	166	57 (18.2)	109 (31.3)	<0.001 *	1 (2.5)	0 (0)	0.385	1 (2.1)	2 (3.4)	>0.99	23 (22.3)	41 (42.7)	0.002 *	32 (26)	66 (50.8)	<0.001 *
Reported breastfeeding practices	324	153 (47.7)	171 (48.6)		15 (37.5)	35 (54.7)		26 (53.1)	32 (55.2)		53 (48.6)	45 (45)		59 (48)	59 (45.4)	
Done breastfeeding	167	77 (50.3)	90 (52.6)		10 (66.7)	21 (60)		17 (65.4)	22 (68.8)		33 (62.3)	27 (60)		17 (28.8)	20 (33.9)	
Mixed	105	43 (28.1)	62 (36.3)		4 (26.7)	11 (31.4)		8 (30.8)	9 (28.1)		10 (18.9)	13 (28.9)		21 (35.6)	29 (49.2)	
Exclusive breastfeeding	48	30 (19.6)	18 (10.5)	0.050 *	1 (6.7)	3 (8.6)	>0.99	1 (3.8)	1 (3.1)	>0.99	9 (17)	5 (11.1)	0.501	19 (32.2)	9 (15.3)	0.121
Under 1 year old	45	30 (100)	15 (83.3)	0.047 *	1 (100)	1 (33.3)	>0.99	1 (100)	1 (100)	--	9 (100)	4 (80)	0.357	19 (100)	9 (100)	--
Under 6 months old	35	23 (76.7)	12 (66.7)	0.513	0 (0)	1 (33.3)	>0.99	0 (0)	1 (100)	>0.99	5 (55.6)	4 (80)	0.580	18 (94.7)	6 (66.7)	0.084

[a] *P values calculated using Pearson's Chi Square or Fisher's exact test*

Table 2.2: Water and sanitation practices of cases and controls, stratified by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. Reported p-values test the null hypothesis that there is no difference between the sites. Asterisks indicate p-values that are significant at the alpha=0.05 level.

		All Subjects			Rural Communities			Borbon			Esmeraldas			Quito		
		Controls 321	Cases 352		Controls 40	Cases 64		Controls 49	Cases 58		Controls 109	Cases 100		Controls 123	Cases 130	
	Total N	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**	**n (%)**	**n (%)**	**p-value[a]**
Water and Sanitation																
Reported sanitation practices at home	668	321 (100)	347 (98.6)		40 (100)	64 (100)		49 (100)	58 (100)		109 (100)	95 (95)		123 (100)	130 (100)	
Improved sanitation[b]	602	296 (92.5)	306 (88.4)	0.080	26 (66.7)	35 (55.6)	0.270	39 (79.6)	47 (81)	0.850	109 (100)	94 (98.9)	0.466	122 (99.2)	130 (100)	0.486
Flush toilet	280	138 (43)	142 (40.9)	0.590			0.400	0 (0)	1 (1.7)	>0.99	50 (45.9)	42 (44.2)	0.810	88 (71.5)	99 (76.2)	0.400
Open defecation	14	6 (1.9)	8 (2.3)	0.690	3 (7.5)	8 (12.5)	0.524	2 (4.1)	0 (0)	0.207	0 (0)	0 (0)	--	1 (0.8)	0 (0)	0.486
Community latrine	9	7 (2.2)	2 (0.6)	0.096	5 (12.5)	2 (3.1)	0.104	1 (2)	0 (0)	0.458	1 (0.9)	0 (0)	>0.99	0 (0)	0 (0)	--
Diaper	165	86 (26.8)	79 (22.8)	0.230	6 (15)	15 (23.4)	0.300	19 (38.8)	13 (22.4)	0.070	33 (30.3)	24 (25.3)	0.430	28 (22.8)	27 (20.8)	0.700
Hole	51	19 (5.9)	32 (9.2)	0.110	11 (27.5)	20 (31.3)	0.680	8 (16.3)	11 (19)	0.720	0 (0)	1 (1.1)	0.466	0 (0)	0 (0)	--
Private latrine	32	13 (4)	19 (5.5)	0.390	4 (10)	5 (7.8)	0.730	0 (0)	5 (8.6)	0.061	3 (2.8)	6 (6.3)	0.309	6 (4.9)	3 (2.3)	0.323
Septic tank	117	53 (16.5)	64 (18.4)	0.510	11 (27.5)	13 (20.3)	0.400	19 (38.8)	28 (48.3)	0.320	23 (21.1)	22 (23.2)	0.720	0 (0)	1 (0.8)	>0.99
River	2	1 (0.3)	1 (0.3)	>0.99	1 (2.5)	1 (1.6)	>0.99	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	0 (0)	--
Reported sanitation practices while traveling	53	27 (8.4)	26 (7.4)		1 (2.5)	1 (1.6)		5 (10.2)	3 (5.2)		5 (4.6)	10 (10)		16 (13)	12 (9.2)	
Improved sanitation[b]	50	27 (100)	23 (88.5)	0.111	1 (100)	0 (0)	>0.99	5 (100)	3 (100)	--	5 (100)	8 (80)	0.524	16 (100)	12 (100)	--
Flush toilet	26	12 (44.4)	14 (53.8)	0.490	0 (0)	0 (0)	--	0 (0)	0 (0)	--	1 (20)	3 (30)	>0.99	11 (68.8)	11 (91.7)	0.139
Open defecation	2	0 (0)	2 (7.7)	0.236	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	2 (20)	0.524	0 (0)	0 (0)	--
Community latrine	2	2 (7.4)	0 (0)	0.491	1 (100)	0 (0)	>0.99	0 (0)	0 (0)	--	0 (0)	0 (0)	--	1 (6.3)	0 (0)	>0.99
Diaper	13	8 (29.6)	5 (19.2)	0.380	0 (0)	0 (0)	--	3 (60)	1 (33.3)	>0.99	2 (40)	3 (30)	>0.99	3 (18.8)	1 (8.3)	0.613
Hole	1	0 (0)	1 (3.8)	0.491	0 (0)	1 (100)	>0.99	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	0 (0)	--
Own latrine	3	1 (3.7)	2 (7.7)	0.610	0 (0)	0 (0)	--	0 (0)	2 (66.7)	0.107	0 (0)	0 (0)	--	1 (6.3)	0 (0)	>0.99
Septic tank	6	4 (14.8)	2 (7.7)	0.669	0 (0)	0 (0)	--	2 (40)	0 (0)	0.464	2 (40)	2 (20)	0.560	0 (0)	0 (0)	--
Reported water source at home	672	321 (100)	351 (99.7)		40 (100)	64 (100)		49 (100)	58 (100)		109 (100)	99 (99)		123 (100)	130 (100)	
Improved water source[c]	646	311 (96.9)	335 (95.4)	0.330	38 (95.0)	55 (85.9)	0.197	43 (87.8)	51 (87.9)	0.980	108 (99.1)	99 (100)	>0.99	122 (99.2)	130 (100)	0.300
Purchased	203	97 (30.2)	106 (30.2)	1.000	11 (27.5)	11 (17.2)	0.210	20 (40.8)	29 (50)	0.340	37 (33.9)	35 (35.4)	0.830	29 (23.6)	31 (23.8)	0.486
Tap Inside	359	184 (57.3)	175 (49.9)	0.050 *	3 (7.5)	6 (9.4)	>0.99	17 (34.7)	15 (25.9)	0.320	60 (55)	46 (46.5)	0.220	104 (84.6)	108 (83.1)	0.750
Tap outside	46	16 (5)	30 (8.5)	0.070	2 (5.0)	5 (7.8)	0.705	2 (4.1)	4 (6.9)	0.685	12 (11)	20 (20.2)	0.070	0 (0)	1 (0.8)	>0.99
Neighbor's tap	5	2 (0.6)	3 (0.9)	>0.99	1 (2.5)	3 (4.7)	>0.99	1 (2)	0 (0)	0.458	0 (0)	0 (0)	--	0 (0)	0 (0)	--
Rain	57	24 (7.5)	33 (9.4)	0.370	21 (52.5)	30 (46.9)	0.580	3 (6.1)	3 (5.2)	>0.99	0 (0)	0 (0)	--	0 (0)	0 (0)	--
Tank	15	7 (2.2)	8 (2.3)	0.930	1 (2.5)	4 (6.3)	0.647	6 (12.2)	4 (6.9)	0.507	0 (0)	0 (0)	--	0 (0)	0 (0)	--
River	13	4 (1.2)	9 (2.6)	0.220	2 (5.0)	6 (9.4)	0.708	0 (0)	3 (5.2)	0.248	1 (0.9)	0 (0)	>0.99	1 (0.8)	0 (0)	0.486
Treat water	294	159 (49.5)	135 (38.5)	0.004 *	7 (17.5)	16 (25)	0.370	13 (26.5)	10 (17.2)	0.240	53 (48.6)	32 (32.3)	0.020 *	86 (69.9)	77 (59.2)	0.080
Reported water source while traveling	58	28 (8.7)	30 (8.5)		2 (5.0)	3 (4.7)		5 (10.2)	5 (8.6)		5 (4.6)	10 (10)		16 (13)	12 (9.2)	
Improved water source[c]	56	26 (92.9)	30 (100)	0.229	2 (100)	3 (100)	--	5 (100)	5 (100)	--	4 (80)	10 (100)	0.333	15 (93.8)	12 (100)	>0.99
Purchased	39	16 (57.1)	23 (76.7)	0.110	2 (100)	3 (100)	--	5 (100)	5 (100)	--	2 (40)	8 (80)	0.251	7 (43.8)	7 (58.3)	0.450
Tap Inside	14	8 (28.6)	6 (20.0)	0.450	0 (0)	0 (0)	--	0 (0)	0 (0)	--	1 (20)	1 (10)	>0.99	7 (43.8)	5 (41.7)	0.910
Tap outside	2	2 (7.1)	0 (0)	0.229	0 (0)	0 (0)	--	0 (0)	0 (0)	--	1 (20)	0 (0)	0.333	1 (6.3)	0 (0)	>0.99
Rain	1	0 (0)	1 (3.3)	>0.99	0 (0)	0 (0)	--	0 (0)	0 (0)	--	0 (0)	1 (10)	>0.99	0 (0)	0 (0)	--
River	2	2 (7.1)	0 (0)	0.229	0 (0)	0 (0)	--	0 (0)	0 (0)	--	1 (20)	0 (0)	0.333	1 (6.3)	0 (0)	>0.99
Treat water	15	10 (35.7)	5 (16.7)	0.100	0 (0)	0 (0)	--	0 (0)	0 (0)	--	3 (60)	1 (10)	0.077	7 (43.8)	4 (33.3)	0.705

[a]*P values calculated using Pearson's Chi Square or Fisher's exact test*
[b]*Includes flush toilet, latrines, diaper and septic tank*
[c]*Includes purchased, taps and rain*

Table 3.1: Duration of travel in the past year, by destination, among all participants Ecuador, 2014-2015. Frequencies and percents of each group are shown.

	Quito n=38		San Lorenzo n=35		Santo Domingo n=26		Guayaquil n=69		Esmeraldas n=72		Borbon n=76		Rural communities n=48[a]	
Duration	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1 day	7	18.4	24	68.6	6	23.1	4	5.8	10	13.9	59	77.6	41	85.4
2-6 days	21	55.3	10	28.6	14	53.9	34	49.3	51	70.8	15	19.7	20	41.7
7-14 days	8	21.1	1	2.9	4	15.4	17	24.6	6	8.3	1	1.3	2	4.2
2-4 weeks	1	2.6	0	0.0	1	3.9	3	4.4	3	4.2	1	1.3	0	0.0
1-2 months	0	0.0	0	0.0	0	0.0	9	13.0	1	1.4	0	0.0	0	0.0
2+ months	1	2.6	0	0.0	1	3.9	2	2.9	1	1.4	0	0.0	0	0.0

[a]*Denotes total number of people that traveled ot rural communities. Each person could have made more than one trip.*

Table 3.2: Frequency of travel in the past year, by destination, among all participants Ecuador, 2014-2015. Frequencies and percents of each group are shown.

	Quito n=38		Esmeraldas n=72		Guayaquil n=69		Santo Domingo n=26		San Lorenzo N=35		Borbon n=76	
Frequency of travel	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Once	13	34.2	7	9.7	32	47.1	9	34.6	5	14.3	7	9.2
Twice	8	21.1	15	20.8	16	23.5	9	34.6	3	8.6	9	11.8
3 to 5 times	14	36.8	44	61.1	18	26.5	6	23.1	18	51.4	36	47.4
Every other month	2	5.3	4	5.6	1	1.5	0	0.0	7	20.0	16	21.1
Every month	0	0.0	2	2.8	0	0.0	1	3.9	1	2.9	2	2.6
Every other week	1	2.6	0	0.0	1	1.5	1	3.9	1	2.9	6	7.9

Table 3.3: Destination of travel in the past week, by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. The symbol (--) indicates that particular destination is not applicable to that site.

	Total N	Rural communities n=5	Borbon n=10	Esmeraldas n=15	Quito n=29
Destination	**59**	**n(%)**	**n(%)**	**n(%)**	**n(%)**
Borbon	6	5 (100)	0 (0)	1 (6.7)	0 (0)
Rural communities	8	0 (0)	0 (0)	5 (33.3)	3 (10.3)
Esmeraldas	3	0 (0)	3 (30)	--	0 (0)
Esmeraldas Province	2	0 (0)	0 (0)	0 (0)	2 (6.9)
Guayaquil	4	0 (0)	1 (10)	0 (0)	3 (10.3)
Quito	3	0 (0)	0 (0)	3 (20)	--
San Lorenzo	9	0 (0)	6 (60)	3 (20)	0 (0)
Santo Domingo	5	0 (0)	0 (0)	1 (6.7)	4 (13.8)
Other	19	0 (0)	0 (0)	2 (13.3)	17 (58.6)

-- destination not applicable for that site

Table 3.4: Reason for travel in the past year, all participants and by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. The symbol (--) denotes a destination that was not a response option for that site.

All Sites

	Borbon n=76		Esmeraldas n=72		Guayaquil n=69		Quito n=38		Santo Domingo n=26		San Lorenzo n=35		Rural communities n=48	
Reason	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shopping	19	25.0	15	20.8	1	1.5	0	0.0	5	19.2	11	34.4	1	2.1
Sports	0	0.0	3	4.2	0	0.0	2	5.3	0	0.0	1	3.1	6	12.5
Medical	53	69.7	8	11.1	6	8.7	8	21.1	1	3.9	5	15.6	3	6.3
School	4	5.3	2	2.8	0	0.0	0	0.0	0	0.0	1	3.1	1	2.1
Family	7	9.2	41	56.9	30	43.5	8	21.1	9	34.6	8	25.0	28	58.3
Party	1	1.3	1	1.4	1	1.5	0	0.0	0	0.0	1	3.1	7	14.6
Work	6	7.9	9	12.5	7	10.1	8	21.1	7	26.9	0	0.0	4	8.3
Religion	1	1.3	0	0.0	0	0.0	0	0.0	1	3.9	0	0.0	1	2.1
Buisness	1	1.3	0	0.0	1	1.5	0	0.0	0	0.0	0	0.0	0	0.0
Transit	3	4.0	7	9.7	3	4.4	8	21.1	0	0.0	7	21.9	1	2.1
Vacation	3	4.0	4	5.6	22	31.9	6	15.8	7	26.9	1	3.1	0	0.0

Rural Communities

	Borbon n=57		Esmeraldas n=29		Guayaquil n=6		Quito n=2		Santo Domingo n=3		San Lorenzo n=10		Rural Communities n=27	
Reason	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shopping	12	21.1	6	20.7	0	0.0	0	0.0	1	33.3	6	60.0	1	3.7
Sports	0	0.0	1	3.5	0	0.0	0	0.0	0	0.0	0	0.0	2	7.4
Medical	39	68.4	4	13.8	2	33.3	0	0.0	0	0.0	2	20.0	3	11.1
School	2	3.5	1	3.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Family	5	8.8	16	55.2	6	100.0	0	0.0	1	33.3	3	30.0	18	66.7
Party	1	1.8	1	3.5	0	0.0	0	0.0	0	0.0	0	0.0	4	14.8
Work	4	7.0	1	3.5	0	0.0	1	50.0	1	33.3	0	0.0	0	0.0
Religion	1	1.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.7
Buisness	1	1.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Transit	3	5.3	2	6.9	0	0.0	1	50.0	0	0.0	0	0.0	1	3.7
Vacation	3	5.3	4	13.8	0	0.0	0	0.0	1	33.3	0	0.0	0	0.0

Borbon

	Borbon n=18		Esmeraldas n=43		Guayaquil n=15		Quito n=12		Santo Domingo n=8		San Lorenzo n=16		Rural Communities n=21	
Reason	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shopping	7	38.9	9	20.9	1	6.7	0	0.0	3	37.5	5	31.3	0	0.0
Sports	0	0.0	2	4.7	0	0.0	1	8.3	0	0.0	0	0.0	4	19.1
Medical	14	77.8	4	9.3	2	13.3	2	16.7	0	0.0	3	18.8	0	0.0
School	2	11.1	1	2.3	0	0.0	0	0.0	0	0.0	1	6.3	1	4.8
Family	2	11.1	25	58.1	8	53.3	4	33.3	4	50.0	0	0.0	10	47.6
Party	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	14.3
Work	1	5.6	8	18.6	1	6.7	5	41.7	2	25.0	0	0.0	4	19.1
Religion	0	0.0	0	0.0	0	0.0	0	0.0	1	12.5	0	0.0	0	0.0
Buisness	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Transit	0	0.0	5	11.6	2	13.3	2	16.7	0	0.0	7	43.8	0	0.0
Vacation	0	0.0	0	0.0	2	13.3	0	0.0	0	0.0	0	0.0	0	0.0

Table 3.4 (continued): Reason for travel in the past year, all participants and by site, Ecuador, 2014-2015. Frequencies and percents of each group are shown. The symbol (--) denotes a destination that was not a response option for that site.

Esmeraldas

	Borbon n=1		Esmeraldas		Guayaquil n=27		Quito n=24		Santo Domingo n=7		San Lorenzo n=5		Rural Communities	
Reason	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shopping	1	100.0	--	--	0	0.0	0	0.0	0	0.0	0	0.0	--	--
Sports	0	0.0	--	--	0	0.0	1	4.2	0	0.0	0	0.0	--	--
Medical	0	0.0	--	--	2	7.4	6	25.0	0	0.0	0	0.0	--	--
School	0	0.0	--	--	0	0.0	0	0.0	0	0.0	0	0.0	--	--
Family	0	0.0	--	--	12	44.4	4	16.7	2	28.6	4	80.0	--	--
Party	0	0.0	--	--	1	3.7	0	0.0	0	0.0	1	20.0	--	--
Work	0	0.0	--	--	2	7.4	2	8.3	1	14.3	0	0.0	--	--
Religion	0	0.0	--	--	0	0.0	0	0.0	0	0.0	0	0.0	--	--
Buisness	0	0.0	--	--	1	3.7	0	0.0	0	0.0	0	0.0	--	--
Transit	0	0.0	--	--	1	3.7	5	20.8	0	0.0	0	0.0	--	--
Vacation	0	0.0	--	--	8	29.6	6	25.0	4	57.1	0	0.0	--	--

Quito

	Borbon n=0		Esmeraldas n=0		Guayaquil n=21		Quito		Santo Domingo n=8		San Lorenzo n=3		Rural Communities	
Reason	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shopping	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Sports	0	0.0	0	0.0	0	0.0	--	--	0	0.0	1	33.3	--	--
Medical	0	0.0	0	0.0	0	0.0	--	--	1	12.5	0	0.0	--	--
School	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Family	0	0.0	0	0.0	4	19.1	--	--	2	25.0	1	33.3	--	--
Party	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Work	0	0.0	0	0.0	4	19.1	--	--	3	37.5	0	0.0	--	--
Religion	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Buisness	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Transit	0	0.0	0	0.0	0	0.0	--	--	0	0.0	0	0.0	--	--
Vacation	0	0.0	0	0.0	13	61.9	--	--	2	25.0	1	33.3	--	--

Table 4.1: Adjusted effect of traveling to Quito in the past year, among participants from Esmeraldas, Borbón and the rural communities, Ecuador, 2014-2015. Adjusted odds ratios and accompanying 95% confidence intervals come from a logistic regression model with case status as the outcome (n=419).

	aOR	95% Wald CI	
Male	1.22	0.83	1.81
Treat Water	0.59	0.39	0.90
Travel to Quito	1.92	0.94	3.93

Table 4.2: Adjusted effect of traveling to Esmeraldas in the past year, among participants from Quito, Borbón and the rural communities, Ecuador, 2014-2015. Adjusted odds ratios and accompanying 95% confidence intervals come from a logistic regression model with case status as the outcome (n=464).

	aOR	95% Wald CI	
Male	1.24	0.86	1.79
Treat Water	0.69	0.47	1.01
Travel to Esmeraldas	0.94	0.56	1.59

Table 4.3: Adjusted effect of traveling to each destination in the past year, by site, Ecuador, 2014-2015. Four separate logistic regression models (one per site) were fit with case status as the outcome. Each model controls for sex and water treatment at home and contains dichotomous variables indicating travel to all possible destinations.

Rural Communities (n=104)			
	aOR	95% Wald CI	
Male	1.16	0.46	2.87
Treat Water	1.54	0.52	4.51
Borbon	1.44	0.56	3.67
Rural Communities	0.30	0.11	0.80
Esmeraldas	0.23	0.04	1.37
Guayaquil	0.13	0.01	1.22
San Lorenzo	0.21	0.03	1.37
Santo Domingo	0.07	0.00	1.46
Other	0.19	0.02	1.40

Esmeraldas (n=208)			
	aOR	95% Wald CI	
Male	1.25	0.70	2.22
Treat Water	0.43	0.24	0.79
Rural Communities	4.59	0.49	43.26
Guayaquil	2.27	0.96	5.41
Quito	2.51	0.99	6.39
San Lorenzo	0.94	0.15	6.13
Santo Domingo	0.72	0.15	3.50
Other	1.61	0.34	7.72

Borbon (n=104)			
	aOR	95% Wald CI	
Male	1.49	0.61	3.60
Treat Water	0.35	0.11	1.10
Borbon	4.52	1.21	16.85
Rural Communities	0.90	0.30	2.64
Esmeraldas	0.23	0.03	1.52
Guayaquil	0.40	0.07	2.44
Quito	0.68	0.15	3.17
San Lorenzo	3.64	0.85	15.50
Santo Domingo	2.32	0.31	17.44
Other	0.20	0.03	1.44

Quito (n=253)			
	aOR	95% Wald CI	
Male	1.30	0.78	2.16
Treat Water	0.68	0.40	1.16
Rural Communities	0.58	0.09	3.66
Esmeraldas Province	1.99	0.65	6.11
Guayaquil	0.75	0.29	1.94
San Lorenzo	0.84	0.06	11.86
Santo Domingo	0.60	0.14	2.66
Other	0.98	0.56	1.73

Table 4.4: Logistic regression results and adjusted effect of number of trips to each destination in the past year, by site, Ecuador, 2014-2015. Four separate logistic regression models (one per site) were fit with case status as the outcome. Each model controls for sex and water treatment at home and contains a continuous variable indicating total number of trips to each possible destination in the past year.

Rural Comunities (n=104)

	Estimate	Std. Error	p-value	aOR	95% Wald CI	
Intercept	0.7923	0.4292	0.065			
Male	0.0866	0.4623	0.852	1.09	0.44	2.70
Treat Water	0.3931	0.539	0.466	1.48	0.52	4.26
# of trips to:						
Borbon	-0.0675	0.0569	0.236	0.94	0.84	1.05
Rural Communities	-0.7603	0.3724	0.041	0.47	0.23	0.97
Esmeraldas	0.0659	0.1562	0.673	1.07	0.79	1.45
Guayaquil	-0.0342	0.313	0.913	0.97	0.52	1.79
Santo Domingo	-1.0182	0.8699	0.242	0.36	0.07	1.99
San Lorenzo	-0.0179	0.1332	0.893	0.98	0.76	1.28

*Quito (n=2) removed because of convergence problems

Borbon (n=107)

	Estimate	Std. Error	p-value	aOR	95% Wald CI	
Intercept	-0.0342	0.3652	0.925			
Male	0.4063	0.4394	0.355	1.50	0.63	3.55
Treat Water	-0.6409	0.5305	0.227	0.53	0.19	1.49
# of trips to:						
Borbon	-0.00601	0.045	0.894	0.99	0.91	1.09
Rural Communities	0.0334	0.3577	0.926	1.03	0.51	2.08
Esmeraldas	-0.0242	0.1005	0.810	0.98	0.80	1.19
Quito	0.0121	0.2219	0.956	1.01	0.66	1.56
Guayaquil	-0.1158	0.101	0.252	0.89	0.73	1.09
Santo Domingo	-0.0474	0.1129	0.674	0.95	0.76	1.19
San Lorenzo	0.3366	0.1638	0.040	1.40	1.02	1.93

Esmeraldas (n=209)

	Estimate	Std. Error	p-value	aOR	95% Wald CI	
Intercept	-0.0699	0.2536	0.783			
Male	0.2487	0.2904	0.392	1.28	0.73	2.27
Treat Water	-0.8253	0.3049	0.007	0.44	0.24	0.80
# of trips to:						
Quito	0.2961	0.1845	0.108	1.35	0.94	1.93
Guayaquil	0.336	0.2027	0.097	1.40	0.94	2.08
Santo Domingo	-0.00011	0.3162	1.000	1.00	0.54	1.86
San Lorenzo	0.1085	0.2776	0.696	1.12	0.65	1.92

*Borbon (n=1) removed because of convergence problems

Quito (n=253)

	Estimate	Std. Error	p-value	aOR	95% Wald CI	
Intercept	0.2308	0.2522	0.360			
Male	0.2465	0.2556	0.335	1.28	0.78	2.11
Treat Water	-0.4396	0.2673	0.100	0.64	0.38	1.09
# of trips to:						
Guayaquil	-0.025	0.1886	0.894	0.98	0.67	1.41
Santo Domingo	-0.1814	0.2092	0.386	0.83	0.55	1.26
San Lorenzo	0.5305	0.8237	0.520	1.70	0.34	8.54

Table 4.5: Logistic regression results and adjusted effect of number of total number of days spent at each destination in the past year, by site, Ecuador, 2014-2015. Four separate logistic regression models (one per site) were fit with case status as the outcome. Each model controls for sex and water treatment at home and contains a continuous variable indicating total number of days spent at each possible destination in the past year.

Rural communities

	Estimate	Std. Error	p-value	aOR	95% Wald Cis	
Intercept	0.4883	0.4003	0.223			
Male	0.175	0.4373	0.689	1.19	0.51	2.81
Treat Water	0.4109	0.5368	0.444	1.51	0.53	4.32
# of trips to:						
Rural communities	-0.2558	0.146	0.080	0.77	0.58	1.03
Borbon	0.0874	0.1537	0.570	1.09	0.81	1.48
San Lorenzo	-0.2305	0.3376	0.495	0.79	0.41	1.54
Santo Domingo	-0.147	0.1437	0.307	0.86	0.65	1.14
Guayaquil	-0.1077	0.0874	0.218	0.90	0.76	1.07
Esmeraldas	0.0384	0.0494	0.438	1.04	0.94	1.15

*Quito (n=2) removed because of convergence problems

Borbon

	Estimate	Std. Error	p-value	aOR	95% Wald Cis	
Intercept	-0.379	0.3858	0.326			
Male	0.1963	0.4419	0.657	1.22	0.51	2.89
Treat Water	-0.9745	0.5711	0.088	0.38	0.12	1.16
# of trips to:						
Rural communities	0.0658	0.1319	0.618	1.07	0.83	1.38
Borbon	1.2464	0.6205	0.045	3.48	1.03	11.74
San Lorenzo	1.1603	0.673	0.085	3.19	0.85	11.93
Santo Domingo	0.097	0.1433	0.499	1.10	0.83	1.46
Quito	-0.0335	0.0891	0.707	0.97	0.81	1.15
Guayaquil	0.0331	0.0251	0.187	1.03	0.98	1.09
Esmeraldas	0.0509	0.0583	0.383	1.05	0.94	1.18

Esmeraldas

	Estimate	Std. Error	p-value	aOR	95% Wald CI	
Intercept	-0.0129	0.2514	0.959			
Male	0.1844	0.2933	0.529	1.20	0.68	2.14
Treat Water	-0.8955	0.3118	0.004	0.41	0.22	0.75
# of trips to:						
San Lorenzo	-0.0733	0.1902	0.700	0.93	0.64	1.35
Santo Domingo	0.0785	0.119	0.510	1.08	0.86	1.37
Quito	0.2644	0.1032	0.011	1.30	1.06	1.60
Guayaquil	0.013	0.0197	0.510	1.01	0.98	1.05

*Borbon (n=1) removed because of convergence problems

Quito

	Estimate	Std. Error	p-value	aOR	95% Wald Cis	
Intercept	0.231	0.2514	0.358			
Male	0.2255	0.2562	0.379	1.25	0.76	2.07
Treat Water	-0.4761	0.268	0.076	0.62	0.37	1.05
# of trips to:						
San Lorenzo	0.1407	0.3114	0.651	1.15	0.63	2.12
Santo Domingo	0.0338	0.0505	0.503	1.03	0.94	1.14
Guayaquil	0.0111	0.0551	0.840	1.01	0.91	1.13

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