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Impact of Human Movement along an Urban-Rural Gradient on Diarrheal Risk and Pathogen-Specific Diarrhea: Case Control Study in Ecuador, 2014 - 2015

By

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Master in Public Health

Global Epidemiology

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By

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B.S., University of Miami, 2014

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Abstract

Impact of Human Movement along an Urban-Rural Gradient on Diarrheal Risk and Pathogen-Specific Diarrhea: Case Control Study in Ecuador, 2014 - 2015

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Diarrheal diseases are a common cause of morbidity and mortality, affecting millions of people worldwide. Diarrhea-related deaths disproportionally affect young children and low-income nations. Diarrheagenic *E. coli* (DEC) infections in particular are associated with diarrheal presence globally, including throughout Latin America and Ecuador. Despite reductions seen in diarrheal deaths, Ecuador still maintains a high burden of disease. Thus there is a need to further the understanding of diarrheal risk and pathogen-specific diarrhea, and to understand how the burden of specific pathogens varies between urban and rural locations. Within-country human movement between urban and rural locations has the potential to increase disease transmission and should be included in the assessment of diarrheal risk.

The EcoZur study is a case-control study of diarrheal diseases along an urban-rural gradient in Ecuador. At each study site, ~100 diarrheal cases were recruited from Ministry of Health clinics and age-matched to ~100 non-diarrheal controls from the same facility. Demographics, medical history, WASH practices, animal contacts, and recent travel history information was collected on all participants using an electronic survey. Additionally, stool samples were collected within 24 hours from all participants for enteric pathogen testing.

The study found that the urban-rural gradient accurately represented a gradient of socioeconomic status and access to clean and safe water/sanitation. Treatment of drinking water was significantly protective against diarrhea in urban sites (Quito aOR: 0.58, 95% CI: 0.34, 0.97; Esmeraldas aOR: 0.41, 95% CI: 0.22, 0.75) and improved sanitation practices were protective against diarrhea in rural sites, specifically in the town of Borbón (aOR: 0.28; 95% CI: 0.09, 0.73). Travel in the past year was significantly associated with diarrhea among all participants (aOR: 1.36; 95% CI: 1.05, 1.77), and specifically among participants from Esmeraldas (aOR: 2.53; 95% CI: 1.36, 4.81), with travel to Quito being a greater risk for not only diarrheal disease, but also DEC infections in general. Urban sites were also found to be associated with a higher proportion of DAEC infection compared to rural sites that had higher EPEC-a and ETEC infections. Interestingly, DAEC infections were significantly associated with diarrhea only in urban centers and ETEC infections were significantly associated with diarrhea in the rural center of Borbón only. This study highlights the differential etiologic agents of diarrhea in urban versus rural areas of one country, and identifies travel as a risk factor for diarrhea and DEC, in addition to the known water and sanitation risk factors.

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I. BACKGROUND

Global Diarrheal Disease Burden

Diarrhea, defined as three or more loose stools within the previous 24-hours, is a common illness that affects millions of people worldwide, and diarrhea-related morbidity and mortality disproportionally affects young children [1]. In 2010, more than 7.5 million children died before their fifth birthday, with two-thirds of these deaths attributed to preventable infectious diseases, including diarrheal diseases [2]. It is well documented that diarrhea is among one of the most attributable causes of death among children less than five [2-5]. Diarrheal diseases account for one in nine child deaths worldwide, which is more than AIDs, malaria and measles combined [6]. This translates to diarrhea causing approximately 17% of all deaths among children less than 5 years old [2-4], and 72% of these deaths are concentrated in children younger than 2 years old [7]

As part of the Millennium Development Goals, which called for a two-thirds reduction in the mortality rate among children under 5 between 1990 and 2015, treatment and prevention strategies were implemented worldwide to reduce diarrheal disease mortality. From 2000 to 2010, global mortality in children under five decreased by 2 million, with some of the greatest progress seen in Latin America [2, 7, 8]. Deaths associated with diarrhea decreased by more than 350,000, contributing to 17.9% of the reduction in child mortality observed between 2000 and 2010 [2]. Despite this sizeable reduction in child mortality, diarrheal diseases are still highly abundant and continue to contribute to child morbidity due to insufficient program coverage in rural areas compared to urban areas.

Low- and middle-income countries in Africa, Asia and Latin America remain the most affected by diarrheal diseases, often developing more severe outcomes due to poor living conditions and lack of access to quality health care [9, 10]. Kosek et. al. reviewed studies conducted in developing countries published in 1992 and 2000, and found that diarrhea still accounts for a median of 21% of all deaths among children less than 5 years old in these developing regions [11]. Case-fatality and incidence ratios have remained much higher in low- and middle-income countries compared to high-income countries [7]. Additionally, these low resource regions tend to be more conducive to the development of several diarrheal episodes per year. Traditionally, a single episode of diarrhea is self-limiting and has no long-term sequela; conversely, in low-income countries, children suffer from multiple episodes of diarrhea annual and as a result are more likely to be nutrient deficient, stunted and cognitively impaired [7, 12-15].

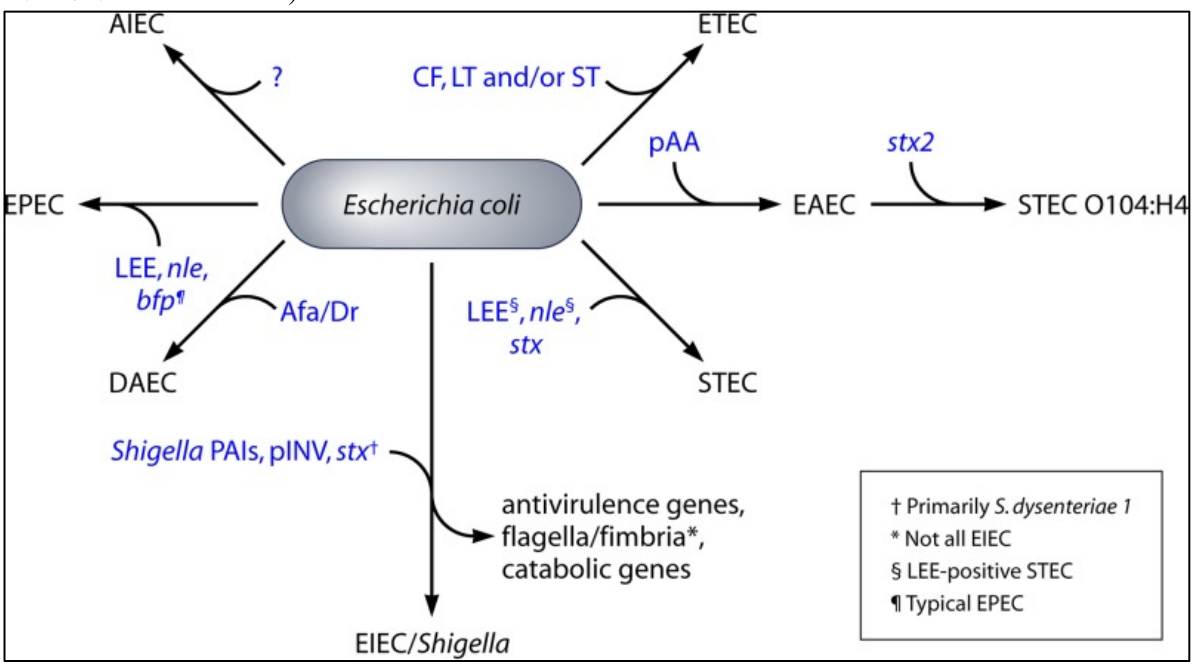
From 1990 to 2010, it was estimated that the incidence of diarrhea in low- and middle-income countries declined from 3.4 episodes/child year to 2.9 episodes/child year [16]. In the Americas, children on average experience three episodes of diarrhea a year with a total of 4.8 million severe episodes, indicating that diarrheal diseases are still a tremendous burden in low-income countries requiring enhanced prevention and treatment strategies [7, 16].

Pathogen-Specific Diarrheal Disease

In order to develop adequate strategies for diarrheal disease reduction, a better understanding of diarrheal disease etiology is needed. Diarrhea can be associated with viruses (e.g., rotavirus, norovirus), bacteria (e.g., *Escherichia coli*, *Shigella*, *Campylobacter* and *Salmonella*), and parasites (e.g., *Giardia* and *Cryptosporidium*). Each pathogen has differential survival and life history strategies, and requires a different treatment and prevention approach. While rotavirus has been repeatedly implicated as a significant contributor to the development of diarrheal disease, the relationship between *Escherichia coli* infections and the development of diarrhea is more complicated.

Most *E. coli* strains live harmlessly within the human digestive tract; however, there are a number of pathogenic strains that can cause illness. Theses pathotypes are collectively known as diarrheagenic *E. coli* (DEC) and are classified as enteropathogenic *E. coli* (EPEC), enterohemorrhagic (shiga toxin-producing) *E. coli* (EHEC/STEC), enteroaggregative *E. coli* (EAEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), and diffusely-adherent *E. coli* (DAEC) [17, 18]. Each pathotype differs in their preferential host colonization sites, virulence mechanisms and clinical presentation [17]. Croxen et. al. classified the virulence genes gained and lost between each pathotypes as shown in Figure 1 (below) [9].

Figure 1. Diagram of *Escherichia coli* Pathotype Virulence Gene Distribution. Describes the virulence genes gained and lost within each pathotypes classification. Enteropathogenic *E. coli* (EPEC), enterohemorrhagic (shiga toxin-producing) *E. coli* (EHEC/STEC), enteroaggregative *E. coli* (EAEC), enterotoxigenic *E. coli* (ETEC), and diffusely-adherent *E. coli* (DAEC). (Adopted from Croxen et. al. 2013)



The different virulence genes contribute to the diverse pathogenicity seen amongst these six groups. Typical EPEC is known to be associated with diarrheal disease, specifically among infants in low-income countries, but little is know about the association between atypical EPEC and diarrhea [18, 19]. EAEC is often associated acute and persistent watery diarrhea and is also responsible for diarrhea in children less than five in low-income countries [17]. ETEC represents the most common form of diarrhea and is the major cause of traveler's diarrhea as well as diarrhea in children from low-income countries [17, 18]. EIEC is a causative agent for dysentery and often related to socioeconomic conditions [9, 17-19].

A systematic review of the literature on pathogenic associations with diarrhea found that rotavirus, calicivirus, *Enteropathogenic E. coli* (EPEC) and *Enterotoxigenic E. coli* (ETEC) make up more than half of all diarrheal deaths among children less than 5 years old worldwide [20]. The Global Enteric Multicenter Study (GEMS) was conducted to better define diarrheal disease incidence, etiology and clinical presentation in seven low resource countries of Sub-Saharan Africa and South Asia [15]. GEMS identified four pathogens that were significantly associated with moderate-to-severe diarrhea across all sites: rotavirus, *Cryptosporidium*, *Shigella* and *Enterotoxigenic E. coli* (ETEC) [15]. Typical *Enteropathogenic E. coli* (EPEC) was also associated with acute and persistent diarrhea often leading to nutritional deficiencies and death [15]. However, the distribution of these leading diarrheal pathogens differed across the numerous study sites, which is also an emerging theme in the MAL-Ed study [15, 21]. GEMS was the first study of its kind to look across multiple pathogens to characterize the pathogenic distribution across various high diarrheal burdened countries as well as identify strong associations between the different pathogens and diarrhea disease. Unfortunately, GEMS did not include any study sites from Latin America, where diarrheal diseases nevertheless persist.

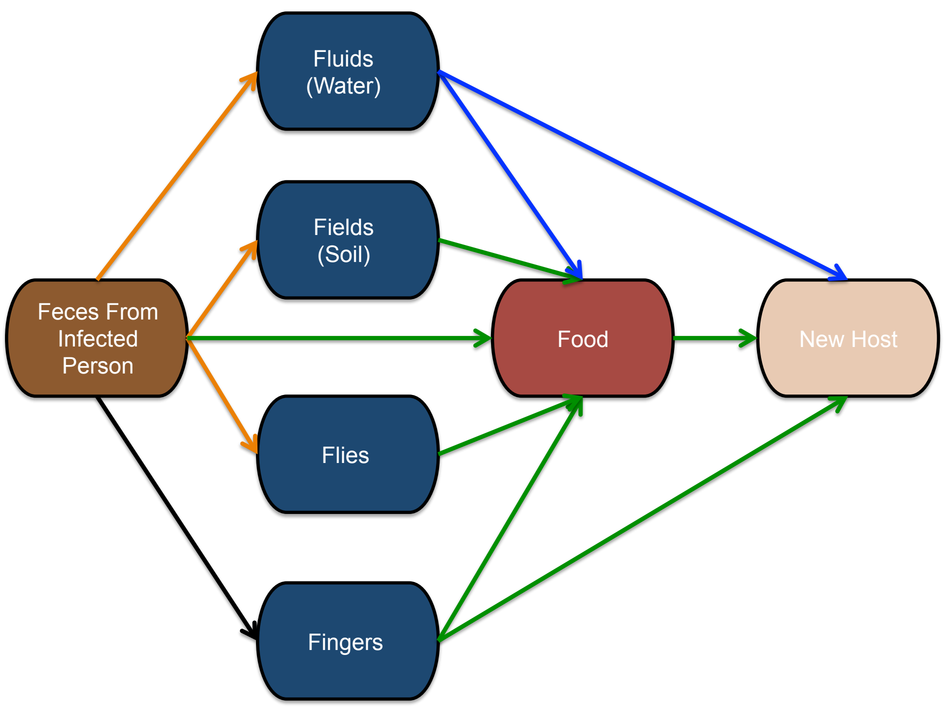
Diarrheal Diseases in Latin America and Ecuador

In 2002, diarrheal diseases were responsible for about 10 percent of all childhood deaths in Latin America, which is an approximate 50% decrease since 1990 [7, 22]. In Ecuador specifically, there were 225,734 cases of diarrhea reported in 2000 with 52% occurring on the coast, and 16% of all cases affecting one to four year olds [22]. However, diarrheal disease morbidity and mortality in Ecuador saw a decline into 2010, with disability-adjusted life years (DALYs) for diarrheal diseases reduced by 82% since 1990 [23]. Despite this dramatic reduction in DALYs, diarrheal disease in Ecuador has higher rates of DALYs than other comparator countries [23].

Water, Sanitation and Hygiene (WASH) Risk Factors for Diarrheal Diseases

A large proportion of diarrheal diseases are caused by fecal-oral pathogens such as those previously described. "Fecal-oral" refers to the route of transmission for these infectious pathogens. This pathway is often characterized by fecal contamination of water, food, and hands, and how proper water supply, sanitation and hand hygiene can prevent the spread from one host's feces to a new host [24]. Figure 2 (adapted from Wagner and Lanoix) illustrates the multiple fecal-oral infection routes [25]. Diarrheal diseases in low resources settings are often attributed to numerous socioeconomic and environmental factors such as safe and adequate water supply, latrine availability, and knowledge of hygienic activities and communicable disease prevention practices that are associated with this fecal-oral pathway [26].

Figure 2. The F-Diagram. Represents the multiple fecal-oral routes for diarrheal disease transmission. The implementation of proper sanitation (orange arrows), safe water supply (blue arrows) and proper hygiene (green arrows) could interrupt each of the pathways. (Adapted from Wagner and Lanoix [25])



About 1.5 million child deaths and about 88% of diarrhea-associated deaths can be attributed to unsafe water, inadequate sanitation and hygiene [27, 28]. Nineteen percent of all

diarrhea cases can be attributed to inadequate sanitation; 20% attributed to inadequate hand washing; and 34% attributed to inadequate drinking water [29]. Adequate sanitation and drinking water is categorized by WHO Joint Monitoring Programme (JMP) as improved water and sanitation [30]. Improved water sources include piped water, public tap, boreholes, protected dug wells, protected spring and rainwater collection. Improved sanitation facilities include piped sewer systems, septic tanks, pit latrines, and composting toilets.

Previous studies have identified water and sanitation as risk factors for diarrhea morbidity and mortality [31, 32]. Additionally, multiple systematic reviews have shown that improvements in access to water and sanitation, water quality and personal hygiene are effective at reducing diarrhea morbidity [33, 34]. WHO and UNICEF report that 89% of the world's population has access to improved (not necessarily safe) drinking water sources, but only 64% have access to improved sanitation facilities with at least 14% practicing open defection [35, 36]. Furthermore, there is currently insufficient evidence to support the idea that water source-based improvements and water treatment reduce diarrheal diseases [37]. Thus it is important to continue to investigate the effectiveness of improved water and sanitation on diarrheal diseases.

Travel as a Risk Factor for Diarrheal Diseases

Travel can be characterized as a temporary departure from one's permanent city or village of residence. As countries become more urbanized and economically driven, there is an increase in human movement to and from urban centers. This sort of travel can be a potent force in the emergence and spread of diseases by increasing mixing among previously disconnected communities, which increases the potential for pathogen transmission [38, 39]. While traveler's diarrhea is a well-known affliction for travelers from developed countries visiting developing countries, travel by residents within their own country also has the potential to cause local traveler's diarrhea.

This phenomenon of human movement as a risk factor for spread of infectious diseases within-country is well-established for vector-borne diseases. Vector-borne disease transmission often highlights human movement as a risk for the transmission of disease by influencing the spread of the disease beyond the range of the vector [40]. Chaparro et. al. study of dengue transmission and internal travel showed that dengue cases reported in non-endemic regions of Colombia were often connected to prior travel to recreation or tourist sites in endemic regions [41]. They also highlighted holiday travel patterns as being associated with increased dengue cases in non-endemic regions [41]. Not only is it necessary to understand travel patterns for disease surveillance, but it is also important for the development and targeting of interventions in resource limited countries with variable disease distribution [42].

Furthermore, human movement enables the transfer of resistance genes and genetic recombinants to otherwise naive genetic pools [39]. Zelner et. al. discuss how remoteness of rural Ecuadorian villages is associated with a lower prevalence of diarrheal disease due to their reduced contact with outside individuals [43]. The question then becomes, if these remote individuals travel to more urban centers, are they at an increased risk of developing diarrheal diseases assuming that travel is increasing their risk of encountering these genetically different pathogens.

Study Significance

There is a need to identify the key risk factors (WASH and travel) associated with diarrheal diseases and pathogen-specific diarrhea as well as a need to characterize the distribution of pathogen-specific diarrhea within a single Latin American country. This study focused on three main objectives: (1) To characterize risk factors for diarrheal diseases in Ecuador as a whole and regionally from 2014 to 2015; (2) To characterize risk factors for pathogenic *E. coli* in Ecuador as a whole and regionally from 2014 to 2015; and (3) To determine the distribution of pathogenic *E. coli* in Ecuador and characterize the association between pathogenic *E. coli* and symptomatic diarrhea. This study is imperative to the understanding of pathogen-specific diarrheal disease incidence and the risk factors associated with diarrheal diseases not only regionally but also across the country of Ecuador. The overall goal is to expand upon the knowledge of diarrheal disease risk and pathogen distribution in Latin American countries as well as to highlight the importance of human movement on pathogenic diarrheal distribution.

II. METHODS

The data in this thesis was generated through the EcoZUR (E. coli *en Zonas Urbanas y Rurales*), study conducted by Dr. Karen Levy, in collaboration with researchers at Universidad San Francisco de Quito to assess pathogenic *E. coli* along a rural-urban gradient in Ecuador.

Study Design

EcoZUR is a case-control study conducted in four different study locations along an urban-rural gradient in the northern region of Ecuador (Figure 3). The study sites included were Quito, Esmeraldas, Borbón and rural river communities. Quito is the capital of Ecuador and has a population of about 1.6 million [44]. Esmeraldas, a coastal city in the northwest of Ecuador, is the capital of Esmeraldas Province and has a population of about 162,000 [44]. Borbón is a town in the Esmeraldas province with approximately 5,000 people and is located at the junction of three rivers. The rural river communities/villages incorporate about 125 villages along theses same three rivers: Rio Cayapas, Rio Santiago and Rio Onzole. These rural river communities consist of populations of about 50 to 500 individuals. This study was designed to understand how factors associated with living conditions (e.g., population density, human travel, water-sanitation-hygiene conditions, animal contact) affect the enteric pathogens in circulation. These four sites were selected because

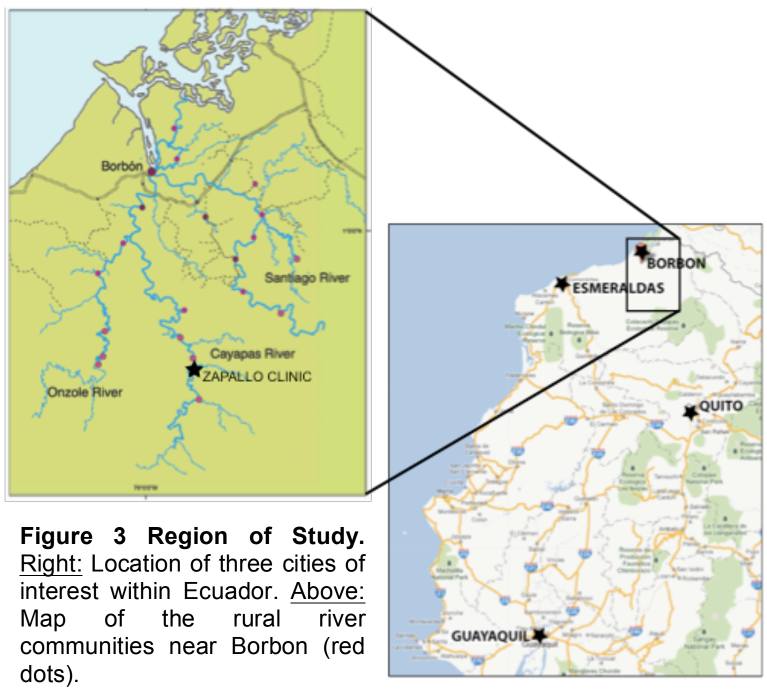


Figure 3 Region of Study. Right: Location of three cities of interest within Ecuador. Above: Map of the rural river communities near Borbon (red dots).

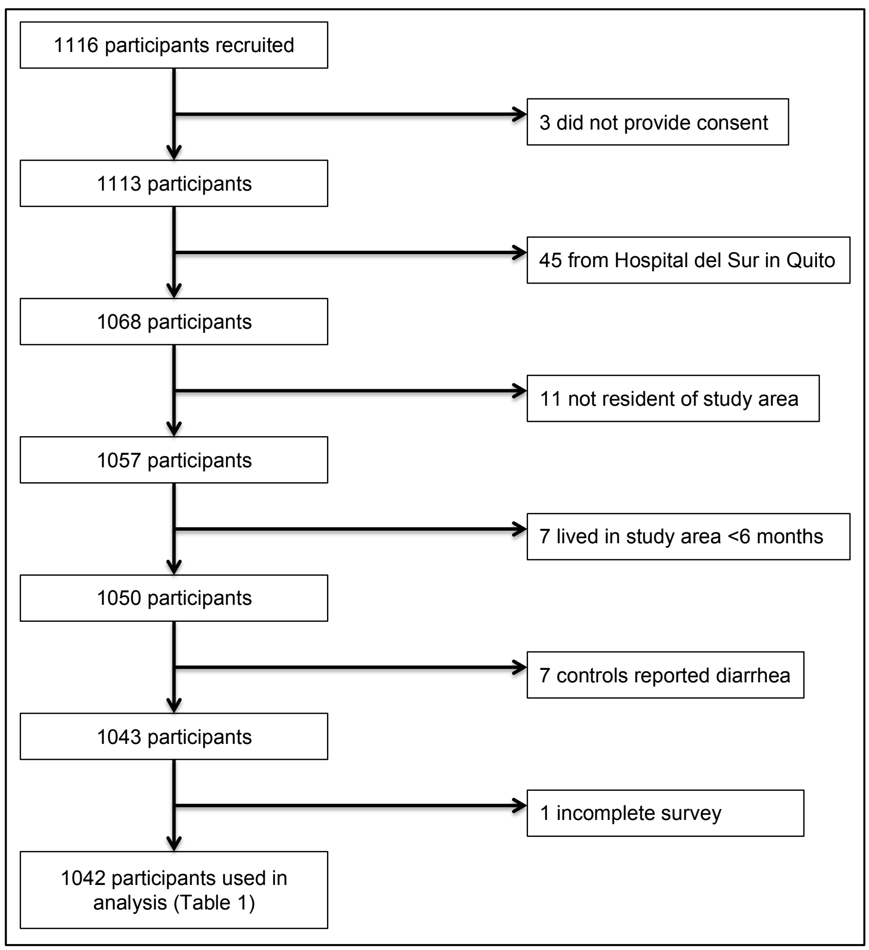
they share an overlapping culture and receive visitors from across the different sites. This study design allows one to explore the pathogenic distribution between urban and rural communities.

Study Participants

About 100 subjects with diarrhea were recruited as cases with 100 age-matched non-diarrheal controls (1:1 matched study) at each of the four study sites. Diarrheal cases were identified as individuals presenting with three or more loose stools within the previous 24 hours. Controls were patients presenting to the same facility with any other illness and age-matched to cases based on the following criteria: 0-24 months (+/- 6 months), 25-60 months (+/- 12 months), 61-180 months (+/- 24 months) and >181 months. The case-control study design allows the study to capture both symptomatic and asymptomatic enteric infections. All participants were recruited from Ministry of Health facilities (hospitals/clinics) at each study site. In Quito, patients were initially recruited from Hospital del Sur; however, this hospital represented an older demographic then desired for a diarrheal study, thus recruitment moved to a local clinic called Chilibulo Subcentro de Salud. In Esmeraldas, patients were recruited from Hospital Delfina Torres de Concha. Participants from Borbón were recruited from the Borbón Hospital as wells as from community visits. Those recruited directly from the hospital are classified as "Borbón-Borbón" whereas those recruited directly from the community were classified as "Borbón-Casas". These sites were left separate due to potential bias associated with the severity of illness between those presenting to the hospital compared to those recruited directly from the community. The participants from the rural communities were either recruited from rotating traveling rural clinics conducted by the Ministry of Health, or by recruiting rural community members if they visited the Borbón Hospital.

Participants of all ages were recruited for each site (*n*=1116) with a focus on patients less than 15 years old (or 181 months old). Furthermore, the initial 45 participants recruited from Hospital del Sur in Quito were excluded from this analysis because they predominately represented an older demographic that differed from the population we wished to focus on. From this pool of recruits (*n*=1068), 11 participants were excluded for not being resident of the designated study site; 7 participants were excluded for not being a resident of the study site for at least 6 months; 7 controls were excluded for reporting diarrhea in the past 7 days; and 1 participant was excluded for not completing the survey (Figure 4).

Figure 4. Summary of Participant Exclusion Criteria. The number of participants excluded along with the reason for exclusion can be found on the right. The left column summarizes remaining participants after each criterion.



Data Collection

Permission for the study and approval of human subjects was obtained from the Ministry of Health, Emory Institutional Review Board (IRB) and the Universidad San Francisco de Quito

(USFQ) Ethical Committee. Data was collected for all participants from April 2014 to February 2015. Identical study protocols were used at each site.

All consenting participants or parents of participants (*n* = 1113) were administered an electronic survey to assess patient/family demographics, socioeconomic status, medical history, water and sanitation practices, recent travel and travel patterns. For individuals indicating having traveled in the past week to a year, additional questions were asked to determine travel destination(s), frequency, duration of stay, and water and sanitation practices away from home. The electronic survey was developed using Open Data Kit program (http://opendatakit.org). Study staff administered the surveys verbally in Spanish and recorded responses via an Android device. At the conclusion of the survey, the participant's responses (without identifiers) were uploaded to an online server that aggregated all survey data.

In addition, to collecting survey data, participants were asked to provide a stool sample for the evaluation of enteric infections. Heath workers provided the participant with a stool collection container and instructions to return a stool sample within 24 hours. Of all consenting participants, 953 provided a stool sample within 24 hours and of those 931 participant samples were evaluated for DEC pathotypes and rotavirus. Twenty-one of these participants were excluded from pathogen-specific analysis based on use of antibiotics in the past 7 days.

Pathogen Identification

A portion of the patient's stool sample was used to test for rotavirus infections. The presence of rotavirus antigens was determined by a RIDA Quick Rotavirus test (r-biopharm, Darmstadt, Germany). The stool was suspended in an extraction buffer and about 200uL of supernatant was pipetted onto the test cassette. Results were read within 5 minutes; the presence of red and blue bands indicated a positive result.

Remaining stool was cultured and tested for DEC pathotypes based on the presence of different virulence factors. Stool samples were first cultured on MacConkey's agar media. After a

24-hour incubation period, five lactose-positive colonies were selected for culture on nutrient agar, and then pooled together in a tube containing 300 uL of sterile distilled water. This mixture was boiled for 10 minutes to release the DNA. The resulting supernatant was used in PCR testing. The PCR assay used a set of 9 different primers to detect the virulence genes associated with each diarrheagenic *E. coli* pathotype. The target virulence genes used for each pathotype were: *lt* and *sta* for Enterotoxigenic *E. coli* (ETEC); *ipaH* for Enteroinvasive *E. coli* (EIEC) and *Shigella; aggR* for Enteroaggregative *E. coli* (EAEC); *afa* for Diffusely adherent *E. coli* (DAEC); *bfp* for typical Enteropathogenic *E. coli* (EPEC); and *eaeA* for atypical EPEC. Positive pools for *eaeA* were subsequently tested for *stx1* and *stx2* genes for the differentiation of potential enterohemorrhagic *E. coli* (EHEC) infections. For each pooled result that tested positive for one of the 9 virulence factors, each isolate was then re-evaluated individually to identify the positive isolate.

Data Cleaning

Survey data from each of the four study sites was merged into one dataset for cleaning and analysis. Response such as ".", "nosabe", "nr" or blanks were encoded as missing data. Furthermore, categorical responses with multiple answers were disaggregated into individual binary response variables representing each option chosen by the participant. Variables with multiple response answers included sanitation facilities, drinking water sources, animal contact type, travel destinations, and travel reasons. The final analysis dataset included all demographic, socioeconomic, water and sanitation, animal contact, travel, and pathogen variables.

Bivariate Analysis

All analysis was completed using R Studio Statistical Software (http://www.rstudio.org/). Data analyzed for this study was restricted based on previously mentioned inclusion and exclusion criteria (Figure 4). Bivariate analysis was used to confirm the existence of an economic and water access gradient between urban and rural sites designated in this project. We hypothesized that the more rural areas would have lower economic status as measured by job and government welfare indicators.

The identification of potential risk factors for diarrheal disease was conducted using a bivariate analysis across all survey variables, such as demographic, medical history, travel history, and water and sanitation practices. Results were stratified by site when applicable. Similar analysis was conducted using any pathogenic *E. Coli* and just DAEC infections as outcomes, other DEC pathotypes were not analysis due to insufficient number of cases available. Any participant reporting antibiotic use was excluded from these pathogen-specific analyses since antibiotic can hinder the accuracy of enteric pathogen detection. As a whole, we hypothesized that travel history in addition to water and sanitation practices would be identified as key risk factors across all outcomes (diarrheal disease, pathogenic *E. coli* infections, or just DAEC infections).

Unadjusted odds ratios and *p*-values were produced using the Pearson's Chi Square Test. If any expected cell counts were less than five, the Fisher's Exact Test was used instead. Significant associations were determined using an alpha level of 0.05 for all p-values in addition to assessing Wald's 95% confidence intervals for the inclusion of the null.

When performing Chi Square analysis, some variable responses were consolidated to provide comparable data across the strata. This was done for variables looking at sanitation practices in the home and during travel. All responses were categorized as either improved or unimproved sanitation according to the guidelines provided by WHO Joint Monitoring Programme (JMP) for Water Supply and Sanitation [30]. Drinking water in the home and during travel was also characterized as improved or unimproved based on WHO JMP with the exception of purchased bottled water. Based on our understanding of this region, purchased bottled water is a much safer and cleaner water source than other available sources. Since we are essentially interested in assessing the correlations between clean, presumably pathogen- free water and diarrheal disease, we decided to reclassify bottled water as an improved water source.

Some of our travel variables were also adjusted to better answer our research question. Travel for this analysis was defined as having visited the following destinations within Ecuador: Guayaquil, Quito, Santo Domingo, Esmeraldas, San Lorenzo, Borbón, and rural communities near Borbón. We categorize travel destinations provided by participants as either urban or rural compared to their site location to determine if there was an association between the types of cities they visited and diarrheal disease. We also converted categorical travel frequency and duration responses into numerical data to provide a better understanding of the average frequency and duration of stay for each travel destination.

Multivariate Analysis

After identifying key risk factors of diarrheal disease using bivariate analysis, diarrheal disease outcomes were modeled using multivariate mixed-effect logistic regression controlling for sex, race, government welfare status, antibiotic use, water treatment at home, and travel in the past year, with study site included as a random effect. This approach adjusts for potential confounders as well as the confounding effect of study site for all participant models. Government welfare status was the only indicator used for economic status due to heavy correlation with job status and home ownership. Birth status, breastfeeding, and contact with poultry were also included in separate models for the subset of participants for which these variables applied. Additionally, models evaluating travel to a specific destination dropped travel in the past year due to 100% correlation with travel destination. Table 1 lists all models used in diarrheal risk factor analysis across all sites. The lme4 R package was used to run all mixed models (https://cran.r-project.org/web/packages/lme4/lme4.pdf)

Table 1. Multivariate Mixed-Effect Logistic Models for Diarrheal Disease. All models included the study location as a random effect. Additional variables under consideration are listed.

	Variables Included
Model 1	Sex, race, government welfare, antibiotics, home water treated, travel in the past year
Model 2	Model 1 variables + Birth type

Model 3	Model 1 variables + Breastfeeding,
Model 4	Model 1 variables + Poultry Contact
Model 5	Model 1 variables, with Specific Travel destination in place of travel in the past year

Logistic regression models were used to evaluate risk factors among the individual study sites for diarrheal diseases. All models for the study sites included any significant variables found by site in the bivariate analysis. Each model included at a minimum sex, government welfare, race, antibiotic use, travel in the past year, and treatment of water in home.

Additional multivariate mixed-effect models were used to look at any pathogenic *E. coli* infection as the outcome as well as a subset with DAEC infections. Similar to the bivariate analyses, those reporting antibiotic use were excluded from the models because antibiotics could have diminished the yield of bacterial cultures, resulting in a bias. Since the original study design only age-matched based on cases and controls for diarrheal disease, age needed to be included in the models for pathogen-specific outcomes in addition to any significant variables from bivariate analysis. Table 2 lists the models used in assessing pathogenic *E. coli* outcomes, and Table 3 lists the models used in assessing DAEC outcomes.

Table 2. Multivariate Mixed-Effect Logistic Models for Any Pathogenic *E. Coli* Infections. All models included the study location as a random effect.

	Variables Included
Model 1	Age, sex, race, government welfare, education, home sanitation, travel in the past year
Model 2	Model 1 variables + Animal contact around the home
Model 3	Model 1 variables, with Specific Travel destination in place of travel in the past year

Table 3. Multivariate Mixed-Effect Logistic Models for DAEC Infections. All models included the study location as a random effect. Additional variables under consideration are listed.

	Variables Included
Model 1	Age, sex, race, government welfare, travel in the past year
Model 2	Model 1 variables + Birth type
Model 3	Model 1 variables, with Specific Travel destination in place of travel in the past year

Furthermore a mixed-effect model was run for rotavirus infections using all significant variables for bivariate analysis. The only significant variable from bivariate analysis was travel to Borbón in the past year. For this reason, we only ran one model for the association rotavirus infections and travel to Borbón in the past year while controlling for age, race, government welfare, and sex.

III. RESULTS

Participant Characteristics

One thousand one hundred and sixteen (*n*=1116) participants were recruited for this study, and 1042 participants met the inclusion criteria for analysis. The four study sites: Quito (*n*=263), Esmeraldas (*n*=223), Borbón (*n*=245 from hospital recruitment, *n*=209 from community recruitment), and the rural river communities (*n*=202), represent an urban-rural gradient. Table 4 characterizes the expected differences in sociodemographics between urban and rural sites to support the existence of this urban-rural gradient (*Appendix:* see Full Table 4). This gradient also represents a reduction of access to clean and safe water and sanitation.

Table 4. Characteristics of all participants, by site, Ecuador, 2014 – 2015

	Urban --> Rural					
	Quito n=263	Esmeraldas n=223	Borbon-Borbon n=245	Borbon-Casas n=109	Rural River Communities n=202	p-value*
	n (%)	n (%)	n (%)	n (%)	n (%)	
Sociodemographics						
Patient family receives bono	15 (5.7)	44 (19.7)	56 (22.9)	31 (28.4)	97 (48.0)	<0.001
Family member holds a job	203 (77.2)	97 (43.5)	105 (43.2)	41 (37.6)	39 (19.3)	<0.001
University Level Education	102 (38.8)	87 (39.2)	49 (20.1)	16 (14.7)	14 (6.9)	<0.001
Animal Contact						
Reported Animal Contact	147 (55.9)	101 (45.5)	100 (40.8)	41 (37.6)	64 (31.8)	<0.001
Water and Sanitation						
Report Improved Sanitation❖	206 (78.3)	152 (69.7)	150 (61.2)	78 (71.6)	85 (42.1)	<0.001
Report Improved water⚩	262 (99.6)	220 (99.5)	226 (92.2)	103 (94.5)	187 (92.6)	<0.001
Treat water at home	169 (64.3)	87 (39.4)	39 (16.0)	26 (23.9)	44 (21.8)	<0.001
Travel						
Reported Travel in past 12 months	53 (20.2)	66 (29.6)	178 (72.7)	63 (57.8)	125 (61.9)	<0.001

*Pearson's Chi-Squared or Fisher's exact test was used to test whether the distribution of each characteristic differs across groups
❖Improved sanitation includes: Personal latrines, septic tanks and pour-over flush
⚩Improved water includes: Tap inside, Tap outside, neighbor's tap, bottled water and rainwater

As the sites become more rural, there is an increase in the proportion of individuals receiving government assistance ($p < 0.001$) and a decrease in the proportion of individuals with family members holding a job ($p < 0.001$). Urban-rural sociodemographic differences are also highlighted in the decrease in university level education at the more rural sites ($p < 0.001$), with the river communities having the lowest proportion (6.9%) of university-educated participants. Furthermore, urban sites reported higher proportions of animal contact ($p<$ 0.001). The urban sites also reported higher proportions of participants using improved sanitation, improved drinking water and treating drinking water at home, but fewer reporting travel in the past 12 months ($p < 0.001$). Using this significant urban-rural gradient, we can assess the differences in risk factors for diarrheal disease and pathogen-specific diarrhea.

Bivariate Analysis

Risk Factors for Diarrheal Disease

Unadjusted bivariate risk factor data is summarized by site in Table 5. Diarrhea cases across all participants had greater odds of being male (OR: 1.29; 95% CI: 1.01, 1.65; $p = 0.04$), but no individual site had a significant association with sex. Both among all participants and in the rural communities, cases were about three times more likely to be indigenous than black compared to controls (OR: 2.77; 95% CI: 1.46, 5.26; $p = 0.001$ and OR: 3.13; 95% CI: 1.31, 7.45; $p = 0.008$, respectively). This difference in race is most likely an artifact of recruitment in the rural river communities, where indigenous cases were age-matched with black. Cases were 1.4 times more likely to report being home-birthed compared to hospital vaginal delivery (OR: 1.81; 95% CI: 1.00, 3.29; $p = 0.05$). Mixed breastfeeding compared to exclusive breastfeeding was also significantly associated with diarrheal disease among all participants (OR: 1.81; 95% CI: 1.00, 3.29; $p = 0.05$) and in just Quito (OR: 3.12; 95% CI: 1.18, 8.20; $p = 0.02$).

Animal contact was only significantly associated with diarrheal disease within the Borbón-Borbón participants (OR: 1.90; 95% CI: 1.13, 3.21; $p = 0.02$). However, cases from Quito were less likely to have reported animal contact within the home (OR: 0.34; 95% CI: 0.13, 0.88; $p = 0.02$). Across all cases as well as the Borbon-Borbón subset, both production and domestic chickens were seen as protective against being a diarrheal case, which may be an indicator for socioeconomic status not adequately captured in our survey. The rural subset was the only site where contact with cats presented an increased risk of diarrhea; cases were >7 times more likely to have reported contact with cats (OR: 7.33; 95% CI: 2.35, 22.88; $p < 0.001$).

Table 5. Unadjusted estimated odds ratios (OR) and 95% confidence intervals (CI) for risk factors of diarrheal disease amongst subjects enrolled in a case-control study in Ecuador stratified by site, 2014-2015. Statistically significant results are shown in red.

	All Participants n = 1042					Quito n = 263					Esmeraldas n = 223				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Demographics															
Age															
<2 years	184	335	1.00	ref.	ref.	47	93	1.00	ref.	ref.	38	74	1.00	ref.	ref.
2-5 years	108	207	0.90	0.63	1.27	20	39	1.03	0.49	2.18	19	43	0.75	0.35	1.60
5-15 years	99	198	0.82	0.58	1.17	22	46	0.90	0.44	0.01	24	49	0.91	0.44	1.87
15+ years	164	302	0.98	0.71	1.33	48	85	1.27	0.70	2.29	30	57	1.05	0.53	2.10
Male	312	555	**1.29**	**1.01**	**1.65**	71	130	1.22	0.75	1.98	68	125	1.53	0.90	2.60
Race															
Black	207	408	1.00	ref.	ref.	2	3	1.00	ref.	ref.	42	93	1.00	ref.	ref.
White	5	9	1.21	0.32	4.58	5	8	0.83	0.05	13.63	0	1	0.00	0.00	-
Indigenous	40	54	**2.77**	**1.46**	**5.26**	3	5	0.75	0.04	14.97	1	1	Inf	-	Inf
Manaba	32	66	0.91	0.54	1.54	2	4	0.50	0.02	11.09	3	8	0.73	0.16	3.23
Mixed	271	504	1.13	0.87	1.47	125	243	0.53	0.05	5.92	65	119	1.46	0.85	2.52
Sociodemographics															
Home ownership status															
Owned	366	695	1.00	ref.	ref.	44	86	1.00	ref.	ref.	75	160	1.00	ref.	ref.
Rented	136	253	1.04	0.78	1.39	81	152	1.09	0.64	1.85	24	38	1.94	0.94	4.03
Loaned	52	93	1.14	0.74	1.76	12	25	0.88	0.36	2.15	12	25	1.05	0.45	2.43
Patient family receives bono	130	243	1.01	0.76	1.35	5	15	0.44	0.15	1.32	22	44	1.01	0.52	1.96
Family member holds a job	258	485	0.99	0.78	1.27	108	203	1.22	0.68	2.16	49	97	1.05	0.62	1.79
Highest level of education in Household															
University	131	268	1.00	ref.	ref.	49	102	1.00	ref.	ref.	40	87	1.00	ref.	ref.
High School	339	624	1.24	0.93	1.66	73	130	1.39	0.82	2.33	60	117	1.24	0.71	2.16
Elementary	79	137	1.42	0.94	2.16	14	30	0.95	0.42	2.14	10	15	2.35	0.74	7.45
None	4	11	0.60	0.17	2.09	1	1	Inf	-	Inf	0	3	0.00	0.00	-
Live in Mining Community	27	55	0.55	0.30	1.01	-	-	-	-	-	-	-	-	-	-
Live in Palm farming Community	43	75	0.84	0.48	1.48	-	-	-	-	-	-	-	-	-	-
Patient employed in mining															
Never	103	191	1.00	ref.	ref.	-	-	-	-	-	-	-	-	-	-
Formerly	1	2	0.85	0.05	13.86	-	-	-	-	-	-	-	-	-	-
Currently	0	2	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-
Patient employed in palm industry															
Never	90	171	1.00	ref.	ref.	-	-	-	-	-	-	-	-	-	-
Formerly	6	11	1.08	0.32	3.67	-	-	-	-	-	-	-	-	-	-
Currently	8	13	1.44	0.45	4.58	-	-	-	-	-	-	-	-	-	-
Child Day Care Attendance	61	112	0.99	0.65	1.51	9	15	1.53	0.51	4.59	10	19	1.22	0.45	3.28
Medical History															
Antibiotics Taken in Past 7 Days	19	26	**2.43**	**1.01**	**5.83**	7	10	2.21	0.56	8.73	11	14	**4.00**	**1.08**	**14.74**
Rotavirus Vaccination Status															
Received 1st Dose	72	140	1.59	0.61	4.12	31	57	4.17	0.80	21.85	13	29	1.22	0.18	8.42
Received 2nd Dose	57	116	0.58	0.23	1.43	27	52	0.27	0.03	2.58	11	26	0.37	0.03	4.57
Birth Description															
Hospital - Vaginal Birth	325	639	1.00	ref.	ref.	81	163	1.00	ref.	ref.	57	109	1.00	ref.	ref.
Hospital - Cesarean Birth	92	168	1.17	0.83	1.64	33	63	1.11	0.62	1.99	33	62	1.04	0.56	1.94
Homebirth	106	179	**1.40**	**1.00**	**1.96**	22	35	1.71	0.81	3.63	10	25	0.61	0.25	1.47
Breastfeeding Practices															
Exclusively	28	65	1.00	ref.	ref.	9	28	1.00	ref.	ref.	7	16	1.00	ref.	ref.
Mixed	81	140	**1.81**	**1.00**	**3.29**	31	52	**3.12**	**1.18**	**8.20**	14	24	1.80	0.50	6.46
Done breastfeeding	160	285	1.69	0.98	2.91	21	39	2.46	0.89	6.78	31	66	1.14	0.38	3.42
Never	1	4	0.44	0.04	4.46	1	3	1.06	0.08	13.23	0	1	0.00	0.00	-
Animal Contact															
Reported Animal Contact	246	453	1.08	0.85	1.39	75	147	0.91	0.56	1.48	55	101	1.43	0.84	2.44
Type of Animal Contact															
Animal breeding	22	35	1.47	0.72	2.99	2	3	1.95	0.17	21.93	0	1	0.00	0.00	-
Animals in home	198	376	0.67	0.41	1.11	57	122	**0.34**	**0.13**	**0.88**	46	90	0.23	0.05	1.14
Animals around home	28	50	1.08	0.60	1.95	17	8	2.34	0.94	5.84	8	9	7.66	0.92	63.73
Animals Contacted															
Cows	5	10	0.84	0.24	2.94	0	1	0.00	0.00	-	0	1	0.00	0.00	-
Production Chickens	27	65	**0.55**	**0.32**	**0.93**	4	12	0.45	0.13	1.57	0	3	0.00	0.00	-
Domestic Chickens	23	56	**0.54**	**0.31**	**0.96**	2	7	0.37	0.07	1.96	0	3	0.00	0.00	-
Pigs	21	40	0.92	0.48	1.77	2	3	1.95	0.17	21.93	0	1	0.00	0.00	-
Dogs	177	336	0.77	0.51	1.19	64	129	0.63	0.23	1.72	37	68	0.99	0.43	2.29
Cats	109	184	1.40	0.96	2.04	19	38	0.95	0.45	1.98	29	52	1.12	0.51	2.44
Wild Game	3	5	1.27	0.21	7.65	0	0	-	-	-	1	2	0.83	0.05	13.70
Rat	1	0	Inf	-	Inf	1	1	Inf	-	Inf	0	0	-	-	-
Other	2	9	0.23	0.05	1.14	1	4	0.31	0.03	3.06	1	2	0.83	0.05	13.70

	Borbon-Borbon n = 245					Borbon-Casas n = 109					Rural River Communities n = 202				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Demographics															
Age															
<2 years	48	85	1.00	ref.	ref.	16	29	1.00	ref.	ref.	35	54	1.00	ref.	ref.
2-5 years	21	34	1.25	0.55	2.81	14	34	0.57	0.21	1.55	34	57	0.80	0.37	1.73
5-15 years	23	43	0.89	0.42	1.85	8	18	0.65	0.20	2.12	22	42	0.60	0.26	1.36
15+ years	42	83	0.79	0.43	1.45	15	28	0.94	0.33	2.66	29	49	0.79	0.35	1.75
Male	78	133	1.42	0.85	2.35	30	59	1.21	0.57	2.58	65	108	1.07	0.61	1.88
Race															
Black	72	134	1.00	ref.	ref.	33	70	1.00	ref.	ref.	58	108	1.00	ref.	ref.
White	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Indigenous	7	10	2.01	0.50	8.10	0	1	0.00	0.00	-	29	37	**3.13**	**1.31**	**7.45**
Manaba	14	27	0.93	0.41	2.12	3	12	0.37	0.09	1.50	10	15	1.72	0.55	5.38
Mixed	41	74	1.07	0.60	1.89	17	26	2.12	0.83	5.39	23	42	1.04	0.51	2.13
Sociodemographics															
Home ownership status															
Owned	104	193	1.00	ref.	ref.	40	78	1.00	ref.	ref.	103	178	1.00	ref.	ref.
Rented	17	36	0.77	0.38	1.56	7	16	0.63	0.21	1.95	7	11	1.27	0.36	4.51
Loaned	12	15	3.42	0.94	12.50	6	15	0.74	0.25	2.18	10	13	2.43	0.65	9.12
Patient family receives bono	28	56	0.78	0.43	1.42	17	31	1.42	0.61	3.27	58	97	1.03	0.59	1.81
Family member holds a job	52	105	0.69	0.41	1.15	20	41	1.01	0.47	2.19	29	39	**2.29**	**1.05**	**5.02**
Highest level of education in Household															
University	21	49	1.00	ref.	ref.	9	16	1.00	ref.	ref.	12	14	1.00	ref.	ref.
High School	102	179	1.77	0.93	3.34	35	78	0.63	0.21	1.87	69	120	0.23	0.05	1.05
Elementary	10	15	2.67	0.79	8.97	9	15	1.17	0.28	4.87	36	62	0.23	0.05	1.12
None	0	1	0.00	0.00	-	0	0	-	-	-	3	6	0.17	0.02	1.49
Live in Mining Community	1	1	Inf	-	Inf	-	-	-	-	-	26	54	**0.53**	**0.28**	**1.00**
Live in Palm farming Community	7	10	1.27	0.24	6.82	-	-	-	-	-	36	65	0.79	0.44	1.44
Patient employed in mining															
Never	53	101	1.00	ref.	ref.	18	35	1.00	ref.	ref.	32	55	1.00	ref.	ref.
Formerly	0	0	-	-	-	0	0	-	-	-	1	2	0.72	0.04	12.10
Currently	0	1	0.00	0.00	-	0	0	-	-	-	0	1	0.00	0.00	-
Patient employed in palm industry															
Never	45	85	1.00	ref.	ref.	15	32	1.00	ref.	ref.	30	54	1.00	ref.	ref.
Formerly	3	7	0.67	0.14	3.16	2	2	Inf	-	Inf	1	2	0.80	0.05	13.47
Currently	5	10	0.89	0.24	3.30	1	1	Inf	-	Inf	2	2	Inf	-	Inf
Child Day Care Attendance	14	25	0.92	0.37	2.25	5	10	1.00	0.26	3.91	23	43	**0.39**	**0.17**	**0.92**
Medical History															
Antibiotics Taken in Past 7 Days	1	2	0.83	0.05	13.38	0	0	-	-	-	0	0	-	-	-
Rotavirus Vaccination Status															
Received 1st Dose	7	20	0.27	0.02	3.52	6	11	Inf	-	Inf	15	23	0.00	0.00	-
Received 2nd Dose	5	15	0.75	0.09	6.04	3	5	1.50	0.14	16.54	11	18	0.39	0.04	4.28
Birth Description															
Hospital - Vaginal Birth	88	174	1.00	ref.	ref.	30	67	1.00	ref.	ref.	69	126	1.00	ref.	ref.
Hospital - Cesarean Birth	12	18	1.95	0.70	5.44	8	17	1.10	0.38	3.19	6	8	2.48	0.48	12.75
Homebirth	32	49	1.84	0.95	3.56	12	21	1.64	0.61	4.42	30	49	1.30	0.67	2.56
Breastfeeding Practices															
Exclusively	6	8	1.00	ref.	ref.	1	5	1.00	ref.	ref.	5	8	1.00	ref.	ref.
Mixed	15	30	0.33	0.06	1.92	5	10	4.00	0.32	49.60	16	24	1.20	0.23	6.34
Done breastfeeding	43	73	0.48	0.09	2.53	23	43	4.60	0.47	44.60	42	64	1.15	0.25	5.24
Never	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Animal Contact															
Reported Animal Contact	64	100	**1.90**	**1.13**	**3.21**	18	41	0.74	0.34	1.61	34	64	0.69	0.38	1.26
Type of Animal Contact															
Animal breeding	10	16	0.93	0.31	2.80	3	4	4.40	0.42	46.43	7	11	1.69	0.44	6.44
Animals in home	55	85	1.22	0.40	3.76	14	31	1.24	0.29	5.26	26	48	1.18	0.38	3.67
Animals around home	0	4	0.00	0.00	-	1	6	0.21	0.02	2.00	2	6	0.41	0.07	2.40
Animals Contacted															
Cows	3	4	1.72	0.17	17.19	1	1	Inf	-	Inf	1	3	0.42	0.04	4.93
Production Chickens	9	22	**0.29**	**0.11**	**0.77**	6	11	1.80	0.45	7.25	8	17	0.72	0.24	2.18
Domestic Chickens	8	19	**0.32**	**0.12**	**0.91**	5	10	1.38	0.33	5.79	8	17	0.72	0.24	2.18
Pigs	11	20	0.62	0.23	1.68	3	5	2.10	0.31	14.15	5	11	0.69	0.19	2.54
Dogs	42	68	0.73	0.30	1.79	14	32	0.97	0.22	4.31	20	39	0.83	0.30	2.27
Cats	36	56	1.03	0.45	2.34	3	10	0.46	0.10	2.10	22	28	**7.33**	**2.35**	**22.88**
Wild Game	0	0	-	-	-	0	0	-	-	-	2	3	1.81	0.16	21.06
Rat	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Other	0	1	0.00	0.00	-	0	0	-	-	-	0	2	0.00	0.00	-

Table 5. (Cont.) Unadjusted Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk of Diarrheal Disease among a Case-Control Study in Ecuador stratified by site, 2014-2015

	All Participants n = 1042					Quito n = 263				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Water and Sanitation										
Sanitation facility used during travel:										
Improved Sanitation❖	23	45	1.00	ref.	ref.	12	24	1.00	ref.	ref.
Unimproved Sanitation❖❖	13	26	0.96	0.36	2.51	1	5	0.25	0.02	2.58
None	6	10	1.43	0.36	5.78	0	0	-	-	-
Sanitation facility used at home:										
Improved Sanitation❖	348	665	1.00	ref.	ref.	109	206	1.00	ref.	ref.
Unimproved Sanitation❖❖	201	366	1.11	0.86	1.43	28	57	0.86	0.48	1.55
Mixed	1	5	0.18	0.02	1.57	0	0	-	-	-
Drinking water source during travel:										
Improved water♐	42	79	1.00	ref.	ref.	13	28	1.00	ref.	ref.
Unimproved water♐♐	0	2	0.00	0.00 -		0	1	0.00	0.00	-
Drinking water source at home:										
Improved water♐	520	974	1.00	ref.	ref.	137	262	1.00	ref.	ref.
Unimproved water♐♐	23	42	1.06	0.57	1.97	0	1	0.00	0.00	-
Mixed	10	24	0.62	0.27	1.42	0	0	-	-	-
Treat water during travel	5	15	0.39	0.12	1.27	4	11	0.57	0.12	2.66
Treat water at home	178	365	**0.76**	**0.59**	**0.99**	80	169	**0.58**	**0.35**	**0.97**
Travel										
Reported Travel in past 12 months	274	485	**1.28**	**1.00**	**1.63**	27	53	0.94	0.52	1.72
Number of locations visited in the past 12 months										
One destination	170	293	1.00	ref.	ref.	26	51	1.00	ref.	ref.
Two destinations	56	111	0.74	0.48	1.14	1	2	0.96	0.06	16.22
Three destinations	28	49	0.96	0.52	1.78	-	-	-	-	-
Four destinations	18	28	1.30	0.58	2.92	-	-	-	-	-
Five destinations	2	3	1.45	0.13	16,14	-	-	-	-	-
Six destinations	0	1	0.00	0.00	-					
Destination Type*										
Urban	174	308	1.00	ref.	ref.	8	19	1.00	ref.	ref.
Rural	46	79	1.07	0.65	1.77	18	32	1.77	0.56	5.57
Mixed	44	84	0.85	0.52	1.37	1	2	1.38	0.07	25.43
Reported Travel in the past month	25	50	0.84	0.46	1.54	-	-	-	-	-
Reported Travel in the past week	43	82	0.96	0.61	1.52	14	30	0.78	0.37	1.68

	Esmeraldas n = 223					Borbon-Borbon n = 245				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Water and Sanitation										
Sanitation facility used during travel:										
Improved Sanitation❖	5	8	1.00	ref.	ref.	2	5	1.00	ref.	ref.
Unimproved Sanitation❖❖	6	8	1.80	0.21	15.41	3	8	0.90	0.09	8.90
None	0	0	-	-	-	3	5	2.25	0.18	28.25
Sanitation facility used at home:										
Improved Sanitation❖	75	151	1.00	ref.	ref.	87	149	1.00	ref.	ref.
Unimproved Sanitation❖❖	31	66	0.90	0.50	1.60	47	95	0.70	0.42	1.17
Mixed	0	1	0.00	0.00	-	0	1	0.00	0.00	-
Drinking water source during travel:										
Improved water♐	11	15	1.00	ref.	ref.	8	18	1.00	ref.	ref.
Unimproved water♐♐	0	1	0.00	0.00	-	0	0	-	-	-
Drinking water source at home:										
Improved water♐	109	220	1.00	ref.	ref.	123	223	1.00	ref.	ref.
Unimproved water♐♐	0	1	0.00	0.00	-	9	19	0.73	0.29	1.87
Mixed	0	0	-	-	-	2	3	1.62	0.15	18.19
Treat water during travel	1	4	0.07	0.00	1.02	0	0	-	-	-
Treat water at home	34	87	**0.50**	**0.29**	**0.87**	20	39	0.86	0.43	1.70
Travel										
Reported Travel in past 12 months	41	66	**2.04**	**1.13**	**3.67**	101	178	1.35	0.77	2.37
Number of locations visited in the past 12 months										
One destination	39	61	1.00	ref.	ref.	48	84	1.00	ref.	ref.
Two destinations	2	5	0.38	0.06	2.43	26	51	0.78	0.39	1.57
Three destinations	-	-	-	-	-	17	25	1.59	0.62	4.10
Four destinations	-	-	-	-	-	9	15	1.13	0.37	3.45
Five destinations	-	-	-	-	-	1	2	0.75	0.05	12.40
Six destinations	-	-	-	-	-	0	1	0.00	0.00	-
Destination Type*										
Urban	34	55	1.00	ref.	ref.	56	103	1.00	ref.	ref.
Rural	6	10	0.93	0.23	3.67	11	17	1.54	0.53	4.48
Mixed	1	1	Inf	-	Inf	24	44	1.01	0.50	2.05
Reported Travel in the past month	-	-	-	-	-	15	32	0.75	0.33	1.66
Reported Travel in the past week	11	16	2.35	0.79	7.01	8	18	0.64	0.24	1.68

	Borbon-Casas n = 109					Rural River Communities n = 202				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Water and Sanitation										
Sanitation facility used during travel:										
Improved Sanitation❖	2	3	1.00	ref.	ref.	2	5	1.00	ref.	ref.
Unimproved Sanitation❖❖	1	1	Inf	-	Inf	2	4	1.50	0.11	21.31
None	0	1	0.00	0.00	-	3	4	4.50	0.25	80.57
Sanitation facility used at home:										
Improved Sanitation❖	32	77	1.00	ref.	ref.	45	82	1.00	ref.	ref.
Unimproved Sanitation❖❖	21	31	**2.95**	**1.23**	**7.11**	74	117	1.41	0.80	2.51
Mixed	0	1	0.00	0.00	-	1	3	0.41	0.04	4.71
Drinking water source during travel:										
Improved water♐	3	5	1.00	ref.	ref.	7	13	1.00	ref.	ref.
Unimproved water♐♐	0	0	-	-	-	0	0	-	-	-
Drinking water source at home:										
Improved water♐	49	102	1.00	ref.	ref.	102	167	1.00	ref.	ref.
Unimproved water♐♐	3	6	1.08	0.21	5.61	11	15	1.75	0.54	5.74
Mixed	1	1	Inf	-	Inf	7	20	0.34	0.13	0.91
Treat water during travel	0	0	-	-	-	0	0	-	-	-
Treat water at home	14	26	1.32	0.54	3.18	30	44	1.62	0.80	3.29
Travel										
Reported Travel in past 12 months	31	63	1.06	0.49	2.26	74	125	0.98	0.55	1.74
Number of locations visited in the past 12 months										
One destination	20	39	1.00	ref.	ref.	37	58	1.00	ref.	ref.
Two destinations	5	16	0.43	0.13	1.48	22	37	0.83	0.36	1.94
Three destinations	4	5	3.80	0.39	37.13	7	19	0.33	0.11	0.97
Four destinations	2	3	1.90	0.16	22.72	7	10	1.32	0.31	5.67
Five destinations	-	-	-	-	-	1	1	Inf	-	Inf
Six destinations	-	-	-	-	-	-	-	-	-	-
Destination Type*										
Urban	20	41	1.00	ref.	ref.	56	90	1.00	ref.	ref.
Rural	6	12	1.05	0.26	4.18	5	8	1.01	0.23	4.51
Mixed	5	10	1.05	0.29	3.80	13	27	0.56	0.24	1.34
Reported Travel in the past month	9	12	3.35	0.84	13.41	1	6	0.13	0.01	1.18
Reported Travel in the past week	3	5	1.62	0.26	10.10	7	13	0.78	0.25	2.43

Note: OR reference is to the absence of the stated variable unless otherwise specified
❖Improved sanitation includes: Personal latrines, septic tanks and pour-over flush
❖❖Unimproved sanitation includes: Open field, hole in ground, river, diaper, community latrines, and neighbor latrines
♐Improved water includes: Tap inside, Tap outside, neighbor's tap, purchased water and rainwater
♐♐Unimproved water includes: River and well water
*Destination type is in relation to origin. (i.e. Esmeraldas is urban compared to a Borbon origin but Rural compared to a Quito origin)

The cases from the Borbón-Casa subset were nearly 3 times more likely to report using unimproved sanitation in the home (OR: 2.95; 95% CI: 1.23, 7.11; $p = 0.01$). Water treatment at home was found to not only be protective within the aggregated data (OR: 0.76; 95% CI: 0.59, 0.99; $p = 0.04$) but also in both Quito (OR: 0.58; 95% CI: 0.35, 0.97; $p = 0.04$) and Esmeraldas (OR: 0.50; 95% CI: 0.29, 0.87; $p = 0.01$).

As for travel, all participants and the subset from Esmeraldas showed travel in the past year to be more likely in those with diarrhea (OR: 1.28; 95% CI: 1.00, 1.63; $p = 0.05$ and OR: 2.04; 95% CI: 1.13, 3.67; $p = 0.02$, respectively).

Bivariate analysis was also conducted on only participants less than 5 years old (*Appendix:* Table 6). Additional risk factors of interest were significantly associated with diarrhea in that subsetted analysis are as follows. Cases from the Borbón-Borbón site were less likely to have received government welfare (OR: 0.31; 95% CI: 0.10, 0.97; $p = 0.04$). Animal contact was significantly associated with diarrheal in both the Esmeraldas subset (OR: 2.87; 95% CI: 1,35, 6.11; $p = 0.006$) and the Borbón-Casas subset (OR: 4.71; 95% CI: 1.99, 11.15; $p < 0.001$). Cases under the age of five in the rural communities were also eleven times more likely to have reported animal contact within the home (OR: 11.37; 95% CI: 1.27, 101.45; $p = 0.01$). Cases from Borbón-Casas were more than three times as likely to reporting having treated their water at home (OR: 3.21; 95% CI: 1.07, 9.59; $p = 0.03$) which may be due to the fact that families tend to treat their water once a child in the family presents with illness. Travel in the past year remained significant for all participants under the age of 5 (OR: 1.49, 95% CI: 1.05, 2.11, $p = 0.03$).

Since travel in the past year was significantly associated with diarrhea using all participant data, we further investigated travel patterns such as destination, duration, frequency, and reason as more travel specific risk factors for diarrheal disease. Figure 4 characterizes the distribution of travel between each of the four study sites. Figure 5 describes participant travel to multiple locations within Ecuador including: Guayaquil, Santo Domingo, and San Lorenzo. Note that both Borbón sub-studies were combined for this travel analysis.

There was a greater tendency for participants to travel to more urban destinations and destinations closest to them. The destination with the greatest proportion of visits was Esmeraldas. In addition to assessing travel destination we also looked at duration of stay (Table 7). Due to the duration being anywhere between 1 to 61 days, both means and median durations were reported to eliminate outlier bias when applicable. On average, participants tended to spend more time in urban location versus rural locations.

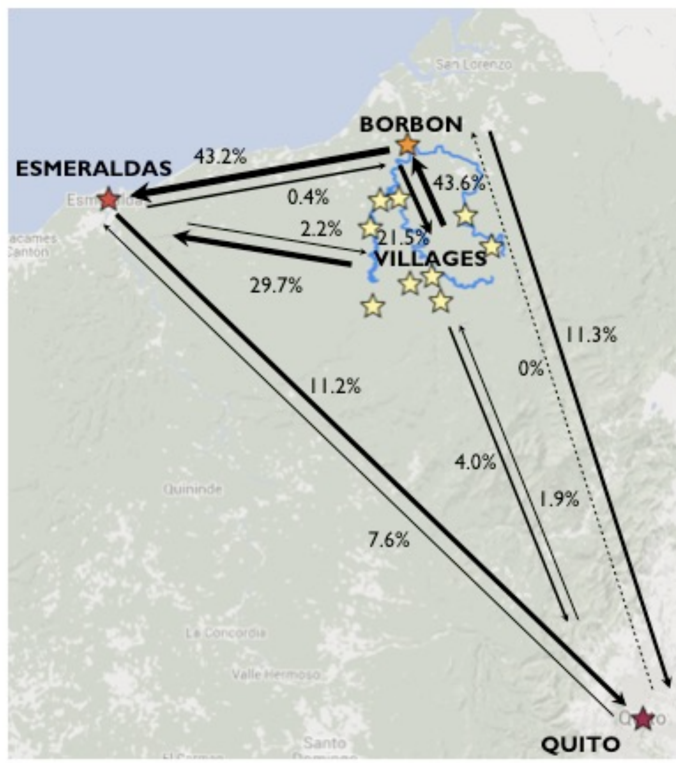


Figure 5. (Right) Map of Travel Distribution in the Past Year Map of Ecuador encompassing all four study sites (Quito, Esmeraldas, Borbón, Rural villages). Arrows denote direction of travel and are weighted by the proportion reporting history of travel to designated location in the past year.

Frequency of travel was also evaluated in Table 8, again reporting both mean and median values. The highest destination frequency was to Borbón, with an average of six visits annually by participants; this is highly driven by the increased frequency seen in the rural communities as well as within Borbón participants visiting other communities within Borbón. Furthermore on average Borbón and the rural communities had a higher frequency of travel compared to participants from Quito and Esmeraldas.

Figure 6. Destination of Travel reported in the past year, by site, Ecuador 2014-2015. Each row represents responses from each of the four study site. Each column represents a specific destination of travel. The darker the shade of green the higher proportion of participants reporting travel to this location. The thatched boxes represent matching study site and destination, since participants cannot report traveling to their own location these boxes are thatched.

		Travel Destination Urban --> Rural							
		Guayaquil	Quito	Santo Domingo	Esmeraldas	San Lorenzo	Borbon	Rural Com.	Other
Study Site	Quito	8.0%		3.4%	7.6%	0.0%	0.0%	1.9%	0.0%
	Esmeraldas	12.1%	11.2%	3.6%		2.2%	0.4%	2.2%	0.0%
	Borbon	12.1%	7.3%	5.6%	43.2%	22.6%		21.5%	4.0%
	Rural Communities	6.9%	4.0%	4.0%	29.7%	10.4%	43.6%	15.8%	1.5%

Table 7. Average Travel Duration (in days) in the past year, by destination, Ecuador, 2014 – 2015

		All Participants			Quito			Esmeraldas			Borbon			Rural Communities		
		n	mean (sd)	median	n	mean (sd)	median	n	mean (sd)	median		mean (sd)	median		mean (sd)	median
Destination	Guayaquil	105	15 (16.5)	6	21	10 (5.7)	6	27	19 (22.9)	6	43	14 (15.8)	6	14	17 (14.5)	14
	Quito	58	9 (11.1)	6				25	9 (11.7)	6	25	8 (5.9)	6	8	12 (20.1)	6
	Santo Domingo	45	8 (9.9)	6	9	13 (19.6)	6	8	8 (8.2)	6	20	6 (3.6)	6	8	9 (4.1)	6
	Esmeraldas	211	7 (8.0)	6	0	0 (0.0)	0				151	6 (4.1)	6	60	10 (13.1)	6
	San Lorenzo	109	3 (3.9)	1	3	6 (0.0)	6	5	8 (3.6)	6	80	2 (3.7)	1	21	3 (4.1)	1
	Borbon	112	3 (3.4)	1	0	0 (0.0)	0	1	28 (NA)	28	23	2 (2.1)	1	88	2 (2.5)	1
Total		**640**	**7 (10.3)**	**6**	**33**	**11 (11.0)**	**6**	**66**	**13 (17.3)**	**6**	**342**	**6 (7.6)**	**6**	**199**	**6 (10.3)**	**6**

Table 8. Average Annual Travel Frequency, by destination, Ecuador, 2014-2015

		All Participants			Quito			Esmeraldas			Borbon			Rural Communities		
		n	mean (sd)	median	n	mean (sd)	median	n	mean (sd)	median		mean (sd)	median		mean (sd)	median
Destination	Guayaquil	105	3 (5.5)	2	21	4 (11)	1	27	2 (1.1)	1	43	3 (3.8)	2	14	3 (1.3)	4
	Quito	58	3 (3.4)	2				25	3 (5.0)	2	25	3 (1.4)	2	8	2 (1.4)	1
	Santo Domingo	45	3 (4.0)	2	9	3 (3.5)	2	8	2 (1.2)	2	20	3 (5.4)	2	8	3 (1.3)	2
	Esmeraldas	211	3 (1.8)	4	0	0 (0.0)	0				151	4 (1.8)	4	60	3 (1.7)	4
	San Lorenzo	108	4 (2.8)	4	3	2 (1.7)	1	5	3 (2.2)	2	79	4 (3.0)	4	21	4 (2.4)	4
	Borbon	112	5 (5.3)	4	0	0 (0.0)	0	1	1 (NA)	1	23	9 (8.3)	6	88	4 (3.7)	4
Total		**639**	**4 (3.9)**	**4**	**33**	**4 (8.9)**	**1**	**66**	**2 (3.2)**	**2**	**341**	**4 (3.7)**	**4**	**199**	**4 (2.9)**	**4**

Differences in travel destination, frequency, duration and reasons were then assessed among cases and controls reporting travel in the past year for potential associations with diarrheal disease (*Appendix:* Table 9). Cases were nearly twice as likely to report traveling to Quito (OR: 1.80; 95% CI: 1.02, 3.17; $p = 0.04$) and about 1.5 times more likely to have traveled to Borbón (OR: 1.53; 95% CI: 1.02, 2.29; $p = 0.04$) in the past 12 months. Furthermore, participants reporting traveling to Borbón for leisure versus business had lower odds of being a case.

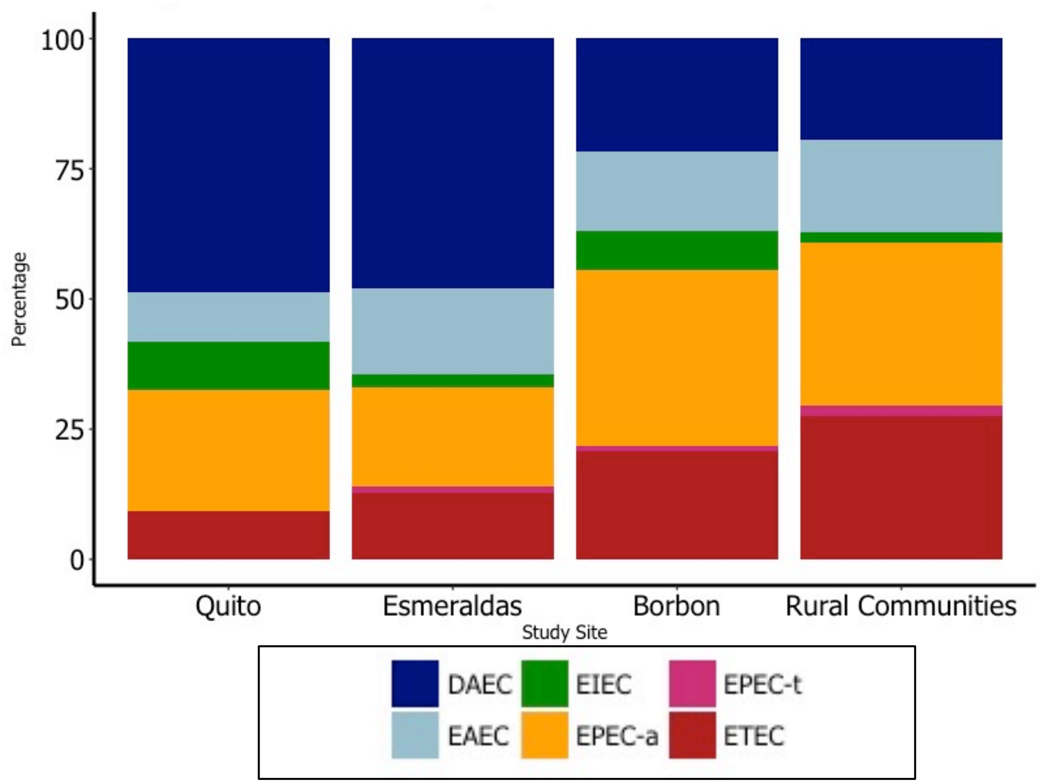
Pathogen-Specific Risk Factors for Diarrheal Disease

The distribution of *E. coli* pathotypes by site is shown in Figure 7. There is a clear difference in the distribution of the various *E. coli* pathotypes across this urban-rural gradient. The urban study sites, Quito and Esmeraldas, have a higher proportion of DAEC infection than the two more rural sites. The two rural sites, Borbón and the rural communities, have higher proportions of EPEC-a and ETEC.

In addition to looking at pathogen distribution, we also wanted to assess pathogen specific risk factors and if these differed from the previously identified risk factors for general diarrheal disease. An initial bivariate analysis was performed to calculate unadjusted odds ratios for all pathogenic *E. coli* infection across each site and is summarized in Table 10.

Across individual study sites there was some variation in the associations between *E. Coli*

Figure 7. Distribution of *E. Coli* Pathotypes detected Among Participants across all sites, Ecuador 2014-2015



and the numerous potential risk factors. Among all participants as well as in Esmeraldas only, some of the older ages were less likely to have pathogenic *E. coli* infections. Pathogenic *E. coli* cases from Esmeraldas were twice as likely to be males (OR: 2.00; 95% CI: 1.09, 3.69; $p = 0.02$), but those from Borbón-Borbón were less likely to be male (OR: 0.53; 95% CI: 0.28, 0.99; $p = 0.04$). Mixed race participants from Borbón-Borbón were more likely to be a case (OR: 2.54; 95% CI: 1.28, 5.03; $p = 0.007$) than black participants, but less likely among the rural communities (OR: 0.26; 95% CI: 0.09, 0.80; $p = 0.01$). Among all participants, cases were less likely to report a family member holding a job (OR: 0.73; 95% CI: 0.54, 0.99; $p = 0.04$), and low levels of household education were also associated with pathogenic *E. coli* infections for all participants as well as in the Quito and Esmeraldas subsets.

Among all participants, *E. coli* cases were about 2.5 times more likely to have reported animal contact around their home (OR: 2.54; 95% CI: 1.28, 5.02; $p = 0.006$). When evaluating water and sanitation as risk factors for pathogenic *E. coli* infections it was found that use of unimproved sanitation facilities both during travel (OR: 4.06; 95% CI: 1.12, 14.73; $p = 0.05$) and at home (OR: 1.36; 95% CI: 1.00, 1.86; $p = 0.05$) was significantly associated with having pathogenic *E. coli* infections across all study participants. Pathogenic *E. coli* cases from the Esmeraldas subset were also twice as likely to have reported use of unimproved sanitation facilities at home (OR: 2.03; 95% CI: 1.05, 3.90; $p = 0.03$).

As for travel being associated with pathogenic *E. coli* infections, travel in the past year was significantly higher among cases within the Quito subset only (OR: 2.64; 95% CI: 1.25, 5.60; $p = 0.01$). No other sites reported any significant travel associated with pathogenic *E. coli*.

Next we evaluated to see if there were any variations among the potential risk factors when defining the outcome as cases of DAEC, which had the largest samples size among the DEC infections. We also performed this risk analysis for the outcome of rotavirus to see if there were any variations between bacterial and viral diarrheal risk factors. Due to small proportion of

Table 10. Unadjusted Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk of Any Pathogenic E. coli Infection among All Study Participants Stratified by Site, Ecuador, 2014-2015. Statistically significant results are shown in red.

	All Participants n=875*					Quito n=185					Esmeraldas n=192					Borbon-Borbon n=215					Borbon-Casas n=104					Rural River Communities n=179				
	E. Coli Positive N	**Total N**	**OR**	**95% CI**		**E. Coli Positive N**	**Total N**	**OR**	**95% CI**		**E. Coli Positive N**	**Total N**	**OR**	**95% CI**		**E. Coli Positive N**	**Total N**	**OR**	**95% CI**		**E. Coli Positive N**	**Total N**	**OR**	**95% CI**		**E. Coli Positive N**	**Total N**	**OR**	**95% CI**	
Demographics																														
Age																														
<2 years	86	261	1.00	ref.	ref.	12	66	1.00	ref.	ref.	28	59	1.00	ref.	ref.	23	72	1.00	ref.	ref.	9	28	1.00	ref.	ref.	14	46	1.00	ref.	ref.
2-5 years	49	272	0.81	0.53	1.23	11	26	2.69	0.98	7.36	7	37	**0.26**	**0.10**	**0.68**	9	28	1.01	0.40	2.57	12	33	1.21	0.42	3.50	10	48	0.60	0.24	1.54
5-15 years	40	177	**0.59**	**0.38**	**0.92**	7	37	0.86	0.30	2.42	15	46	0.54	0.24	1.19	6	36	0.43	0.16	1.17	3	18	0.42	0.10	1.84	9	40	0.66	0.25	1.75
15+ years	61	265	**0.61**	**0.41**	**0.89**	13	66	0.90	0.37	2.17	17	50	0.57	0.26	1.24	16	79	0.54	0.26	1.13	4	25	0.40	0.11	1.52	11	45	0.74	0.29	1.87
Male	134	462	1.25	0.92	1.68	21	93	0.93	0.47	1.84	43	102	**2.00**	**1.09**	**3.69**	23	117	**0.53**	**0.28**	**0.99**	18	55	1.90	0.78	4.64	29	95	2.02	0.99	4.11
Race																														
Black	106	366	1.00	ref.	ref.	0	1	1.00	ref.	ref.	31	82	1.00	ref.	ref.	23	118	1.00	ref.	ref.	20	66	1.00	ref.	ref.	32	99	1.00	ref.	ref.
White	0	8	0.00	0.00	-	0	7	-	-	-	0	1	0.00	0.00	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Indigenous	9	44	0.63	0.29	1.36	2	5	-	-	-	1	1	Inf	-	Inf	1	8	0.59	0.07	5.04	0	1	0.00	0.00	-	5	29	0.44	0.15	1.25
Manaba	14	64	0.69	0.36	1.29	2	4	-	-	-	0	7	0.00	0.00	-	6	26	1.24	0.45	3.44	3	12	0.77	0.19	3.13	3	15	0.52	0.14	1.99
Mixed	107	392	0.92	0.67	1.26	39	168	-	-	-	35	100	0.89	0.48	1.63	24	63	**2.54**	**1.28**	**5.03**	5	25	0.58	0.19	1.75	4	36	**0.26**	**0.09**	**0.80**
Sociodemographics																														
Home ownership status																														
Owned	152	599	1.00	ref.	ref.	10	63	1.00	ref.	ref.	49	137	1.00	ref.	ref.	38	168	1.00	ref.	ref.	16	74	1.00	ref.	ref.	39	157	1.00	ref.	ref.
Rented	59	203	1.20	0.85	1.72	31	109	0.96	0.18	5.02	11	35	0.82	0.37	1.82	10	33	1.49	0.65	3.40	5	15	1.81	0.54	6.06	2	11	0.67	0.14	3.25
Loaned	25	72	1.56	0.93	2.63	2	13	2.11	0.95	4.66	7	20	0.97	0.36	2.58	6	13	2.93	0.93	9.25	7	15	3.17	1.00	10.07	3	11	1.13	0.29	4.49
Patient family receives bono	49	213	0.76	0.53	1.09	2	14	0.53	0.11	2.46	12	38	0.83	0.39	1.78	9	44	0.72	0.32	1.61	7	29	0.82	0.30	2.20	19	88	0.73	0.37	1.44
Family member holds a job	93	393	**0.73**	**0.54**	**0.99**	35	142	1.43	0.61	3.37	25	85	0.64	0.35	1.18	18	93	0.56	0.29	1.07	9	39	0.73	0.29	1.82	6	34	0.60	0.23	1.57
Highest level of education in Household																														
University	44	221	1.00	ref.	ref.	11	76	1.00	ref.	ref.	17	71	1.00	ref.	ref.	8	47	1.00	ref.	ref.	6	15	1.00	ref.	ref.	2	12	1.00	ref.	ref.
High School	149	527	**1.59**	**1.08**	**2.32**	27	87	**2.66**	**1.21**	**5.82**	41	106	**2.00**	**1.02**	**3.92**	42	154	1.83	0.79	4.23	16	76	0.40	0.12	1.29	23	104	1.42	0.29	6.94
Elementary	40	116	**2.12**	**1.28**	**3.51**	5	22	1.74	0.53	5.68	7	12	**4.45**	**1.25**	**15.84**	4	12	2.44	0.59	10.09	6	13	1.29	0.29	5.77	18	57	2.31	0.46	11.63
None	2	9	1.15	0.23	5.73	0	0	-	-	-	1	2	3.18	0.19	53.55	0	1	0.00	0.00	-	0	0	-	-	-	1	6	1.00	0.07	13.87
Live in Mining Community	12	52	0.94	0.45	1.99	-	-	-	-	-	-	-	-	-	-	0	1	0.00	0.00	-	-	-	-	-	-	12	51	0.92	0.43	1.98
Live in Palm farming Community	15	64	0.96	0.48	1.94	-	-	-	-	-	-	-	-	-	-	0	7	0.00	0.00	-	-	-	-	-	-	15	57	1.15	0.56	2.36
Patient employed in mining																														
Never	38	176	1.00	ref.	ref.	-	-	-	-	-	-	-	-	-	-	18	93	1.00	ref.	ref.	5	32	1.00	ref.	ref.	15	51	1.00	ref.	ref.
Formerly	0	2	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-	0	0	-	-	-	0	0	-	-	-	0	2	0.00	0.00	-
Currently	0	2	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-	0	1	0.00	0.00	-	0	0	-	-	-	0	1	0.00	0.00	-
Patient employed in palm industry																														
Never	33	157	1.00	ref.	ref.	-	-	-	-	-	-	-	-	-	-	15	77	1.00	ref.	ref.	5	30	1.00	ref.	ref.	13	50	1.00	ref.	ref.
Formerly	1	11	0.38	0.05	3.04	-	-	-	-	-	-	-	-	-	-	0	7	0.00	0.00	-	0	2	0.00	0.00	-	1	2	2.85	0.17	48.86
Currently	4	12	1.88	0.53	6.62	-	-	-	-	-	-	-	-	-	-	3	10	1.77	0.41	7.67	0	0	-	-	-	1	2	2.85	0.17	48.86
Child Day Care Attendance	26	89	0.91	0.54	1.54	0	9	0.00	0.00	-	4	11	0.91	0.24	3.37	4	19	0.52	0.16	1.74	5	10	2.54	0.63	10.25	13	40	1.71	0.63	4.62
Medical History																														
Rotavirus Vaccination Status																														
Received 1st Dose	33	106	1.36	0.34	5.34	10	35	0.40	0.05	3.24	11	24	Inf	-	Inf	4	15	0.73	0.05	10.39	4	10	Inf	-	Inf	4	22	Inf	-	Inf
Received 2nd Dose	27	86	1.07	0.37	3.08	9	32	0.78	0.06	9.74	10	21	1.82	0.14	23.25	3	11	1.13	0.08	15.51	1	4	0.33	0.02	5.33	4	18	Inf	-	Inf
Birth Description																														
Hospital - Vaginal Birth	143	533	1.00	ref.	ref.	28	111	1.00	ref.	ref.	32	94	1.00	ref.	ref.	36	150	1.00	ref.	ref.	20	64	1.00	ref.	ref.	27	114	1.00	ref.	ref.
Hospital - Cesarean Birth	43	132	1.32	0.87	1.99	7	42	0.59	0.24	1.48	24	52	1.66	0.83	3.32	5	16	1.44	0.47	4.42	5	15	1.10	0.33	3.64	2	7	1.29	0.24	7.03
Homebirth	40	158	0.92	0.62	1.39	8	30	1.08	0.43	2.69	5	22	0.57	0.19	1.69	13	45	1.29	0.61	2.71	2	21	0.23	0.05	1.09	12	40	1.38	0.62	3.08
Breastfeeding Practices																														
Exclusively	14	44	1.00	ref.	ref.	3	14	1.00	ref.	ref.	5	12	1.00	ref.	ref.	2	7	1.00	ref.	ref.	1	5	1.00	ref.	ref.	3	6	1.00	ref.	ref.
Mixed	33	112	0.90	0.42	1.90	8	34	1.13	0.25	5.07	9	22	0.81	0.22	2.90	8	25	1.18	0.19	7.42	3	10	1.71	0.13	22.51	5	21	0.32	0.05	2.07
Done breastfeeding	70	229	0.94	0.47	1.89	6	23	1.29	0.27	6.28	19	52	0.97	0.23	4.04	19	61	1.13	0.20	6.36	14	41	2.07	0.21	20.37	12	52	0.30	0.05	1.68
Never	0	1	0.00	0.00	-	0	1	0.00	0.00	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Animal Contact																														
Reported Animal Contact	94	369	0.87	0.64	1.18	22	98	0.91	0.46	1.80	29	85	0.94	0.52	1.71	23	89	1.07	0.57	1.99	10	40	0.85	0.35	2.09	10	57	0.54	0.25	1.20
Type of Animal Contact																														
Animal breeding	5	30	0.56	0.21	1.51	1	2	3.57	0.21	59.54	1	1	Inf	-	Inf	1	14	0.19	0.02	1.50	2	4	3.50	0.42	28.91	0	9	0.00	0.00	-
Animals in home	75	309	0.69	0.38	1.26	16	84	0.31	0.10	1.03	24	76	0.37	0.09	1.50	22	76	4.89	0.60	39.90	5	30	**0.20**	**0.04**	**0.96**	8	43	1.37	0.25	7.38
Animals around home	17	39	**2.54**	**1.28**	**5.02**	6	15	2.79	0.87	8.98	4	8	2.08	0.48	9.01	2	4	3.05	0.40	23.00	3	6	3.86	0.64	23.41	2	6	2.69	0.42	17.22
Animals Contacted																														
Cows	1	10	0.32	0.04	2.54	0	1	0.00	0.00	-	0	1	0.00	0.00	-	1	4	0.95	0.09	9.66	0	1	0.00	0.00	-	0	3	0.00	0.00	-
Production Chickens	12	60	0.69	0.35	1.37	3	10	1.56	0.37	6.60	2	3	4.07	0.35	46.94	2	20	0.25	0.05	1.19	2	11	0.58	0.10	3.31	3	16	1.12	0.25	5.00
Domestic Chickens	10	53	0.64	0.31	1.34	2	6	1.80	0.31	10.55	2	3	4.07	0.35	46.94	2	18	0.30	0.06	1.41	1	10	0.26	0.03	2.36	3	16	1.12	0.25	5.00
Pigs	7	37	0.66	0.28	1.55	0	3	0.00	0.00	-	1	1	Inf	-	Inf	5	18	1.13	0.35	3.62	1	5	0.72	0.07	7.34	0	10	0.00	0.00	-
Dogs	63	271	0.65	0.39	1.09	20	87	1.34	0.27	6.73	16	57	0.45	0.18	1.15	14	62	0.58	0.22	1.58	9	31	3.27	0.36	30.10	4	34	0.38	0.10	1.53
Cats	39	154	0.99	0.61	1.59	6	27	0.98	0.34	2.85	15	46	0.86	0.35	2.12	12	49	0.86	0.33	2.21	1	9	0.31	0.03	2.81	5	23	1.61	0.41	6.35
Wild Game	0	5	0.00	0.00	-	-	-	-	-	-	0	2	0.00	0.00	-	0	0	-	-	-	0	0	-	-	-	0	3	0.00	0.00	-
Rat	1	1	Inf	-	Inf	1	1	Inf	-	Inf	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Other	3	6	2.99	0.59	15.07	1	1	Inf	-	Inf	0	2	0.00	0.00	-	1	1	Inf	-	Inf	0	0	-	-	-	1	2	5.11	0.29	89.46

Table 10. (cont.) Unadjusted Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk of Any Pathogenic E. coli Infection among All Study Participants Stratified by Site, Ecuador, 2014-2015

	All Participants n=875*					Quito n=185					Esmeraldas n=192					Borbon-Borbon n=215					Borbon-Casas n=104					Rural River Communities n=179				
	E. Coli Positive N	Total N	OR	95% CI		E. Coli Positive N	Total N	OR	95% CI		E. Coli Positive N	Total N	OR	95% CI		E. Coli Positive N	Total N	OR	95% CI		E. Coli Positive N	Total N	OR	95% CI		E. Coli Positive N	Total N	OR	95% CI	
Water and Sanitation																														
Sanitation facility used during travel:																														
Improved Sanitation❖	5	38	1.00	ref.	ref.	3	18	1.00	ref.	ref.	1	7	1.00	ref.	ref.	0	5	1.00	ref.	ref.	1	3	1.00	ref.	ref.	0	5	1.00	ref.	ref.
Unimproved Sanitation❖❖	8	21	**4.06**	**1.12**	**14.73**	2	3	10.00	0.67	149.04	3	6	6.00	0.42	85.35	1	7	Inf	-	Inf	0	1	0.00	0.00	-	2	4	Inf	-	Inf
None	4	8	**6.60**	**1.24**	**35.23**	0	0	-	-	-	0	0	-	-	-	2	5	Inf	-	Inf	0	0	-	-	-	2	3	Inf	-	Inf
Sanitation facility used at home:																														
Improved Sanitation❖	140	562	1.00	ref.	ref.	38	152	1.00	ref.	ref.	42	134	1.00	ref.	ref.	29	128	1.00	ref.	ref.	16	73	1.00	ref.	ref.	15	75	1.00	ref.	ref.
Unimproved Sanitation❖❖	94	302	**1.36**	**1.00**	**1.86**	5	33	0.54	0.19	1.49	25	52	**2.03**	**1.05**	**3.90**	25	86	1.40	0.75	2.61	11	30	2.06	0.82	5.21	28	101	1.53	0.75	3.13
Mixed	2	6	1.51	0.27	8.32	0	0	-	-	-	0	1	0.00	0.00	-	0	1	0.00	0.00	-	1	1	Inf	-	Inf	1	3	2.00	0.17	23.56
Drinking water source during travel:																														
Improved water♐	17	67	1.00	ref.	ref.	5	21	1.00	ref.	ref.	4	13	1.00	ref.	ref.	3	17	1.00	ref.	ref.	1	4	1.00	ref.	ref.	4	12	1.00	ref.	ref.
Unimproved water♐♐	1	1	Inf	-	Inf	1	1	Inf	-	Inf	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Drinking water source at home:																														
Improved water♐	220	813	1.00	ref.	ref.	42	184	1.00	ref.	ref.	66	190	1.00	ref.	ref.	49	196	1.00	ref.	ref.	26	97	1.00	ref.	ref.	37	146	1.00	ref.	ref.
Unimproved water♐♐	8	37	0.74	0.33	1.65	1	1	Inf	-	Inf	0	1	0.00	0.00	-	5	16	1.36	0.45	4.12	2	6	1.37	0.24	7.90	0	13	**0.00**	**0.00**	**-**
Mixed	7	24	1.11	0.45	2.71	0	0	-	-	-	0	0	-	-	-	0	3	0.00	0.00	-	0	1	0.00	0.00	-	7	20	1.58	0.59	4.28
Treat water during travel	3	11	1.05	0.25	4.49	1	8	0.26	0.02	2.73	2	3	8.00	0.46	139.29	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-
Treat water at home	72	292	0.84	0.61	1.16	26	116	0.88	0.44	1.78	26	80	0.85	0.47	1.57	6	32	0.65	0.25	1.67	8	26	1.29	0.49	3.42	6	38	0.51	0.20	1.31
Travel																														
Reported Travel in past 12 months	117	439	0.97	0.72	1.30	16	42	**2.64**	**1.25**	**5.60**	22	60	1.12	0.59	2.12	38	162	0.71	0.36	1.41	16	62	0.87	0.36	2.09	25	113	0.70	0.35	1.41
Number of locations visited in the past 12 months																														
One destination	81	261	1.00	ref.	ref.	16	40	1.00	ref.	ref.	22	55	1.00	ref.	ref.	20	76	1.00	ref.	ref.	13	39	1.00	ref.	ref.	10	51	1.00	ref.	ref.
Two destinations	21	103	**0.57**	**0.33**	**0.98**	0	2	0.00	0.00	-	0	5	0.00	0.00	-	11	46	0.88	0.38	2.06	2	16	0.29	0.06	1.45	8	34	1.18	0.36	3.93
Three destinations	5	47	**0.26**	**0.10**	**0.69**	-	-	-	-	-	-	-	-	-	-	2	24	0.25	0.05	1.18	0	5	0.00	0.00	-	3	18	3.60	0.82	15.86
Four destinations	10	24	1.59	0.68	3.72	-	-	-	-	-	-	-	-	-	-	5	13	1.75	0.51	5.98	1	2	2.00	0.12	34.60	4	9	0.00	0.00	-
Five destinations	0	3	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-	0	2	0.00	0.00	-	-	-	-	-	-	0	1	-	-	-
Six destinations	0	1	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-	0	1	0.00	0.00	-	-	-	-	-	-	-	-	-	-	-
Destination Type**																														
Urban	78	278	1.00	ref.	ref.	7	14	1.00	ref.	ref.	16	50	1.00	ref.	ref.	26	94	1.00	ref.	ref.	12	41	1.00	ref.	ref.	17	79	1.00	ref.	ref.
Rural	14	80	1.25	0.71	2.20	9	26	0.53	0.14	1.99	6	9	4.25	0.94	19.20	3	15	0.65	0.17	2.51	4	12	1.21	0.31	4.78	1	8	0.52	0.06	4.53
Mixed	23	70	0.54	0.29	1.02	0	2	0.00	0.00	-	0	1	0.00	0.00	-	7	42	0.52	0.21	1.32	0	9	0.00	0.00	-	7	26	1.34	0.48	3.72
Reported Travel in the past month	9	48	0.65	0.30	1.41	-	-	-	-	-	-	-	-	-	-	5	30	0.55	0.19	1.60	3	12	0.98	0.24	4.05	1	6	0.55	0.07	4.94
Reported Travel in the past week	18	68	0.97	0.56	1.70	6	22	1.28	0.47	3.50	4	13	0.82	0.24	2.76	3	17	0.62	0.17	2.24	1	4	0.90	0.09	9.04	4	12	1.59	0.45	5.55

*Includes participants who provided a stool sample for pathogen testing and excludes participants reporting taken antibiotics within the past week
❖Improved sanitation includes: Personal latrines, septic tanks and pour-over flush
❖❖Unimproved sanitation includes: Community latrines, neighbor latrines, open field, hole in ground, river, diaper
♐Improved water includes: Tap inside, Tap outside, neighbor's tap, bottled water and rainwater
♐♐Unimproved water includes: River and well water
**Destination type is in relation to origin. (i.e. Esmeraldas is urban compared to a Borbon origin but Rural compared to a Quito origin)

Note: OR reference is to the absence of the stated variable unless otherwise specified

Table 11. Unadjusted Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk Factors of Pathogen-Specific Infection among All Study Participants, Ecuador, 2014-2015. Statistically significant results are shown in red.

	Rotavirus n = 877 | pos n = 64					DAEC n = 875 | pos n = 89				
	RV Positive N	**Total N**	**OR**	**95% CI**		**DAEC Positive N**	**Total N**	**OR**	**95% CI**	
Demographics										
Age										
<2 years	21	256	1.00	ref.	ref.	38	261	1.00	ref.	ref.
2-5 years	14	176	0.97	0.48	1.96	10	172	**0.36**	**0.17**	**0.75**
5-15 years	12	175	0.82	0.39	1.72	15	177	0.54	0.29	1.02
15+ years	17	270	0.75	0.39	1.46	26	265	0.64	0.38	1.09
Male	32	458	0.91	0.55	1.51	56	462	**1.59**	**1.01**	**2.50**
Race										
Black	21	362	1.00	ref.	ref.	35	366	1.00	ref.	ref.
White	1	8	2.32	0.27	19.74	0	8	0.00	0.00	-
Indigenous	5	47	1.93	0.69	5.40	3	44	0.69	0.20	2.35
Manaba	5	63	1.40	0.51	3.86	5	64	0.80	0.30	2.13
Mixed	32	396	1.43	0.81	2.52	46	392	1.26	0.79	2.00
Sociodemographics										
Home ownership status										
Owned	42	601	1.00	ref.	ref.	54	599	1.00	ref.	ref.
Rented	16	199	1.16	0.64	2.12	25	203	1.42	0.86	2.35
Loaned	6	76	1.14	0.47	2.78	10	72	1.63	0.79	3.36
Patient family receives bono	16	213	1.04	0.58	1.88	20	213	0.89	0.53	1.50
Family member holds a job	30	395	1.08	0.65	1.80	36	393	0.81	0.52	1.27
Highest level of education in Household										
University	17	222	1.00	ref.	ref.	21	221	1.00	ref.	ref.
High School	37	528	0.91	0.50	1.65	55	527	1.11	0.65	1.88
Elementary	9	116	1.01	0.44	2.35	11	116	1.00	0.46	2.15
None	0	9	0.00	0.00	-	1	9	1.19	0.14	9.99
Live in Mining Community	3	51	0.56	0.16	2.03	1	52	0.27	0.03	2.18
Live in Palm farming Community	6	63	1.11	0.40	3.09	4	64	1.24	0.35	4.39
Patient employed in mining										
Never	11	176	1.00	ref.	ref.	11	176	1.00	ref.	ref.
Formerly	1	2	15.00	0.88	256.28	0	2	0.00	0.00	-
Currently	0	2	0.00	0.00	-	0	2	0.00	0.00	-
Patient employed in palm industry										
Never	12	157	1.00	ref.	ref.	10	157	1.00	ref.	ref.
Formerly	0	11	0.00	0.00	-	0	11	0.00	0.00	-
Currently	0	12	0.00	0.00	-	1	12	1.34	0.16	11.42
Child Day Care Attendance	7	93	0.88	0.37	2.10	7	89	0.60	0.26	1.41
Medical History										
Rotavirus Vaccination Status										
Received 1st Dose	8	107	Inf	-	Inf	11	106	0.35	0.08	1.48
Received 2nd Dose	8	84	Inf	-	Inf	10	86	2.50	0.30	20.75
Birth Description										
Hospital - Vaginal Birth	42	535	1.00	ref.	ref.	46	533	1.00	ref.	ref.
Hospital - Cesarean Birth	9	132	0.86	0.41	1.81	22	132	**2.12**	**1.22**	**3.66**
Homebirth	8	157	0.63	0.29	1.37	15	158	1.11	0.60	2.05
Breastfeeding Practices										
Exclusively	2	48	1.00	ref.	ref.	7	44	1.00	ref.	ref.
Mixed	10	107	2.37	0.50	11.26	14	112	0.76	0.28	2.02
Done breastfeeding	20	228	2.21	0.50	9.80	23	229	0.59	0.24	1.47
Never	0	2	0.00	0.00	-	0	1	0.00	0.00	-
Animal Contact										
Reported Animal Contact	30	371	1.22	0.73	2.03	35	369	0.88	0.56	1.37
Type of Animal Contact										
Animal breeding	2	31	0.77	0.17	3.39	1	30	0.31	0.04	2.34
Animals in home	26	311	1.28	0.43	3.80	29	309	0.93	0.37	2.35
Animals around home	2	37	0.62	0.14	2.73	7	39	2.36	0.95	5.83
Animals Contacted										
Cows	0	10	0.00	0.00	-	0	10	0.00	0.00	-
Production Chickens	3	59	0.57	0.17	1.93	5	60	0.85	0.31	2.28
Domestic Chickens	3	52	0.55	0.19	2.27	5	53	0.99	0.37	2.69
Pigs	1	37	0.29	0.04	2.21	2	37	0.52	0.12	2.25
Dogs	25	274	1.85	0.69	4.97	21	271	0.50	0.25	1.04
Cats	14	153	1.27	0.60	2.69	16	154	1.20	0.59	2.41
Wild Game	0	4	0.00	0.00	-	0	5	0.00	0.00	-
Rat	0	1	0.00	0.00	-	0	1	0.00	0.00	-
Other	0	6	0.00	0.00	-	1	6	1.94	0.22	17.05

	Rotavirus n = 877 | pos n = 64					DAEC n = 875 | pos n = 89				
Water and Sanitation										
Sanitation facility used during travel:										
Improved Sanitation❖	2	37	1.00	ref.	ref.	2	38	1.00	ref.	ref.
Unimproved Sanitation❖❖	1	20	0.92	0.08	10.83	4	21	4.24	0.71	25.44
None	0	9	0.00	0.00	-	1	8	2.57	0.20	32.39
Sanitation facility used at home:										
Improved Sanitation❖	37	561	1.00	ref.	ref.	53	562	1.00	ref.	ref.
Unimproved Sanitation❖❖	27	310	1.35	0.81	2.27	35	302	1.26	0.80	1.98
Mixed	0	6	0.00	0.00	-	1	5	1.92	0.22	16.75
Drinking water source during travel:										
Improved water♐	3	66	1.00	ref.	ref.	6	67	1.00	ref.	ref.
Unimproved water♐♐	0	1	0.00	0.00	-	1	1	Inf	-	Inf
Drinking water source at home:										
Improved water♐	57	817	1.00	ref.	ref.	83	813	1.00	ref.	ref.
Unimproved water♐♐	5	36	2.15	0.81	5.74	3	37	0.78	0.23	2.58
Mixed	2	23	1.27	0.29	5.55	2	24	0.80	0.18	3.46
Treat water during travel	0	10	0.00	0.00	-	2	11	2.31	0.39	13.79
Treat water at home	20	290	0.91	0.53	1.58	32	292	1.16	0.73	1.83
Travel										
Reported Travel in past 12 months	35	433	1.26	0.75	2.10	39	439	0.75	0.48	1.17
Number of locations visited in the past 12 months										
One destination	23	256	1.00	ref.	ref.	29	261	1.00	ref.	ref.
Two destinations	10	102	1.10	0.50	2.40	5	103	0.41	0.15	1.09
Three destinations	1	46	0.23	0.03	1.71	3	47	0.54	0.16	1.87
Four destinations	1	25	0.42	0.05	3.26	2	24	0.73	0.16	3.25
Five destinations	0	3	0.00	0.00	-	0	3	0.00	0.00	-
Six destinations	0	1	0.00	0.00	-	0	1	0.00	0.00	-
Destination Type**										
Urban	23	280	1.00	ref.	ref.	27	278	1.00	ref.	ref.
Rural	5	65	0.93	0.34	2.55	8	70	1.20	0.52	2.77
Mixed	3	79	0.44	0.13	1.51	4	80	0.49	0.17	1.44
Reported Travel in the past month	1	48	0.23	0.03	1.72	1	48	0.38	0.05	2.95
Reported Travel in the past week	3	67	0.58	0.18	1.89	7	68	1.01	0.45	2.29

*Includes participants who provided a stool sample for pathogen testing and excludes participants reporting taken antibiotics within the past week
❖Improved sanitation includes: Personal latrines, septic tanks and pour-over flush
❖❖Unimproved sanitation includes: Community latrines, neighbor latrines, open field, hole in ground, river, diaper
♐Improved water includes: Tap inside, Tap outside, neighbor's tap, bottled water and rainwater
♐♐Unimproved water includes: River and well wate
**Destination type is in relation to origin. (i.e. Esmeraldas is urban compared to a Borbon origin but Rural compared to a Quito origin)

Note: OR reference is to the absence of the stated variable unless otherwise specified

DAEC and rotavirus infection detected, these risk factor analyses were not stratified by site. A summary of unadjusted odds ratios can be found in Table 11.

For DAEC cases, age was found to be a significant risk factor, and males had significantly higher rates of infection than females (OR: 1.59; 95% CI: 1.01, 2.50; $p = 0.04$). DAEC cases were also twice as likely to have been a cesarean birth (OR: 2.16; 95% CI: 1.22, 3.66; $p = 0.006$). No other associations were significant for DAEC cases and none of the listed risk factors were significantly associated with rotavirus.

Further analysis was conducted on the association between pathogen-specific diarrhea and specific travel patterns such as destination, duration, frequency and reason to determine if there were any additional relationships between travel and any pathogenic *E. coli* or DAEC infections. A summary of the findings is displayed in Table 12. The primary finding from this analysis was that cases of any pathogenic *E. coli* were significantly less likely to have reported travel to Esmeraldas in the past year (OR: 0.68; 95% CI: 0.46, 1.00; $p = 0.05$). No other significant associations were found between any pathogenic *E. coli* and travel history.

DAEC cases, on the other had, were twice as likely to have reported traveled to Guayaquil in the past year (OR: 2.07; 95% CI: 1.09, 3.95; $p = 0.02$). DAEC cases were also nearly 20 times more likely to have traveled to Quito more than 3 times in the past year (OR: 19.09; 95% CI: 2.07, 176.26; $p = 0.001$). Lastly, rotavirus cases were more than twice as likely to have reported traveling to Borbón in the past year (OR: 2.18; 95% CI: 1.14, 4.18; $p = 0.02$). No other significant associations were found between rotavirus infections and travel history.

Table 12. Unadjusted Estimated Exposure Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Travel Patterns associated with Pathogen-Specific Diarrheal Disease from a Case-Control Study in Ecuador, 2014 – 2015. Statistically significant results shown in red.

	Any Pathogenic E. Coli					DAEC					Rotavirus				
Travel Patterns	**E. Coli Positive N**	**Total N**	**OR**	**95% CI**		**DAEC Positive N**	**Total N**	**OR**	**95% CI**		**RV Positive N**	**Total N**	**OR**	**95% CI**	
Travel to Guayaquil	26	95	1.01	0.62	1.65	14	95	**2.07**	**1.09**	**3.95**	5	95	0.65	0.25	1.68
Annual Visit Frequency															
Less than 3 times per year	19	61	1.00	ref.	ref.	10	61	1.00	ref.	ref.	4	63	1.00	ref.	ref.
3 or more times per year	7	34	0.57	0.21	1.55	4	34	0.68	0.20	2.36	1	32	0.48	0.05	4.44
Duration of stay															
Less than 7 days	11	50	1.00	ref.	ref.	6	50	1.00	ref.	ref.	1	51	1.00	ref.	ref.
7 or more days	15	45	1.77	0.71	4.41	8	45	1.59	0.50	4.98	4	44	5.00	0.54	46.52
Reason															
Business[Ψ]	5	22	1.00	ref.	ref.	4	22	1.00	ref.	ref.	1	20	1.00	ref.	ref.
Leisure[θ]	18	68	1.22	0.39	3.80	7	68	0.52	0.14	1.96	4	70	1.15	0.12	10.92
Both	3	5	5.10	0.66	39.55	3	5	6.75	0.83	54.66	0	5	0.00	0.00	-
Travel to Quito	13	54	0.84	0.44	1.60	7	54	1.64	0.70	3.81	5	51	1.38	0.52	3.64
Annual Visit Frequency															
Less than 3 times per year	6	36	1.00	ref.	ref.	1	36	1.00	ref.	ref.	2	32	1.00	ref.	ref.
3 or more times per year	6	17	2.73	0.72	10.27	6	17	**19.09**	**2.07**	**176.26**	3	18	3.00	0.45	19.93
Duration of stay															
Less than 7 days	10	39	1.00	ref.	ref.	6	39	1.00	ref.	ref.	3	39	1.00	ref.	ref.
7 or more days	2	14	0.48	0.09	2.54	1	14	0.42	0.05	3.86	2	11	2.67	0.39	18.42
Reason															
Business[Ψ]	9	33	1.00	ref.	ref.	5	33	1.00	ref.	ref.	1	31	1.00	ref.	ref.
Leisure[θ]	3	18	0.53	0.12	2.29	2	18	0.70	0.12	4.03	3	17	6.43	0.61	67.43
Both	0	2	0.00	0.00	-	0	2	0.00	0.00	-	1	2	30.00	0.99	911.20
Travel to Santo Domingo	11	39	1.06	0.51	2.17	3	39	0.87	0.26	2.91	1	39	0.31	0.04	2.31
Annual Visit Frequency															
Less than 3 times per year	8	27	1.00	ref.	ref.	2	27	1.00	ref.	ref.	0	26	1.00	ref.	ref.
3 or more times per year	3	12	0.79	0.17	3.71	1	12	1.14	0.09	13.89	1	13	Inf	-	Inf
Duration of stay															
Less than 7 days	10	34	1.00	ref.	ref.	2	34	1.00	ref.	ref.	1	34	1.00	ref.	ref.
7 or more days	1	5	0.60	0.06	6.06	1	5	4.00	0.29	54.71	0	5	0.00	0.00	-
Reason															
Business[Ψ]	4	14	1.00	ref.	ref.	1	14	1.00	ref.	ref.	1	13	1.00	ref.	ref.
Leisure[θ]	7	24	1.03	0.24	4.41	2	24	1.18	0.10	14.35	0	24	0.00	0.00	-
Both	0	1	0.00	0.00	-	0	1	0.00	0.00	-	0	2	0.00	0.00	-
Travel to Esmeraldas	43	196	**0.68**	**0.46**	**1.00**	11	196	0.54	0.27	1.06	13	198	0.82	0.43	1.58
Annual Visit Frequency															
Less than 3 times per year	12	71	1.00	ref.	ref.	4	71	1.00	ref.	ref.	3	70	1.00	ref.	ref.
3 or more times per year	30	123	1.57	0.75	3.34	7	123	1.01	0.29	3.58	10	126	1.93	0.51	7.24
Duration of stay															
Less than 7 days	39	172	1.00	ref.	ref.	11	172	1.00	ref.	ref.	9	174	1.00	ref.	ref.
7 or more days	3	22	0.54	0.15	1.92	0	22	0.00	0.00	-	3	22	2.89	0.72	11.62
Reason															
Business[Ψ]	7	40	1.00	ref.	ref.	2	40	1.00	ref.	ref.	1	40	1.00	ref.	ref.
Leisure[θ]	25	123	1.20	0.48	3.04	8	123	1.32	0.27	6.50	10	125	3.39	0.42	27.35
Both	11	32	2.47	0.83	7.38	1	32	0.61	0.50	7.08	2	32	2.60	0.22	30.05
Travel to San Lorenzo	30	98	1.22	0.76	1.95	6	98	0.65	0.27	1.55	6	92	0.78	0.32	1.87
Annual Visit Frequency															
Less than 3 times per year	12	30	1.00	ref.	ref.	2	30	1.00	ref.	ref.	2	28	1.00	ref.	ref.
3 or more times per year	20	69	0.61	0.25	1.50	6	69	1.33	0.25	7.02	4	71	0.78	0.13	4.50
Duration of stay															
Less than 7 days	30	95	1.00	ref.	ref.	8	95	1.00	ref.	ref.	6	95	1.00	ref.	ref.
7 or more days	2	5	1.44	0.23	9.10	0	5	0.00	0.00	-	0	5	0.00	0.00	-
Reason															
Business[Ψ]	14	39	1.00	ref.	ref.	3	39	1.00	ref.	ref.	2	40	1.00	ref.	ref.
Leisure[θ]	16	50	0.84	0.35	2.03	4	50	1.04	0.22	4.96	4	49	1.69	0.29	9.73
Both	2	11	0.40	0.07	2.10	1	11	1.20	0.11	12.83	0	11	0.00	0.00	-
Travel to Borbon	22	99	0.75	0.46	1.24	5	99	0.44	0.17	1.12	13	98	**2.18**	**1.14**	**4.18**
Annual Visit Frequency															
Less than 3 times per year	6	26	1.00	ref.	ref.	1	26	1.00	ref.	ref.	3	23	1.00	ref.	ref.
3 or more times per year	16	73	0.94	0.32	2.72	4	73	1.45	0.15	13.59	10	75	1.03	0.26	4.09
Duration of stay															
Less than 7 days	21	97	1.00	ref.	ref.	4	97	1.00	ref.	ref.	13	97	1.00	ref.	ref.
7 or more days	1	2	3.62	0.22	60.33	1	2	**23.25**	**1.22**	**442.87**	0	1	0.00	0.00	-
Reason															
Business[Ψ]	13	58	1.00	ref.	ref.	3	58	1.00	ref.	ref.	7	56	1.00	ref.	ref.
Leisure[θ]	4	22	0.77	0.22	0.68	0	22	0.00	0.00	-	2	22	0.70	0.13	3.66
Both	5	19	1.24	0.37	4.08	2	19	2.16	0.33	13.99	4	20	1.75	0.45	6.76

Note: OR reference is to the absence of the stated variable unless otherwise specified
Ψ Business includes: Work, School, Medical Attention, to do paperwork, and general business
θ Leisure includes: Shopping, sports, visit family, religious motivation, festivals/parties, and vacation

Multivariate Analysis

The adjusted odds ratios of the multivariate models are presented in Table 13 – 16.

Table 13. Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Risk Factors associated with Diarrheal Disease from a Case-Control Study in Ecuador, 2014 – 2015. Statistically significant results shown in bold.

Diarrheal Disease					
	EXPOSURES	aOR	95% CI Lower Limit	95% CI Upper Limit	p-value
ALL SITES	**Male**	**1.28**	**1.00**	**1.64**	**0.05***
	Race: Indigenous	**2.90**	**1.52**	**5.56**	**0.001***
	Antibiotic Use past 7 days	2.37	0.97	5.80	0.06
	Birth: Hospital Cesearan	1.17	0.82	1.66	0.40
	Birth: Homebirth	1.33	0.94	1.90	0.11
	Breastfeeding: Mixed	1.70	0.92	3.14	0.09
	Breastfeeding: Done	1.58	0.89	2.79	0.12
	Breastfeeding: None	0.32	0.02	4.15	0.38
	Contact w/ Production Chickens	**0.49**	**0.28**	**0.85**	**0.01***
	Contact w/ Domestic Chickens	**0.47**	**0.26**	**0.86**	**0.01***
	Treatment of drinking water at home	0.77	0.59	1.01	0.06
	Travel in the past year	**1.36**	**1.05**	**1.77**	**0.02***
	Travel history to Guayaquil	0.84	0.55	1.27	0.40
	Travel history to Quito	**1.82**	**1.02**	**3.23**	**0.04***
	Travel history to Esmeraldas	1.07	0.77	1.48	0.70
	Travel history to Borbon	1.48	0.97	2.25	0.07
QUITO	**Breastfeeding: Mixed**	**3.74**	**1.37**	**11.01**	**0.01***
	Breastfeeding: Done	2.79	0.10	8.49	0.06
	Breastfeeding: None	0.00	NA	Inf	0.99
	Contact w/ Animals in the Home	**0.36**	**0.12**	**0.93**	**0.04***
	Treatment of drinking water at home	**0.58**	**0.34**	**0.97**	**0.04***
	Travel in the past year	0.85	0.46	1.60	0.62
ESM.	Antibiotic Use past 7 days	3.58	0.98	17.26	0.07
	Treatment of drinking water at home	**0.41**	**0.22**	**0.75**	**0.004***
	Travel in the past year	**2.53**	**1.36**	**4.81**	**0.004***
BORBON	**Animal contact**	**2.01**	**1.17**	**3.47**	**0.01***
	Contact w/ Production Chickens	NA	NA	NA	NA
	Contact w/ Domestic Chickens	NA	NA	NA	NA
	Treatment of drinking water at home	0.80	0.39	1.63	0.53
	Travel in the past year	1.30	0.72	2.37	0.39
CASAS	**Improved Sanitation at home**	**0.28**	**0.09**	**0.73**	**0.01***
	Treatment of drinking water at home	1.38	0.52	3.70	0.52
	Travel in the past year	1.29	0.55	3.08	0.57
RURAL	**Race: Indigenous**	**3.32**	**1.43**	**8.51**	**0.008***
	Contact w/ Cats	**9.21**	**2.63**	**38.84**	**0.001***
	Treatment of drinking water at home	1.71	0.84	3.61	0.14
	Travel in the past year	1.13	0.60	2.14	0.71

When evaluating all participants and controlling for confounders, diarrheal cases were more likely to be male, indigenous, report travel in the past year and report traveling to Quito in the past year. Contact with domestic and production chickens was protective against diarrhea, which may still be confounded by economic status not captured in this study. Within the Quito study site, cases were more likely to have received non-exclusive breastfeeding. Additionally, contact with animals around the home and treatment of drinking water at home were both protective against diarrheal disease. Among the Esmeraldas subset, diarrheal cases were more likely to report travel in the past year, on the other hand treatment of drinking water at home was again protective against diarrhea. In the Borbón study site, animal contact remained a risk factor for diarrheal disease. In the Casas study site, improved sanitation at home was protective against diarrheal. Lastly, in the rural study site, cases were more likely to be indigenous and report contact with cats.

Table 14. Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Risk Factors associated with Any Pathogenic *E. Coli* Infection from a Case-Control Study in Ecuador, 2014 – 2015. Statistically significant results shown in bold.

Any Pathogenic E. Coli					
	EXPOSURES	aOR	95% CI Lower Limit	95% CI Upper Limit	p-value
ALL SITES	Age: 2-5 years old	0.83	0.52	1.33	0.43
	Age: 5-15 years old	**0.57**	**0.34**	**0.96**	**0.03***
	Age: >15 years old	0.68	0.42	1.1	0.12
	Education: High School	**1.72**	**1.15**	**2.57**	**0.008***
	Education: Elementary	**2.92**	**1.64**	**5.18**	**0.0002***
	Education: None	1.57	0.3	8.31	0.59
	Government Welfare	**0.67**	**0.45**	**0.99**	**0.05***
	Contact w/ Animals around the Home	**2.5**	**1.18**	**5.31**	**0.02***
	Improved Sanitation during travel	**0.1**	**0.01**	**0.84**	**0.04***
	Improved Sanitation at home	0.88	0.59	1.32	0.55
	Travel in the past year	1.1	0.78	1.56	0.59
	Travel history to Guayaquil	1.06	0.61	1.86	0.83
	Travel history to Quito	0.98	0.46	2.1	0.96
	Travel history to Esmeraldas	**0.65**	**0.42**	**0.99**	**0.05***
	Travel history to Borbon	0.073	0.41	1.28	0.27

Mixed-effect models for pathogenic *E. coli* revealed that cases of *E. coli* were more likely to report high school or elementary as highest household education as well as contact with animals around the home. DEC cases were also less likely to be between the ages of 5 and 15 and receive government welfare. Improved sanitation during travel and travel to Esmeraldas were protective against any pathogenic *E. coli* infections.

Table 15. Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Risk Factors associated with DAEC infections from a Case-Control Study in Ecuador, 2014 – 2015. Statistically significant results shown in bold.

DAEC					
	EXPOSURES	aOR	95% CI Lower Limit	95% CI Upper Limit	p-value
ALL SITES	**Age: 2-5 years old**	**0.38**	**0.18**	**0.79**	**0.01***
	Age: 5-15 years old	**0.59**	**0.25**	**0.94**	**0.03***
	Age: >15 years old	0.7	0.4	1.22	0.21
	Male	1.55	0.97	2.48	0.07
	Birth: Hospital Cesearan	1.59	0.88	2.9	0.13
	Birth: Homebirth	1.25	0.63	2.46	0.52
	Travel in the past year	1.06	0.63	1.77	0.83
	Travel history to Guayaquil	1.75	0.86	3.56	0.12
	Travel history to Quito	1.07	0.41	2.82	0.88
	Travel history to Esmeraldas	0.63	0.28	1.45	0.28
	Travel history to Borbon	0.66	0.23	1.89	0.44

Mixed effect models for DAEC infections resulted in only age being predictive of DAEC cases. Children aged 2 to 15 were less likely to be cases compared to children less than 2 years old. Lastly, rotavirus cases were more likely to report having traveled to Borbón in the past year when controlling for age, sex, government assistance, and study site.

Table 16. Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for Risk Factors associated with rotavirus infections from a Case-Control Study in Ecuador, 2014 – 2015. Statistically significant results shown in bold.

Rotavirus					
	EXPOSURES	aOR	95% CI Lower Limit	95% CI Upper Limit	p-value
ALL SITES	Age: 2-5 years old	0.95	0.46	1.93	0.88
	Age: 5-15 years old	0.82	0.39	1.73	0.6
	Age: >15 years old	0.73	0.37	1.44	0.37
	Male	0.91	0.54	1.53	0.72
	Travel history to Borbon	**2.3**	**1.16**	**4.57**	**0.02***

Association between enteric infections and diarrheal diseases

The final analysis evaluated each enteric infection to determine if there was a significant association between a pathogenic infection and the development of diarrheal disease. All associations are summarized in Table 17 in the Appendix. Forest plots were created to better visualize the associations between pathogenic infections and diarrhea (Figure 8 and 9).

Figure 8. Pathogen-specific Associations with Diarrhea Across all participants. Assessment of odds ratios between different pathogenic infections and diarrheal disease.

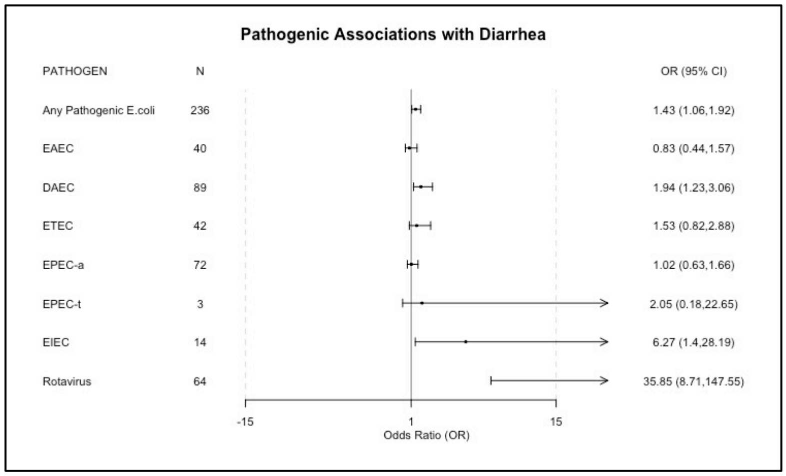
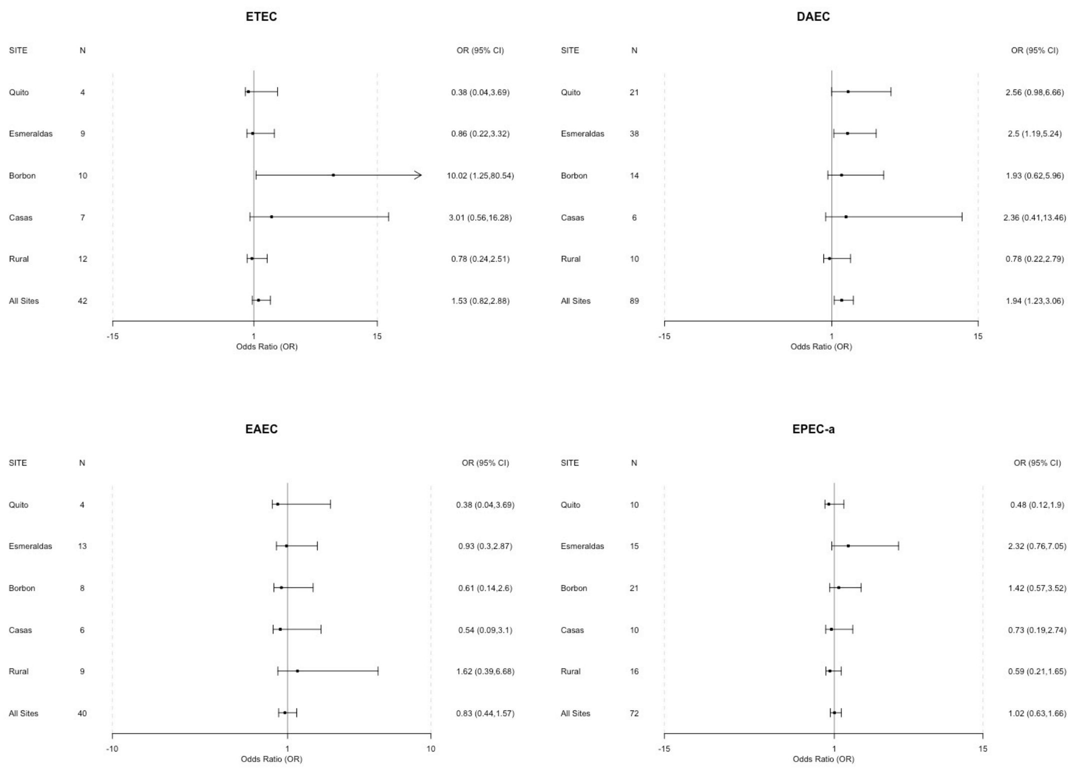


Figure 9. Site-Specific Pathogenic Associations with Diarrhea. EPEC-t and EIEC were excluded due to small sample sizes.



Based on this analysis, non-specific pathogenic *E. coli*, DAEC, EIEC, and rotavirus infections were all significantly associated with diarrheal disease. Nearly all EIEC infections across all sites exhibited diarrheal symptoms. Across the site, DAEC was associated with diarrhea in Quito and Esmeraldas but not in Borbón or the rural communities. On the other hand ETEC was associated with diarrhea in Borbón but not in the urban centers.

IV. DISCUSSION

Risk Factors for Diarrheal Diseases

In order to better understand diarrheal disease distribution in Ecuador, it is imperative to define the potential risk factors associated with the disease. The literature has pointed to unimproved water and sanitation, among others, as key contributors to diarrheal disease. Due to the high proportion (>90%) of participants using improved drinking water in this study, we were unable to detect any significant difference between improved and unimproved drinking water as a potential risk factor for diarrheal cases. Interestingly, treatment of drinking water was significantly protective against diarrheal cases in urban sites (Quito and Esmeraldas), even though 99.6% and 99.5%, respectively, of participants in these sites reported an improved drinking water source. When adjusting for confounding, cases from both sites were about 50% less likely to report treatment of their drinking water, highlighting this practice as an important protective factor against diarrheal diseases among these populations. The majority (98.2% in Quito and 96.6% in Esmeraldas) of participants reported boiling as their treatment method. On the other hand, sanitation practices in the home were more associated with the rural sites (Casas and rural communities). Analysis from both sites showed an elevated odds of being a diarrheal case for individuals with unimproved sanitation; however, only the Casas site showed sanitation to be a significant risk factor associated with diarrheal disease when controlling for confounding. Animal contact is also thought to be a risk factor for diarrheal disease and may pose as an indicator for hygienic practices. In this study, there were inconsistent finding across each site for the effect of animal contact on case development; however, diarrheal cases from Borbón had a significant association with animal contact. Cases were twice as like to report contact with animals, which means that animal contact may be regionally specific, especially with the differences in animal populations and access along the urban-rural gradient.

Other important risk factors identified in this analysis were sex, breastfeeding practices, contact with chicken, and race. Across all study participants, cases were about 1.3 times more likely to be male. As for breastfeeding practices, each individual site (excluding Borbón) and all sites combines showed an elevated odds of diarrhea among individuals who did not exclusively breastfeed. This association was only found to be significant for the Quito, but this points to the importance of exclusive breastfeeding of children. If a child is exclusively breastfed, than they have fewer opportunities to be exposed to enteric pathogens through food and water ingestion.

The associations made regarding race may be a result of selection bias in the study. This difference in race is most likely an artifact of recruitment in the rural river communities, where indigenous cases were age-matched with black. Furthermore, many controls in the rural communities were recruited from day care facilities by field clinicians, thus explaining why child day care attendance was seen as protective against diarrhea (OR: 0.39; 95% CI: 0.17, 0.92; *p*-value = 0.03). Additionally, contact with chickens may not be directly protective against diarrhea, but acting as an economic indicator that was not otherwise measured in this study. In rural settings, owning chickens is often a sign of wealth and it may be inferred that this association is driven by this phenomenon.

A key finding was that travel in the past year was significantly associated with diarrhea when looking at all participants, and particularly for subjects from Esmeraldas. Cases for Esmeraldas were more than twice as likely to have reported travel in the past year. Of those who reported traveling, the majority went to Quito and Guayaquil, the two more urban and heavily populated cities in Ecuador. An additional analysis showed that diarrheal cases were more than twice as likely to have reported traveling specifically to Quito in the past year. With this evidence, we can infer that diarrheal disease in Esmeraldas is associated with travel to the more urban region of Quito.

Risk Factors for Pathogen-Specific Diarrhea

For pathogen-specific diarrhea, we wanted to assess if there were any differences or stronger associations with specific risk factors than there were with just general diarrhea. Again no significant association could be made regarding improved water due to the low proportion of the population reporting use of unimproved drinking water sources. Water treatment at home was seen to be protective across all study sites in the bivariate analysis but was not significantly associated with reduced pathogenic *E. coli* infections in multivariate analysis. Improved sanitation on the other hand was significantly associated with a protective affect against pathogenic *E. coli*. More specifically, among all participants use of improved sanitation during travel was found to be significantly associated with reduced odds of being infected with pathogenic *E. coli*. Controls were 90% more likely to report using improved sanitation during travel compared to cases. Furthermore, sanitation practice at home showed that the use of unimproved sanitation within each individual study site (except Quito) was associated with higher odds of diarrheal disease in bivariate analysis, but these findings were not found to be significant when controlling for other factors in the multivariate analysis.

Other risk factors from pathogen-specific diarrhea include age, education, economic status, and animal contact around the home. Participants under the age of two had a high risk of infection with any diarrheagenic *E. coli* than participants between the ages of 2 and 15. This is consistent with previous literature that specified young children and infants as being at higher risk for these infections [18, 20]. Participants who reported the highest household education to be university level were less likely to have pathogenic *E. coli* infections than those with only high school or elementary education. This speaks to the importance of community education beyond a structured setting. If higher educated individuals have a better understanding of risky behaviors associated with diarrheagenic *E. coli* infections than this highlights the importance of hygiene education during primary and secondary school. Education may also be associated with economic status. However, the direct influence of economic status on diarrheal disease and pathogen-specific infections is still unclear from our study. Those reporting collection of government welfare were less likely to be infected with any *E. coli*. This can mean one of two things. One is that the very poor are not receiving proper government support and thus feeding into a higher risk for pathogenic diarrhea. Or two, those receiving support are economically more well off and able to provide clean and safe food and water to their families to prevent transmission of diarrheagenic *E. coli* infections.

One of the most interesting findings was the linkage between specific enteric infections and travel. Bivariate analysis revealed that *E. coli* cases from Quito were more than 2.5 times more likely to have reported travel in the past year. Although this was not validated with our models for any pathogenic *E. coli* since low samples sizes inhibited stratification by site, this is still of importance since a majority of persons traveling from Quito report going to Guayaquil, which is a more urban area. This again speaks to the trend of urban centers being the source of diarrheal diseases. Especially since DAEC infections were highly associated (in bivariate analysis) with travel to Guayaquil and with the development of diarrheal disease. We also found that travel to Esmeraldas was protective against pathogen-specific diarrhea, which is mostly driven by Borbón and other rural communities who frequent this city most. It is unclear as to why Esmeraldas is protective against diarrheal; however, it is likely related to improved living conditions compared to the more rural communities. We expected rural travel to Esmeraldas to be risk factor for pathogen-specific diarrhea especially with the clear difference in DAEC distribution across the two locations.

Our investigation unexpectedly found a strong association between rotavirus and travel history to Borbón. Rotavirus cases were more than twice as likely to have reported travel to

Borbón in the past year. This is may be due to higher incidence of rotavirus infections in Borbón, or lower vaccination coverage in Borbón, however further investigation is required.

Pathogen-Specific Associations with Diarrheal Disease

As expected, rotavirus was significantly associated with diarrheal disease across the board. The *E. coli* pathotypes commonly associated with diarrhea are ETEC, DAEC, EIEC and atypical EPEC. Among all participants DAEC and EIEC were significantly associated with diarrheal disease. More interesting was looking at which pathogens were more likely to cause diarrheal disease across the different study locations. DAEC was significantly associated with diarrheal disease in the urban sites of Quito and Esmeraldas but not in the more rural sites, whereas ETEC was significantly associated with diarrhea only in the rural site of Borbón. This is important because these are also the pathotypes that dominate in these regions, and highlights regional difference in pathogen-specific diarrhea. It is important to note that these relationships are limited by sample size, with only few cases of EPEC-t and sparse distribution of others among sites for comparison.

Strengths and Weaknesses

This study is one of the first to assess within-country travel as a risk factor for diarrheal disease and a driver for enteric pathogen distribution within a country. Most studies that assess travel and diarrheal disease focus on international travel and traveler's diarrhea. However, we were able to assess in country travel at four different study locations within Ecuador, along an urban-rural gradient, which allowed us to not only assess risk factor differenced among study site but also allowed us to capture how travel patterns may be influencing the spread of diarrheagenic *E. coli*. Furthermore, this study is able to build off of previous studies such as GEMS to highlight the pathogenic distribution associated with diarrheal diseases in a Latin American country. GEMS also identified enteric infection variability between countries, and our study emphasis that this variability also exists within country.

Limitations

Using a case-control study, we can only estimate risk and are more susceptible to selection bias. In addition our survey relied on patient travel recall, which is also subject to recall bias. Beyond bias, some of our results for pathogen-specific diarrhea were limited by samples size and thus the inability to stratify the data by site that may point to additional links to pathogenic diarrhea.

The generalizability of this study is limited to Latin American countries with a similar in country urban and rural gradient since enteric pathogens vary regionally. Moreover, because pathogen distribution is highly dependent upon environmental suitability and regional diversity, the specific distribution of *E. coli* pathotypes found along this urban-rural gradient may not be applicable to other countries.

For the purpose of this study, we focused on pathogenic *E.coli* as a specific cause of diarrheal disease, however there are multiple enteric pathogens, including viruses and parasites, that may influence diarrheal disease in other regions of study. The pathogen-specific risk factors highlighted in this study are more related to diarrheagenic *E. coli* and rotavirus, and may not reflect diarrheal caused by parasitic or other viral infections. However, despite these limitations, it is important to conduct region specific diarrheal risk factor analysis in order to add to the global understanding of diarrhea disease presentation and associations.

Future Direction

The future goal for this project is to take this risk factor analysis and link it to whole genome sequencing and metagenomic analysis of each specific pathogenic isolate collected from study participants to further understand pathogenic *E. coli* distribution along this urban-rural gradient in Ecuador. The assessment of travel will provide evidence for the linkage between the different pathogens across each study site. This is a novel approach to understanding and explaining the impact of human movement on diarrheal disease and pathogen-specific diarrhea.

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VI. APPENDIX. Supplemental Tables and Figures

Table 4. Characteristics of all participants, by site Ecuador, 2014 – 2015 (Full Table)

			Urban	-------------	-------------	-------------	**> Rural**		
	N	All Participants n=1042	Quito n=263	Esmeraldas n=223	Borbon-Borbon n=245	Borbon-Casas n=109	Rural River Communities n=202	p-value*	Interpretation
		n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**		
Cases	1042	555 (53.3)	137 (52.1)	111 (49.8)	134 (54.7)	53 (48.6)	120 (59.4)	0.25	No significant difference across site
Demographics									
Age	1042								
<2 years		335 (32.1)	93 (35.4)	74 (33.2)	85 (34.7)	29 (26.6)	54 (26.7)		There is a significant difference in the distribution of age with Quito and Esmeraldas having a greater percent of participants <2 years old
2-5 years		207 (19.9)	39 (14.8)	43 (19.3)	34 (13.9)	34 (31.2)	57 (28.2)	<0.001	
5-15 years		198 (19.0)	46 (17.5)	49 (22.0)	43 (17.6)	18 (16.5)	42 (20.8)		
15+ years		302 (29.0)	85 (32.3)	57 (25.6)	83 (33.9)	28 (25.7)	49 (24.3)		
Male	1042	555 (53.3)	130 (49.4)	125 (56.1)	133 (54.3)	59 (54.1)	108 (53.5)	0.66	No significant difference across site
Race	1041								
White		9 (0.9)	8 (3.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)		Significant differences in race distribution across site. With Urban loacation have greater proportion of mixed race individuals and rural communities having greater indigenous population.
Indigenous		54 (5.2)	5 (1.9)	1 (0.5)	10 (4.1)	1 (0.9)	37 (18.3)		
Black		408 (39.2)	3 (1.1)	93 (41.9)	134 (54.7)	70 (64.2)	108 (53.5)	<0.001	
Manaba		66 (6.3)	4 (1.5)	8 (3.6)	27 (11.0)	12 (11.0)	15 (7.4)		
Mixed		504 (48.4)	243 (92.4)	119 (53.6)	74 (30.2)	26 (23.9)	42 (20.8)		
Sociodemographics									
Home ownership status	1041								Significant difference in home ownership across site. Rural communities have more ownership and urban areas have greater rental opportunities
Owned		695 (66.8)	86 (32.7)	160 (71.7)	193 (79.1)	78 (71.6)	178 (88.1)	<0.001	
Rented		253 (24.3)	152 (57.8)	38 (17.0)	36 (14.8)	16 (14.7)	11 (5.4)		
Loaned		93 (8.9)	25 (9.5)	25 (11.2)	15 (6.1)	15 (13.8)	13 (6.4)		
Items owned by the family	552								
Land/Farm		310 (56.2)	-	-	102 (42.3)	37 (33.9)	171 (84.7)	<0.001	Among the more rural communities there are differences in the items owned by each family. With the less rural communities having more access to technology and more rural communities having greater access to personal land, livestock and canoes.
Canoe		113 (20.5)	-	-	18 (7.5)	2 (1.8)	93 (46.0)	<0.001	
Livestock		35 (6.3)	-	-	12 (5.0)	4 (3.7)	19 (9.4)	0.07	
Business		52 (9.4)	-	-	31 (12.9)	13 (11.9)	8 (4.0)	0.004	
Motorcycle		75 (13.6)	-	-	47 (19.5)	16 (14.7)	12 (5.9)	<0.001	
Cellphone		369 (66.8)	-	-	216 (89.6)	77 (70.6)	76 (37.6)	<0.001	
None of these items		49 (8.9)	-	-	20 (8.3)	22 (20.2)	7 (3.5)	<0.001	
Patient family receives bono	1042								As the study site becomes more rural, the proportion of families receiving bono increases.
Yes		243 (23.3)	15 (5.7)	44 (19.7)	56 (22.9)	31 (28.4)	97 (48.0)	<0.001	
No		799 (76.7)	248 (94.3)	179 (80.3)	189 (77.1)	78 (71.6)	105 (52.0)		
Family member holds a job	1040								As the study site becomes more rural, the proportion of families holding jobs decreases.
Yes		485 (46.6)	203 (77.2)	97 (43.5)	105 (43.2)	41 (37.6)	39 (19.3)	<0.001	
No		555 (53.4)	60 (22.8)	126 (56.5)	138 (56.8)	68 (62.4)	163 (80.7)		
Highest level of education in Household	1040								
None		11 (1.1)	1 (0.4)	3 (1.4)	1 (0.4)	0 (0.0)	6 (3.0)		As the study site becomes more rural, fewer families have individuals holding university level education
Elementary		137 (13.2)	30 (11.4)	15 (6.8)	15 (6.1)	15 (13.8)	62 (30.7)	<0.001	
High School		624 (60.0)	130 (49.4)	117 (52.7)	179 (73.4)	78 (71.6)	120 (59.4)		
University		268 (25.8)	102 (38.8)	87 (39.2)	49 (20.1)	16 (14.7)	14 (6.9)		

	N	All Participants n=1042	Quito n=263	Esmeraldas n=223	Borbon-Borbon n=245	Borbon-Casas n=109	Rural River Communities n=202	p-value*	Interpretation
			Urban	------------------	------------------	------------------	**--> Rural**		
		n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**		
Live in Mining Community	229								
Yes		55 (24.0)	-	-	1 (3.7)	-	54 (26.7)	0.007	The rural river communities have a greater porportion of individuals living in mining communities
No		174 (76.0)	-	-	26 (96.3)	-	148 (73.3)		
Live in Palm farming Community	228								
Yes		75 (32.9)	-	-	10 (37.0)	-	65 (32.3)	0.79	No significant difference across site
No		153 (67.1)	-	-	17 (63.0)	-	136 (67.7)		
Patient employed in mining	195								
Currently		2 (1.0)	-	-	1 (1.0)	0 (0.0)	1 (1.7)	0.28	No significant difference across site
Formerly		2 (1.0)	-	-	0 (0.0)	0 (0.0)	2 (3.4)		
Never		191 (97.9)	-	-	101 (99.0)	35 (100.0)	55 (94.8)		
Patient employed in palm industry	195								
Currently		13 (6.7)	-	-	10 (9.8)	1 (2.9)	2 (3.4)	0.45	No significant difference across site
Formerly		11 (5.6)	-	-	7 (6.9)	2 (5.7)	2 (3.4)		
Never		171 (87.7)	-	-	85 (83.3)	32 (91.4)	54 (93.1)		
Child Day Care Attendance	496								
Yes		112 (22.6)	15 (12.3)	19 (17.8)	25 (22.5)	10 (17.2)	43 (43.9)	<0.001	As the study site becomes more rural, a greater proportion of paricipants use child daycare
No		384 (77.4)	107 (87.7)	88 (82.2)	86 (77.5)	48 (82.8)	55 (56.1)		
Medical History									
Antibiotics Taken in Past 7 Days	1042								
Yes		26 (2.5)	10 (3.8)	14 (6.3)	2 (0.8)	0 (0.0)	0 (0.0)	<0.001	Urban sites have a greater use of anitbiotics which may be point to greater medical access
No		1016 (97.5)	253 (96.2)	209 (93.7)	243 (99.2)	109 (100.0)	202 (100.0)		
Rotavirus Vaccination Status									
Received 1st Dose	160	140 (87.5)	57 (86.4)	29 (85.3)	20 (87.0)	11 (91.7)	23 (92.0)	0.96	No significant difference across site
Received 2nd Dose	140	116 (82.9)	52 (91.2)	26 (89.7)	15 (75.0)	5 (45.5)	18 (78.3)	0.005	
Birth Description	986								
Homebirth		179 (18.2)	35 (13.4)	25 (12.8)	49 (20.3)	21 (20.0)	49 (26.8)		
Hospital - Vaginal Birth		639 (64.8)	163 (62.5)	109 (55.6)	174 (72.2)	67 (63.8)	126 (68.9)	<0.001	Rural site have a greater proportion of homebirths which may speak to medical accessibility in addition to local customs.
Hospital - Cesarean Birth		168 (17.0)	63 (24.1)	62 (31.6)	18 (7.5)	17 (16.2)	8 (4.4)		
Breastfeeding Practices	494								
Never		4 (0.8)	3 (2.5)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)		
Done breastfeeding		285 (57.7)	39 (32.0)	66 (61.7)	73 (65.8)	43 (74.1)	64 (66.7)	<0.001	There is a significant difference in breastfeeding practices across sites.
Mixed		140 (28.3)	52 (42.6)	24 (22.4)	30 (27.0)	10 (17.2)	24 (25.0)		
Exclusively		65 (13.2)	28 (23.0)	16 (15.0)	8 (7.2)	5 (8.6)	8 (8.3)		
Duration of diarrheal episode	555								
<2 days		117 (21.1)	51 (37.2)	17 (15.3)	21 (15.7)	9 (17.0)	19 (15.8)		
2-5 days		364 (65.6)	73 (53.3)	68 (61.3)	106 (79.1)	43 (81.1)	74 (61.7)	<0.001	There is a significant difference in duration of diarrheal episodes across sites.
> 5 days		74 (13.3)	13 (9.5)	26 (23.4)	7 (5.2)	1 (1.9)	27 (22.5)		
Recent Bowel Movements	555								
Watery		480 (86.5)	123 (89.8)	105 (94.6)	127 (94.8)	38 (71.7)	87 (72.5)	<0.001	There is a significant difference in stool characteristics across sites.
Mucousy		247 (44.5)	43 (31.4)	68 (61.3)	35 (26.1)	28 (52.8)	73 (60.8)	<0.001	
Bloody		24 (4.3)	2 (1.5)	10 (9.0)	7 (5.2)	2 (3.8)	3 (2.5)	0.05	

	N	All Participants n=1042	Quito n=263	Esmeraldas n=223	Borbon-Borbon n=245	Borbon-Casas n=109	Rural River Communities n=202	p-value*	Interpretation
		Urban ---> Rural							
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		
Animal Contact									
Reported Animal Contact	1040								
Yes		453 (43.6)	147 (55.9)	101 (45.5)	100 (40.8)	41 (37.6)	64 (31.8)	<0.001	As the study site becomes more rural, animal contact decreases.
No		587 (56.4)	116 (44.1)	121 (54.5)	145 (59.2)	68 (62.4)	137 (68.2)		
Type of Animal Contact	453								
Animal breeding		35 (7.7)	3 (2.0)	1 (1.0)	16 (16.0)	4 (9.8)	11 (17.2)	<0.001	There is a significant difference in the proportion of animal breeding contact and animal contact around the home.
Animals in home		376 (83.0)	122 (83.0)	90 (89.1)	85 (85.0)	31 (75.6)	48 (75.0)	0.11	
Animals around home		50 (11.0)	25 (17.0)	9 (8.9)	4 (4.0)	6 (14.6)	6 (9.4)	0.02	
Other		1 (0.2)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.68	
Animals Contacted	453								
Cows		10 (2.2)	1 (0.7)	1 (1.0)	4 (4.0)	1 (2.4)	3 (4.7)	0.16	
Production Chickens		65 (14.3)	12 (8.2)	3 (3.0)	22 (22.0)	11 (26.8)	17 (26.6)	<0.001	There is a significant difference in the proportion of chickens, pigs, dogs and cats contacted across the different sites.
Domestic Chickens		56 (12.4)	7 (4.8)	3 (3.0)	19 (19.0)	10 (24.4)	17 (26.6)	<0.001	
Pigs		40 (8.8)	3 (2.0)	1 (1.0)	20 (20.0)	5 (12.2)	11 (17.2)	<0.001	
Dogs		336 (74.2)	129 (87.8)	68 (67.3)	68 (68.0)	32 (78.0)	39 (60.9)	<0.001	
Cats		184 (40.6)	38 (25.9)	52 (51.5)	56 (56.0)	10 (24.4)	28 (43.8)	<0.001	
Wild Game		5 (1.1)	0 (0.0)	2 (2.0)	0 (0.0)	0 (0.0)	3 (4.7)	0.02	
Rat		1 (0.2)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.00	
Other		9 (2.0)	4 (2.7)	2 (2.0)	1 (1.0)	0 (0.0)	2 (3.1)	0.80	
Water and Sanitation									
Sanitation facility used during travel:	81								
Improved Sanitation[❖]		45 (55.6)	24 (82.8)	8 (50.0)	5 (27.8)	3 (60.0)	5 (38.5)	0.002	There is a significant difference across site in those that used improved sanitation during travel.
Community Latrine		4 (4.9)	1 (3.4)	0 (0.0)	1 (5.6)	1 (20.0)	1 (7.7)	0.35	
Hole in ground		3 (3.7)	0 (0.0)	0 (0.0)	2 (11.1)	0 (0.0)	1 (7.7)	0.19	
Open Field		3 (3.7)	0 (0.0)	2 (12.5)	1 (5.6)	0 (0.0)	0 (0.0)	0.24	
Diaper		16 (19.8)	4 (13.8)	6 (37.5)	4 (22.2)	0 (0.0)	2 (15.4)	0.33	
None		10 (12.3)	0 (0.0)	0 (0.0)	5 (27.8)	1 (20.0)	4 (30.8)	0.001	
Sanitation facility used at home:	1037								
Improved Sanitation[❖]		671 (64.7)	206 (78.3)	152 (69.7)	150 (61.2)	78 (71.6)	85 (42.1)	<0.001	There is a significant difference across site in those that used improved sanitation at home. With rural communities having smaller proportion of participants using improved sanitation.
Community Latrine		6 (0.6)	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)	4 (2.0)	0.06	
Neighbor's Latrine		12 (1.2)	0 (0.0)	0 (0.0)	5 (2.0)	3 (2.8)	4 (2.0)	0.03	
Hole in ground		78 (7.5)	0 (0.0)	1 (0.5)	26 (10.6)	4 (3.7)	47 (23.3)	<0.001	
Open Field		17 (1.6)	1 (0.4)	0 (0.0)	3 (1.2)	0 (0.0)	13 (6.4)	<0.001	
River		2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0.08	
Diaper		257 (24.8)	56 (21.3)	65 (29.8)	61 (24.9)	25 (22.9)	50 (24.8)	0.30	

		Urban ---				> Rural		
	N	All Participants n=1042	Quito n=263	Esmeraldas n=223	Borbon-Borbon n=245	Borbon-Casas n=109	Rural River Communities n=202	p-value*	Interpretation
		n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**		
Drinking water source during travel:	81								There is a significant difference across site in those that used improved water during travel. With rural communities having smaller proportion of participants using
Improved water⚦		79 (97.5)	28 (96.6)	15 (93.8)	18 (100.0)	5 (100.0)	13 (100.0)	<0.001	
River		2 (2.5)	1 (3.4)	1 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.84	
Drinking water source at home:	1040								
Improved water⚦		998 (96.0)	262 (99.6)	220 (99.5)	226 (92.2)	103 (94.5)	187 (92.6)	<0.001	There is a significant difference across site in the source of drinking water used in the home
Well water		32 (3.1)	0 (0.0)	0 (0.0)	17 (6.9)	6 (5.5)	9 (4.5)	<0.001	
River		34 (3.3)	1 (0.4)	1 (0.5)	5 (2.0)	1 (0.9)	26 (12.9)	<0.001	
Treat water during travel:	81								
Yes		15 (18.5)	11 (37.9)	4 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.002	There is a significant difference across site in whether or not participants treat their drinking water when they travel
No		66 (81.5)	18 (62.1)	12 (75.0)	18 (100.0)	5 (100.0)	13 (100.0)		
Water Treatment during travel:	15								
Boiled		15 (100.0)	11 (100.0)	4 (100.0)	-	-	-	-	
Chlorine		-	-	-	-	-	-		
Filter		-	-	-	-	-	-		No significant difference
UV		-	-	-	-	-	-		
Larvicide		-	-	-	-	-	-		
Settling techniques		-	-	-	-	-	-		
Treat water at home:	1039								
Yes		365 (35.1)	169 (64.3)	87 (39.4)	39 (16.0)	26 (23.9)	44 (21.8)	<0.001	There is a significant difference across site in whether or not participants treat their drinking water at home.
No		674 (64.9)	94 (35.7)	134 (60.6)	205 (84.0)	83 (76.1)	158 (78.2)		
Water Treatment at home:	363								
Boiled		321 (88.4)	165 (98.2)	84 (96.6)	26 (66.7)	19 (73.1)	27 (62.8)	<0.001	
Chlorine		32 (8.8)	0 (0.0)	0 (0.0)	13 (33.3)	5 (19.2)	14 (32.6)	<0.001	There is a significant difference in treatment type across site with Urban sites relying more on boiling and rural sites relying multiple methods.
Filter		7 (1.9)	3 (1.8)	2 (2.3)	0 (0.0)	1 (3.8)	1 (2.3)	0.85	
UV		-	-	-	-	-	-		
Larvicide		6 (1.7)	0 (0.0)	1 (1.1)	2 (5.1)	1 (3.8)	2 (4.7)	0.06	
Settling techniques		-	-	-	-	-	-		
Travel									
Reported Travel in past 12 months	1042	485 (46.5)	53 (20.2)	66 (29.6)	178 (72.7)	63 (57.8)	125 (61.9)	<0.001	Significant difference in travel across site
Reported Travel in the past month	311	50 (16.1)	-	-	32 (25.0)	12 (14.3)	6 (6.1)	<0.001	Significant difference in travel across site
Reported Travel in the past week	1042	82 (7.9)	30 (11.4)	16 (7.2)	18 (7.3)	5 (4.6)	13 (6.4)	0.14	No significant difference across site

*Pearson's Chi-Squared or Fisher's exact test was used to test whether the distribution of each characteristic differs across groups

❖Improved sanitation includes: Personal latrines, septic tanks and pour-over flush

⚦Improved water includes: Tap inside, Tap outside, neighbor's tap, bottled water and rainwater

Table 6. Unadjusted Estimated Exposure Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk of Diarrheal Disease among Children <5 from a Case-Control Study in Ecuador, 2014 – 2015

	All Participants n = 542					Quito n = 132				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Demographics										
Age										
<2 years	184	335	1.00	ref.	ref.	47	93	1.00	ref.	ref.
2-5 years	108	207	0.90	0.63	1.27	20	39	1.03	0.49	2.18
Male	171	303	1.26	0.90	1.78	39	75	1.12	0.56	2.23
Race										
Black	98	202	1.00	ref.	ref.	2	2	1.00	ref.	ref.
White	2	3	2.12	0.19	23.78	2	2	-	-	-
Indigenous	20	27	**3.03**	**1.23**	**7.49**	0	0	-	-	-
Manaba	16	31	1.13	0.53	2.41	2	2	-	-	-
Mixed	156	278	1.36	0.94	1.95	61	126	0.00	0.00	-
Sociodemographics										
Home ownership status										
Owned	185	343	1.00	ref.	ref.	22	38	1.00	ref.	ref.
Rented	69	138	0.85	0.58	1.27	36	78	0.62	0.28	1.36
Loaned	38	61	1.41	0.81	2.47	9	16	0.94	0.29	3.04
Patient family receives bono	60	116	0.90	0.59	1.35	0	2	0.00	0.00	-
Family member holds a job	123	235	0.90	0.64	1.26	54	104	1.24	0.54	2.88
Highest level of education in Household										
University	68	133	1.00	ref.	ref.	22	51	1.00	ref.	ref.
High School	187	340	1.17	0.78	1.75	40	73	1.60	0.77	3.29
Elementary	37	66	1.22	0.67	2.21	5	8	2.20	0.47	10.20
None	0	3	0.00	0.00	-	0	0	-	-	-
Live in Mining Community	11	25	**0.34**	**0.14**	**0.83**	-	-	-	-	-
Live in Palm farming Community	24	39	0.81	0.37	1.78	-	-	-	-	-
Child Day Care Attendance	61	112	1.00	0.65	1.52	9	15	1.53	0.51	4.59
Medical History										
Antibiotics Taken in Past 7 Days	10	14	2.18	0.68	7.04	3	4	3.00	0.30	29.61
Rotavirus Vaccination Status										
Received 1st Dose	69	137	1.27	0.47	3.41	28	54	3.77	0.72	19.82
Received 2nd Dose	54	113	0.55	0.22	1.36	24	29	0.24	0.03	2.30
Birth Description										
Hospital - Vaginal Birth	200	369	1.00	ref.	ref.	42	87	1.00	ref.	ref.
Hospital - Cesarean Birth	68	125	1.01	0.67	1.51	23	43	1.23	0.59	2.56
Homebirth	24	48	0.85	0.46	1.54	2	2	Inf	-	Inf
Breastfeeding Practices										
Exclusively	28	65	1.00	ref.	ref.	9	28	1.00	ref.	ref.
Mixed	81	140	1.18	1.00	3.29	31	52	**3.12**	**1.18**	**8.20**
Done breastfeeding	159	284	1.68	0.98	2.90	21	39	2.46	0.89	6.78
Never	1	4	0.44	0.04	4.46	1	3	1.05	0.08	13.23
Animal Contact										
Reported Animal Contact	125	214	1.36	0.96	1.93	36	70	1.06	0.53	2.10
Type of Animal Contact										
Animal breeding	1	4	0.23	0.02	2.26	0	1	0.00	0.00	-
Animals in home	106	181	1.04	0.49	2.21	26	55	0.45	0.14	1.48
Animals around home	19	32	1.05	0.49	2.25	10	16	1.79	0.57	5.64
Animals Contacted										
Cows	0	1	0.00	0.00	-	0	1	0.00	0.00	-
Production Chickens	1	13	**0.05**	**0.01**	**0.41**	0	6	**0.00**	**0.00**	**-**
Domestic Chickens	0	9	**0.00**	**0.00**	**-**	0	3	0.00	0.00	-
Pigs	3	5	1.07	0.18	6.54	0	1	0.00	0.00	-
Dogs	95	163	0.98	0.52	1.85	32	61	1.38	0.34	5.64
Cats	65	104	1.39	0.80	2.40	8	18	0.69	0.23	2.01
Wild Game	2	2	Inf	-	Inf	0	0	-	-	-
Other	0	2	0.00	0.00	-	0	2	0.00	0.00	-

	Esmeraldas n = 117					Borbon-Borbon n = 119				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Demographics										
Age										
<2 years	38	74	1.00	ref.	ref.	77	155	1.00	ref.	ref.
2-5 years	19	43	0.75	0.35	1.60	34	76	0.82	0.47	1.42
Male	32	66	0.99	0.47	2.03	63	129	1.07	0.64	1.81
Race										
Black	16	42	1.00	ref.	ref.	16	40	1.00	ref.	ref.
White	0	1	0.00	0.00	-	2	3	3.00	0.25	35.91
Indigenous	0	0	-	-	-	0	0	-	-	-
Manaba	0	0	-	-	-	2	2	Inf	-	Inf
Mixed	41	73	2.08	0.96	4.52	91	185	1.45	0.72	2.91
Sociodemographics										
Home ownership status										
Owned	35	81	1.00	ref.	ref.	48	106	1.00	ref.	ref.
Rented	15	23	2.46	0.94	6.46	47	96	1.16	0.67	2.02
Loaned	7	13	1.53	0.47	4.97	16	29	1.49	0.65	3.40
Patient family receives bono	9	20	0.84	0.32	2.20	4	17	**0.31**	**0.10**	**0.97**
Family member holds a job	24	48	1.09	0.52	2.28	74	144	1.43	0.84	2.44
Highest level of education in Household										
University	27	49	1.00	ref.	ref.	43	92	1.00	ref.	ref.
High School	27	60	0.67	0.31	1.42	60	124	1.07	0.62	1.83
Elementary	3	6	0.81	0.15	4.44	8	14	1.52	0.49	4.73
None	0	2	0.00	0.00	-	0	1	0.00	0.00	-
Live in Mining Community	-	-	-	-	-	0	0	-	-	-
Live in Palm farming Community	-	-	-	-	-	0	0	-	-	-
Child Day Care Attendance	10	19	1.22	0.45	3.28	17	31	1.37	0.63	2.95
Medical History										
Antibiotics Taken in Past 7 Days	7	9	4.06	0.81	20.44	10	13	**3.86**	**1.03**	**14.42**
Rotavirus Vaccination Status										
Received 1st Dose	13	29	0.81	0.10	6.58	37	88	1.80	0.50	6.49
Received 2nd Dose	11	26	0.37	0.03	4.57	31	70	0.26	0.05	1.41
Birth Description										
Hospital - Vaginal Birth	32	66	1.00	ref.	ref.	61	137	1.00	ref.	ref.
Hospital - Cesarean Birth	24	46	1.16	0.55	2.46	47	87	1.46	0.85	2.51
Homebirth	1	5	0.27	0.03	2.50	3	7	0.93	0.20	4.33
Breastfeeding Practices										
Exclusively	7	16	1.00	ref.	ref.	16	43	1.00	ref.	ref.
Mixed	14	24	1.80	0.50	6.46	42	73	**2.29**	**1.05**	**4.95**
Done breastfeeding	31	66	1.14	0.38	3.42	43	92	1.48	0.71	3.11
Never	0	1	0.00	0.00	-	1	4	0.56	0.05	5.88
Animal Contact										
Reported Animal Contact	33	53	**2.87**	**1.35**	**6.11**	57	111	1.31	0.78	2.21
Type of Animal Contact										
Animal breeding	0	0	-	-	-	0	1	0.00	0.00 -	
Animals in home	25	44	0.16	0.02	1.43	41	89	**0.32**	**0.11**	**0.89**
Animals around home	7	8	5.12	0.58	45.13	7	22	2.40	0.89	6.45
Animals Contacted										
Cows	0	0	-	-	-	0	1	0.00	0.00 -	
Production Chickens	0	2	0.00	0.00	-	0	8	**0.00**	**0.00 -**	
Domestic Chickens	0	2	0.00	0.00	-	0	5	**0.00**	**0.00 -**	
Pigs	0	0	-	-	-	0	1	0.00	0.00 -	
Dogs	22	36	0.86	0.26	2.84	47	90	1.20	0.46	3.11
Cats	18	28	1.20	0.39	3.65	18	38	0.78	0.36	1.72
Wild Game	1	1	Inf	-	Inf	0	0	-	-	-
Other	0	0	-	-	-	0	2	0.00	0.00	-

	Borbon-Casas n = 63					Rural River Communities n = 111				
	Cases N	Total N	OR	95% CI		Cases N	Total N	OR	95% CI	
Demographics										
Age										
<2 years	37	74	1.00	ref.	ref.	70	106	1.00	ref.	ref.
2-5 years	21	35	1.50	0.66	3.39	53	96	0.63	0.36	1.12
Male	34	57	1.72	0.81	3.69	74	117	1.26	0.71	2.24
Race										
Black	24	51	1.00	ref.	ref.	58	111	1.00	ref.	ref.
White	0	0	-	-	-	0	0	-	-	-
Indigenous	1	3	0.56	0.05	6.60	19	24	**3.47**	**1.21**	**9.96**
Manaba	4	7	1.50	0.30	7.39	22	22	0.76	0.30	1.91
Mixed	29	48	1.72	0.77	3.81	36	45	**3.66**	**1.61**	**8.30**
Sociodemographics										
Home ownership status										
Owned	42	82	1.00	ref.	ref.	95	155	1.00	ref.	ref.
Rented	11	21	1.05	0.40	2.74	11	21	0.69	0.28	1.74
Loaned	5	6	4.76	0.53	42.56	17	26	1.19	0.50	2.85
Patient family receives bono	14	29	0.76	0.33	1.79	42	70	0.94	0.52	1.71
Family member holds a job	20	43	0.64	0.30	1.39	29	48	0.97	0.50	1.89
Highest level of education in Household										
University	15	25	1.00	ref.	ref.	10	16	1.00	ref.	ref.
High School	39	76	0.70	0.28	1.76	88	140	1.02	0.35	2.96
Elementary	4	6	1.33	0.20	8.71	25	46	0.71	0.22	2.29
None	0	2	0.00	0.00	-	0	0	-	-	-
Live in Mining Community	-	-	-	-	-	10	24	**0.29**	**0.12**	**0.74**
Live in Palm farming Community	-	-	-	-	-	23	38	0.75	0.34	1.67
Child Day Care Attendance	9	18	0.87	0.32	2.46	35	63	0.61	0.33	1.14
Medical History										
Antibiotics Taken in Past 7 Days	0	1	0.00	0.00	-	0	0	-	-	-
Rotavirus Vaccination Status										
Received 1st Dose	7	20	0.27	0.02	3.52	25	29	0.89	0.07	10.75
Received 2nd Dose	7	17	Inf	-	Inf	16	26	0.71	0.17	2.94
Birth Description										
Hospital - Vaginal Birth	51	91	1.00	ref.	ref.	88	141	1.00	ref.	ref.
Hospital - Cesarean Birth	7	14	0.78	0.25	2.42	14	24	0.84	0.35	2.03
Homebirth	0	4	0.00	0.00 -		21	37	0.79	0.38	1.65
Breastfeeding Practices										
Exclusively	5	7	1.00	ref.	ref.	7	15	1.00	ref.	ref.
Mixed	11	25	0.31	0.05	1.94	28	42	2.29	0.69	7.59
Done breastfeeding	37	69	0.46	0.08	2.55	79	123	2.05	0.70	6.04
Never	0	0	-	-	-	0	0	-	-	-
Animal Contact										
Reported Animal Contact	31	41	**4.71**	**1.99**	**11.15**	37	62	0.93	0.50	1.71
Type of Animal Contact										
Animal breeding	0	0	-	-	-	1	3	0.32	0.03	3.73
Animals in home	29	37	3.63	0.44	29.91	36	55	**11.37**	**1.27**	**101.45**
Animals around home	2	4	0.28	0.03	2.28	2	6	0.30	0.05	1.78
Animals Contacted										
Cows	0	0	-	-	-	0	0	-	-	-
Production Chickens	1	3	0.13	0.01	1.66	0	2	0.00	0.00	-
Domestic Chickens	0	2	0.00	0.00 -		0	2	0.00	0.00	-
Pigs	2	2	Inf	-	Inf	1	2	0.67	0.04	11.18
Dogs	21	29	0.53	0.09	2.94	27	44	1.27	0.42	3.86
Cats	21	29	0.53	0.09	2.94	26	37	**3.01**	**1.04**	**8.67**
Wild Game	1	1	Inf	-	Inf	1	0	Inf	-	Inf
Other	0	0	-	-	-	0	0	-	-	-

Table 6. (Cont.) Unadjusted Estimated Exposure Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Risk of Diarrheal Disease among Children <5 from a Case-Control Study in Ecuador, 2014 – 2015

Water and Sanitation																														
Sanitation facility used during travel:																														
Improved Sanitation❖	3	9	1.00	ref.	ref.	3	6	1.00	ref.	ref.	0	1	1.00	ref.	ref.	3	7	1.00	ref.	ref.	0	0	1.00	ref.	ref.	0	2	1.00	ref.	ref.
Unimproved Sanitation❖❖	9	17	2.25	0.42	12.09	1	4	0.33	0.02	5.33	5	7	Inf	-	Inf	6	10	2.00	0.28	14.20	0	4	-	-	-	3	3	Inf	-	Inf
None	2	3	4.00	0.25	63.95	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	2	3	Inf	-	Inf
Sanitation facility used at home:																														
Improved Sanitation❖	121	229	1.00	ref.	ref.	39	75	1.00	ref.	ref.	22	47	1.00	ref.	ref.	55	110	1.00	ref.	ref.	25	39	1.00	ref.	ref.	41	80	1.00	ref.	ref.
Unimproved Sanitation❖❖	165	304	1.06	0.75	1.49	28	57	0.89	0.45	1.78	30	65	0.97	0.46	2.07	56	120	0.88	0.52	1.47	28	64	**0.44**	**0.19**	**0.99**	81	120	**1.98**	**1.10**	**3.53**
Mixed	1	4	0.30	0.03	2.90	0	0	-	-	-	0	0	-	-	-	0	1	0.00	0.00	-	0	1	0.00	0.00	-	1	2	0.95	0.06	15.74
Drinking water source during travel:																														
Improved water♐	13	27	1.00	ref.	ref.	3	9	1.00	ref.	ref.	5	7	1.00	ref.	ref.	8	15	1.00	ref.	ref.	0	1	1.00	ref.	ref.	5	8	1.00	ref.	ref.
Unimproved water♐♐	0	1	0.00	0.00	-	0	0	-	-	-	0	1	0.00	0.00	-	0	1	0.00	0.00	-	0	3	-	-	-	0	0	-	-	-
Drinking water source at home:																														
Improved water♐	273	509	1.00	ref.	ref.	67	132	1.00	ref.	ref.	56	116	1.00	ref.	ref.	110	230	1.00	ref.	ref.	56	104	1.00	ref.	ref.	107	175	1.00	ref.	ref.
Unimproved water♐♐	14	21	1.73	0.69	4.36	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	2	4	0.86	0.12	6.32	12	17	1.52	0.51	4.52
Mixed	4	11	0.49	0.14	1.71	0	0	-	-	-	0	0	-	-	-	0	0	-	-	-	0	1	0.00	0.00	-	4	10	0.42	0.12	1.56
Treat water during travel	1	6	0.17	0.02	1.67	0	3	0.00	0.00	-	1	3	0.13	0.00	3.22	1	5	0.14	0.01	1.76	0	1	-	-	-	0	0	-	-	-
Treat water at home	105	203	0.88	0.62	1.24	43	92	0.59	0.28	1.24	26	55	0.93	0.45	1.92	62	139	0.72	0.42	1.23	15	20	**3.21**	**1.07**	**9.59**	28	44	1.16	0.58	2.32
Travel																														
Reported Travel in past 12 months	128	214	**1.49**	**1.05**	**2.11**	15	29	1.05	0.46	2.40	19	29	**2.50**	**1.04**	**5.99**	25	51	1.42	0.76	2.66	34	58	1.59	0.75	3.40	66	105	1.19	0.67	2.09
Number of locations visited in the past 12 months																														
One destination	90	153	1.00	ref.	ref.	14	28	1.00	ref.	ref.	18	27	1.00	ref.	ref.	27	49	1.00	ref.	ref.	23	42	1.00	ref.	ref.	40	62	1.00	ref.	ref.
Two destinations	29	45	1.27	0.64	2.53	1	1	Inf	-	Inf	1	2	0.50	0.03	8.95	1	2	0.81	0.05	13.79	8	11	2.20	0.51	9.48	20	32	0.92	0.38	2.22
Three destinations	4	10	0.47	0.13	1.72	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	0.40	0.03	4.91	3	7	0.41	0.08	2.01
Four destinations	5	6	3.50	0.40	30.69	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	2	Inf	-	Inf	3	4	1.65	0.16	16.83
Destination Type*																														
Urban	82	139	1.00	ref.	ref.	3	9	1.00	ref.	ref.	16	23	1.00	ref.	ref.	14	27	1.00	ref.	ref.	25	44	1.00	ref.	ref.	43	68	1.00	ref.	ref.
Rural	29	48	1.06	0.54	2.07	11	19	2.75	0.52	14.44	3	6	0.44	0.07	2.73	13	23	1.21	0.39	3.69	6	9	1.52	0.34	6.87	10	16	0.97	0.31	2.99
Mixed	10	20	0.70	0.27	1.78	1	1	Inf	-	Inf	0	0	-	-	-	1	1	Inf	-	Inf	2	4	0.76	0.10	5.90	7	15	0.51	0.16	1.57
Reported Travel in the past month	7	11	1.43	0.40	5.11	-	-	-	-	-	-	-	-	-	-	0	0	-	-	-	3	3	Inf	-	Inf	4	8	0.81	0.19	3.42
Reported Travel in the past week	14	29	0.79	0.37	1.67	4	10	0.62	0.17	2.32	5	8	1.82	0.42	8.02	9	17	1.24	0.46	3.32	0	4	**0.00**	**0.00**	**-**	5	8	1.07	0.25	4.62

Note: OR reference is to the absence of the stated variable unless otherwise specified
❖Improved sanitation includes: Personal latrines, community latrines, neighbor latrines, septic tanks and pour-over flush
❖❖Unimproved sanitation includes: Open field, hole in ground, river, diaper
♐Improved water includes: Tap inside, Tap outside, neighbor's tap, and rainwater
♐♐Unimproved water includes: River, well water, purchased water
*Destination type is in relation to origin. (i.e. Esmeraldas is urban compared to a Borbon origin but Rural compared to a Quito origin)

Table 9. Unadjusted Estimated Exposure Odds Ratios (OR) and 95% Confidence Inte (CI) for Travel Patterns Associated with Diarrheal Disease from a Case-Control Study Ecuador, 2014 – 2015

Travel Patterns	All Participants Cases N	 Total N	 OR	 95% CI	
Travel to Guayaquil	53	105	0.81	0.54	1.22
Annual Visit Frequency					
Less than 3 times per year	35	70	1.00	ref.	ref.
3 or more times per year	18	35	1.06	0.47	2.38
Duration of stay					
Less than 7 days	27	56	1.00	ref.	ref.
7 or more days	26	49	1.21	0.56	2.62
Reason					
Business[Ψ]	13	22	1.00	ref.	ref.
Leisure[θ]	38	78	0.66	0.26	1.72
Both	2	5	0.46	0.06	3.35
Travel to Quito	40	59	**1.80**	**1.02**	**3.17**
Annual Visit Frequency					
Less than 3 times per year	25	39	1.00	ref.	ref.
3 or more times per year	14	19	1.57	0.47	5.27
Duration of stay					
Less than 7 days	29	44	1.00	ref.	ref.
7 or more days	10	14	1.29	0.35	4.82
Reason					
Business[Ψ]	26	37	1.00	ref.	ref.
Leisure[θ]	12	19	0.73	0.23	2.33
Both	1	2	0.42	0.02	7.39
Travel to Santo Domingo	20	45	0.64	0.35	1.17
Annual Visit Frequency					
Less than 3 times per year	16	31	1.00	ref.	ref.
3 or more times per year	4	14	0.38	0.10	1.46
Duration of stay					
Less than 7 days	15	37	1.00	ref.	ref.
7 or more days	5	8	2.44	0.51	11.80
Reason					
Business[Ψ]	6	14	1.00	ref.	ref.
Leisure[θ]	13	29	1.08	0.30	3.92
Both	1	2	1.33	0.07	25.91
Travel to Esmeraldas	117	213	1.00	0.73	1.37
Annual Visit Frequency					
Less than 3 times per year	41	77	1.00	ref.	ref.
3 or more times per year	75	134	1.12	0.64	1.96
Duration of stay					
Less than 7 days	99	186	1.00	ref.	ref.
7 or more days	17	25	1.87	0.77	4.54
Reason					
Business[Ψ]	20	43	1.00	ref.	ref.
Leisure[θ]	71	134	1.46	0.73	2.91
Both	22	35	1.95	0.78	4.84
Travel to San Lorenzo	59	106	1.03	0.68	1.56
Annual Visit Frequency					
Less than 3 times per year	17	33	1.00	ref.	ref.
3 or more times per year	44	75	1.34	0.59	3.04
Duration of stay					
Less than 7 days	60	104	1.00	ref.	ref.
7 or more days	1	5	0.18	0.02	1.70
Reason					
Business[Ψ]	25	44	1.00	ref.	ref.
Leisure[θ]	32	54	1.11	0.49	2.48
Both	4	11	0.43	0.11	1.70
Travel to Borbon	70	112	**1.53**	**1.02**	**2.29**
Annual Visit Frequency					
Less than 3 times per year	19	27	1.00	ref.	ref.
3 or more times per year	51	85	0.63	0.25	1.61
Duration of stay					
Less than 7 days	68	110	1.00	ref.	ref.
7 or more days	2	2	Inf	-	Inf
Reason					
Business[Ψ]	44	63	1.00	ref.	ref.
Leisure[θ]	9	22	**0.30**	**0.11**	**0.82**
Both	17	27	0.73	0.28	1.90
Travel to Rural Communities	64	118	0.95	0.64	1.44
Annual Visit Frequency					
Less than 3 times per year					
3 or more times per year					
Duration of stay					
Less than 7 days					
7 or more days					
Reason					
Business[Ψ]					
Leisure[θ]					
Both					

Note: OR reference is to the absence of the stated variable unless otherwise specified
Ψ Business includes: Work, School, Medical Attention, to do paperwork, and general business
θ Leisure includes: Shopping, sports, visit family, religious motivation, festivals/parties, and vacation

Table 17. Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Association between Diarrheal Disease and Pathogenic *E. coli* or Rotavirus infection among All Study Participants, Ecuador, 2014 – 2015

Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	95% CI Lower Limit	95% CI Upper Limit	p-value
Any Pathogenic E. Coli						
Quito	23 (26.7)	20 (20.2)	1.44	0.73	2.86	0.29
Esmeraldas	41 (44.6)	26 (26.0)	2.29	1.25	4.2	0.007
Borbon-Borbon	33 (31.1)	21 (19.3)	1.89	1.01	3.55	0.04
Borbon-Casas	14 (28.6)	14 (25.5)	1.17	0.49	2.79	0.72
River communities	21 (0.65)	23 (29.1)	0.65	0.33	1.28	0.23
All sites combined	132 (30.5)	104 (0.24)	1.43	1.06	1.92	0.02
Enteroaggregative E. coli (aggr)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	1 (1.2)	3 (3.0)	0.38	0.04	3.69	0.62
Esmeraldas	6 (6.5)	7 (7.0)	0.93	0.30	2.87	0.90
Borbon-Borbon	3 (2.8)	5 (4.6)	0.61	0.14	2.60	0.72
Borbon-Casas	2 (4.1)	4 (7.3)	0.54	0.09	3.10	0.68
River communities	6 (6.0)	3 (3.8)	1.62	0.39	6.68	0.73
All sites combined	18 (4.2)	22 (5.0)	0.83	0.44	1.57	0.56
Diffusely adherente E. coli (afa)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	14 (16.3)	7 (7.1)	2.56	0.98	6.66	0.05
Esmeraldas	25 (27.2)	13 (13.0)	2.50	1.19	5.24	0.01
Borbon-Borbon	9 (8.5)	5 (4.6)	1.93	0.62	5.96	0.28
Borbon-Casas	4 (8.2)	2 (3.6)	2.36	0.41	13.46	0.42
River communities	5 (5.0)	5 (6.3)	0.78	0.22	2.79	0.75
All sites combined	57 (13.2)	32 (7.2)	1.94	1.23	3.06	0.004
Enterotoxigenic E. coli (lt or sta)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	1 (1.2)	3 (3.0)	0.38	0.04	3.69	0.62
Esmeraldas	4 (4.3)	5 (5.0)	0.86	0.22	3.32	1.00
Borbon-Borbon	9 (8.5)	1 (0.9)	10.02	1.25	80.54	0.009
Borbon-Casas	5 (10.2)	2 (3.6)	3.01	0.56	16.28	0.25
River communities	6 (6.0)	6 (7.6)	0.78	0.24	2.51	0.77
All sites combined	25 (5.8)	17 (3.8)	1.53	0.82	2.88	0.21
Atypical Enteropathogenic E. Coli (eaeA)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	3 (3.5)	7 (7.1)	0.48	0.12	1.9	0.34
Esmeraldas	10 (10.9)	5 (5.0)	2.32	0.76	7.05	0.18
Borbon-Borbon	12 (11.3)	9 (8.3)	1.42	0.57	3.52	0.50
Borbon-Casas	4 (8.2)	6 (10.9)	0.73	0.19	2.74	0.75
River communities	7 (7.0)	9 (11.4)	0.59	0.21	1.65	0.43
All sites combined	36 (8.3)	36 (8.1)	1.02	0.63	1.66	0.93
Typical Enteropathogenic E. Coli (bfp)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	0 (0.0)	0 (0.00)	-	-	-	-
Esmeraldas	1 (1.1)	0 (0.00)	Inf	-	-	0.48
Borbon-Borbon	0 (0.0)	1 (0.9)	0	0	0	1.00
Borbon-Casas	0 (0.0)	0 (0.00)	-	-	-	-
River communities	1 (1.0)	0 (0.0)	Inf	-	Inf	1.00
All sites combined	2 (0.5)	1 (0.2)	2.05	0.18	22.65	0.62
Enteroinvasive E. coli (ipaH)						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	4 (4.7)	0 (0.0)	Inf	-	Inf	0.04
Esmeraldas	2 (2.2)	0 (0.0)	Inf	-	Inf	0.23
Borbon-Borbon	5 (4.7)	1 (0.9)	5.35	0.61	46.55	0.12
Borbon-Casas	0 (0.0)	1 (1.8)	0.00	0.00	-	1.00
River communities	1 (1.0)	0 (0.0)	Inf	Inf	-	1.00
All sites combined	12 (2.8)	2 (0.5)	6.27	1.4	28.19	0.006
Rotavirus						
Study Site	Cases Infected n (%)	Controls Infected n (%)	OR	Lower Limit	Upper Limit	p-value
Quito	14 (15.1)	0 (0.0)	Inf	-	Inf	<0.001
Esmeraldas	11 (0.13)	1 (1.0)	13.86	1.75	1.09	0.001
Borbon-Borbon	18 (17.0)	0 (0.0)	Inf	-	Inf	<0.001
Borbon-Casas	7 (13.7)	0 (0.0)	Inf	-	Inf	0.004
River communities	12 (11.9)	1 (1.3)	10.65	1.35	83.77	0.006
All sites combined	62 (14.1)	2 (0.5)	35.85	8.71	147.55	<0.001