Diarrheal Disease Risk Associated with Village-level Mass Gatherings in Rural Coastal Ecuador

Author
Morris, Christina D

Publication Date
2017-10-01

Diarrheal Disease Risk Associated with Village-level Mass Gatherings in Rural Coastal Ecuador

by

Christina Decker Morris

A thesis submitted in partial satisfaction of the

Requirements for the degree of

Master of Science

in

Health and Medical Sciences

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Ndola Prata, Co-Chair
Justin Remais, Co-Chair
John Swartzberg

Fall 2017

Acknowledgements

Thesis Committee: Ndola Prata, Justin Remais, John Swartzberg
Remais Lab: Phillip Collender, Christopher Hoover, Rosie Glenn-Finer
Statistics consultation: Howard Chang, Alan Hubbard
Thesis working group: Josh Pepper, Wilson Ly, Daniel Morberg
Field research team: Denis David Tenorio Castillo, Mauricio Ayovi, Liliana Requené
After-hours R help / moral support: Stephanie Gogarten, Jan Overgoor, Daniel Greene

Table of Contents

1: Literature Review

Introduction

Despite impressive progress at reducing morbidity and mortality from infectious diarrheal disease, it remains one of the top causes of child mortality, and the fourth leading cause of disability adjusted life years (DALYs) lost among all age groups worldwide.[1,2] Infectious diarrhea, as defined by the World Health Organization (WHO), is three or more loose stools in a 24-hour period, and can be caused by a wide variety of viral, bacterial, and protozoal pathogens.[3] A recent meta-analysis of diarrheal disease epidemiology research reviewed a large body of literature identifying transmission pathways and interventions. It then called for a deeper understanding of the ecological and social drivers of diarrheal disease, while considering the interdependence of multiple pathways and risk factors. [4]

In the rural, coastal province of Esmeraldas, Ecuador, a long-term study documents diarrheal disease incidence alongside socioeconomic, social network, temperature, and rainfall data. A number of insights have emerged from this work, including the important role of social connection and movement, and the significant variation in diarrheal disease incidence in a single year that is only partially accounted for by rainfall patterns. A hypothesis has emerged from this work that common-place gatherings of social and religious life may amplify diarrheal disease transmission and shape timing of outbreaks through increased travel between villages, overcrowding of sanitation infrastructure, food sharing, or other associated activities.

To lay the foundation for investigating the potential relationship between mass gatherings and diarrheal disease transmission, this literature review addresses three main topics. The first section, describing the study site in Esmeraldas, Ecuador, emphasizes the unique ecological, cultural, and socioeconomic context of the study. After a brief overview of worldwide trends in diarrheal disease, the second section focuses on the pathogenesis and epidemiology of diarrheal disease in Ecuador. In the final section on mass gatherings, I review the literature on mass gatherings and infectious disease, propose mechanisms by which mass gatherings might impact diarrheal disease transmission, and conclude with a anthropological description of mass gatherings in coastal Ecuador.

Esmeraldas, Ecuador

Ecuador is a country of remarkable environmental and cultural diversity. Spanning just under 300,000 square kilometers, slightly smaller than the state of Nevada, the country encompasses costal plain, cloud forests, high Andean peaks, volcanoes, and to the east, rolling jungle down to the rainforest of the Amazon. About half of the population resides in the central Andean highland valleys, while the majority of the rest inhabit the western coastal plains. Primarily indigenous communities sparsely populate the eastern rainforests. Three quarters of the country identify as mestizo—mixed Amerindian and white—while Montubio, Amerindian, white, and Afro-Ecuadorian people make up about equal proportions of the remaining quarter.[5]

Significant income inequality exists among the people of Ecuador, with rural, indigenous, and mixed race groups experiencing high rates of poverty; the country as a whole has a 2010 GINI coefficient of 49 (on a scale of 0 being perfect equality and 100 being perfect inequality).[6] Rates of poverty have decreased in recent years, with the percent of people making less than $1.25 a day reducing from 21% in 2000 to 5% in 2010.[7] The GDP per capital today is $11,000, which makes Ecuador ranked 208 worldwide.[5] The country is currently in a recession, and has the lowest level of foreign investment in the region due to unstable economic regulations. The country depends on petroleum exports for half of its export earnings, while agricultural and marine exports, textiles, wood products, and food processing make up the majority of the remainder.[5]

Among comparator countries such as Peru, Colombia, and Thailand, Ecuador ranks first for life expectancy and 5th for age-standardized years lived with disability (YLD) rate.[6] In 2010, the top 3 causes of DALYs in Ecuador were road injury, lower respiratory infection, and interpersonal violence, while the three risk factors accounting for the greatest burden of disease were alcohol use, dietary risks, and high blood pressure. This reflects global trends in the reduction in communicable diseases and the increase in non-communicable diseases and injuries. [6]

Also like the rest of the world, Ecuador has made significant progress in diarrheal disease reduction, likely linked to increased investment in public infrastructure. Between 1990 and 2015, the percent of rural households with treated water piped in increased from 38% to 72%, and improved sanitation facilities increased from 41% to 90%.[8] Over the same time period, the DALYs associated diarrheal diseases fell 82%, moving diarrheal diseases from the number one cause of years of life lost to the 17th.[6] The under-five mortality rate has also decreased from 56 deaths per 1000 live births to 25. Despite this drop, among 15 comparable countries, Ecuador ranked 12th in terms of age-standardized rates of DALYs from diarrheal diseases in 2010.

This study examines a longitudinal diarrheal disease data set from Esmeraldas province in northwestern coastal Ecuador. In Canton Eloy Elfaro, 150 small, mainly Afro-Ecuadoran communities are distributed along the Cayapas, Santiago, and Onzole rivers (figure 1). These rivers drain toward the main town of Borbon, a community of approximately 6,000.[9]

Figure 1. Rio Cayapas[10]

The region is located at the southern end of the Choco rainforest—part of the Tumbes-Choco-Magdalena biodiversity Hotspot that encompasses parts of Panama, Colombia, Ecuador, and northern Peru. The climate is tropical megathermal humid, with a yearly average temperature between 24-26 C. The high rainfall in the area results from clouds forming as the air is forced up the foothills of the Andes, with most of the rain falling in March, April, and May, with significant variation year to year, especially with the arrival of El Nino.[10]

According to the 2001 Ecuadorian national census, the canton is approximately 55% Afro-Ecuadorian, 13% Chachi, and the remainder mestizo, mulatto, or white. The Chachi migrated down from the Andes to the Cayapas river basin likely to escape the growing Spanish Conquest of the Andes.[10] As one anthropologist, DeBoer, writes, "If one had to give a thumbnail sketch of the Chachi ethnography, one should emphasize that they are river people, equally at home in a dugout canoe as on land, that they tend to live in single-house settlements dispersed along rivers, that plantains and fish are staples of their diet, and that they speak a language related to the Colorado and Kwaiker."[11]

Afro-Ecuadorians arrived in the area in several waves, beginning around the same time as the Chachi migration in the mid to late 1500s, when a boat carrying 27 African slaves shipwrecked off the coast. One of these slaves—Alonso de Illescas—who was fluent in Spanish, became the leader of the growing community in Esmeraldas and was the first governor of the region called the "Zambo Republic" in 1577. At this time, primarily indigenous groups lived in the area, and the nascent community of Afro-Ecuadorians intermarried and socialized with these groups, while establishing political ties with the Spanish authorities in Quito. A second wave began in the 17th century with the arrival of escaped or freed slaves over the border from Colombia and the Andean Highlands of Ecuador. Finally, during the 19th and 20th centuries, smaller numbers of African descendants came to Esmeraldas as slaves to pan for gold along the rivers, as part of the liberation armies of Simon Bolivar, during the construction of the railroad from Quito to Guayaquil, and migrating from Colombia during the palm nut and banana booms. [10,12,13]

Overlaid on a foundational livelihood of subsistence agriculture, the canton has followed a boom and bust economy since the beginning of urbanization in the 19th century. The ports in Esmeraldas have been key export locations for products such as lumber during wartime, bananas from the 1940s to 1960s, and most recently shrimp. Since the 1980s, commercial logging and export agriculture have led to high rates of deforestation.[14] After the completion of a paved highway connecting Borbon to the coast and the Andes in 2001, rates of economic and environmental change accelerated, as did migration into and out of the region leading to a growing Mestizo population.[9] Still, in the villages surveyed, 91% of participants identified as Afro-Ecuadorian,[9] and the majority of communities live predominately from subsistence agriculture, hunting, and fishing.[13]

The size and stability of village populations in the study vary greatly, with populations ranging from 53 to 770, and percent of residents born in each village ranging from 0% to 79%.[9] Some villages are easily accessible by road, while others are only accessible by riverboat. Infrastructure for safe water and sanitation, while improving, is still sparse in the area, and communities depend on the rivers as their primary water source. Sanitation facilities, such as in-house and public latrines, are rudimentary.[15]

Eloy Elfaro has been the ongoing focus of studies on linkages between environmental and social change and infectious diseases, beginning with the Ecologia, Desarrollo, Salud, y Sociedad (EcoDESS) project from which the data for this analysis was drawn.[9,15–20] Previous analysis utilizing EcoDESS data have emphasized the roles of nearby roads,[9] social cohesion,[16,19] safe water, sanitation and hygiene practices such as handwashing[15], and extreme rainfall events[20] in shaping regional diarrheal disease risks. A recent study found that heavy rainfall was associated with increased diarrhea following relatively dry periods--and decreased diarrhea incidence following relatively wet periods. They hypothesized that heavy rainfall after regular rainfall dilutes pathogens from the community, while a buildup of pathogens over a dry period may be flushed into water sources in a “concentrated pulse” leading to increased diarrheal disease incidence. In addition, drinking water treatment was found to reduce the impact of these heavy rainfall events following drought. These results explain the diversity in previous findings of rainfall’s influence on diarrhea, and highlight the importance of time-varying risk factors and social context—in this case, in the form of water treatment infrastructure.[20,21]

Secular and religious festivals, which occur in communities throughout the region, may represent temporal confounders of environmental risk factors such as rainfall, transient effect modifiers of social and environmental processes driving risk, or important independent drivers of the spatiotemporal distribution of risk.

Diarrheal Disease

Health Burden

Prior to oral rehydration therapy (ORT) being introduced, diarrhea was the leading cause of death of children worldwide. ORT has helped reduced diarrhea-associated mortality from 5 million to 2.5 million deaths per year.[4] The under-5 incidence rate has reduced from 3.4 episodes per child per year in 1990 to 2.9 episodes per child in 2010, a decline that strongly correlates with significantly decreased under-5 mortality rates over the same period.[22]

Despite sustained public health efforts and medical innovations, diarrheal disease remains one of the top causes of child mortality, and the fourth leading cause of disability adjusted life years (DALYs) lost among all age groups worldwide.[1,2] A recent WHO meta-analysis estimated 1.9 billion cases of diarrheal diseases in the 2000 decade. This burden primarily rests on children low-income countries.[3] 39% of all diarrheal disease affects children under the age of 5, with the most vulnerable age (age with the highest incidence) is 6-11 months.[22] Furthermore, the rate of death due to diarrhea in children under 5 years of age is 8.37 x the rate of death in those over 5 years of age. [3] Recurrent infections during early childhood, are associated with physical and mental stunting, wasting, and malnutrition.[23]

The disease burden in the developing world can be traced primarily to overcrowding, substandard water sources, and inadequate sanitation infrastructure.[24] Given current trajectories of population growth, as well as looming threats to water quality related to climate change, there is a potential for a rebound in risk.[21,25,26]

Pathogenesis

Pathogens responsible for diarrhea differ depending on the location as well as the population. After briefly reviewing general pathogenic mechanisms, I will discuss the most common pathogens in the coastal Ecuador study site in more detail.

Pathogens differ widely in their infectious dose –or the number of organisms that must be ingested to cause illness –from *Giardia lamblia*, which can cause disease with only 10-100 cysts, to *Vibrio cholerae,* which requires 10^5-10^8 organisms.[23] They also differ in their transmission mechanisms and incubation times. Once ingested, pathogens use a variety of adherence mechanisms to attach to the intestinal cell wall and colonize the mucosa. The nature of this adherence mechanism—in bacteria, a cell surface protein—is part of what determines where in the digestive tract the pathogen will cause the most damage. After colonizing the mucosa, pathogens may produce one or more exotoxins that lead to diarrhea. Enterotoxins, produced by cholera and some enterotoxigenic strains of *E. coli*, are proteins that cause secretory diarrhea by causing the intestinal mucosa to increase Cl^- secretion and decrease Na^+ absorption, leading to a massive loss of fluid and watery diarrhea. Pathogens producing enterotoxins cause *non-inflammatory* diarrhea. Cytotoxins, on the other hand, produced by *Shigella* and Shiga-toxin producing strains of *E. coli*, directly destroy mucosal cells and cause bloody stool containing inflammatory cells, called dysentery, or *inflammatory* diarrhea. Hemorrhagic colitis and hemolytic-uremic syndrome are associated with cytotoxin-producing pathogens. In addition to producing toxins that result in diarrhea, some pathogens like *Shigella* and *Salmonella* can also invade the mucosal cells themselves, called *invasive* diarrhea (which is a type of inflammatory diarrhea).

Figure 2. Summary of published data on the presence of enteric pathogens in Ecuador[28]

TABLE 1

Summary of published data on the presence of enteric pathogens in Ecuador*

	Year of publication	Number of tested samples	Age range	% positive cases	Measure of Association	Setting	Reference
Campylobacter	1987	100	0 to 24 months	23	–	Urban	11
Campylobacter	1994	177	Under 5 years	3,37	–	Urban	12
Cryptosporidium	1986	169	Under 5 years	11.24	–	Urban	13
Shigellae	1987	100	0 to 24 months	12	–	Urban	11
Shigellae	1994	177	Under 5 years	3.7	–	Urban	12
Shigellae	2007	915	All ages	0.9	0.6 (0.06, 2.7)†	Rural	14
Shigellae	2012	2936	All ages	–	1.6 (1.1–2.4)‡	Rural	15
Shigellae and EIEC	2012	3314	All ages	17.1	3.6 (2.4, 5.0)‡	Rural	16
Entamoeba histolytica	1987	100	0 to 24 months	1	–	Urban	11
Enteroinvasive *E. coli*	2007	915	All ages	8.9	3.1 (1.6, 6.0)†	Rural	14
Enteropathogenic *E. coli*	2007	915	All ages	1.7	1.9 (0.4, 8.2)†	Rural	14
Enterotoxigenic *E. coli*	2007	915	All ages	7.6	6.9 (2.8, 18.6)	Rural	14
Giardia lamblia	1987	100	0 to 24 months	5	–	Urban	11
Giardia lamblia	1994	177	Under 5 years	63	–	Urban	12
Giardia lamblia	2012	244	Under 5 years	18.3	–	Urban	17
Giardia lamblia	2012	3314	All ages	31.5	2.6 (2.1, 3.2)‡	Rural	16
Giardia lamblia	2012	2936	All ages	–	1.5 (1.0, 2.2)‡	Rural	15
Norovirus	2012	244	Under 5 years	29.5	–	Urban	17
Rotavirus	1981	702	Under 3 years	21.1	–	Urban	18
Rotavirus	1986	1722	Under 3 years	21.8	–	Urban	19
Rotavirus	1987	100	0 to 24 months	21	–	Urban	11
Rotavirus	1994	177	Under 5 years	7.5	–	Urban	12
Rotavirus	2007	1656	All ages	23.35	9.2 (6.1, 13.9)†	Rural	20
Rotavirus	2008	728	Under 5 years	37	–	Urban	21
Rotavirus	2009	3300	All ages	22.3	10.6 (7.9, 14.3)†	Rural	22
Rotavirus	2012	3314	All ages	22.2	10.7 (7.9, 15.1)‡	Rural	16
Rotavirus	2012	2936	All ages	–	1.7 (1.1, 2.5)‡	Rural	15
Salmonella spp.	1987	100	0 to 24 months	3	–	Urban	11

*Studies that reported % positive cases used a cross-sectional design, and studies that reported an odds ratio or risk ratio used a case-control design.
†Odds ratio (OR) (95% confidence interval [CI]), OR compared the odds of having diarrhea given infection with the odds of not having diarrhea given infection.
‡Crude risk ratio (95% CI).

E. Coli, *Shigella*, and rotavirus are the most common causes globally, while *Cryptosporidium* has recently emerged as a major protozoan cause.[27] A recent review of pathogens in Ecuador (figure 2) identified *Camplyobacter*, *Cryptosporidium*, *Shigella*, *Entamoeba histolytica,* Enteroinvasive *E. coli* (EIEC), Enteropathogenic *E.coli* (EPEC), Enterotoxigenic *E.coli* (ETEC)*, Giardia lamblia*, norovirus, rotavirus, and *Salmonella* as associated with diarrhea.[28] In the rural, coastal Ecuador study site, a case-control study found high levels of rotavirus and *Giardia*, while a previous study identified high levels of pathogenic *E.Coli* (ETEC, *Shigella*, EPEC) in addition.[28,29] These findings are consistent with global trends, where *Giardia* infection is common in developing countries and pathogenic *E. coli* and rotavirus are the leading causes of diarrhea in infants.[27] As compared with a low-income study site in Quito, in the rural study site there are a higher number of co-infections, a higher odds of pathogen-associated diarrhea, and a higher overall pathogen detection rate.[28]

Pathogenic *E. coli* are gram-negative, rod-shaped, motile bacteria. A number of different species have been implicated in diarrheal disease: Enteropathogenic *E. coli*, Enterotoxigenic *E. coli*, Enteroinvasive *E. coli*, Enterohaemorrhagic *E. coli*, Enteroaggregative *E. coli,* and diffusely adherent *E. coli*.[30] These bacteria are primarily harbored in the intestines of mammals and birds, and in tropical conditions—which approximate the environment of mammalian bodies—*E. coli* may be able to survive and reproduce outside of animal hosts.[30] In soil, manure, and water, they may survive for up to 12 months.[31–33] The various species have different transmission profiles and pathogenesis. EPEC is thought to be primarily transmitted person-to-person, and after an incubation period of 9-12 hours, causes diarrhea by adhering to the small intestinal epithelium and disrupting the brush border surface, leading to a decrease in functional surface area for water reabsorption.[30,34] ETEC, in contrast, is thought to be transmitted primarily through contamination of food and water, has a longer incubation period of 24-72 hours, and causes watery diarrhea by the production of heat-labile and heat-stable enterotoxins. It is often the cause of "traveler's" diarrhea due to a lack of immunity. [30,35] While both EPEC and ETEC are non-invasive, EIEC has the ability to adhere to the intestinal epithelium, produce toxins, as well as invade the mucosa, causing necrosis and inflammation that result in dysenteric (bloody) diarrhea along with fever.[30,35] EIEC's transmission period is intermediate at 10-18 hours, and transmission includes person-to person and contaminated food and water. Finally, Shigella is quite similar to EIEC in pathogenesis, transmission, and clinical manifestations, however has a lower infectious dose and a longer incubation period, on the order of 1-4 days.[36]

Rotavirus is a common cause of fatal diarrhea in children under two years. It is a double-stranded, linear RNA virus with a double icosahedral capsule that attacks epithelial cells of the small intestine, leading to secretory and osmotic diarrhea. [37,38] Humans are rotavirus' primary host, and though the virus may survive for hours to months in the environment (hours on hands; days in air; surfaces and food; weeks in water; months in fecal mater), it cannot multiply.[37] It is primarily transmitted fecalorally from person to person, with an incubation period of one to three days and an infection period of around 8 days.[38]

Giardia lamblia is a common protozoan cause of diarrhea worldwide across all age groups.[39] The cyst form enters the small intestine, releases trophozoites, which then multiply by binary fission and adhere to the small intestine epithelium by ventral sucking disks. This damages the mucosa, triggers an immune response, and leads to bloating, flatulence, and fatty, foul-smelling diarrhea.[35] Primary hosts of Giardia are humans and beavers, along with other mammals.[39] Giardia cysts can survive in the environment, up to one year in cold water, and are usually transmitted via the consumption of this contaminated water, person to person, or via fomites.[39] The incubation period of Giardia is longer than for E. Coli or Rotavirus, ranging from 1 to 60 days with an average of 8 days. The infectious period is also longer, lasting up to months.[40]

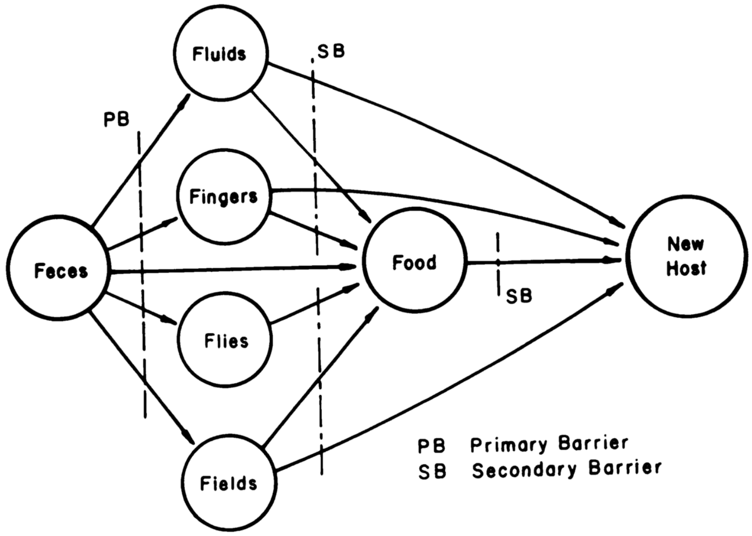
Treatment of diarrhea begins with rehydration, in particular with oral rehydration solution containing sodium chloride, sodium bicarbonate, potassium chloride, and glucose, to replace the loss of electrolytes as well as improve the absorption of water. Depending on the pathogen, antimicrobial agents can also be used, and rotavirus vaccines can be administered as a preventative measure.[23]

Epidemiology

Importantly, all of these pathogens can be transmitted to varying degrees through direct person-to-person contact as well as through food, water, and surfaces. In the 1970s, a shift occurred in epidemiology of diarrheal disease, from the biomedical perspective focusing on individual risk factors and medical treatment to an ecological perspective that directed focus to environmental and social context.[4] The seminal paper of this time (Kawata 1978) introduced the "F-diagram" to highlight the environmental and social role in diarrheal disease transmission, by identifying "food, flies, fields, fingers, and fluids" as transmission pathways (figure 3).[41] This contributed to the shift of focus in research and intervention strategies from individual risk factors and hygiene to environmental and social determinants, which in turn contributed to the increased success in global reduction in the burden of disease.[42]

More broadly at this time, there was increasing focus on social epidemiology and the bio-psycho-social model of health and disease, which considers individual, biological risk factors as rooted in multilevel, interacting environmental, cultural, and societal contexts. In the bio-psycho-social model, a person's relative income may be as important to their risk of diarrheal disease as their immune status.[43]

Figure 3. The F-diagram describing transmission of enteric pathogens[41]



The ensuing period of research on diarrheal disease epidemiology investigated the single transmission pathways implicated by the F-diagram, including water, food and food hygiene, sanitation, domestic hygiene, and person-to-person transmission.[4] The majority of single transmission pathway studies—about half—focus on water systems. Significant advancements from this body of work include the differentiation between source and point of use water treatment, the importance of clean water for hygiene purposes in addition to drinking and preparing food, and the relationship between water accessibility and water quality.[4] The food pathway has primarily been investigated in the context of large-scale food production and service in developed countries, which facilitate the emergence of salmonella and *E. coli*.[42] In the developing world, the food pathway has been investigated in terms of food storage and contamination. [44,45] WHO estimates that 29% of cases of diarrhea in the 2000 decade were transmitted by contaminated food in total, with 38% of cases being foodborne in children under 5 years of age.[3] Studies about the hygiene pathway similarly had a divide in focus between the developing and the developed world. In the developing world, research focused on the "private domain," including hand-washing, soap, and cleaning utensils. In the developed world, research focused more on the community level, such as cleaning practices in daycares and cruise ships. Research on person-to-person transmission focused on spread of disease within households or with household contacts. Finally, the literature on the sanitation pathway was exclusively centered on the developing world, emphasizing the use of latrines, disposal of child feces, improved sewage systems, and the potential spread of disease by irrigating crops with wastewater.[46–49]

The transmission dynamics of certain pathogens vary considerably—for instance, cholera spreads primarily through contaminated water sources and thus is determined by geography and hydrology, while Shigella survives less well in the environment, is primarily transmitted person to person, and therefore patterns of disease spread are more likely to be socially-mediated. However, the majority of diarrheal pathogens can be transmitted meaningfully through both environmental and person-to-person pathways, and therefore will "reflect both social and geographic patterns of populations." [16]

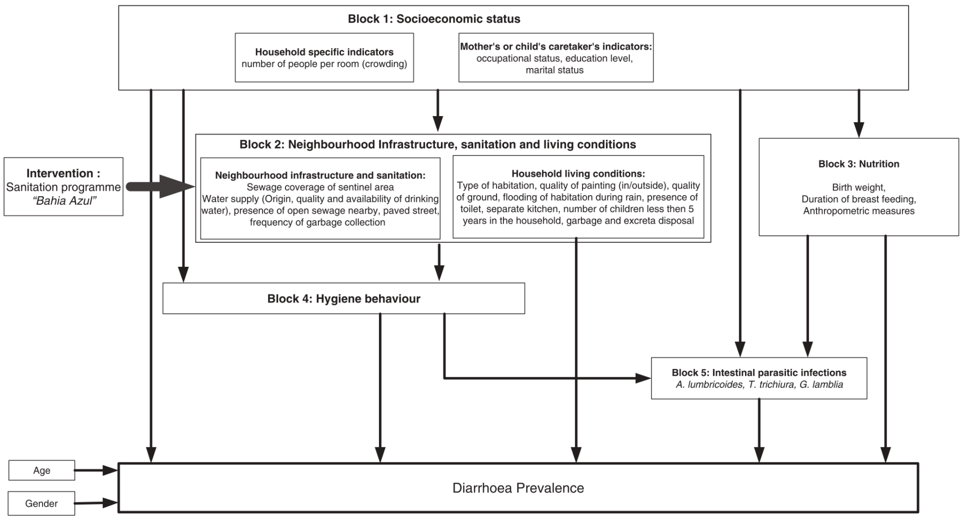
Few studies have investigated the relative importance of these pathways, or their interdependence. A minority of studies investigated the "classic trinity" of water, sanitation, and hygiene in conjunction, and only 1% looked at the interdependencies between pathways.[4]

Nevertheless, these observational studies significantly influenced public heath practice, and intervention trials and their meta-analyses have proliferated since. While hand-washing interventions have consistently reduced diarrheal disease incidence by over 30%,[24] significant heterogeneity has been noted in other single-pathway interventions, most notably water treatment. A number of context-dependent factors have been identified to explain this, and reviews identified the relationship between water-quality interventions, sanitation, and hygiene. One found that point-of-use interventions are ineffective or insignificant when sanitation and hygiene practices are inadequate,[50] while another found that point-of-use water quality interventions have more impact when a high proportion of households have adequate hygiene and sanitation.[51] Furthermore, evidence suggests that behavior change and community education need to be included in interventions to preserve benefits over time.[52]

Eisenberg (2012) suggests that diarrheal disease research now requires yet another evolution, from single-pathway transmission research and single-pathway interventions to the consideration of interdependencies, multiple interventions and varying social and environmental context.[42]

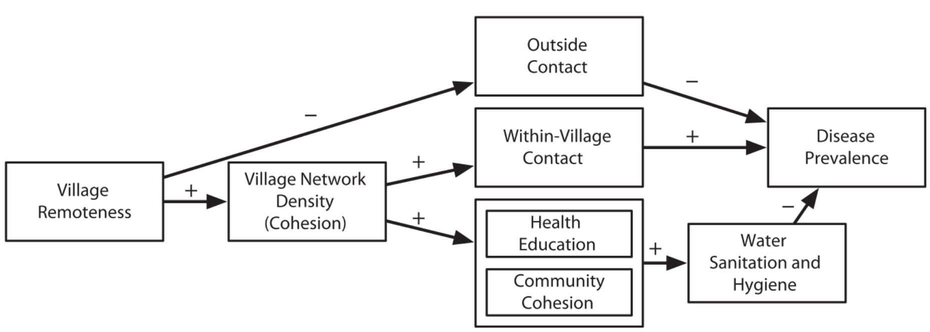
In the social realm, some research has begun this project by looking into the importance of power, gender, and socioeconomic status (SES) [53] as well as infrastructure and community organization change.[16,54] While many studies simply assessed socioeconomic status as a confounder when investigating other risk factors, others investigated socioeconomic status in more detail, identifying mediating factors such as crowded housing, cost and access to clean water, and low levels of education as important risk factors for diarrheal disease.[55] For example, one study found that while a composite measure of socioeconomic status, including household construction, wealth, and technology, did not independently influence diarrheal disease incidence, it was the root cause of other important risk factors such as lack of sufficient sanitation, hygiene and water treatment (figure 4).[53] Another study looked at the attributable risk associated with socioeconomic status before and after a city-wide intervention in Northeast Brazil, finding that poverty was a major determinant of diarrhea (attributable risk 24%) before the study. After the intervention, the risk attributable to SES reduced to 13%, suggesting that interventions may be able to affect the contribution of SES to diarrheal disease risk without altering SES itself.[56]

Figure 4. Conceptual framework visualizing the inter-relationships between potential risk factors, the sanitation intervention and diarrhea prevalence[56]



In recent years, studies have begun focusing on the importance of sociogeographic landscapes to diarrheal disease risk—such as social networks within communities and the degree to which communities are connected to or isolated from one another. In both Papua New Guinea and Ecuador, studies have documented that more remote communities—as defined by time and cost of travel to the nearest population center—have lower levels of diarrheal disease.[9,54] Follow-up studies have explored the mechanisms for this relationship, which may be representative of social, geographic, and environmental factors, using the following conceptual model as a guide (figure 5).

Figure 5. Postulated conceptual model: effects of social relationships on disease outcomes, Esmeraldas, Ecuador, 2007, from Zelner et al. 2012[19]



Note. Solid arrows illustrate the hypothesized pathway by which remoteness affects risk of infection. Plus or minus signs indicate the directionality of the relationship.

Remoteness has been postulated to effect diarrheal disease prevalence through two main pathways: internal characteristics of the villages associated with remoteness, and connection to other villages. More remote villages have higher housing density and denser social networks (cohesion), while villages closer to the road have lower housing density and more diffuse social networks. These characteristics may be related to longer tenure of inhabitants. Interestingly, these two characteristics seem to have opposing effects on diarrheal disease incidence. Holding social network degree constant, higher housing density is associated with an *increase* in diarrheal disease. Holding housing density constant, higher social network degree is associated with a *decrease* diarrheal disease.[16] Follow-up studies found that remoteness was associated with higher levels of intra-village social connectedness, which was hypothesized to decrease diarrheal disease risk due to investment in social goods such as water quality and sanitation measures.[16] In models accounting for all these factors—household size, average network degree, and improved sanitation and water treatment—remoteness itself was no longer a significant predictor of diarrheal illness, suggesting that these variables are the important mediating factors.

Traditionally, more highly connected social networks are seen as more efficient disease transmission systems, especially in terms of sexually transmitted disease.[57,58] Transmissibility of infectious disease has been proposed to be a function of the mean number of contacts and the extent of clustering.[59] It has been proposed in multiple studies that R0—the basic reproduction number using in epidemic modeling, derived from the product of the contact rate, the probability of transmission per contact, and the duration of the infection period—will be affected by social networks, in that we would expect higher values in crowded—more dense—contact networks.[60] The work on remoteness lends nuance to the typical view within infectious disease literature that social networks are pathways for pathogen spread, by linking increased social network density (cohesion) to increased investment in social goods that may dampen disease transmission.

This work also expands upon the traditional and simplistic view of diarrheal disease transmission, by which community effects are emphasized. One study found that community disease dynamics are affected by those in surrounding communities, where the effectiveness of interventions (latrines and water treatment) depended on regional prevalence.[15] More specifically, the protective effect of water treatment was lessened when regional prevalence was high.[15] Other observational studies have shown that neighbors benefit from household latrines even if they do not have their own[61], water filtration in one household benefits neighboring households without filters[62], and household sanitation improvements can provide herd protection against stunting.[63] A clustered randomized experiment empirically demonstrated these community effects [64], and other community-based sanitation and water interventions have been effective.[48,56]

Mass Gatherings

Mass gatherings and infectious disease

Mass gathering events are one potential social driver for periods of enhanced diarrheal disease transmission. Mass gatherings are defined by the World Health Organization as events involving "a concentration of people at a specific location for a specific purpose over a set period of time… which has the potential to strain the planning and response resources of the country or community".[65]

In the past decade, there has been increasing interest in infectious disease transmission during mass gatherings – especially gatherings involving inter-region or international travel. Recent public health crises, exemplified by diseases such as Zika and Ebola, have focused attention on appropriate surveillance and planning to protect attendees of mass gatherings and prevent the import or export of ongoing epidemics from host locales.[66–69] In 2015 the World Health Organization published *Public Health For Mass Gatherings: Key Considerations* which includes a section on *Protection of Food and Water,* focusing specifically on the dangers of enteric disease transmission.[65]

Multiple routes of infectious disease transmission have been documented during mass gatherings, including respiratory, gastrointestinal, vector-borne, and sexual routes.[70] Much research into communicable disease transmission during mass gatherings has been done in the context of the Hajj and Umrah pilgrimages in Saudi Arabia, where outbreaks of meningitis, respiratory tract infections, and infectious diarrhea have all been documented in depth.[70–73] Additional reports have traced disease transmission sequences at diverse events, including religious meetings, sporting events, and large-scale open air festivals (for comprehensive reviews, see Botelho-Nevers and Gautret, Gautret and Steffen).[74,75] Among these, at least 15 reports of gastrointestinal infections associated with inadequate hygiene and sanitation have surfaced.[71,74,75] Case studies of transmission of gastrointestinal illness outbreaks associated with festivals found that a small number of initial infections proceed to a peak in cases over a 1 to 2 week period, with complete outbreak epidemic curves lasting approximately 3 weeks.[76,77]

Despite mounting evidence implicating mass gathering events in the amplification and dissemination of diarrheal and other infectious diseases, retrospective analyses in the literature have consisted primarily of case-control studies and outbreak reports, and have only rarely been extended to explicitly consider the role of mass gatherings in long-term epidemiological patterns. Notably, Finger et al. recently used mobile phone data to model the critical role of a large religious pilgrimage in amplifying a nationwide outbreak of cholera in Senegal in 2005.[78]

Furthermore, the bulk of existing research has emphasized particularly large mass gathering events, such as the Hajj, with few exceptions including the documentation of a rotavirus outbreak amplified by a national independence holiday in South Tarawa, Kiribati, in 2013.[77] While the WHO emphasizes that the importance of mass gatherings is "not linked to the size of the gathering or the number of people…because each community has a different capacity," there has been no rigorous investigation of the role of smaller scale events in local epidemiological patterns to date.[65]

The particular characteristics of mass gatherings—food sharing, crowding, migration, and stresses on sanitation and hygiene infrastructure—present plausible mechanisms by which diarrheal disease transmission may be amplified or disseminated between population centers.

One possible mechanism for the relationship between festivals and diarrheal illness is environmental contamination due to insufficient sanitation infrastructure to accommodate visiting populations. One notable example is the Rainbow Family gathering in the US in 1987, where a large outbreak of shigellosis was traced to the contamination of drinking water due to inadequate sanitation.[74] In the Ecuador study site, not everyone in each village has a toilet, and people often use neighbors' toilets or public toilets.[15] It is plausible that, with an influx of visitors, there may be an overwhelming of sanitation infrastructure simply by overuse.[72] There also may be situations in which people don't have access to sanitary facilities because they are visiting from out of town and can't use "a neighbor's" toilet, and therefore defecate outdoors (A. Acevedo, personal communication, August 17, 2016). Finally, there may be more alcohol and food consumption leading to more frequent and less careful bathroom use.[74]

A second potential mechanism is a failure of hygiene, specifically hand-washing hygiene among food handlers and the public, production of large quantities of food by multiple handlers, unsanitary or crowded food prep conditions, and lack of clean water in sufficient quantities. These conditions have been documented in previous studies of large-scale open-air festivals. [70,76,79–81] In general, food contamination has repeatedly been identified as an important diarrheal disease transmission pathway.[82,83] In the Ecuador study site, one study documented extensive and heterogeneous food-sharing networks, where less remote villages have more aggregated food-sharing networks with lower network degree and more remote villages have more diffuse networks with higher network degree.[84] Ethnographic observations have shown the presence of extensive food sharing at festivals within this study region, including crowding at local eating establishments and mass food preparation.[13,85] In cultures with extensive sharing of food across households, the secondary spread of diarrhea from food-borne pathogens can be important in disease transmission.[24]

Finally, festival-associated national, regional, and local migration may result in the introduction of new pathogens, strains, or the addition of a new susceptible population. The revelers at each festival are not isolated to the particular village hosting the festival, rather the village becomes nodal in the region: visitors come from neighboring towns, from villages located in other river basins, and on particularly important festivals that coincide with work holidays, migrants return home from nationwide.[13] New technologies that allow the geographic tracking of mobile phone use document the increased mobility associated with mass gatherings. In one study, sudden peaks in travel and mobility were found to occur around mass gatherings.[78] Previous studies in this region have pointed toward the importance of inter-village transmission in diarrheal disease incidence. Remoteness—defined by length and cost of travel to the central town of Borbón—was found to be associated with lower rates of diarrheal disease.[9] Remoteness was associated with a decreased rate of inter-village migration, as defined by the proportion of households with a visitor from outside the village in the previous week; higher proportions of households with visitors were associated with increased diarrheal disease risk.[19]

While social connectedness on a village level may decrease risk due to increased investment in collective mitigation strategies (as described in the section on diarrhea epidemiology), social connectedness at the scale of regional migration networks—which may intensify during festival periods—may facilitate the spread of pathogens. This is theoretically consistent with the sexually transmitted infection (STI) literature, in which high frequencies of repeated contacts are associated with smaller and slower growing epidemics, while high concurrency (simultaneity) of contacts is associated with larger and faster growing epidemics. [86]

Mass Gatherings in Ecuador

It is impossible to overstate the diversity and complexity of mass gatherings in Ecuador. Mass gatherings may be religious or secular, national or local, draw large tourist attendance or be restricted to the community, may be concentrated in the home or located in large, outdoor public spaces, may be informal and spontaneous or orchestrated over a year's planning period. [13] I will draw from a few cultural anthropologies, specific to northwestern coastal Ecuador, for examples of specific mass gatherings and then will extrapolate some notable characteristics of mass gatherings in the study region.

Kimbra Smith, an anthropologist writing about tourism and the politics of authenticity in coastal Ecuador, describes one festival called *Festival de la Balsa Mantena*, which is held on October 12 *Dia De La Raza* (an Ecuadorian national holiday) in the region of Agua Blanca.

> "They had invited folkloric dance groups from all over the country to participate, and would be hosting a series of events including the launching of

> balsa rafts to the nearby Isla Salango and back, an event they somewhat self-consciously referred to as a regatta; various cultural performances; a food fair; and the election of a Señorita Manteña, an indigenous princess. Each visiting community, plus some local organizations and their peers from Puerto López, would be sponsoring a candidate who would present a short speech and some kind of performance."[85]

This description highlights a number of important aspects of festivals in coastal Ecuador. Dances and cultural performances, mass food sharing, and contests are all nearly ubiquitous in mass gatherings, as are the collaboration of surrounding communities. This festival in particular also involves the attraction of tourists, both national and international.

In *Kings for Three Days*, anthropologist Jean Rahier describes the Afro-Esmeraldian *Festival of the Kings* in great detail, which takes place from January 6 to January 8 in northern Esmeraldas. This holiday celebrates the Catholic festival of the Epiphany. Despite the ostensible foundation in Catholic tradition, the festival is an example of the syncretism wide-spread in the festivals of coastal Ecuador. The primary activities of *Festival of the Kings* are complex and multi-day theatrical parodies, reenactments and satires of race, gender, and Ecuadorian politics. Interestingly, when the three kings are acted out, they are representing the three racial groups of the province: the white-mestizos, the Chacis, and the Afro-Esmeraldians.[13]

Religion and spirituality play a central role in the gatherings of Esmeraldas, representing a syncretism of indigenous Ecuadorian, African, and colonial religious traditions. Seventy-one percent of Ecuador is Roman Catholic,[5] and this cosmology is central to many of the holidays celebrating the study region.[87] Anthropologist Quiroga writes,

> "The Virgen del Carmen, Santa Rosa, El Hermano Gregorio, and San Antonio are among the figures who provide the space of the *divino* with its healing and ordering powers. These figures are celebrated in rituals called *arrullos*, which punctuate the year. Led by women, a male rhythmic ensemble composed of two large drums (*bombos),* two conga-like drums (*cununos),* accompanies female singers (*cantadoras)* who sing the *arrullos* (spirituals), shake maracas, dance, tell stories, and open a passageway to heaven. During these celebrations, the spirit of the saint or virgin is said to come to the world of the living." P156

Holidays such as Dia de los Muertos and Semana Santa are thought to be times at which the divine comes to interact with the human realm, which can be times of peril as evil spirits also come along.[87]

Another important religious holiday, Christmas, is often more of an intimate event as opposed to a mass gathering *per se* – Nativity plays are performed in schools, gifts are given, crèches are created in the house, and hot chocolate and sweets are shared on Christmas eve.[85]

Communities also place great importance on the festivals of their patron saints. For instance, Smith describes the festival of San Isidro Labrador in one coastal Ecuadorian community. Organized by a committee and paid for collectively, the festival lasts 2 days. The first day includes a volleyball tournament and an evening mass, during which people bring their agricultural products to be blessed. Afterward, a queen of the festival is elected, and a dance party continues until dawn. The second day, a morning soccer tournament brings together teams from the entire region, and other traditional games follow, such as egg-on-a-spoon races. Another mass is held where baptisms are performed for all children born that year. In the evening, a competition is held for the "mother" of the community, and dancing again continues all night. Aguardiente, either purchased or brewed, is a large part of these celebrations.[85]

Migrants often schedule visits home during the festival of San Isidro Labrador, above even Christmas and New Years. Mass gatherings, overall, are important periods of travel. As Smith describes,

> "Emigrants return to Agua Blanca for the fiesta from all over the country and even from abroad. If people are planning a trip home from abroad, they almost always schedule it around this event, preferring it even to Christmas or the New Year. The fiesta is not included on the regional touristic calendar, however, and outsiders are not generally present unless they are particular friends of those who travel to the fiesta. All local baptisms take place during this fiesta; migrants' ties to the community are often reinvigorated through invitations to become godparents to the children being baptized, a commitment most take quite seriously."[85]

As mentioned here, New Year's Eve is another very important festival in coastal Ecuador and many migrants use the holiday to return home. The celebration often includes a sports (soccer) tournament in the day, and large, all night dances. These dances include collective meals, theatrical performances, and a ceremony in which effigies representing politicians, public figures, or unlucky community members are burned in a bonfire to represent "burning the bad luck of the previous year to start afresh." [85] In one community described by Smith, celebrants form two concentric circles, and rotate around hugging one another.

The inclusion of public figures in the festivities of New Years highlights another important part of festivals in the region: politics. A common feature of festivals is a speech by local government officials. In one festival witnessed by the author, speeches were given by a panel of local dignitaries, including a public health official rallying support for her effort to find a doctor to stay in the community over night so there would be reliable medical care.

Some gatherings are organized by the local government itself while others are organized by small, rotating committees of community members.[85] Another important aspect of festival organization is their cost. While gatherings are extremely important to the communities of coastal Ecuador, they are also quite expensive. Towns often struggle to procure funds for festivals, and there may be conflict over the use of these funds.[10] Sometimes money comes from the government, while in other instances, everyone in the community is expected to contribute to a collective fund that goes to musical acts, food, beautification, and prizes.[85] The planning phase of mass gatherings presents an opportunity for public health education and mitigation strategies addressing potential risk factors.[65]

Conclusion

Despite increasing public health attention and the introduction of oral rehydration therapy, diarrheal disease remains a major cause of child mortality and overall loss of Disability Adjusted Life Years worldwide.[3,24] Targeted intervention strategies require an understanding of processes that sustain the transmission of diarrheal pathogens through both social and environmental pathways.[4] Mass gatherings represent a discrete socio-environmental context in which to examine diarrheal disease transmission. Traditionally, mass gatherings have been the subject of anthropological and sociological inquiry. However, in the past decade, there has been increasing interest in infectious disease during mass gatherings, and research has found that large mass gatherings are associated with increased rates of enteric infections.[71,74,75]. Outbreaks such as Zika and Ebola highlight the importance of understanding how human movement and density affect infectious disease transmission.

The behaviors and conditions involved in mass gatherings—food sharing, crowding, migration, and overwhelmed sanitation and hygiene infrastructure—present plausible mechanisms by which diarrheal disease transmission may be amplified. However, no studies have attempted to explicitly link the common-place mass gatherings of religious and social life to patterns of diarrheal incidence. This research examines a longitudinal diarrheal disease data set from northwestern coastal Ecuador to explore the relationship between festivals and diarrheal disease transmission. In the subsequent analysis, I will pursue the following three questions:

1. Is there a relationship between mass gatherings and diarrheal incidence?
2. Over what time frame does this relationship occur?
3. Does this relationship differ depending on characteristics of the mass gathering, such as event length or associated activities?

By investigating the effect of mass gatherings on diarrheal disease incidence, this project attempts to integrate anthropological insights into environmental epidemiology. Diarrheal disease, in particular, requires this type of analysis, as pathogens causing diarrheal disease can be transmitted through the environment, contaminated food and water, as well as social contact, and major risk factors that have already been identified—including sanitation infrastructure, hygiene, and water quality—are highly dependent on social systems. It has been hypothesized that varying socio-environmental context is responsible for the heterogeneity of outcomes from intervention trials, and that understanding how transmission varies in different socio-environmental contexts is critical for choosing appropriate interventions.[42]

2: Original Research Paper

Introduction

Despite sustained public health efforts and medical innovations such as oral rehydration therapy, diarrheal disease remains one of the top causes of child mortality, and the fourth leading cause of disability adjusted life years (DALYs) lost among all age groups worldwide.[1,2] The disease burden in the developing world can be traced primarily to overcrowding, substandard water sources, and inadequate sanitation infrastructure.[24] Given current trajectories of population growth, as well as looming threats to water quality related to climate change, there is a potential for a rebound in risk.[21,25,26] Targeted intervention strategies require an understanding of processes that sustain the transmission of diarrheal pathogens through both social and environmental pathways.[42]

Mass gatherings have been consistently linked to the spread of infectious disease. They are defined by the World Health Organization as events characterized by "the concentration of people at a specific location for a specific purpose over a set period of time and which have the potential to strain the planning and response resources of the country or community." [65] The particular characteristics of mass gatherings—food sharing, crowding, migration, and overwhelmed sanitation and hygiene infrastructure—present plausible mechanisms by which diarrheal disease transmission may be amplified or disseminated between population centers.

In the past decade, there has been increasing interest in infectious disease transmissions during mass gatherings – especially gatherings involving inter-region or international travel. Recent public health crises, exemplified by diseases such as Zika and Ebola, have focused attention on appropriate surveillance and planning to protect attendees of mass gatherings and prevent the import or export of ongoing epidemics from host locales.[66–69] Much research into communicable disease transmission during mass gatherings has been done in the context of the Hajj and Umrah pilgrimages in Saudi Arabia, where outbreaks of meningitis, respiratory tract infections, and infectious diarrhea have all been documented in depth.[70–73] Additional reports have traced disease transmission sequences at diverse events, including religious meetings, sporting events, and large-scale open air festivals (for comprehensive reviews, see Botelho-Nevers and Gautret, Gautret and Steffen[74,75]). Among these, at least 15 reports of gastrointestinal infections associated with inadequate hygiene and sanitation have surfaced. [71,74,75]

Despite mounting evidence implicating mass gathering events in the amplification and dissemination of diarrheal and other infectious diseases, retrospective analyses in the literature have consisted primarily of case-control studies and outbreak reports, and have only rarely been extended to explicitly consider the role of mass gatherings in long-term epidemiological patterns. Notably, Finger et al. recently used mobile phone data to model the critical role of a large religious pilgrimage in amplifying a nationwide outbreak of cholera in Senegal in 2005.[78] Furthermore, the bulk of existing research has emphasized particularly large mass gathering events, such as the Hajj, and there has been no rigorous investigation of the role of smaller scale events in local epidemiological patterns to date.

This secondary data analysis examines a longitudinal diarrheal disease data set from northwestern coastal Ecuador to explore the relationship between festivals and diarrheal disease transmission. The canton of Eloy Elfaro in Esmeraldas province, Ecuador, has been the ongoing focus of studies on linkages between environmental and social change and infectious diseases, beginning with the Ecologia, Desarrollo, Salud, y Sociedad (EcoDESS) project from which the data for this analysis was drawn.[9,15–20] Consisting of numerous small, mainly Afro-Ecuadoran communities along the Cayapas, Santiago, and Onzole rivers, and a small town (Borbon) at the mouth of the river system (figure 6), the canton represents an ideal setting to study the impacts of social and environmental processes affected by economic development and climate change on the health of vulnerable populations. Since the 1980s, commercial logging and export agriculture have led to high rates of deforestation.[14] After the completion of a paved highway connecting Borbon to the coast and the Andes in 2001, rates of economic and environmental change accelerated, as did migration into and out of the region.[9] Previous analysis utilizing the EcoDESS data have emphasized the roles of nearby roads[9], social cohesion[16,19], safe water, sanitation and hygiene practices[15,20], and extreme rainfall events[20] in shaping regional diarrheal disease risks. Secular and religious festivals, which occur in communities throughout the region, may represent temporal confounders of environmental risk factors, such as rainfall, transient effect modifiers of social and environmental processes driving risk, or important independent drivers of the spatiotemporal distribution of risk.

Here, I present initial time-series regression analyses evaluating the association of local festivals with the incidence of diarrheal disease in 19 villages to determine the potential effects of festival events on average disease risks in the region. This study attempts to answer the following three questions:

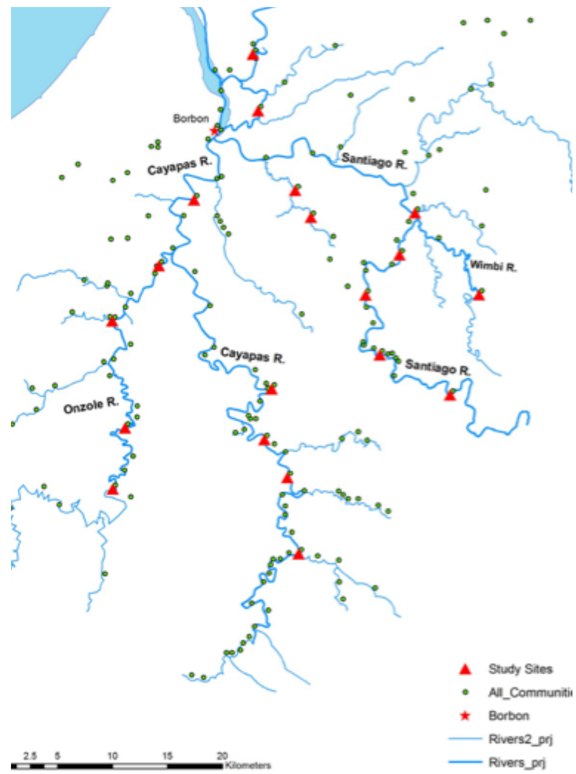
1. Is there a relationship between festivals and diarrheal incidence?
2. On what time frame (lag time) does this relationship occur?
3. Does this relationship differ depending on characteristics of the mass gathering, such as event length or associated activities?

Methods

Study Population

This study takes place in Esmeraldas province, northwestern Ecuador, at the southern end of the Choco rainforest. In Canton Eloy Elfaro, 150 small villages are distributed along the Cayapas, Santiago, and Onzole rivers (figure 6). These rivers drain toward the main town of Borbon, a community of approximately 6,000.

Figure 6. Study Region, Esmeraldas Province, Ecuador



According to the 2001 Ecuadorian national census, the canton is approximately 55% Afro-Ecuadorian, 13% Chachi, and the remainder mestizo, mulatto, or white. Since the 1980s, increasing commercial logging and export agriculture led to high rates of deforestation.[14] A paved highway was finished in 2001 connecting Borbon to the coast and the Andes, leading to increasing development, migration and a growing mestizo population. Still, in the villages surveyed, 91% of participants identified as Afro-Ecuadorian.

The size and stability of village populations in the study vary greatly, with populations ranging from 53 to 770, and percent of residents born in the village ranging from 0% to 79%. Some villages are easily accessible by road, while others are only accessible by riverboat. Infrastructure for safe water and sanitation, while improving, is still sparse in the area, and communities depend on the rivers as their primary water source. Sanitation facilities, such as in-house and public latrines, are rudimentary. The region is described in further detail elsewhere.[9,14]

Primary Data Collection

Data on the incidence of diarrheal disease, village population characteristics, and environmental exposures were collected previously as part of the EcoDESS project, which investigates linkages between environmental change and diarrheal diseases in the region.[9] The diarrheal disease data assessed in this study was collected from 21 villages, selected by block randomization to represent the region. Of the 21 surveyed villages, only 19 are included in the present analysis due to the poor quality surveillance data in 2 villages, as determined by previous quality control analyses of the data.[20]

Reported cases of diarrhea were recorded during weekly surveys from February 18, 2004 through July 4, 2007 by the local EcoDESS field team. Self-identified heads of household were interviewed about illness and symptoms experienced by any of the household members in the previous week. Cases of diarrhea were identified following the WHO-accepted definition of 3 or more loose stools in a 24-hour period. Across all villages, total diarrhea incidence for all age groups was 4.12 cases per 1,000 person-weeks. In children under 5, total incidence was 13.08 cases per 1,000 person-weeks. In some weeks, diarrheal incidence data could not be collected for certain villages (due to logistical difficulties encountered by the field team). This missing data accounts for 5% of total village-weeks, and these village-weeks were excluded from the analysis.

In addition to population characteristics collected during weekly surveys (age, gender), access to improved sanitation and improved drinking water sources were assessed during annual village censuses, social networks were measured during a complete census conducted in 2004 and again in 2007, and water treatment and hygiene were determined during a case-control study of diarrhea in the same villages between 2003 and 2008.[9] Institutional review boards at the University of California, Berkeley, University of Michigan, and Universidad San Francisco de Quito approved all human subjects protocols. Environmental exposures in the form of extreme rainfall events were previously derived from data collected by four HOBO rain gauges (Onset Corporation, Borne, Massachusetts) placed across the region, and found to be significantly associated with the incidence of diarrhea when antecedent rainfall over the past 2 months was relatively low.[20]

Festival Data Collection

Dates of secular and religious festivals hosted annually in each study village were obtained from an anthropologist local to the study region (A. Acevedo, personal communication, June 25, 2016). Twenty-three annual festivities were identified. Eleven of these represented common celebrations which all communities hosted, including New Year's, Carnival, Holy Week, Father's Day, Mother's Day, Day of the Dead, and Christmas, or which all Afro-Ecuadoran communities hosted, including Las Carmen, San Antonio, Las Marias, and El Rosario (Table 1). The remainder represented events hosted in single communities, such as village-specific Saint's days, community and school celebrations, etc. (Table 2). Festivals were indicated to be secular (39% of events) or religious (61% events) in theme, and some were indicated to be Saint's Days (28% of events). Festival events had inferred lengths of 1 (38%), 2 (33%), 3 (5%), 4 (20%), or 7 (2%) days, which were defined from the identity and location of the festival, and are thus strongly correlated with other festival characteristics. Festivals occur on the same date each year, except for Carnival and Holy Week, which follow the Gregorian calendar, as well as Father's Day and Mother's Day, which fall on specific days of the week.

Table 1. Regional Festivals and their Characteristics

Hosting Villages	Name	Type	End Date	Length (Days)
all	Año Nuevo	Secular	1-Jan	2
all	Carnaval	Religious	Late Feb / Early Mar	4
all	Semana Santa	Religious	Late Mar / Early Apr	4-7
all	Dia de las Madres	Secular	2 Sunday May	1
all	San Antonio	Saint Day	14-Jun	2-3
all	Dia de los Padres	Secular	3 Sunday June	1
all	Las Cármenes	Saint Day	16-Jul	1
all	Las Marías	Saint Day	8-Sep	1
all	El Rosario	Saint Day	8-Oct	2-3
all	Día de los Difuntos	Religious	3-Nov	2
all	Navidad	Religious	25-Dec	2

Table 2. Village-Specific Festivals and their Characteristics

Hosting Village	Name	Type	End Date	Length (Days)
3	San Agustín	Saint Day	28-Aug	1
4	Fiesta del Pueblo	Secular	10-Aug	1
5	Fundación Escuela	Secular	26-Oct	1
7	Fundación Escuela	Secular	23-Oct	1
10	Fiesta del Pueblo	Secular	12-Oct	1
11	Las Mercedes	Saint Day	25-Sep	3
11	Fiesta del Pueblo	Secular	5-Oct	2
17	Santo Domingo	Secular	14-May	1
17	San Martín de Porres	Saint Day	3-Nov	1
20	Santísima Trinidad	Saint Day	15-Jun	4
20	Las Mercedes	Saint Day	24-Sep	1
21	Fiesta del Pueblo	Secular	29-Sep	2

To convert these data into a weekly time series describing the characteristics of events hosted in each village each week, weekly binary ($host_{yn}$) and categorical ($host_{length}$) variables were created for each village, representing whether or not a festival was hosted and the maximum length of any festival ending within a given week, respectively. The choice of a categorical variable representing festival length was motivated by the direct relationship between the length of any given festival and the type of festival. If different activities or differences in population mixing are associated with festival duration, categorical variables for festival length, referenced to the last date of the festival, may better explain disease outcomes than a binary definition of festival.

Statistical Analyses

Descriptive Analyses

Descriptive statistics were examined across the 19 villages studied, including the mean and variance of weekly incidence of diarrhea, and yearly festival days hosted. Time series plots of diarrheal incidence per 1,000 person-weeks as well as weekly festival days were generated. Village-specific standardized incidence rates for each village-week were estimated as:

$$SIR_{v,t} = \frac{Y_{v,t}}{P_{v,t} * \frac{\sum_t Y_{v,t}}{\sum_t P_{v,t}}} \tag{1}$$

where $SIR_{v,t}$ is the standardized weekly incidence rate; $Y_{v,t}$ is the number of incident cases of diarrhea; and $P_{v,t}$ is the population at risk in village v during time period t. Village-specific standardized incidence rates were examined against time-since-festival events, cumulatively and stratified by festival duration.

Base Regression Models

In order to estimate the effect of festival hosting and attendance on short-term variations in diarrheal incidence, a separate Poisson regression model was constructed for each version (binary and categorical) of the hosting variable:

$$Y_{v,t} \sim Poisson\left(P_{v,t} * e^{\alpha_v + \beta X_t}\right) \tag{2}$$

where $P_{v,t}$ is as above; α_v is a village-specific intercept included to accommodate underlying differences in the average risk of diarrheal disease across sites; and β is vector of coefficients describing the effects of exposures X_t. To control for autocorrelation in the outcome, a Generalized Estimating Equation (GEE) approach was chosen to estimate α_v, β, and robust bootstrap methods were employed to estimate the standard errors of model parameters.[88] A distributed lag model was used with separate effects estimated for festival variables at 0, 1, 2, 3, and 4 week lags, thought to encompass the likely scale of incubation periods and probable duration of primary and secondary transmission related to festival events.

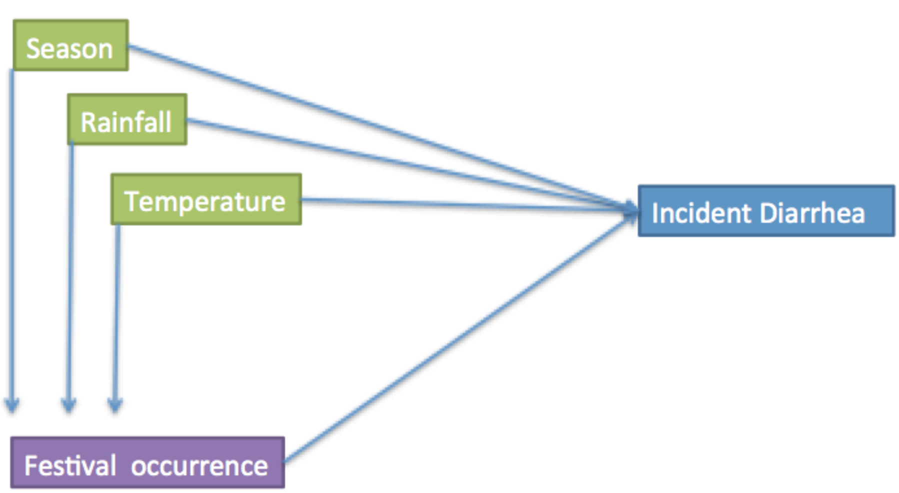
Adjusted Models

Confounding from variables operating on a similar time-scale to festivals was considered, including the effects of seasonality and heavy rainfall events (figure 7). Temperature was initially considered as a potential confounder, but previous analysis found no effect of temperature on diarrhea in this region, and so it was not considered further here.[89] Other factors known to be associated with diarrheal disease incidence —such as sanitation,[4] housing density,[16] and remoteness[9]—which vary over much larger time scales in our dataset, were not considered to be potential confounders.[90] Bivariate models were built for each potential confounder – described in further detail below – and tested for an association with the outcome of diarrheal incidence. Confounders with relationships to the outcome were included in adjusted models with the binary and categorical festival variables.

Seasonality
Seasonality was assessed using a time-stratified approach with quarterly (based on calendar year) and seasonal ("rainy" and "dry") indicator variables.

Rainfall
Indicator variables were included for the occurrence of heavy rainfall events (defined previously[20] by exceedance of 90% of daily rainfall records across the study period on any day in a given week), stratified by the tertile of antecedent rainfall over the prior 8 weeks, were included as potential confounders.[20] Following previous findings, rainfall events were considered to operate at a 2-week lag.[20]

Figure 7. Causal diagram indicating potential confounders



Results

Distribution and Characteristics of Diarrheal Incidence

Community population ranged from 49 to 770 individuals, and a total of 5170 people in 19 villages were surveyed over the study period. Over the study period of 177 weeks, there were a total of 749 village-weeks in which a festival occurred. The number of weeks in which a festival was hosted in a given village ranged from 38 to 44 (Table 3). Village-level diarrhea incidence ranged from 1.9 per 1,000 person weeks to 11.6 per 1,000 person weeks (Table 3).

Diarrheal incidence does not show distinct seasonal patterns, with the timing of diarrheal incidence peaks varying each year (figure 8A). 2006 and 2007 both have overall lower diarrheal incidence than 2004 and 2005.

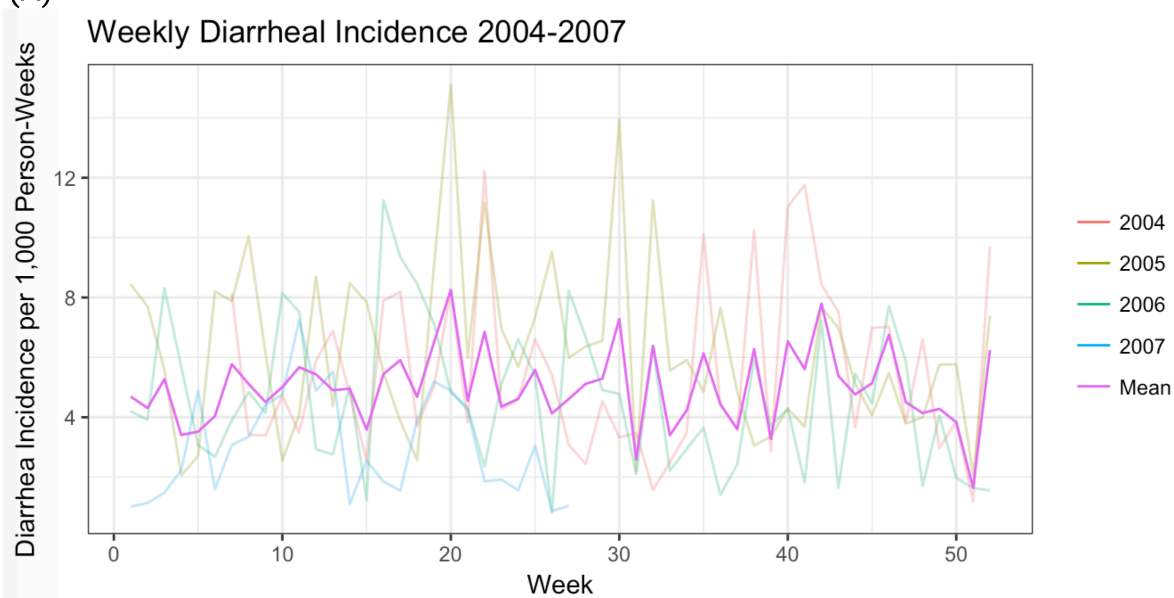
Festivals are hosted relatively regularly throughout the year. Festival dates based on the Gregorian calendar vary each year, leading to greater variability between years in the first half of the year, when these festivals (Carnival and Holy Week) take place. More village-specific festivals occur in the latter half of the year (figure 8B).

Table 3. Relevant Characteristics of Study Villages

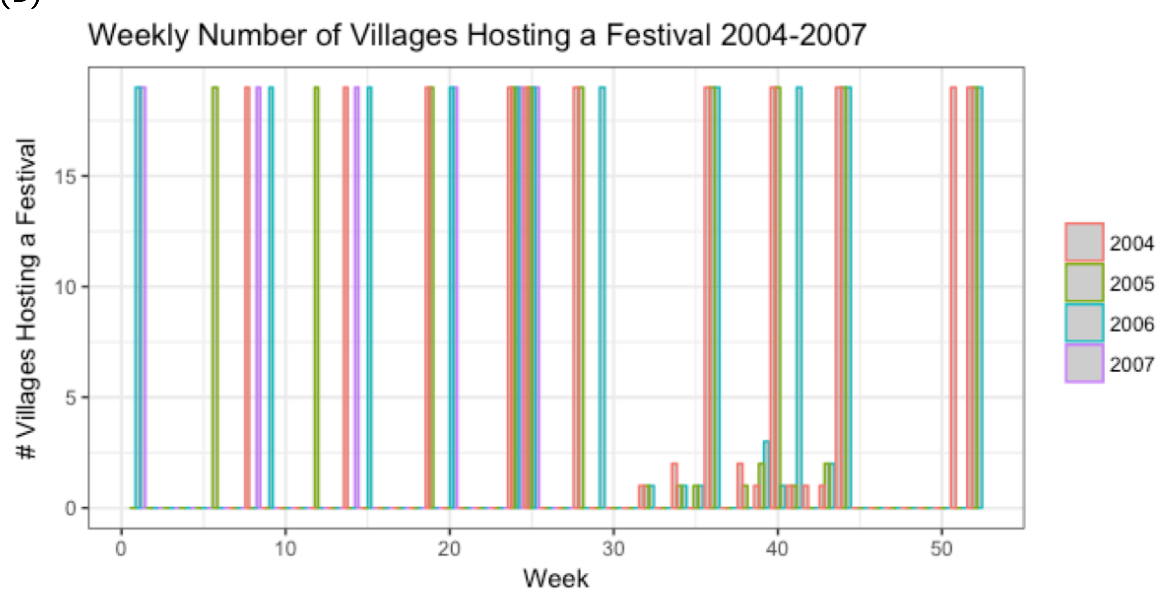
Village	Total Survey Weeks	Mean (SD) Population	Mean (SD) Diarrheal Incidence per 1000 person-weeks	Weeks with Festival
1	175	52.85 (0.82)	4.26 (11.07)	38
2	175	120.45 (16.77)	4.93 (6.89)	38
3	155	262.28 (28.35)	8.06 (8.83)	41
4	173	484.11 (46.42)	4.83 (5.34)	41
5	176	770.01 (70.92)	2.90 (2.60)	41
7	172	75.99 (5.00)	3.56 (8.46)	41
8	162	144.99 (8.42)	6.68 (8.82)	38
9	173	296.72 (16.19)	4.65 (7.46)	38
10	154	123.66 (12.80)	2.38 (6.72)	40
11	168	238.65 (8.40)	1.94 (4.50)	42
12	135	49.44 (20.63)	11.56 (22.53)	38
13	160	86.96 (21.59)	6.87 (13.45)	38
15	159	78.92 (5.51)	3.32 (14.49)	38
16	176	93.86 (7.73)	5.45 (12.49)	38
17	171	430.15 (11.37)	4.38 (5.34)	38
18	159	107.94 (5.74)	8.09 (15.60)	38
19	174	299.91 (42.27)	3.59 (7.56)	38
20	175	88.74 (11.04)	2.26 (6.46)	44
21	172	131.19 (12.02)	7.74 (10.06)	41

Figure 8. Weekly diarrheal incidence (A) and number of villages hosting a festival (B) in 19 villages in a study of festival events and diarrhea incidence, Ecuador, Feb 2004-July 2007.

(A)



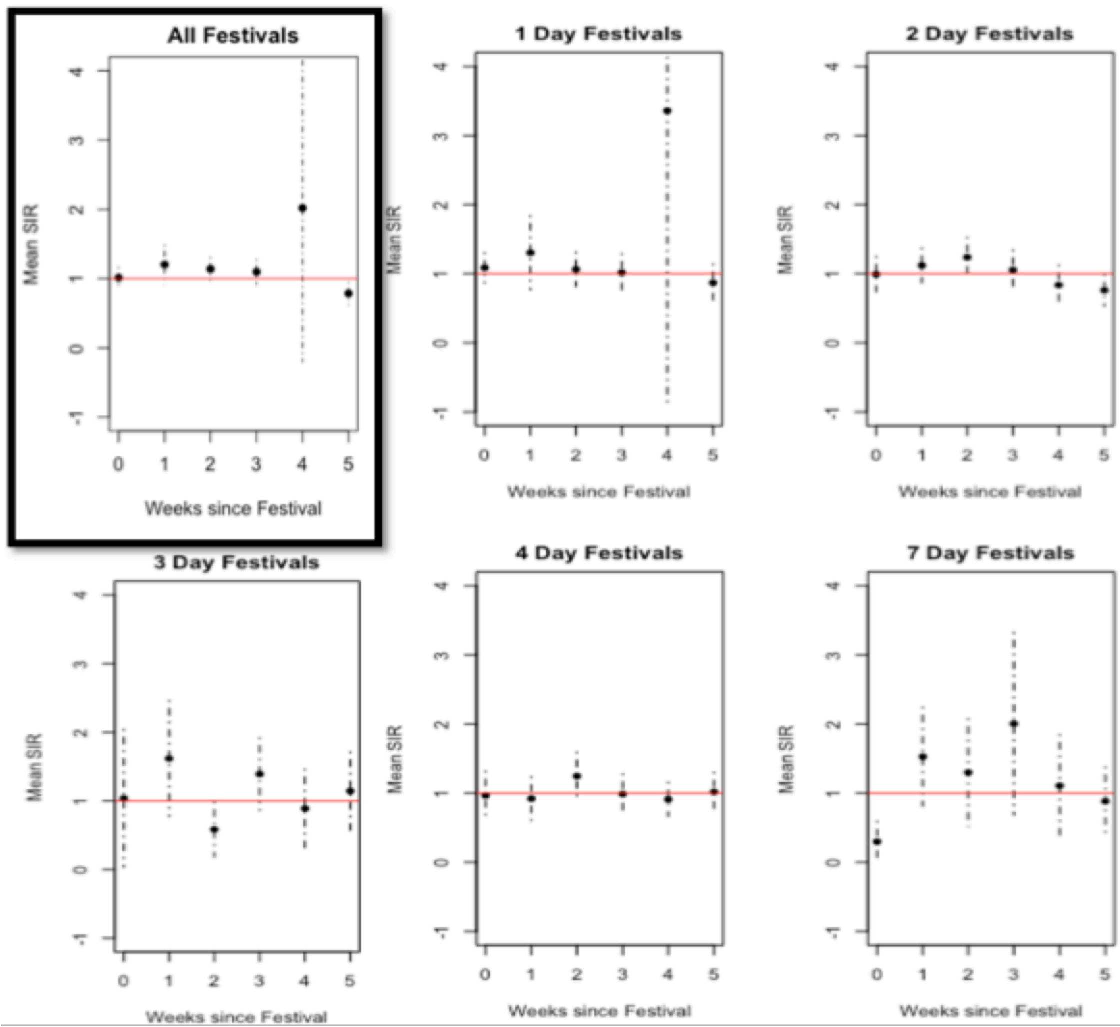
(B)



Village-specific standardized incidence rates show a temporal signature over the first 5 weeks after the last festival was hosted (figure 9). When considering all festivals, average SIR spikes at 1 week since the last festival, gradually attenuates toward baseline, and then drops below baseline on week 5. When stratifying by festival length, similar trends are found for festival durations of 1, 2, 4, and 7 days, though 2 and 4-day festivals peak at a 2-week lag and 7-day festivals peak at a 3-week lag. 3-day festivals are unusual in that they show a decrease in mean SIR below baseline at a 2-

week lag. The standard errors of 3 and 7-day festivals are large due to the paucity of data points. For all festival lengths, the mean SIR returns to 1 by 4 weeks post-festival, so regression analyses explored festival exposures over a 0-4 week lag.

Figure 9. Mean standardized incidence ratios (SIR) vs. weeks since last festival (cumulative and stratified by festival length). Dashed lines represent 95% confidence intervals of the mean SIR.



Adjusted Model Variable Selection

Each potential confounder was tested individually in a bivariate model for a significant relationship with the outcome of diarrheal incidence. Neither season (IRR 1.01, 95% CI 0.9,1.13) nor quarter (IRR 1, 95% CI 0.96,1.05) was found to have any significant relationship with the outcome. Heavy rainfall events, stratified by 8-week prior rainfall, were found to have a significant relationship with the outcome and were thus the sole additional variable included in the adjusted model.

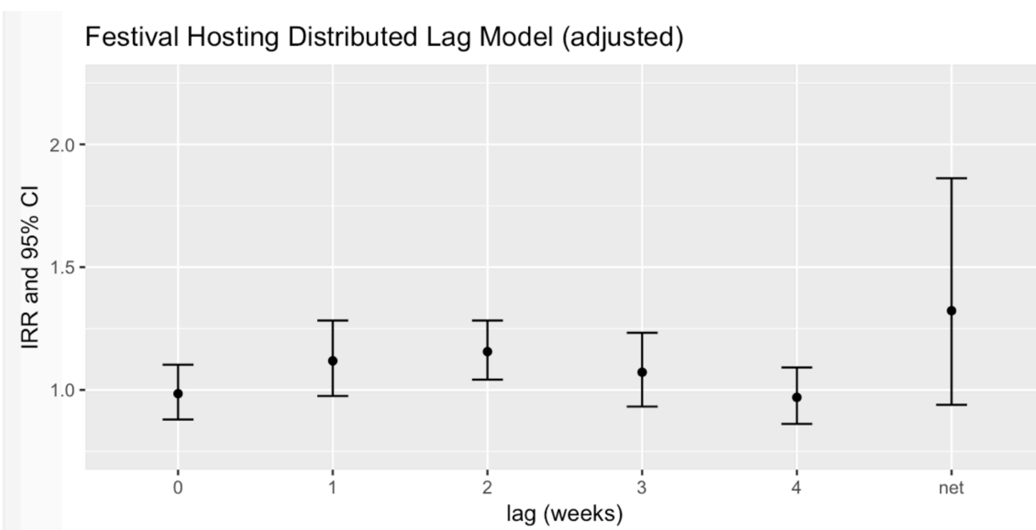
Associations Between Festival Events and Diarrheal Incidence

In the adjusted model, hosting a festival was associated with a 16% increase (95% CI 6%, 31%) in diarrheal incidence 2 weeks later (Table 4). 1 and 3 week lag times showed smaller effects trending toward significance (12% increase and 7% increase, respectively) and the 4 week lag time showed attenuation of the association over time (visual representation in figure 10).

Table 4. Association between hosting festival events and diarrhea incidence, at lag times 0-4 weeks from end of festival. Results adjusted for heavy rainfall events. IRR (CI).

	Hosting	
	Unadjusted	Adjusted
Lag 0	0.97 (0.88, 1.08)	0.98 (0.88, 1.10)
Lag 1	1.12 (0.98, 1.29)*	1.12 (0.98, 1.28)
Lag 2	1.11 (0.99, 1.23)*	1.16 (1.04, 1.28)***
Lag 3	1.08 (0.94, 1.23)	1.07 (0.93, 1.23)
Lag 4	0.98 (0.87, 1.10)	0.97 (0.86, 1.09)
	p<0.1; **p<0.05**;** p<0.01***	

Figure 10. Lagged IRRs associated with festival hosting, with net effect over 4 weeks. Error bars represent 95% confidence intervals of effects.



Festival Length as an Effect Modifier

Given the significance of the 2-week lag in the binary model, this lag time was chosen to examine festival length as a potential effect modifier. When stratifying hosting effects by festival duration, significant associations were present for hosting two and 7-day festivals. Hosting 1, 3, and 4-day festivals were not found to have any significant associations with diarrheal incidence. In the adjusted model, hosting a 2-day festival was associated with a 24% increase (95% CI 1%, 52%) in diarrheal incidence 2 weeks later (Table 5). Hosting a 7-day festival was associated with a 48% increase (95% CI 0%, 119%) in diarrheal incidence 2 weeks later (Table 5).

Table 5. Association between the length of hosted festivals and diarrhea incidence at 2 weeks from end of festival, with categorical treatment of festival length exposure. Results adjusted for heavy rainfall events. IRR (95% CI)

	Hosting	
Festival Length	Unadjusted	Adjusted
1 day	1.04 (0.91, 1.18)	1.09 (0.93, 1.28)
2 day	1.20 (0.98, 1.47)*	1.24 (1.01, 1.52)**
3 day	0.58 (0.37, 0.92)**	0.65 (0.37, 1.13)
4 day	1.20 (0.86, 1.68)	1.21 (0.87, 1.70)
7 day	1.33 (0.88, 2.00)	1.48 (1.00, 2.19)**
	p<0.1; **p<0.05**;* p<0.01***	

Discussion

The results of this analysis indicate an association between festivals and increased diarrheal disease risk 1 to 3 weeks later. The strength of this relationship varies with festival duration, with the strongest associations observed for 2-day and 7-day events.

Our results indicate that associations between festival hosting and diarrheal disease are observed over a span of 1 to 3 weeks following the events, with the maximum association observed 2 weeks after the week in which the festival ends. The range of lags over which associations were observed may have arisen through a combination of several mechanisms, including variable incubation times of etiologic agents of diarrhea (common pathogens in the region— pathogenic *E. coli*, rotavirus, and *Giardia intestinals* —have typical incubation periods of 1 to 8 days[29]); amplified secondary transmission from index cases infected during festival events, potentially followed by dampened tertiary transmission, or errors in the specification of lag times, resulting from weekly discretization and uncertainty in the exact interview dates for each village. The observed associations distributed over 3 weeks are consistent with previous case studies of transmission of gastrointestinal illness outbreaks associated with festivals, where a small number of initial infections proceed to a peak in cases over a 1 to 2 week period, with complete outbreak epidemic curves lasting approximately 3 weeks.[76,77] The statistically significant effect at 2 weeks is also consistent with findings for heavy rainfall events—the only other short-term temporal risk factor having been investigated in the case of diarrheal disease transmission in this region.[20]

The strength of association between festival events and diarrheal incidence was found to vary with festival duration. 1, 3, and 4-day festivals exhibited no significant association with diarrheal incidence, while 2 and 7-day festivals were associated with a 24% and 48% increased risk of diarrhea 2 weeks later, respectively. If all festival events are equal in terms of the risky exposures they entail, event length would be expected to have a monotonic increasing relationship with diarrheal incidence as a result of additive exposures or accumulation of pathogens in the local environment for each additional day in which a festival is hosted. That such a trend is not apparent across festival durations in our current analysis suggests that any cumulative effects of risk are outweighed by differences in exposures across festival types, which are associated with festival lengths. The heightened association of 2 and 7 day festivals with diarrheal disease in subsequent weeks may have to do with the particular festivals that fall into either category. 2-day festivals are varied—representing various secular celebrations as well as religious events such as Day of the Dead and Christmas. On the other hand, 7-day festivals are hosted only in four specific villages during Holy Week. Holy Week is the largest and most important festival in the region, and entails food sharing of traditional dishes as well as local and regional travel.[91]

While further qualitative investigations are necessary to identify the types of activities that may contribute specifically to risk for a given festival, the particular characteristics of mass gatherings— overwhelmed sanitation and hygiene infrastructure, food sharing, and migration—present plausible mechanisms by which diarrheal disease transmission may be amplified.[74]

One possible mechanism for the relationship between festivals and diarrheal illness is environmental contamination due to insufficient sanitation infrastructure to accommodate visiting populations. Not everyone in each village has a toilet, and people often use neighbors' toilets or public toilets.[15] It is plausible that, with an influx of visitors, there may be an overwhelming of sanitation infrastructure simply by overuse.[72] There also may be situations in which people don't have access to sanitary facilities because they are visiting from out of town and can't use "a neighbor's" toilet, and therefore defecate outdoors. Finally, there may be more alcohol and food consumption leading to more frequent and less careful bathroom use.[74]

A second potential mechanism is a failure of hygiene, specifically hand-washing hygiene among food handlers, production of large quantities of food by multiple handlers, unsanitary food prep conditions, and lack of clean water in sufficient quantities. These conditions have been documented in previous studies of large-scale open-air festivals.[74] Ethnographic observations have shown the presence of extensive food sharing at festivals within this study region, including crowding at local eating establishments and mass food preparation.

Finally, the introduction of new pathogens by inter-village festival attendance is a third potential mechanism. The revelers at each festival are not isolated to the particular village hosting the festival, rather the village becomes nodal in the region: visitors come from neighboring towns and even from villages located in other river basins (A. Acevedo, personal communication, August 17, 2016).

Previous studies in this region have pointed toward the importance of inter-village transmission in diarrheal disease incidence. One study found that community disease dynamics are affected by those in surrounding communities, where the effectiveness of interventions (latrines and water treatment) depended on regional prevalence.[15] In another study, remoteness—defined by length of travel to the central town of Borbón—was found to be associated with lower rates of diarrheal disease.[9] Follow-up studies found that remoteness was associated with higher levels of intra-village social connectedness, which was hypothesized to decrease diarrheal disease risk due to investment in social goods such as water quality and sanitation measures.[16] In addition, remoteness was associated with a decreased rate of inter-village migration, as defined by the proportion of households with a visitor from outside the village in the previous week (higher proportions of households with visitors were associated with increased diarrheal disease risk).[19] While the current analysis does not investigate the interaction between remoteness and festival activity, it is plausible that part of the reason for the decreased risk in more remote villages is reduced connection to nearby festivals, which may be serving as nodes of pathogen transmission.

Traditionally, more highly connected social networks are seen as more efficient disease transmission systems, especially in terms of sexually transmitted disease.[57,58] Transmissibility of infectious disease has been proposed to be a function of the mean number of contacts and the extent of clustering.[59] While social connectedness on a village level may decrease risk due to increased investment in collective mitigation strategies, social connectedness at the scale of regional migration networks—which may intensify during festival periods—may facilitate the spread of pathogens. This is theoretically consistent with the sexually transmitted infection (STI) literature, in which high frequencies of repeated contacts are associated with smaller and slower growing epidemics, while high concurrency (simultaneity) of contacts is associated with larger and faster growing epidemics.[86]

Further data collection is needed to explore attendance patterns at festivals and migration patterns around festival times. In particular, Holy Week is considered a week of migration, as people travel to vacation, see family, or attend festivities. Increased incidence in villages hosting festivals may be due to this migration. In addition, it is likely that any festival-linked outbreak may subsequently reach neighboring communities through local travel, local food or livestock commerce, or waterway contamination.

Further studies identifying the context-specific mechanisms underlying the association between festivals and diarrheal disease may assist in identifying specific supportive interventions for these types of social events. One possible direction is assessing the interaction between baseline risk and protective factors and the effect of festivals. For instance, are festivals in villages with water treatment less likely to experience increased diarrheal incidence than villages without water treatment? Further studies could utilize existing EcoDESS data on the infrastructure in each town (e.g. availability and functionality of public toilets and water treatment facilities) to answer this question. The results of this study already make clear, however, that transmission mitigation techniques are necessary not only for large-scale and infrequent mass gatherings, but smaller scale mass gatherings that occur on an annual basis.

Limitations

The limitations of this analysis are primarily related to assumptions made when retrospectively inferring the occurrence and characteristics of social events. Festival dates were determined in 2017, and assumed to be stable from year to year during the study period of 2004-2007. However, the occurrence and duration of festivals may vary depending on the availability of funds in a given village, or other logistical or environmental factors (A. Acevedo, personal communication, August 17, 2016), and so it is not certain that every festival actually occurred on the dates specified for this analysis. With respect to festival occurrence, this potential source of error would likely be non-differential, and would generally bias associations towards the null.

With respect to festival lengths, some misclassification is also likely. A festival is not limited to the day of its celebration; it may start a couple of days before and be extended so long as the community has the capacity to receive visitors. The data on festival occurrence was not fine-scale enough to account for this variability. Therefore, there is some uncertainty in the stratification of festivals into length categories. For example, it is possible that a festival, currently classified as a 2-day festival in all villages, is actually 2-days in some and 4-days in others.

Another limitation is our reliance on festival length as a proxy for variable exposures. This method is both theoretically unsatisfying and a poor means of separating festivals with variable characteristics. While some length categories, such as 7-day festivals, account for very specific events, others include multiple types of festivities. For instance, 4-day festivals encompass both Carnival celebrations and shorter Holy Week celebrations. Furthermore, there is an inherent assumption that festivals of the same type and/or length have the same effect across all villages, when in reality major differences in risk mechanism are likely between villages. For example, two of the villages in the original study are transient communities, who, while they celebrate all the common festivals, might have primarily been attending other festivals rather than hosting their own. The ecological fallacies implicit in these limitations are likely to bias estimated effects towards the null.

The definition of lagged exposures, referenced to the week in which a festival ended, likely results in some misspecification of actual temporal lags between events and disease occurrence. For instance, a coded lag time of 1 week for a 1 day festival is likely to represent a shorter actual lag from a potential time of exposure than a coded lag time of 1 week for a 7 day festival, since a nearly 1-week lag from the first day of potential exposure occurs in the latter case. This introduces uncertainty into interpretation of the effect estimates in the distributed lag model of the binary festival exposure.

Finally, the lack of microbiological data from diarrheal cases and the aggregation of diarrheal cases at the village level prevent confirmation of pathogen-specific transmission pathways.

Conclusion

Previous research on diarrheal disease has identified multiple causal pathways involved in transmission—food and food hygiene, water, person-to-person, sanitation, personal and domestic hygiene, and flies—but has mostly focused on single-transmission pathways without considering multiple pathways or interdependencies between pathways.[42] Eisenberg et al. (2006) emphasized the importance of moving toward community level analysis that takes into account the interaction of social and environmental pathways. In this analysis of festivals, we do just this by examining social events at the nexus of all of these interconnected pathways.

Results of this analysis indicate that small-scale, annual mass gatherings do play a role in diarrheal disease transmission. Specifically, associations with increased diarrheal disease incidence peak 2 weeks after a festival. 2-day and 7-day festivals are indicated to be the drivers of this association, with 7-day Holy Week associated with a 48% increase in diarrheal incidence 2 weeks later. This has implications for the understanding of inter-community transmission dynamics—as festivals are often hubs of local travel—as well as intervention strategies to mitigate hygienic food preparation and sanitation system breakdown during high-use events. Finally, while the first period of research on diarrheal disease epidemiology consisted primarily of static risk-factor observational studies, this adds to the growing body of research examining temporal factors in timing of diarrheal disease outbreaks, as well as the interrelation of environmental and social factors in infectious disease dynamics.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2095-2128. doi:10.1016/S0140-6736(12)61728-0.
2. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2197-2223.
3. Kirk MD, Pires SM, Black RE, et al. World Health Organization Estimates of the Global and Regional Disease Burden of 22 Foodborne Bacterial, Protozoal, and Viral Diseases, 2010: A Data Synthesis. doi:10.1371/journal.pmed.1001921.
4. Eisenberg JN, Trostle J, Sorensen RJ, Shields KF. Toward a Systems Approach to Enteric Pathogen Transmission: From Individual Independence to Community Interdependence. doi:10.1146/annurev-publhealth-031811-124530.
5. America WS, America S. SOUTH AMERICA :: ECUADOR. 2017:1-13.
6. *Global Burden of Diseases, Injuries, and Risk Factors Study: Ecuador*. Seattle, Washingon; 2010.
7. *Global Nutrition Report: 2014 Country Profile, Ecuador*.; 2014.
8. WHO, UNICEF. *Estimates on the Use of Water Sources and Sanitation Facilities: Ecuador*.; 2017.
9. Eisenberg JNS, Cevallos W, Ponce K, et al. Environmental change and infectious disease: how new roads affect the transmission of diarrheal pathogens in rural Ecuador. *Proc Natl Acad Sci U S A*. 2006;103(51):19460-19465. doi:10.1073/pnas.0609431104.
10. Redvers-lee P. The Serpent without Shame: Economic Development and Change In Afro-Ecuadorian Communities of Northwestern Esmeraldas. 2011.
11. DeBoer WR. *Traces Behind the Esmeraldas Shore*. Tuscaloosa: The University of Alabama Press; 1996.
12. Wellington PJ. Folklorization and Afro-ecuadorian Music in Esmeraldas. 2012.
13. Rahier JM. *Kings for Three Days: The Play of Race and Gender in an Afro-Ecuadorian Festival*. Champaign: University of Illinois Press; 2013.
14. Sierra R. Traditional resource-use systems and tropical deforestation in a multi-ethnic region in North-West Ecuador. *Environ Conserv*. 1999;26(2):136-145. doi:10.1017/S0376892999000181.
15. Goldstick JE, Trostle J, Eisenberg JNS. Ask when--not just whether--it's a risk: How regional context influences local causes of diarrheal disease. *Am J Epidemiol*. 2014;179(10):1247-1254. doi:10.1093/aje/kwu034.
16. Bates SJ, Trostle J, Cevallos WT, Hubbard A, Eisenberg JNS. Relating diarrheal disease to social networks and the geographic configuration of communities in rural Ecuador. *Am J Epidemiol*. 2007;166(9):1088-1095. doi:10.1093/aje/kwm184.
17. Levy K, Hubbard AE, Nelson KL, Eisenberg JNS. Drivers of Water Quality Variability in Northern Coastal Ecuador. *Env Sci Technol*. 2009;43(6):1788-1797.

doi:10.1021/es8022545.
18. Eisenberg JNS, Goldstick J, Cevallos W, et al. In-roads to the spread of antibiotic resistance: regional patterns of microbial transmission in northern coastal Ecuador. *J R Soc Interface*. 2012;9(70):1029 LP-1039.
19. Zelner JL, Trostle J, Goldstick JE, Cevallos W, House JS, Eisenberg JNS. Social connectedness and disease transmission: social organization, cohesion, village context, and infection risk in rural Ecuador. *Am J Public Health*. 2012;102(12):2233-2239. doi:10.2105/AJPH.2012.300795.
20. Carlton EJ, Eisenberg JNS, Goldstick J, Cevallos W, Trostle J, Levy K. Heavy rainfall events and diarrhea incidence: the role of social and environmental factors. *Am J Epidemiol*. 2014;179(3):344-352. doi:10.1093/aje/kwt279.
21. Levy K, Woster AP, Goldstein RS, Carlton EJ. Untangling the Impacts of Climate Change on Waterborne Diseases: A Systematic Review of Relationships between Diarrheal Diseases and Temperature, Rainfall, Flooding, and Drought. *Environ Sci Technol*. 2016;50(10):4905-4922. doi:10.1021/acs.est.5b06186.
22. Fischer Walker CL, Perin J, Aryee MJ, Boschi-Pinto C, Black RE. Diarrhea incidence in low- and middle-income countries in 1990 and 2010: a systematic review. *BMC Public Health*. 2012;12(1):220. doi:10.1186/1471-2458-12-220.
23. Butterton JR, Calderwood SB. Acute Infectious Diarrheal Diseases and Bacterial Food Poisoning. 2007:1-13.
24. Clasen TF, Alexander KT, Sinclair D, et al. Interventions to improve water quality for preventing diarrhoea. *Cochrane database Syst Rev*. 2015;10:CD004794. doi:10.1002/14651858.CD004794.pub3.
25. Hodges M, Belle JH, Carlton EJ, et al. Delays in reducing waterborne and water-related infectious diseases in China under climate change. *Nat Clim Chang*. 2014;4(12):1109-1115.
26. Gentry-Shields J, Bartram J. Human health and the water environment: Using the DPSEEA framework to identify the driving forces of disease. *Sci Total Environ*. 2014;468-469:306-314. doi:10.1016/j.scitotenv.2013.08.052.
27. Fletcher SM, McLaws M-L, Ellis JT. Prevalence of gastrointestinal pathogens in developed and developing countries: systematic review and meta-analysis. *J Public health Res*. 2013;2(9):42-53.
28. Vasco G, Trueba G, Atherton R, et al. Identifying Etiological Agents Causing Diarrhea in Low Income Ecuadorian Communities. *Am J Trop Med Hyg*. 2014;91(3):563-569. doi:10.4269/ajtmh.13-0744.
29. Bhavnani D, Bayas R de los Á, Lopez VK, et al. Distribution of Enteroinvasive and Enterotoxigenic Escherichia coli Across Space and Time in Northwestern Ecuador. *Am J Trop Med Hyg*. 2016;94(2):276-284. doi:10.4269/ajtmh.14-0337.
30. Hunter PR. Drinking water and diarrhoeal disease due to Escherichia coli. *J Water Health*. 2003;1(2):65-72.
31. Dirk Van Elsas J, Semenov A V, Costa R, Trevors JT. Survival of Escherichia coli in the environment: fundamental and public health aspects. *ISME J*. 2011;580(10):173-183. doi:10.1038/ismej.2010.80.
32. Lothigius Å, Sjöling Å, Svennerholm A-M, Bölin I. Survival and gene expression of

enterotoxigenic *Escherichia coli* during long-term incubation in sea water and freshwater. *J Appl Microbiol*. 2010;108(4):1441-1449. doi:10.1111/j.1365-2672.2009.04548.x.
33. Cook KL, Bolster CH. Survival of Campylobacter jejuni and Escherichia coli in groundwater during prolonged starvation at low temperatures. *J Appl Microbiol*. 2007;103(3):573-583. doi:10.1111/j.1365-2672.2006.03285.x.
34. Celli J, Deng W, Finlay BB. Enteropathogenic Escherichia coli (EPEC) attachment to epithelial cells: exploiting the host cell cytoskeleton from the outside. *Cell Microbiol*. 2000;2(1):1-9. doi:10.1046/j.1462-5822.2000.00033.x.
35. Blaser S, ed. *Infections of the Gastrointestinal Tract*. Lippincott Williams and Wilkins; 2002.
36. Sur D, Ramamurthy T, Deen J, Bhattacharya SK. Shigellosis : challenges & management issues. *Indian J Med Res*. 2004;120:454-462.
37. Ansari SA, Springthorpe VS, Sattar SA. Survival and Vehicular Spread of Human Rotaviruses: Possible Relation to Seasonality of Outbreaks. *Clin Infect Dis*. 1991;13(3):448-461. doi:10.1093/clinids/13.3.448.
38. Ramig RF. Pathogenesis of intestinal and systemic rotavirus infection. *J Virol*. 2004;78(19):10213-10220. doi:10.1128/JVI.78.19.10213-10220.2004.
39. Huang DB, White AC, Thomas E, al. et. An updated review on Cryptosporidium and Giardia. *Gastroenterol Clin North Am*. 2006;35(2):291-314, viii. doi:10.1016/j.gtc.2006.03.006.
40. Gilman R, Miranda E, Marquis G, Vestegui M, Martinez H. Rapid reinfection by giardia lamblia after treatment in a hyperendemic third world community. *Lancet*. 1988;331(8581):343-345. doi:10.1016/S0140-6736(88)91131-2.
41. Kawata K. *Minimum Investment*.; 1978.
42. Eisenberg JNS, Trostle J, Sorensen RJD, Shields KF. Toward a systems approach to enteric pathogen transmission: from individual independence to community interdependence. *Annu Rev Public Health*. 2012;33:239-257. doi:10.1146/annurev-publhealth-031811-124530.
43. Honjo K. Social epidemiology: Definition, history, and research examples. *Environ Health Prev Med*. 2004;9(5):193-199. doi:10.1007/BF02898100.
44. Black RE, Brown KH, Becker S, Alim ARMA, Merson MH. Contamination of weaning foods and transmission of enterotoxigenic Escherichia coli diarrhoea in children in rural Bangladesh. *Trans R Soc Trop Med Hyg*. 1982;76(2):259-264. doi:10.1016/0035-9203(82)90292-9.
45. Schmitt R, Bryan FL, Jermini M, et al. Hazards and Critical Control Points of Food Preparation in Homes in Which Persons Had Diarrhea in Zambia. *J Food Prot*. 1997;60(2):161-171. doi:10.4315/0362-028X-60.2.161.
46. AHMED F, CLEMENS JD, RAO MR, BANIK AK. Family Latrines and Paediatric Shigellosis in Rural Bangladesh: Benefit or Risk? *Int J Epidemiol*. 1994;23(4):856-862. doi:10.1093/ije/23.4.856.
47. Makoni FS, Ndamba J, Mbati PA, Manase G. Impact of waste disposal on health of a poor urban community in Zimbambwe. *East Afr Med J*. 2004;81(8):422-426. http://www.ncbi.nlm.nih.gov/pubmed/15622937. Accessed July 15, 2017.

48. Barreto ML, Genser B, Strina A, et al. Effect of city-wide sanitation programme on reduction in rate of childhood diarrhoea in northeast Brazil: assessment by two cohort studies. *Lancet*. 2007;370(9599):1622-1628. doi:10.1016/S0140-6736(07)61638-9.
49. Norman G, Pedley S, Takkouche B. Effects of sewerage on diarrhoea and enteric infections: a systematic review and meta-analysis. *Lancet Infect Dis*. 2010;10(8):536-544. doi:10.1016/S1473-3099(10)70123-7.
50. Gundry S, Wright J, Conroy R. A systematic review of the health outcomes related to household water quality in developing countries. *J Water Health*. 2004;2(1). http://jwh.iwaponline.com.ucsf.idm.oclc.org/content/2/1/1. Accessed July 15, 2017.
51. Waddington H, Snilstveit B. Effectiveness and sustainability of water, sanitation, and hygiene interventions in combating diarrhoea. *J Dev Eff*. 2009;1(3):295-335. doi:10.1080/19439340903141175.
52. Stanton BF, Clemens JD. An Educational Intervention for Altering Water-Sanitation Behaviors to Reduce Childhood Diarrhea in Urban Bangladesh. *Am J Epidemiol*. 1987;125(2):292-301. doi:10.1093/oxfordjournals.aje.a114529.
53. Yeager BA, Lanata CF, Lazo F, Verastegui H, Black RE. Transmission Factors and Socioeconomic Status as Determinants of Diarrhoeal Incidence in Lima, Peru. *J Diarrhoeal Dis Res*. 1991;9:186-193. doi:10.2307/23498080.
54. Jenkins C, Dimitrakalds M, Cook I, Sanders R, Stallman N. Culture change and epidemiological patterns among the Hagahai, Papua New Guinea. *Hum Ecol*. 1988;17(1):27-57. doi:10.1007/BF01047651.
55. Pickering AJ, Davis J, Walters SP, et al. Hands, Water, and Health: Fecal Contamination in Tanzanian Communities with Improved, Non-Networked Water Supplies. *Environ Sci Technol*. 2010;44(9):3267-3272. doi:10.1021/es903524m.
56. Genser B, Strina A, dos Santos LA, et al. Impact of a city-wide sanitation intervention in a large urban centre on social, environmental and behavioural determinants of childhood diarrhoea: analysis of two cohort studies. *Int J Epidemiol*. 2008;37(4):831-840. doi:10.1093/ije/dyn101.
57. Newman MEJ. The spread of epidemic disease on networks. 2002. https://arxiv.org/pdf/cond-mat/0205009.pdf. Accessed April 25, 2017.
58. Kretzschmar M, Morris M. Measures of concurrency in networks and the spread of infectious disease. *Math Biosci*. 1996;133(2):165-195. doi:10.1016/0025-5564(95)00093-3.
59. Meyers LA, Pourbohloul B, Newman MEJ, Skowronski DM, Brunham RC. Network theory and SARS: predicting outbreak diversity. *J Theor Biol*. 2005;232(1):71-81. doi:10.1016/j.jtbi.2004.07.026.
60. Chowell G, Nishiura H, Viboud C. Modeling rapidly disseminating infectious disease during mass gatherings. 2012:1-12.
61. Root GPM. Sanitation, Community Environments, and Childhood Diarrhoea in Rural Zimbabwe. *J Heal Popul Nutr*. 2001;19:73-82. doi:10.2307/23498676.
62. Huq A, Yunus M, Sohel SS, et al. Simple sari cloth filtration of water is sustainable and continues to protect villagers from cholera in Matlab, Bangladesh. *MBio*.

2010;1(1):e00034-10. doi:10.1128/mBio.00034-10.
63. Fuller JA, Villamor E, Cevallos W, Trostle J, Eisenberg JN. I get height with a little help from my friends: herd protection from sanitation on child growth in rural Ecuador. *Int J Epidemiol*. 2016:460-469. doi:10.1093/ije/dyv368.
64. Katz J, Carey VJ, Zeger SL, Sommer A. Estimation of Design Effects and Diarrhea Clustering within Households and Villages. *Am J Epidemiol*. 1993;138(11):994-1006. doi:10.1093/oxfordjournals.aje.a116820.
65. World Health Organization. *Public Health for Mass Gatherings: Key Considerations.* Geneva, Switzerland; 2015. www.who.int/about/licensing/copyright_form/en/index.html. Accessed November 1, 2016.
66. Petersen E, Wilson ME, Touch S, et al. Rapid Spread of Zika Virus in The Americas - Implications for Public Health Preparedness for Mass Gatherings at the 2016 Brazil Olympic Games. *Int J Infect Dis*. 2016;44:11-15. doi:10.1016/j.ijid.2016.02.001.
67. Grassi de Miranda B, Cais D, Nunes J, Duarte L, Moura ML, Costa A. Mass Gatherings: Experience and Difficulties in Elaborating an Ebola Virus Disease Outbreak Response Plan in a Private Hospital in Brazil. *Am J Infect Control*. 2017;44(6):S123-S124. doi:10.1016/j.ajic.2016.04.148.
68. Blumberg L, Regmi J, Endricks T, et al. Hosting of mass gathering sporting events during the 2013–2016 Ebola virus outbreak in West Africa: experience from three African countries. *Int J Infect Dis*. 2016;47:38-41. doi:10.1016/j.ijid.2016.06.011.
69. Elachola H, Gozzer E, Zhuo J, et al. Mass gatherings: A one-stop opportunity to complement global disease surveillance. *J Heal Spec*. 2016;4(3):178. doi:10.4103/2468-6360.186487.
70. Al-Tawfiq J a., Memish Z a. Mass Gatherings and Infectious Diseases. Prevention, Detection, and Control. *Infect Dis Clin North Am*. 2012;26(3):726-737. doi:10.1016/j.idc.2012.05.005.
71. Gautret P. Religious mass gatherings: Connecting people and infectious agents. *Clin Microbiol Infect*. 2015;21(2):107-108. doi:10.1016/j.cmi.2014.11.023.
72. Abubakar I, Gautret P, Brunette GW, et al. Mass Gatherings Health 2 Global perspectives for prevention of infectious diseases associated with mass gatherings. *Lancet Infect Dis*. 2012;12:66-74. doi:10.1016/S1473-3099(11)70246-8.
73. Saeed KMI, Mofleh J, Hafiz Rasooly M, Iabal Aman M. Occurrence of acute respiratory infection, diarrhea and jaundice among Afghan pilgrims, 2010. *J Epidemiol Glob Health*. 2012;2(4):215-220. doi:10.1016/j.jegh.2012.11.003.
74. Botelho-Nevers E, Gautret P. Outbreaks associated to large open air festivals, including music festivals, 1980 to 2012. *Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull*. 2013;18(11):20426.
75. Gautret P, Steffen R. Communicable diseases as health risks at mass gatherings other than Hajj: What is the evidence? *Int J Infect Dis*. 2016;47:46-52. doi:10.1016/j.ijid.2016.03.007.
76. Lee LA, Ostroff SM, McGee HB, et al. An outbreak of shigellosis at an outdoor music festival. *Am J Epidemiol*. 1991;133(6):608-615.
77. Tabunga T, Utiera M, Tekoaua R, et al. Response to a large rotavirus outbreak on

South Tarawa, Kiribati, 2013. *West Pacific Surveill response J WPSAR*. 2014;5(2):9-14. doi:10.5365/WPSAR.2013.4.4.006.
78. Finger F, Genolet T, Mari L, et al. Mobile phone data highlights the role of mass gatherings in the spreading of cholera outbreaks. *Proc Natl Acad Sci*. 2016;113(23):6421-6426. doi:10.1073/pnas.1522305113.
79. Camps N, Dominguez A, Company M, et al. A foodborne outbreak of Salmonella infection due to overproduction of egg-containing foods for a festival. *Epidemiol Infect*. 2005;133(5):817. doi:10.1017/S0950268805004504.
80. Kitamoto M, Kito K, Niimi Y, et al. Food Poisoning by Staphylococcus aureus at a University Festival. *Jpn J Infect Dis*. 2009;62. http://www0.nih.go.jp/JJID/62/242.pdf. Accessed July 15, 2017.
81. Morgan D, Gunneberg C, Gunnell D, et al. An outbreak ofCampylobacter infection associated with the consumption of unpasteurised milk at a large festival in England. *Eur J Epidemiol*. 1994;10(5):581-585. doi:10.1007/BF01719576.
82. Albert MJ, Neira M, Motarjemi Y. The role of food in the epidemiology of cholera. *World Health Stat Q*. 1997;50(1-2):111-118. http://www.ncbi.nlm.nih.gov/pubmed/9282393. Accessed July 15, 2017.
83. Todd EC. Epidemiology of foodborne diseases: a worldwide review. *World Health Stat Q*. 1997;50(1-2):30-50. http://www.ncbi.nlm.nih.gov/pubmed/9282385. Accessed July 15, 2017.
84. Trostle JA, Hubbard A, Scott J, Cevallos W, Bates SJ, Eisenberg JNS. Raising the level of analysis of food-borne outbreaks: food-sharing networks in rural coastal Ecuador. *Epidemiology*. 2008;19(3):384-390. doi:10.1097/EDE.0b013e31816a9db0.
85. Smith K. *Practically Invisible: Coastal Ecuador, Tourism, and the Politics of Authenticity*. Nashville: Vanderbilt University Press; 2015.
86. Bansal S, Read J, Pourbohloul B, Meyers LA. The dynamic nature of contact networks in infectious disease epidemiology. *J Biol Dyn*. 2010;4(5):478-489. doi:10.1080/17513758.2010.503376.
87. Norman E. Millennial Ecuador The Devil and Development in Esmeraldas Cosmology as a System of Critical Thought. 2017.
88. Hubbard AE, Ahern J, Fleischer NL, et al. To GEE or Not to GEE. *Epidemiology*. 2010;21(4):467-474. doi:10.1097/EDE.0b013e3181caeb90.
89. Ahn J, Johnson TD, Bhavnani D, Eisenberg JNS, Mukherjee B. A space-time point process model for analyzing and predicting case patterns of diarrheal disease in northwestern Ecuador. *Spat Spatiotemporal Epidemiol*. 2014;9:23-35. doi:10.1016/j.sste.2014.02.001.
90. Bhaskaran K, Gasparrini A, Hajat S, Smeeth L, Armstrong B. Time series regression studies in environmental epidemiology. *Int J Epidemiol*. 2013;42(4):1187-1195. doi:10.1093/ije/dyt092.
91. Rahier JM. Presence of Blackness and Representations of Jewishness in the Afro-Esmeraldian Celebrations of the Semana Santa (Ecuador). In: *Representations of Blackness and the Performance of Identities*. Vol Westport, Connecticut: Bergin and Garvey; 1999:19-47.