Accounting for Human Behavior and Pathogen Transmission in the Sanitation Paradigm: Opportunities for Improving Child Health

by

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Dedication

This dissertation is dedicated to Dayanara. I met Dayanara in rural Ecuador when she was 15 days old and was with her on the day she died. Dayanara died when she was 19 days old, while in our canoe, making the two-hour trip to the nearest health facility. She had a stack of cards against her: she was black girl, poor, lived in a rural community, and had a young mother that hadn't finished elementary school. Health and wellbeing; neigh, even life and death; are driven by factors beyond the immediate causes of illness. Often referred to as the "cause-of-the-causes", the determinants of health are fundamentally social in nature. Decades of academic research support the rationale that had her status in society been different, her likelihood of celebrating her first birthday, and then her fifth birthday, would have been much greater. Dayanara's death is a reminder to me that there are grave consequences when public health research fails to connect to public health practice. Without integration of this work into policies, there is little hope of changing systems of oppression and improving the health of our people. Breaking down systems and building new ones is challenging and requires a coalition dedicated to do so; but without such work, there are millions of children within the United States and around the globe that face the same fate as Dayanara, to become another number in a nation's infant mortality statistic. It is my hope that Dayanara's short life will serve as a reminder for researchers, myself included, to conduct research that is meaningful and impactful for people's lives.

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Preface

A version of Chapter 2 (*Determinants of Latrine Use Behavior: The Psychosocial Proxies of Individual-level Defecation Practices in Rural Coastal Ecuador*) is currently under review for publication. The full list of authors is: Velma K. Lopez, Veronica J. Berrocal, Betty Corozo Angulo, Pavani K. Ram, James Trostle, Joseph NS. Eisenberg.

A version of Chapter 3 (*Latent variable modeling to develop a robust proxy for sensitive behaviors: application to latrine use behavior and its association with sanitation access in a Middle-Income Country*) will be submitted for publication. The full list of authors is: Velma K. Lopez, Brady T. West, Philippa J. Clarke, Joseph NS. Eisenberg.

A version of Chapter 4 (*Enteric Pathogen Transmission and Child Undernutrition: Use of Mathematical Modeling to Identify Intervention Opportunities*) will be submitted for publication. The full list of authors is: Velma K. Lopez, Yu-Han Kao, Andrew F. Brouwer, Andrew D. Jones, Joseph NS Eisenberg, Marissa C. Eisenberg.

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ORT	Oral Rehydration Therapy
EED	Environmental Enteric Dysfunction
WASH	Water, Sanitation, and Hygiene
LMIC	Low- and Middle- Income Country
ETEC	Enterotoxigenic *Escherichia coli*
ST-ETEC	Heat-stable enterotoxin-producing *Escherichia coli*
CRP	C-reactive protein
AGP	Alpha-1 acid glycoprotein
NEO	Neopterin
AAT	Alpha-anti-trypsin
MPO	Myeloperoxidase
UN	United Nations
SDG	Sustainable Development Goals
LAC	Latin America and the Caribbean
RANAS	Risks, Attitudes, Norms, Abilities, and Self-regulation
IBM-WASH	Integrated Behavior Model of Water, Sanitation, and Hygiene
BCD	Behaviour-Centered Design
SHINE	Sanitation, Hygiene, Infant Nutrition Efficacy
ENET	Elastic Net
SPCA	Supervised Principal Component Analysis
PMSE	Predictive Mean Squared Error
SE	Standard Error
LCA	Latent Class Analysis
BIC	Bayesian Information Criterion
OR	Odds Ratio
CI	Confidence Interval
LHS	Latin Hypercube Sampling
PF	Preventable Fraction
LNS	Lipid-Based Nutritional Supplement

Abstract

Access to sanitation reduces pathogen exposure to improve child health by reducing diarrhea and promoting physical growth. Globally, millions of children under five suffer from diarrheal disease and undernutrition, which are leading causes of child-mortality in low-resource settings and have long term consequences for children that do survive. Recent sanitation interventions, however, have shown no effect on improving child health outcomes. The null results of an established intervention, therefore, require further investigation into the mechanisms linking sanitation access to improved health outcomes. This dissertation seeks to highlight the role of human behavior as it relates to latrine access, as well as address how sanitation and nutrition intervention affect environmental and biological processes driving enteropathogen transmission. In chapter two, we use health behavior theory to identify determinants of latrine use behavior from a sanitation-related ethnography collected in rural, Ecuadorian communities. We then develop a quantitative survey tool to collect information on these determinants, and following primary data collection, apply data reduction approaches and regression analyses to select which determinants in the sample are reflective of self-reported consistent latrine use. We show that latrine use is influenced by a constellation of drivers, including social norms, attitudes about latrine cleanliness, and habitual latrine use behavior. In chapter three, which also uses primary data from rural Ecuador, we use a suite of determinants to predict an individual's propensity to consistently use a latrine via latent class analysis modeling. We find that latrine use behavior is most accurately predicted by community-level norms reflecting other people's latrine use and attitudes towards latrine sharing. We also illustrate that latrine access is not the primary driver of latrine use. In chapter four, we build a community-level environmental-mediated enteropathogen transmission model that reflects the biological interdependencies between enteric infection and undernutrition. By simulating enteric pathogen transmission among a cohort of children, we test the effect of sanitation and nutritional interventions on the overall transmission of disease. The mathematical modeling approach allows for exploration of underlying mechanism inherent in this system, which highlights opportunities to inform intervention design. Overall, in each

chapter, we use a variety of methods to examine environmental, community, and individual-level processes at play in a system of latrine access, latrine use, and diarrhea-related morbidity. Towards the goal of implementing effective sanitation interventions, this dissertation argues for a need to improve measurement of sanitation behavior and incorporate enteric pathogen transmission dynamics in programmatic design, implementation, and evaluation.

Chapter 1
Introduction

1.1 Rationale

Mortality associated with diarrheal disease, the clinical manifestation of enteric infection, have plagued children under five in low resource settings for decades. Although annual child deaths attributed to diarrheal disease have dropped dramatically from five million in the the 1980s (1) to approximately half a million currently (2), largely due to Oral Rehydration Therapy (ORT) (3), millions children still suffer the short and long-term effects of clinical diarrhea and asymptomatic enteric infection. With mortality on the decline, research has shifted to address morbidity associated with enteric infections, most notably long-term implications of repeated enteropathogen exposure that result in undernutrition, known as environmental enteric dysfunction (EED) (4,5). Undernourished children are subject to a vicious cycle of further infection and further nutritional deficiencies. Due to repeated infections, the 36 million children that suffer from severe diarrhea each year have an elevated risk of long term consequences such as stunting, which in turn may result in decreased cognitive function or even death (6–8). These estimates do not account for effects of asymptomatic enteric infection on child growth, which are also thought to be severe. Since treatment of chronic sequelae to diarrheal disease is limited, child health programs have a reinvigorated focus on prevention through water, sanitation, and hygiene (WASH) interventions (9,10). WASH interventions focused on reducing morbidity, however, have not seen the same reductions as ORT has had on mortality. Towards the goal of implementing effective sanitation interventions, this dissertation argues for a need to improve measurement of sanitation behavior and incorporate enteric pathogen transmission dynamics in programmatic design, implementation, and evaluation.

Sanitation interventions, which are designed to reduce several fecal-oral transmission routes of enteric pathogens (11), largely focus on latrine construction in low-and-middle-income countries (LMICs). Although generally deemed efficacious, the results of eight recent trials conducted in South Asia and Subsaharan Africa have challenged assumptions about the protective health effects of latrine access. In India, large-scale sanitation trials have been conducted in Odisha (12), Madya Pradesh (13), and Maharashtra (14). With the exception of the Maharashtra trial, which found improvement in village-level child growth, the Indian interventions yielded no difference in child health outcomes between communities that were targeted for latrine construction and the control communities. Likewise, within the same geographical region, an Indonesian sanitation trial did not attribute observed reductions in diarrhea to the implemented sanitation intervention (15). Sanitation trial results are comparable within the African region. Growth improvement was observed in Malian children enrolled in a sanitation trial, while reductions in diarrhea were not observed (16), whereas in Tanzania, effects on diarrhea, anemia, stunting, and wasting were not observed in communities that received sanitation programming (17). The WASH Benefits trial in Bangladesh and Kenya (18) — which compares child health outcomes under WASH, nutrition, and combined WASH-nutrition interventions — adds to these results. In Kenya, sanitation only improved child growth when combined with water, hygiene, and nutrition and did not reduce diarrheal disease (either alone or in combination with other WASH or with nutrition) (19); whereas in Bangladesh, the sanitation effectively reduced child diarrhea and when sanitation was combined with water, hygiene, and nutrition, child growth also improved (20). Moreover, early results from the Sanitation, Hygiene, Infant Nutrition Efficacy (SHINE) project in Zimbabwe (21) suggest that their results are equivocal.

Three plausible rationales may explain the aforementioned mixed results for such an established health intervention: 1. limited latrine coverage, 2. limited latrine uptake, and 3. high levels of pathogens in the environment. Excluding the Mali study and the WASH Benefits sites, latrine coverage was exceptionally low given the trial designs, ranging from a four percent increase in any latrine coverage in Indonesia to a 36% increase in functional latrine coverage in Odisha (22); it is questionable whether these latrine coverage levels are sufficient to result in meaningful community-level protection (23). Additionally, latrine uptake, i.e., use of the latrines built by the intervention, may impact intervention results. As noted in the Odisha study, more than a third of households reported that no one in their family used the household latrine (12), and open defecation was practiced by individuals living in home with latrine access (12,13). This pattern of limited latrine use was also observed in the other India trials, where self-reported open defecation was prevalent among study participants. While the WASH Benefits studies did not report defecation practices throughout the study period, the authors showed high baseline prevalence of open defecation in children less than three years (85% in Bangladesh (20) and 75% in Kenya (19)), high adult self-reported latrine use in Kenya (94%; (19)), and low adult open defecation in Bangladesh (5% of women and 8% of men; (20)). While there is acceptance that WASH access does not equate to WASH use (24), latrine use behavior is infrequently assessed in sanitation interventions. A systematic review by Garn et al 2017 noted that not even 30% of household sanitation interventions included any defecation behavioral metric. The authors additionally noted that the quality of evidence among these 10 studies was low (25). Without a behavioral metric, it is not possible to determine whether an intervention was insufficient to promote health or poorly used.

Beyond issues of latrine coverage and use, there is also growing concern that WASH interventions are not sufficient to limit ubiquitous exposures to pathogens, specifically, among those most vulnerable to infection, children under five years of age. When examining health outcomes, it is important to understand dynamics between exposures and spread of disease across a range of levels, regardless of whether the disease is non-communicable (26) or infectious (27,28). Enteric pathogen transmission routes are mediated by the environment (29). While water contamination is common in LMCIs, high levels of enteric pathogens have been found in soil (30,31), hands of children's caregivers (32,33), children's toys (34,35) and in prepared food (36–38). It is through pervasive exposure to a host of pathogens that repeated enteric infections occur, one hypothesized pathway leading to growth faltering. Thus, if the goal of sanitation interventions is to improve child health, a better understanding of the dynamics between environmental exposure, infection processes, and intervention synergies at a community-level is needed. It is likely that the minimal success of these interventions is due to both copious pathogens in the environment and the variable latrine use within a community.

The overall objective of this dissertation is to center the WASH intervention paradigm around social and biological processes. The premise of this research is that giving minimal attention to human behavior and pathogen transmission dynamics impedes successful sanitation interventions (see Figure 1. Conceptual Framework). Sanitation interventions are designed to mitigate pathogen transmission on the community-level (see *Enteric Pathogen Transmission* below), and, thus, use of sanitation facilities by adults in the community greatly influences a child's exposure to enteropathogens. The studies in this dissertation seek to better characterize enteric pathogen transmission through elucidation of: 1. the determinants of individual-level latrine use behavior, 2. a quantitative measurement of latrine use behavior, and 3. how biological and environmental processes influence the mechanisms driving enteric pathogen transmission that result in chronic undernutrition. Population health may be influenced by noncompliance with sanitation interventions, increasing pathogen transmission. High pathogen exposure levels, coupled with underlying biological mechanisms of infection, may make it more difficult for sanitation programs to interrupt pathogen transmission. To address knowledge gaps, each study applies unique analytical approaches to examine environmental, community, and individual-level processes at play in a system of latrine access, latrine use, and diarrhea-related morbidity. These study results will add to ongoing research that seeks to better understand the etiology of diarrheal disease and its impact on child health within the context of social development and globalization. The burden of diarrheal-disease morbidity is high, and latrine construction programs will continue to be implemented, necessitating the continued need for research in this area. Broadly, the goal of this dissertation is to generate knowledge and hypotheses that meaningfully inform public health policies and programs promoting healthy child development through upstream routes.

1.2 Specific Aims

Specific Aim 1. Identifying Determinants of Latrine Use Behavior (Chapter 2)

Latrine use behavior has been studied to some extent within South Asia and the African context— areas where mean latrine coverage tends to be lower (39). However, there is limited work examining latrine use in settings with high, but inequitable coverage, such as Latin America. This aim examined the determinants of latrine use among adults (18 years and older) living in heterogeneous rural Ecuadorian communities within a framework based in health behavior theory. While these communities have high mean levels of latrine access, defecation behaviors are variable. Qualitative data was used to understand underlying psychosocial determinants of defecation behavior and to design a quantitative survey tool to capture said determinants. Following primary data collection, data reduction techniques and regression analyses were used to identify which hypothesized determinants were associated with self-reported consistent latrine use. The identified determinants provide important targets for latrine adoption programs, a critical component of sanitation interventions. Importantly, this also provides an example of quantitatively assessing the underlying drivers of latrine use behavior.

Specific Aim 2. To Quantify Latrine Use Behavior as a Latent Construct (Chapter 3)

Lacking a gold-standard for measurement, most studies that include behavioral assessment of defecation practices collect these data via self-report. Self-report of a sensitive behavior, such as substance abuse, may be misclassified in certain settings (40,41). Although validation studies of self-reported defecation behaviors do not exist, qualitative data from the Ecuador site suggests that individuals over-report latrine use behavior and under-report open defecation practices. In this aim, a person's latent propensity to consistently use a latrine was predicted from a set of indicator psychosocial variables. These indicators were hypothesized to represent underlying drivers of latrine use and developed from ethnographic data examining defecation behaviors in the study site (rural, coastal Ecuador) as well as the research presented in Chapter 2. Through this process, groups of latrine users within the population were identified. Following classification of different types of latrine users, the association between access to within-home sanitation and consistent latrine use was then tested via a pseudo-class logistic regression model. Analyses used primary data from a child cohort study designed to assess the relationship between latrine use behavior and child health outcomes in a sample of households in remote Ecuador; specifically, cross-sectional data from individuals 13 years of age and older were used. Individuals living in this study site exhibit a variety of defecation behaviors and also have high levels of latrine access. Overall, these results present a novel approach to measuring a behavior with limited measurement approaches.

Specific Aim 3. To Examine the Interdependencies of Nutritional and Infection Processes and their Impact on Interventions Results (Chapter 4)

In low-resource settings, the outcomes of enteric infection and nutritional processes exhibit a cyclic relationship. Enteric infection reduces absorption of nutrients and causes inflammation to influence overall nutritional status, and nutritional status modifies one's susceptibility to new infections (42,43). Standard analytical tools in epidemiologic analysis, however, rely on assumptions of independence (44) in order to assess relationships between variables. To appropriately investigate the effect of health interventions on an interconnected infection and nutrition pathway, a systems-based analysis allows for examining a true counterfactual in the presence of dependencies. Here, repeated all-cause diarrhea infections were simulated in a cohort of children from birth to two-years of age, which is a critical time for child growth and development (45). Sanitation and nutrition programs were then incorporated into the model simulations as standalone, as well as combined, interventions to test their impact. Such an approach is useful in determining how disease progression is influenced by the infection-malnutrition cycle. Moreover, through exploring theoretical counterfactual contrasts, mechanisms behind the interrelationship between infection and nutrition can be elucidated and inform intervention design.

1.3 Enteric Pathogen Transmission

Individuals are exposed to enteric pathogens when fecal matter is consumed. The primary routes of enteropathogen fecal-oral transmission are mediated by flies, fingers, floors/fields, fluids (i.e., drinking water), and also food (11). Transmission can occur on the individual-level, within a household, and within a community (29). Likewise, movement of people also stimulates enteropathogen transmission between communities (46). With multiple transmission routes across various levels, diarrhea-related illnesses and related-conditions are byproducts of a dynamic system. Within this system, WASH interventions are designed to mitigate these transmission routes. For example, household water treatment and storage programs target individual consumption of fluids. Sanitation, in contrast, affects community-level as well as individual level exposures by reducing environmental contamination (i.e., floors/fields and fluids) and the presence of flies (47). Hence, well designed and implemented sanitation interventions with high uptake have the potential to greatly reduce pathogen transmission and improve child health. For this reason, first two dissertation analyses focus on adult latrine use. Adults are the primary users of sanitation facilities and their defecation behavior accounts for a higher proportion of environmental contamination, of which young children are uniquely vulnerable to health consequences following exposure.

1.4 Enteric Pathogens and Child Health

While a variety of pathogens cause diarrhea, only a handful are primarily responsible for the high burden of enteric infections observed in children under five living in LMICs — *Cryptosporidium*, rotavirus, *Shigella*, enterotoxigenic *Escherichia coli* (ETEC) (48), heat-stable enterotoxin-producing *Escherichia coli* (ST-ETEC), adenovirus, and *Campylobacter* (49). Due to the variety of pathogens that cause infection, as well as their minimal infective doses, high shedding rates, and general pathogenicity (50,51), enteric infection is pervasive. Pathogen burden early in life is large (5), with repeated infection common (52). For example, recurring symptomatic infections have been observed (53–56), as well as repeated asymptomatic enteric infections (53). Additionally, in a case-control study examining the global etiology of moderate to severe diarrhea, 39% of case stool samples had two or more pathogens present (49). Concurrent infections were also evident in both asymptomatic and symptomatic children from a large-scale diarrhea cohort study (57). Likewise, in a small study in Venezuela, 36% of healthy children had more than one enteropathogen in their tested stool (58). High pathogen burden and recurrent infection is of growing concern as evidence is increasing that enteropathogen infection influences long-term malnutrition-related morbidities, such as growth faltering, cognitive development, and chronic inflammation (59).

From a biological perspective, the numerous pathways connecting enteric infection and malnutrition are challenging to disentangle. Central, however, to this system is the role of the gut, an organ that is responsible for absorbing nutrients as well as aiding the immune system in fighting infection. Enteropathogens disrupt gut function through three primary mechanisms: 1) altering the structure and function of the tight junction barrier to make the gut permeable; 2) inducing fluid and electrolyte secretion to reduce absorption of nutrients; and 3) activating the inflammatory cascade (60). Direct physiological changes to the intestinal wall occur when enteric pathogens adhere and/or invade the epithelium (61), and blunted villi are common (62). Cellular invasion not only creates physical disruption, but also triggers an inflammatory response (63,64). Indirectly, enteric infections also increase phosphorylation processes (i.e., energy production) while down-regulating some transport mechanisms (64). With a deteriorated barrier, microbes (65), as well as immune molecules (66), can seep through the intestinal wall, leading to further inflammation. Moreover, synergistic effects between pathogens have been observed, in which inflammation increases (67). Interactions between commensal organisms and enteropathogens also affect gut functioning, usually leading to overgrowth of enteropathogens (68). Such microbiome changes have been linked to undernutrition (69,70); although, the underlying mechanisms between infection, the gut microbiome, and nutrition are not well understood. Aggregately, these complex and interrelated processes spur the reallocation of energy away from growth pathways and toward an immune response during an important time period in child development, while also limiting the nutrients a child absorbs and causing direct harm to specific growth mechanisms (71).

Of the three primary mechanisms by which enteric infection causes undernutrition, evidence suggests that local and systemic inflammation may be the stronger drivers of child undernutrition (71). During infancy, insulin and various amino acids mediate the endocrine system processes responsible for normal child growth; hence adequate nutrition is key during this period (72). However, inflammation, a common consequence of ingested pathogens as well as microbes that translocate across the gut, disrupts molecular mechanisms of growth (72). Indirect effects of inflammation occur through production of pro-inflammatory cytokines (73,74) which modify endochondral ossification processes, that is, creation of bone tissue that occurs in growth plates (75). Additionally, inflammation also increases cortisol levels, which affects growth by inhibition of chrondrocyte proliferation (i.e., cells that make cartilage) (76), hypertrophy (i.e., increases in cell size) (76), cartilage matrix production (76), and anabolic signaling (i.e., stimulation of growth pathways) (77). Elevated clinical markers of inflammation, such as C-reactive protein (CRP), alpha-1 acid glycoprotein (AGP), neopterin (NEO), alpha-anti-trypsin (AAT), and myeloperoxidase (MPO) have been associated with child stunting in settings where enteric infection is common (78,79). Likewise, NEO, AAT, and MPO have also been have been observed among children with high enteric pathogen burden (80), which further highlights the role of infection in these processes.

Scientists are just beginning to understand these pathways and mechanisms, with growing interest in preventing enteric infection from occurring in the first place. Although there is emerging evidence that linear growth retardation may continue past of age of two (81), it is generally thought that child stunting is largely irreversible after two years of age (82). Thus, the first 24 months of life is a critical window for prevention and a target for nutritional interventions, such as complementary feeding, that seek to promote growth (83). The impact of complementary feeding programs on child growth, although overall positive (84), has been variable, especially when considering different types of feeding programs (micronutrient fortification, breastfeeding education, increased energy density, etc.) (83). While a variety of external factors, such as food insecurity or baseline adequacy of diet, influence these results, some have theorized that the failure of some stand-alone nutrition interventions to improve child growth is due to the large burden of subclinical enteric infections (85). As an estimated 7.2 million cases of child stunting are attributable to unimproved sanitation (86), WASH is a unique opportunity to improve overall child health, particularly through sanitation. While it is generally accepted that access to improved sanitation limits child stunting (87), evidence from intervention trials is mixed (88). Further investigation is required to understand why markers of EED have been associated with geophagia (89), animal feces (90,91), and overall contaminated household environments (poor water quality, unimproved sanitation, and unhygienic handwashing conditions) (92), and sanitation trial results do not always improve child growth.

1.5 Sanitation Interventions

In 2010, United Nations (UN) General Assembly and UN Human Rights Council declared water and sanitation a basic human right (93,94). These resolutions recognize WASH as critical components to achieving of other human rights, such as the right to an adequate standard of living and the right to the highest attainable standard of health (95). Importantly, this also means that achieving WASH access must also include components that promote human dignity (96) — every person has intrinsic value and they should be able to consume water and defecate in a manner that reflects their value. Hence, the traditional definition of WASH access must be expanded. To achieve WASH access within a human rights framework, it is necessary to surpass affordability, availability, and quality — the standard components of WASH access — and incorporate community participation, equality, and non-discrimination (97). When monitoring progress towards WASH, assessment should thus account for the social and political context which may inhibit full equality (98) and realize that a one-size-fits-all approach to achieving equality is likely not attainable (99). Hence, the human rights framework of progressive realization becomes a useful tool to ensure that multiple dimensions of health, including equality, disparities, accountability, and compliance (100), are incorporated into WASH implementation and measurement over time. Although much more work is needed to redefine WASH access, this human rights framing has had some influence on the current global commitments towards creating a sustainable future.

WASH as a human right is incorporated into the Sustainable Development Goals (SDG) Initiatives (the intergovernmental goals voted on by UN member states to promote sustainability across throughout the world). SDG 6, specifically, seeks to "ensure access to water and sanitation for all" through four targets that focus on drinking water, sanitation, wastewater, and water-use efficiency (101). The language in the sanitation target (SDG 6.2), which states "By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations" (102), reflects the human rights framing of WASH policy makers. First and foremost, it notes that access should not be universal, but equitable, with specific disenfranchised groups highlighted. Accordingly, measurement of this target requires disaggregation of sanitation access within a population; overall aggregate mean access provides little insight into achieving this goal. Moreover, SDG 6 is the first global WASH goal to incorporate behavior by specifically noting to "end open defecation." Individual-level behaviors, however, remain unmeasured in the context of global WASH measurement. Barriers to WASH use provide insight into the limitations of the various aforementioned components of access. Thus, to apply principles of progressive realization and reduce systems of oppression that result in health disparities, it is imperative to include metrics of WASH behaviors in addition to those of WASH access.

Given global priorities of promoting WASH, water and sanitation access have been globally monitored by the UN since the 1990s. To ensure comparability in water and sanitation coverage estimates, standardized definitions are employed. For example, sanitation access is conceptualized as a ladder (103), with "open defecation" (or no access) at the lowest rung and "safely managed" the highest (where excreta is treated/removed from the household setting). While universal access to safely managed sanitation is the goal, sanitation access is considered adequate when an individual has a non-shared, improved household sanitation facility. A sanitation facility is considered improved if it designed to hygienically separate the user from feces. Following this definition, any latrine that provides a base for sitting is an "improved sanitation facility." Important components of exposure risk are excluded from this definition, such as cleanliness (104), environmental contamination (105), and/or latrine usage, which limits the ability to accurately assess the protective effects provided by a sanitation facility. While global monitoring approaches should not define what practitioners consider to be sufficient WASH access (106), many sanitation interventions are designed merely to meet UN definitions of improved sanitation access: success is measured by the number of basic hardware installed. However, without accounting for latrine use and contamination risks, from sanitation definitions, the link between sanitation access and health promotion is murky; several studies have found that individuals report having access to improved sanitation, but they might not always use them (13,107).

1.6 Sanitation Coverage in Latin America

Sanitation Coverage in Latin American: On the regional level, Latin American and the Caribbean (LAC) exceeded the UN goal for sanitation coverage in 2015 (39), with approximately 90% of households having access to improved sanitation. However, sanitation coverage is greatly variable across the region and within countries (108). For example, of the 35 countries in the region, nearly 3 in 4 countries did not meet the UN sanitation goal, while Belize, Chile, Cuba, Ecuador, Honduras, Mexico, Paraguay, Uruguay, and the United States did. Moreover, regional variations within all countries are evident, with rural areas generally experiencing lower coverage. Lower rural sanitation coverage exists even within countries that have high national coverage estimates, such as Paraguay, where 20 percent of rural household had access to improved sanitation in 2010, relative to approximately 70 percent of urban households (108). In addition to urban-rural disparities in sanitation access, ecological analyses show that sanitation access within the LAC region is correlated with a variety of social position indicators, such a fertility rates, national income, median years of education, life expectancy, and mortality estimates (infant, child, and maternal) (108).

Most of the data used in this dissertation were collected from rural and remote Ecuadorian communities. These communities are in an active state of economic development and are not nationally representative of living conditions within the country. Ecuador, a middle-income country, has a high national average of sanitation coverage (86%) (39). In contrast, some rural communities included in our studies have improved sanitation coverage in fewer than 50 percent of households (23). Such coverage estimates are lower than some the previously discussed sanitation trials in Africa and Asia. In the WASH Benefits trials, for example, sanitation coverage in the Kenyan trial was 89 percent after the first year of the study (19) and 95 percent in the corresponding Bangladesh trial at a comparable time point (20). Given this heterogeneity, the study site reflects generic low-resource settings within and outside of the LAC region. Thus, it provides a unique location to assess sanitation behaviors, which remain unstudied in LAC, while also providing generalizable insights to other low-resource settings.

1.7 Leveraging Social Theories to Measure Defecation Behavior

The epidemiologic triad of disease transmission traditionally focuses on the biological agent of disease, the infected host, and the environment through which infection and transmission occur. By examining these components within a population, the sufficient and necessary causes of disease can be identified, providing insight into causal mechanisms (28,109,110). Arguably, human behavior is at the heart of disease transmission dynamics, for a person must interact with an exposure in some manner when transmission occurs. For example, models that incorporate disease dynamics and dynamic human behavior show that variability in human actions has a substantial impact on population disease transmission (111,112). Behavior, however, is often difficult to accurately quantify, and consequently, it is excluded from most WASH analysis. If models do incorporate behavioral metrics, they are often measured with minimalist proxies, which may insufficiently reflect behavior. In the sanitation literature, defecation behaviors are typically measured via self-report, and as with most self-reported sensitive behavior (for example substance abuse; (40,41)), metrics may be subject to misclassification. Beyond self-reported latrine use, sanitation also measure defecation by a visual inspection of latrines and compounds for feces, which limits inference to an ecological level. These metrics of defecation behavior, thus, limit opportunities to learn about the systems driving the spread of enteric infections, a critical component of designing interventions for child health. With the goal of improving epidemiologic inference in the sanitation field, there is a great need to develop better proxy-measurements of defecations behaviors. Such proxies should be at the individual level and be subject to minimal misclassification. Explanatory social theories of health behavior provide one avenue for creating robust proxies of latrine use by measuring behavioral determinants.

Within the health sector, social theories are applied towards behavior in order to inform study design of a trial or observational study, to evaluate a study, to test theories and learn more about behavior, and to build additional theory explaining people’s actions (113). The early predominating theories of health behavior, such as theory of reasoned action/theory of planned behavior (114), the health belief model (115), and social cognitive theory (116), all draw on a common thread: an individual's ability to act in isolation from their sociocultural context. For example, the theory of reasoned action (Ajzen & Fishbein, 1980) emphasizes that behavior can be changed by changing the way a person thinks, (this is also key to Becker's health belief model (115)), or by changing the strength of intention to perform a certain behavior. Bandura, on the other hand, repeatedly noted that behavior is reflective of one's self-confidence in the ability to act (116–119); which is partially influenced by societal rewards and penalties. On a whole, however, these frameworks, and many others using psychology as a basis for understanding behavior, failed to incorporate social, cultural, organizational, historical, and political influences on behavior (120). Conceptualizing behavior as purely influenced by intrapersonal factors is highly limiting, with growing criticism of individual-level behavioral theories, such as the theory of planned behavior (121). There has been strong urging to shift focus, as noted by Glass and McAtleen (2006), "The study of health behavior in isolation from the broader social and environmental context is incomplete, and has contributed to disappointing results from experiments in behavior change" (122). From the epidemiological perspective, causality and the dynamics of the systems leading to disease and health disparities cannot be determined without a broad understanding of what drives health behaviors.

Ecological models of behavior may provide more insight into the holistic determinants of behavior as they explicitly account for the role of sociocultural and environmental drivers and may better reflect the influence of dynamic social processes on individual behaviors (123). Social factors shape daily life, affecting health in indirect and direct ways, and are often invisible influencers on behavior (124). Humans are influenced by what others in society do (a *descriptive norm*) (125), by what they think others should do (an *injunctive norm*) (125), and even by what they think are they are expected to do by others in their social network (a *normative expectation*) (126). This results in locally-shaped norms (126), meaning behavioral influences in one context may not exist in another context. For example, in examining open defecation patterns in India, Doron and Raja proposed that defecation is reflective of structural inequality and cultural norms that result from the ways in which society views public space (127). They propose that changing defecation behavior patterns in the growing middle class could be induced by changing norms related to perception of filth among members of the caste system (128). The evolving roles of class and caste not only affect who mixes in social spaces, but also how filth is tolerated in public. Dorn and Raja's analysis, thus, exemplifies the interconnectedness of ecological drivers of behavior (cultural, society, politics, history) on a personal behavior.

WASH behaviors are complex and influenced by a host of factors within a complex system. Importantly, an ecological approach to assessing WASH behaviors, as conducted by Dorn and Raja, can identify multiple targets for proxy-measurement of behavior (behavior evaluation) as well as multiple opportunities for behavioral interventions (behavior change). The type of social theory that is used to assess behavior has an impact on how behavior is measured. Within the WASH sector, a variety of frameworks are used to understand behavior, with three primary frameworks that were designed specifically to understand human behavior related to water treatment, hand hygiene, toilet use, etc.: RANAS (Risks, Attitudes, Norms, Abilities, and Self-regulation; (129)); IBM-WASH (Integrative Behavioural Model for Water Sanitation and Hygiene; (130)); and Behaviour Centered Design (131). Each of these behavioral frameworks are based in different social theories of behavior and have been used to assess behavior change with interventions and to explain WASH behaviors. Theses theories, and examples of their explanatory application, are discussed in more details below.

The RANAS model was one of the first WASH specific behavior frameworks. It views behavior as an outcome of underlying psychological processes within an individual (129). RANAS, thus, is based on a suite of psychological theories that groups determinants into five blocks of factors: risk factors (based on the Health Belief Model (115); the Protection Motivation Theory (132); and the Health Action Process Approach (133)), attitudinal factors (based on the Theory of Planned Behavior (134)), normative factors (based on the Theory of Planned Behavior), ability factors (based on the Theory of Planned Behavior), and self-regulation factors (influenced by work from (135,136)). Within this framework, a risk factor is defined by the individual's knowledge, awareness, and understanding of health and disease. In addition to knowledge, the RANA model views self-regulatory factors as important drivers of behavior, which are responsible for the continuance of the behavior via a person's attempt to plan when/where/how to act; to self-monitor their actions and modify the behavior if necessary; to plan how to overcome barriers that might inhibit their desired actions; to remember to perform the behavior; and finally, to feel committed to the behavior. While most of the literature using the RANAS model examines the factors that drive behavior change, the RANAS factors have been used to explain determinants of WASH behaviors in a variety of settings. A few examples include handwashing after toilet use in primary school children in Burundi and Zimbabwe (137), switching an an arsenic-safe well in Bangladesh (138), use of water filters in Ethiopia (139), and cleaning of shared toilets in Uganda (140). Each of these studies relied on self-reported WASH behavior as the analytical outcome and assessed the relationship between psychological variables and said outcome via regression modeling. Generally, the analytical approaches did not account for macro-level determinants, or even upstream factors, that influence behavior.

While the RANAS model is based solely in psychological theory, the IBM-WASH framework is an ecologic model that conceptualizes behaviors as a byproduct of intersecting dimensions of technology, context, and psychosocial factors (130). Social cognitive theory underlies this component of the model, as the intersecting domains reflect principles of reciprocal determinism (i.e., behavior both influences and is influenced by personal factors and the social environment) (116). The IBM-WASH domains influence health through five nested, but interdependent levels: habitual, individual, interpersonal, community, and societal. To develop the IBM-WASH model, Dreibelbeis and colleagues first conducted a literature review of existing WASH-related models and frameworks that examined behavior (129,141–144). They adapted what was learned from the literature through formative research and pilot studies of behavior change programs in Bangladesh. Two strengths of the framework are that it transcends the individual-level of behavioral determinants, while also incorporating theories that are derived from public health practice. The applications of IBM-WASH for implementing behavior change, informing study design, and explaining behavior are numerous. The IBM-WASH framework has been used in most often in qualitative research assessing drivers of WASH behaviors (145–150); furthermore, application to quantitative (151,152), mixed-methods (153), and literature review (154) has also been made. Of these examples, Dreibelbeis and colleagues' 2015 research (152) applied item response methods to variables designed with the IBM-WASH framework, showing that perceptions of latrine attributes and the convenience of latrine use drove open defecation. While their work has some limitations (such as use of self-reported outcomes), this example of integrating social theory and quantitative assessment of WASH behavior is a promising strategy for measuring latrine use.

In contrast to the IBM-WASH and RANAS framework, the Behaviour-Centered Design (BCD) framework is rooted in evolutionary theories of behavior and ecological psychology (131).

The BCD model views behavior as a purposeful and dynamic interactions with the environment that leads to adaptive changes in the mammalian brain. The brain processes these interactions in three different manners (155): reactive (an automatic response), motivated (an evolutionary response made towards meeting a goal, with physical, emotional, and interest-related drivers; (156)), and planned executive control (short to long term motivated planning). Environmental interactions, and the evolutionary processes that accompany them, occur in specific settings and to stimulate a behavioral response that is thus dependent on physical, social, and temporal settings (157). Behavioral assessment using the BCD approach, therefore, is measured across the following factors: the brain, the body, the environment, and the behavior setting. Because the purpose of the BCD framework is to assess behavior and design a population-specific intervention to change it, BCD use in the literature focuses on behavior change rather than behavior evaluation (examples include handwashing (158), nutrition (159), food hygiene (160), use of oral rehydration salts (161), and even combined diarrheal disease interventions (162)). With the growing need to add nuance to behavioral evaluation within population-health studies, there is potential for applying the theories used in BCD to quantitatively evaluate WASH behavior through interdisciplinary collaborations.

Evaluating behavior, and seeking to change it, are cornerstones to public health practice. There exists, however, a disconnect between behavior change practitioners' approaches to behavioral measurement and those of quantitative researchers. Repeatedly, the need to collect behavioral data within WASH has been identified (163–165). Nevertheless, few interventions, let alone epidemiologic observational studies, measure behavior beyond minimalistic attainment. For example, in the WASH Benefits Bangladesh site, study authors noted extensive use of the IBM-WASH framework to encourage uptake of the various interventions (20); however, behavior was not explicitly included as a study variable in the intervention assessment. Instead, the Bangladesh team monitored intervention adherence by proxy measurement: presence of functional latrine and feces disposal hardware, visual inspection of the latrine to determine use and child feces disposal practices, presence and quantity of feces in the living environment, presence of soap at the handwashing station, and detectable free chlorine in stored water. The sister site, in Kenya, nonetheless, did not present a behavior change framework and measured intervention adherence in a similar manner (respondent-reported number of field team visits, respondent-reported sanitation access, presence of water and soap at the handwashing stations, respondent-reported disposal method of child feces, detectable free chlorine in stored water) ((19)). In contrast to the WASH Benefits Study, the SHINE trial group describes the importance of collecting human behavior data in order to distinguish between theory failure (i.e.- the intervention was not appropriate to stop disease/promote health) and implementation failure (i.e.- individuals did not use the intervention) (166). In the SHINE trial evaluation, various WASH behaviors were included via respondent-reported and structured observation. Moreover, the health workers that delivered behavior change messages as well as the households that received the intervention were included in the study's process evaluation by measuring their knowledge-based self-efficacy as a determinant of behavior (167). While measuring behavioral determinants is certainly necessary for developing an enriched understanding of intervention results, there is also room for epidemiologic studies to include social theories of behavior to ameliorate causal relationships.

Disease and wellbeing do not occur in a vacuum, void of humans and their behavior. Arguably, measurement of human behavior is not only required to assess systems of disease transmission, but there is also a specific role for human behavior in the traditional epidemiologic triad and causal thinking. The "environment" of the epidemiologic triad, which brings together the host and the pathogen, naturally accounts for the sociocultural domains driving behavior. Thus, use of proxy-behavioral measurements derived from social theory may prove useful in understanding underlying mechanisms of disease dynamics. Not only does this approach place the people at the center of the research rather than their exposures, but it also promotes systems-thinking. As established by health behavior researchers, behavior is indeed a product of a complex system where various factors across multiple levels interact. While all population-health problems likely result from dependencies influenced by humans, inclusion of behavioral metrics into WASH research presents unique opportunities to broaden WASH knowledge. First, using social theory to develop a variety of proxy-measurements of behavior and test their relationships presents insight into the systems of WASH practices. Such insights are useful for evaluating who practices open defecation and when and why they practice, critical knowledge if the goal of a sanitation program is increase latrine use. Additionally, the generalizability of WASH behavioral drivers, an important component in epidemiologic study of causality, can also be examined. Second, systems-analytical tools can identify data gaps. Like statistical analysis, system-analysis is based on a set of assumptions about how factors are interrelated. If theory exists to support model construction, but data are not available that reflect theoretical constructs, the results from a simple model could generate hypotheses as to what types of data would make the model assumptions more flexible.

1.8 Summary of Background

In summary, children living in LMICs face a large burden of disease due to enteric infection. Clinical enteric infections can lead to diarrheal disease, which increases risk of mortality and acute and chronic undernutrition. Moreover, growing evidence supports hypotheses that asymptomatic enteric infection also results in chronic malnutrition via numerous molecular pathways. WASH programs, therefore, have become central components of child health initiatives. Sanitation, in particular, reduces several pathways of enteric exposure including environmentally-mediated enteropathogen transmission, and important transmission route for young children. Moreover, sanitation access is also a basic human right. As a basic human right, there is a need to reevaluate how the health sector implements and measures sanitation interventions, for it is challenging to promote defecation with dignity without considering use of sanitation facilities. Behavior is also a critical component of WASH interventions, and its measurement may be enhanced by applying social theories. Overall, there is a need to assess the interconnectedness of social and biological processes at play in the system propagating enteric pathogen transmission.

Several other studies have examined the associations between WASH access, pathogen exposure, and child growth, such as the WASH Benefits study (19,20), the SHINE trial (21), the MAL-ED study (168), and the GEMS study (48). Nevertheless, among the intervention studies, latrine use behavior was not a central component of the research, whereas among the pathogen burden studies, dependencies inherent in pathogen transmission were not considered. In light of the conflicting results of the recent high-profile sanitation trials, there is a need to understand how interactions between sanitation access and pathogen exposure lead to child health outcomes. Such information can not only guide future WASH programs, but also provide information for health policies at a time of growing health needs and shrinking resources. To contribute to this goal, this dissertation explicitly studies sanitation as a system-type problem by identifying determinants of latrine use behavior in rural Ecuadorian communities (Aim 1), predicting how latrine use and assessing its association with latrine access (Aim 2), and investigating how biological and environmental processes influence enteropathogen transmission among children (Aim 3).

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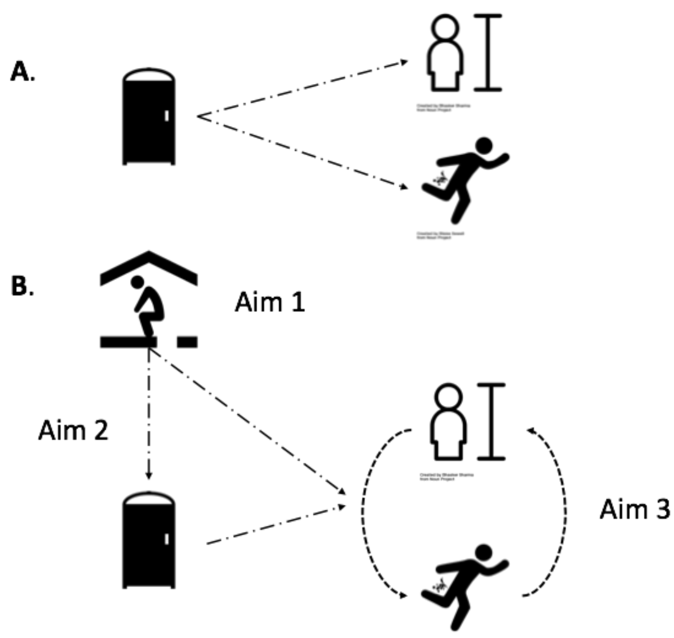
Figure 1.1. Routes of enteric pathogen transmission are mitigated by sanitation interventions. Reduced pathogen transmission, in theory, improves child health outcomes, which is the rationale for the dissertation and connection between the three aims. (A) Research studies examining the relationship between sanitation interventions and child health outcomes (both growth and enteric infections) traditionally conceptualize a linear relationship between sanitation access and child health. Our conceptual framework (B), however, is based on a dynamic relationship between sanitation and health. We suggest that latrine use behavior may have a direct effect on child health outcomes, which occur from dependent biological processes. Thus, we seek to understand this system through first assessing determinants of latrine use (Aim 1) and then testing the association between latrine access and use (Aim 2). Within this framework, we also test the protective effects of sanitation interventions on dynamic biological process leading to undernutrition and enteric infections (Aim 3). Aims 1 and 2 focus on adult latrine use, as this intervention is specifically designed to reduce overall pathogen transmission in the environment. Aim 3 focuses on the connection between intervention coverage and child health.



Chapter 2

Determinants of Latrine Use Behavior: The Psychosocial Proxies of Individual-level Defecation Practices in Rural Coastal Ecuador

2.1 Abstract

There is increasing appreciation that latrine access does not imply use—many individuals who own latrines do not consistently use them. Little is known, however, about the determinants of latrine use. To study latrine use requires populations with variable sanitation access and defecation behaviors. Latrine access is high but inequitable in the Latin American region. Using the Integrated Behavior Model of Water, Sanitation, and Hygiene, a health behavior framework, we sought to characterize the determinants of latrine use behavior in rural Ecuador. We interviewed 197 adults living in three communities with a survey that asked 70 psychosocial-related questions. Questions were excluded from analysis if responses lacked variability or least 10% of respondents did not provide a definitive answer. We applied Adaptive Elastic Nets (ENET) and Supervised Principal Component Analysis (SPCA) to a reduced dataset of 45 questions among 154 individuals with complete data to select determinants that predict self-reported latrine use. Consistent latrine use was commonly reported in the sample (76%). The SPCA model identified six determinants and Adaptive ENET selected five determinants, with similar drivers identified (McNemar's chi-squared statistic = 0.20, p-value = 0.65). Three indicators overlapped between the models: whether other community members use latrines; daily latrine use; and whether the latrine is sufficiently clean to use. Our findings suggest that social norms are important predictors of latrine use; whereas knowledge of the health benefits of sanitation may not be as important. These determinants are informative for promotion of latrine adoption.

2.2 Introduction

Sanitation interventions, alongside clean water and good hygiene, are important strategies to reduce the incidence of pediatric diarrheal disease and malnutrition, particularly in low and middle-income countries (1–4). In the Latin American region, most countries have met the World Health Organization's outlined goals for sanitation under the Millennium Development Goals. Yet disparities in sanitation access persist across the region (5). Examining national estimates of sanitation coverage in the Andes, for example, the proportion of households that have a sanitation facility that separates human excreta from contact with individuals (i.e., an "improved" sanitation facility) is heterogeneous, with Venezuelan households (95%) and Ecuador households (86%) experiencing the highest levels of access to improved sanitation and those in Bolivia the lowest (53%) (6). Likewise, within-countries similar disparities are observed. For example, although access to improved sanitation in Ecuador is high, among rural households, improved sanitation access drops to 80 percent (6). Furthermore, neighborhood-level sanitation access is highly variable: some rural Ecuadorian communities have improved sanitation coverage in fewer than 50 percent of households (7). While sanitation access is indeed important, it may not be sufficient to ensure latrine use and therefore improve child health. For example, results from recent randomized control trials of latrine construction interventions have shown no effect on diarrhea, child growth, or helminth infections, largely due to limited coverage of latrines and low uptake of latrine use (8,9).To effectively mitigate enteric pathogens transmission, we need to understand the drivers of latrine use behavior.

While latrine use behavior has been studied to some extent within South Asia and Africa, there is a dearth of knowledge about Latin America. Existing studies have identified latrine construction and maintenance (10,11) as key factors associated with latrine use. Additionally, because individual-level behavior is influenced by social processes (12), sociocultural factors associated with latrine use behavior are also presented within the literature. Identified sociocultural drivers of defecation behaviors reflect a wide array of determinants, such as enhancement of social status or community norms of latrine use (13,14) or a preference to practice open defecation rather than defecate in a latrine (15). Recent literature examining the intersection of sociocultural factors with physical components of latrines among Indian households noted that open defecation was predicted by perceptions of latrine attributes and the convenience of latrine use (16). This study applied the Integrated Behavior Model of Water, Sanitation, and Hygiene (IBM-WASH) as a basis for understanding defecation practices. The IBM-WASH framework presents intersecting dimensions of technology, context, and psychosocial factors as the intrinsic drivers of behavior (17). Each of these dimensions operate through five nested, but interdependent ecological levels: habitual, individual, interpersonal, community, and societal (17). We add to this literature by providing data on the determinants of individual sanitation practices in rural Ecuadorian communities with distinct cultural practices. More broadly, in combination with results from prior studies, this research provides insight into whether drivers of defecation behavior are generalizable across regions of the globe.

Universal access to adequate and equitable sanitation facilities, and implied use of said facilities with the goal of ending open defecation, is a global priority noted in Sustainable Development Goal (SDG) 6.2 (18). Considering both this SDG and the inequalities present in latrine access throughout Latin America, it is paramount to understand the potential variability of drivers of latrine use behavior in distinct cultural settings throughout the globe. Responding to this need, we aim to characterize the psychosocial drivers of latrine use in rural, coastal Ecuadorian communities. First, we use an ethnography describing defecation practices in communities in the Esmeraldas province to design and implement a survey tool to measure specific social norms, perceptions, and attitudes related to latrine use and open defecation. Second, we use data reduction techniques drawn from machine learning to eliminate survey questions that may not reflect common drivers of behavior at the population-level associated with self-reported latrine use. Through this approach, we identify a subset of latrine use determinants within communities where latrine ownership is common but latrine use is variable. Such drivers of behavior provide important context for the promotion of latrine use and behavior change, which are central to SDG successes.

2.3 Methods

Questionnaire Development

Setting: This research builds upon a 10-year longitudinal study in Esmeraldas, Ecuador that examines enteric pathogen transmission (19). Esmeraldas, the northernmost coast province within Ecuador, is home to indigenous communities, a growing number of *Mestizos*, and a predominant Afro-Ecuadorian population. As an area undergoing social and economic development, the 21 study communities have a gradient of access to sanitation infrastructure (ranging from no facility to a toilet with a septic tank), with construction and maintenance of facilities varying across communities. Likewise, multiple defecation practices also occurred within the communities, such as use of latrines or various forms of open defecation (e.g., defecation in a river or on the ground). Such variability in the physical components of latrines and defecation behaviors, as well as distinct cultural values and practices between communities, presented a unique setting for the study.

Ethnography and Questionnaire Design: Survey development began with a review of existing ethnographic data from the site. A full-time field anthropologist, who has lived in the area for nearly two decades, developed the ethnography as part of a research project examining the influence of road development on diarrheal disease (19); the ethnography specifically described defecation practices of the population from early 2012 until mid-2013. He interviewed both community leaders and other residents of various ages, and spent weeks observing sanitation behaviors, infrastructure, and their effects on the environment.

We used the IBM-WASH model to create a conceptual framework for understanding the drivers of latrine use in our study site (see Figure 2.1). In our conceptual model, we examined the intersection of technology and psychosocial factors as they are related to latrine use behavior; we excluded the community and societal IBM-WASH levels as these data were not available from the ethnography and would be more difficult to obtain in individual-level interviews. Using this conceptual framework as a guide, we reviewed the ethnography to identify determinants of latrine use behavior within the population. Following this review, we drafted survey questions to reflect these determinants. Specifically, we drafted questions across the interpersonal, intrapersonal/individual, and habitual levels. Interpersonal questions reflected *descriptive* and *injunctive* social norms of defecation across age, gender, and seasons (*Descriptive* norms are reports of others' behaviors, while *injunctive* norms are perceptions of how others should behave (20).). These interpersonal questions also solicited attitudes regarding latrine sharing. Intrapersonal/individual questions assessed the benefits of latrine use and attitudes regarding latrine cleanliness, maintenance and personal safety. Other questions assessed daily habits, convenience of latrine use, and open defecation. These survey questions were designed to reflect cultural values as driving forces of latrine use behavior. All survey questions are presented in Supplement 1.

Survey Implementation and Analysis

Data Collection: Data were collected in January and February of 2016. Three communities were preselected for the study based on size, racial/ethnic makeup of the population, and representativeness of the study region in terms of access to clean water and improved sanitation facilities and sanitation practices. Households in communities A and B were censused, whereas a convenience sample was done in community C due to its large size and the associated complex logistics of field visits. We sought to include more than one adult (i.e., those 18 years or older) per household interviewed to capture within household variability and an equal number of men and women. Individuals were selected for interview if they were present at the time of the field visit; however, household clustering was not recorded during fieldwork. See Appendix 2 for background characteristics of the communities.

Data Cleaning and Manipulation: Each psychosocial question in the survey included three possible response categories: “yes”, “no”, or “don’t know/no response”. Questions were removed from analysis if: 1) the percentage of individuals agreeing or disagreeing with a specific question was 90% or greater (deemed to poorly reflect variability in survey questions that would predict latrine use); or 2) 10% or more of those surveyed responded that they did not know/ did not provide a response to the survey question (deemed to reflect that these questions were not drivers of latrine use in this population).

Following removal of some survey questions, the remaining questions were recoded as indicator variables. For questions in which all three of the possible responses were provided, the “don’t know” response was chosen as the referent category. For those questions where only “yes” or “no” responses were provided, the “no” response was used as the referent category. Hence, the final model results reflect whether each selected indicator is associated with consistent latrine use, the outcome variable of interest, relative to the respective referent group response (that is, no association). Those respondents reporting that they always use a latrine for defecation were considered consistent latrine users, whereas those reporting that they sometimes or never used a latrine for defecation were considered inconsistent latrine users. Individuals with missing data were excluded from the analyses.

Data Reduction: Using the cleaned dataset, we fit logistic regression models to assess the association between latrine use and the psychosocial predictors. As identified in the ethnography, factors influencing latrine use behavior are interrelated (see Appendix 3 for assessment of correlation). If strong correlation between survey questions, and the domains they represent, is present, standard regression model results will most likely over-inflate the variance of each predictor, leading to poor prediction and limited interpretation of final models (21). To avoid an erroneous increase in the variance of the estimated regression coefficients, we used Supervised Principal Component Analysis (SPCA) and Adaptive Elastic Nets (ENET), two data reduction techniques that explicitly incorporate covariance matrices within their algorithms, and thus account for correlation among the predictors (see Appendix 4 for details regarding the modeling) (22,23). Through use of these models, we sought to remove questions that were not instrumental in explaining the total variability in the set of questions that predict latrine use behavior, thus reducing the number of predictors to include in the logistic regression models for latrine use.

Given our anticipated small sample size, and because each modeling approach uses a different algorithm, we compared results from these two data-adaptive analytical approaches to increase our confidence that the observed associations were not spurious. In each of these analytical approaches, we employed *k*-fold cross-validation to select model-tuning parameters (specifically, 8-fold validation for SPCA and 5-fold validation for Adaptive ENET). The model-tuning parameters enhance the performance of each model and reduces the variance of the included variables. Because the Adaptive ENET model selects and shrinks the estimates of the unnecessary regression coefficients to zero, the p-values do not have a standard interpretation (24). Here, the p-values are not absolute, but are a relative reflection of the adjusted strength of associations within the entire dataset. Thus, it is important to examine all selected variables in the Adaptive ENET model. The SPCA model, on the other hand ranks the importance of selected variables by producing a relative score. To ease comparison of model results, variables selected by SPCA were subsequently used as predictors in a logistic regression model to quantify the relationship between the selected variables and latrine use.

To assess the extent to which results from the two models were discordant, we compared the questions deemed relevant by each model using the McNemar's test. To assess the internal validity of each analysis, we compared each model's predictive mean squared error (PMSE), a metric of model accuracy that accounts for the squared difference between the fitted values of predicted outcomes and the observed fitted values (i.e., the dataset) (25). The predicted outcome reflects the odds of expected latrine use for each person in the sample given the relationships observed within the dataset. Because the data are binary, the PMSE value fall within a range of zero to one, with a value close to zero indicating a high level of accuracy.

Analyses were conducted using R (version 3.0.2) and R-packages *superpc*, *gcdnet*, *GMCM*, and *matrixStats*. The University of Michigan Institutional Review Board and the Universidad San Francisco de Quito Bioethics Committee approved data collection methods and study procedures.

2.4 Results

Ethnography and Questionnaire Development

Based on ethnographic data, we found that defecation practices in the study site varied between and within communities. On the one hand, most households had access to a latrine -- located within their own home, at a neighbor's home, or within the community -- and reported defecating in the latrine(s) to which they had access. Open defecation, on the other hand, was practiced regardless of latrine ownership. Multiple forms of open defecation occurred: within a leaf or plastic bag (which is not disposed of safely), on the ground within community boundaries, outside of community boundaries, within nearby rivers, and within the boundaries of their households. Demographic characteristics, such as age, gender, place in the family hierarchy, and time spent outside of the home, had some influence on the types of defecation behavior practiced. For example, those who were **confined to the household**, such as the elderly or the sick, were consistent latrine users, whereas individuals who were **able to leave the house** practiced some form of open defecation in addition to using the household's latrine Those working in agricultural fields, most commonly men in Afro-Ecuadorian communities and women in Chachi communities, individuals reported they often defecated on the way to their farms or within their farmlands, which lacked latrines. Once mobile and out of diapers, **young children** defecated wherever and whenever the need arose, frequently on the ground within the community, which was viewed as a nuance to community members. Overall, there was within-household and within-person variability of defecation behaviors were practiced independently of latrine access.

Multiple factors specific to the study site also influenced defecation practices. During the rainy season, latrines were used less frequently. The influence of seasonality on defecation patterns intersects with descriptive defecation norms in unique ways. Some individuals with latrines located outside of their home, most commonly adult men, preferred not to leave their homes and become wet en route to the latrine. They defecated in a receptacle, with the contents disposed of at a later time in a variety of locations, including the latrine, the yard, or the river. Thus, men, who more often defecate on the ground on the farms, are less likely to use a latrine at home during the rainy season. Moreover, seasonality also influences the preference for river defecation. Individuals who normally defecated in the river reported that high water levels in the rainy season resulted in fecal matter quickly sinking out of sight, which was cited as a positive outcome. Defecating in a body of water was thought to avoid contact with feces and, importantly, reduce the likelihood that others would encounter feces.

In addition to seasonality, key drivers of latrine use behavior were related to the latrine itself as well as one's safety and privacy during use. It was commonly reported that dirty latrines as well as latrines with poor construction were less likely to be used. Poor latrine maintenance was noted as both a safety and privacy concern (i.e. a lack of a door or cracks in a wall). Some individuals noted that nighttime use of latrines outside of the household was dangerous. Walking to the latrine in the dark posed hazard, as did the potential for animals in the pit of the latrine or insects that could bite them. Given these threats, river defecation or defecation in a receptacle was noted as a preference should one have to defecate at night.

These ethnographic results were used to both develop new survey questions as well as modify questions obtained from studies previously conducted in India (16,26). The questionnaire was meant to reflect important constructs in the ethnographic data and test the generalizability of the Indian questions in a Latin American context. In total, 70 questions were included spanning seven categories of psychosocial factors used by Dreibelbis et al. 2015 (Table 2.1), along with questions about the frequency of self-reported latrine use and open defecation practice (see Appendix 1 for a complete list of questions).

Survey Implementation and Analysis

Survey and Data Cleaning: Of the 202 individuals approached, 197 consented to participate in the survey. Examining the responses from these 197 people, 25 of the 70 psychosocial questions were removed from the analysis: 18 questions were removed due to lack of variability in the responses and seven were removed because >10 percent of the population responded "did not know" to a specific question (Table 2.1). From the remaining 45 survey questions, 17 questions had yes/no responses and 28 had yes/no/don't know response; thus, 73 indicator variables were created. Three demographic variables (individual's gender, age, and race/ethnicity) were also included in the final dataset alongside the psychosocial indicator variables.

Of 197 individuals who participated in the survey, data from 154 subjects with complete records (those who answered every survey question) were analyzed. We found no difference in latrine use among those with complete data and those without complete records in terms of self-reported latrine use (chi-squared = 0.16, p-value = 0.69), gender (chi-squared = 0.44, p-value = 0.40), or race/ethnicity (chi-squared = 1.3, p-value = 0.25). Approximately 76 percent of the 154 individuals self-reported always using a latrine whereas the remainder of the study participants reported not always using a latrine (Table 2.2). A higher proportion of women, participants aged 18-40, and individuals living in Afro-Ecuadorian communities report consistent latrine use.

Data Reduction: Using SPCA, the dataset was reduced to six questions of importance, whereas the Adaptive ENET identified five psychosocial questions as having an association with reported latrine use (Table 2.3). The models selected psychosocial factors, but not demographic variables, as independent drivers of consistent latrine use. The low PMSE values for both models (less than 15%) imply that each model exhibits good internal validity.

The two models did not yield statistically different results (McNemar's chi-squared statistic = 0.20, p-value = 0.65). Three questions reflecting determinants of latrine use on each of the IBM-WASH domains (interpersonal, individual and habitual levels), were selected by both approaches, and were included in the logistic regression models. Of the common questions, daily latrine use, and perceived cleanliness of the latrine had the strongest association with self-reported consistent latrine use. In contrast, when asking about latrine use norms within the community, disagreement with the statement "During the dry season, I think that majority of the elderly men in my village regularly use a latrine" reflected lower odds of consistent latrine use among individuals, although at varying strength between the Adaptive ENET model and the SPCA model.

In addition to the three common questions, five other psychosocial determinants were identified by the two data-reduction approaches and included in the logistic regression models. These determinants have large standard errors, which limits any possible interpretation of the association between the predictors and the outcome. Nevertheless, the selected predictors unique to ENET reflect attitudes about latrine attributes (small cabin size and small walls) as well as convenience of latrine use at night as important drivers of behavior. On the other hand, the Adaptive ENET model selected the following determinants of individual level latrine use: convenience of returning to home to defecate and the perception that household size is too large for one latrine (Table 2.3).

2.5 Discussion

Understanding individual-level latrine use is an important step towards integrating behavior change into sanitation interventions. To this end, we first used social theories, based on the IBM-WASH framework, to guide our initial selection of potential latrine-use determinants identified in a previously collected ethnography. We then used dimension reduction techniques to narrow down these variables to a select set of latrine-use determinants. Overall, we found that determinants of latrine use are not solely individual-level psychosocial factors or personal characteristics (gender, age, race/ethnicity). Daily latrine use, perceived latrine cleanliness, and a descriptive norm about latrine use among elderly men were also drivers of individual-level behavior for our field site. This constellation of questions provides insight into the sociocultural drivers of behavior to exemplify that individual behavior is a by-product of dynamic social and psychological processes. First and foremost, daily latrine use reflects a personal habit. Habit formation is impacted by a variety of factors, including ease of repeating behavior (27) and sociocultural norms that impact how individuals process information (28,29). Latrine cleanliness has been associated with overall satisfaction of a sanitation facility (30,31). Thus, we conclude that cleanliness creates a favorable environment for latrine use to become habitual. Indeed, latrine cleanliness, among other factors, was identified as an important driver of latrine adoption in a systematic review of the impact of sanitation interventions in South Asia and Sub-Saharan Africa (32). Outside of an intervention setting, latrine cleanliness is consistently cited as a driver of latrine use in places like India (33), Benin (34), South Africa (35), and Uganda (36). Cleanliness, however, is only one factor that leads to daily latrine use. The social environment, which is also included in the study results, greatly influences how behavior patterns form and change.

Like our results, other researchers have also noted the influence of social norms on sanitation practices (37–39). In rural Ethiopia, for example, shared values around latrine use and open defecation were strong indicators of individual defecation behavior; open defecation was practiced more often in communities that noted strong barriers to latrine use, whereas in communities with taboos against open defecation latrine use was practiced commonly (37). O'Reilly and Louis' examination of latrine use behavior in India noted that proximate social pressures to use latrines were important drivers of behavior (38). This is also echoed by Shakya et al.'s social network analysis of latrine access, a precursor to latrine use, which showed latrine ownership was higher among more centrally connected individuals (39). Within our study, we found that a descriptive norm specific to defecation behavior among elderly men during the dry season predicted individual-level latrine use. Men, particularly male elders, are highly respected in the study communities, and due to seasonal flooding, rain often affects activities of daily living. This highlights the intersectional influence of power dynamics (social position, described by age and gender) with temporal factors, such as seasonality, on individuals. Our results, alongside these other studies, highlight the importance of sociocultural determinants of behavior, because individuals are likely to exhibit the same behavior as those around them (40).

Our findings differ from other studies examining latrine use in two fundamental ways. First, we did not find personal characteristics to be independent determinants of latrine use behavior. Nearly all studies examining defecation practices have noted distinct patterns by age, seasonality, and gender (14,41,42). While personal characteristics were not selected within our model, it is of note that themes of seasonality were imbedded in the questions that asked about normative behaviors within the communities (i.e., defecation patterns by demographic groups in the wet and dry seasons). Additionally, our findings deviate from a core principle in early health behavior theories- knowledge as a propagator of behavior change (43–46). Based on this core principle, many sanitation campaigns, most notably the Community Led Total Sanitation program, often rely on knowledge of disease transmission and health benefits of latrine uptake to promote latrine use (47). In our study, however, questions related to knowledge of benefits resulting from latrine use were not selected. Knowledge of benefits stemming from latrine use was high, even among non-users. The fact that people chose to not use latrines even when they understood the health benefits associated with latrine use has been observed elsewhere. In a recent study examining latrine use behavior in Ethiopia, community members identified that latrines could be beneficial for health and simultaneously chose not to use latrines (37). Additionally, Barnard et al. 2013 found similar findings in their assessment of latrine uptake following a large-scale latrine construction intervention (10). Increasingly, health behavior change approaches are relying less on knowledge as a primary driver of behavior (48). Because knowledge alone does not predict behavior, additional work is required to further test whether there are generalizable determinants of latrine use across a wide array of contexts.

One approach to enhance our abilities to determine whether indicators of latrine use behavior generalize across populations is to expand studies to include heterogeneous populations. Latrine use studies, particularly those conducted in India, commonly sampled one person per household and almost exclusively women (16,20). Within-household variability of psychosocial factors or behaviors was not accounted for in their results; nor were the identified psychosocial factors reflective of defecation determinants within the general population. One strength of our approach is the diversity of the study population. Not only did we attempt to sample more than one adult per household, but also, we intentionally sampled both men and women from communities with different cultural values and primary languages spoken. For example, as described in the ethnography, open defecation was less stigmatized in Chachi communities than in Afro-Ecuadorian communities and latrine access varied between the two ethnic groups. Yet, latrine cleanliness was a driver of latrine use among both groups. If we had limited our sample to either type of community, we would likely present different results with limited generalizability. Additionally, we also observed households in which individuals practiced defecation behaviors different from their family members. For example, one individual primarily openly defecated while others were consistent latrine users. If we had estimated only household-level drivers of latrine use, the variability in individual-level behavior would have been missed. Thus, sampling homogeneous populations presents challenges for assessing whether common psychosocial determinants of latrine use exist between and within populations.

Beyond the issue of generalizability, a few caveats with our approach are important to highlight. First, as noted in the results section, the PMSE value is low. This suggests that the selected predictors present a near perfect proxy of latrine use. It is improbable that the questionnaire captured all of the psychosocial determinants of latrine use behavior and we would thus expect a higher margin of error, which is common in questionnaire-based proxies of measurement (49). As is always the case in face-to-face interviews, there is a possibility that the predictors themselves may also be subject to some misclassification, which could result in the observed low margin of error. Perceived sensitivity of survey questions can lead to social desirability bias in responses (50). We hypothesize that misclassification inherent in the selected determinants is minimal, as these questions were perceived to be less sensitive than self-reported defecation questions. Furthermore, because the design of the questionnaire is rooted in qualitative data, which increase the validity of the questions, we believe that any misclassification of the predictors is minimal. Our confidence that the group of identified questions truly reflect drivers of behavior is supported by an out-of-sample analysis. In this analysis, we compared two datasets containing six common psychosocial variables and self-reported latrine use by fitting logistic regression models to test the association between these variables. The model PMSE value were similar, providing evidence that the variables selected in this study have some degree of external validity (see Appendix 5 for details).

Second, the current R packages we used for data reduction do not account for the nested clustering we observed in our data. If the outcomes are correlated and their correlation is ignored in the analysis, the standard errors presented in Table 2.3 are narrower than they would otherwise be. A sensitivity analysis examining this question is presented in Appendix 5 and the results suggest that clustering of behaviors is unlikely to impact our results.

Third, there is no gold standard measurement of individual latrine use. Although we are using psychosocial determinants to predict behavior, it is likely that our outcome variable, self-reported latrine use, is subject to social desirability bias with over-reporting of latrine use behavior. It should also be noted that self-reported defecation behavior has not been previously validated as a metric of latrine use. Thus, misclassification of latrine use behavior may have influenced which attitudes, norms, habits, etc. were associated with latrine use behavior. The use of multiple cross-validation methods to select questions predicting latrine use, however, mitigates errors in variable selection.

Fourth, our analysis presents psychosocial factors influencing latrine use behavior at the population level and does not disaggregate by gender, ethnicity, or age. These contextual factors, in particular gender, are likely associated with unique psychosocial factors that influence sanitation practices and are not included within our analyses. For example, women require latrines to be sufficiently outfitted for menstrual hygiene management (51). Additionally, women consistently report that privacy and safety are of concern and are, therefore, important determinants of latrine use for women more so than for men (14,52). For these reasons, SDG 6.2 specifically notes the importance of considering the needs of girls and women while improving latrine access for the entire population. Importantly, our study does not address individual-drivers of behavior among children, but rather focuses on determinants of latrine use among adults. Future work examining latrine use behavior should incorporate contextual factors alongside psychosocial factors influencing latrine use behavior.

Achieving universal access to water, sanitation, and hygiene (WASH), the stated goal of SDG 6, will require a focus on equity across different populations. One implication of this goal is the need to re-focus on regions like Latin America where coverage is high overall but where pockets of low coverage can still be found. In addition to this regional variation, there is growing evidence that individuals exhibit a variety of sanitation practices, including both open defecation and latrine use, even when a household has access to a sanitation facility (53,54). This evidence highlights the fact that access does not equate to use. Teasing apart this complicated relationship by identifying psychosocial determinants of individual-level use across multiple domains is an important step. Extension of this work is needed to test hypotheses that assess whether psychosocial proxies of latrine use are robust indicators of latrine use behavior and whether latrine use is a good indicator of reduced exposure to pathogens that mitigates poor child health outcomes

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Figure 2.1. Conceptual Framework. Our framework is a modified IBM-WASH model. Here, we measure the determinants of latrine use that intersect at two domains (technology and psychosocial) across three levels (interpersonal, intrapersonal, and habitual). This diagram provides example themes of the types of questions included in the survey.

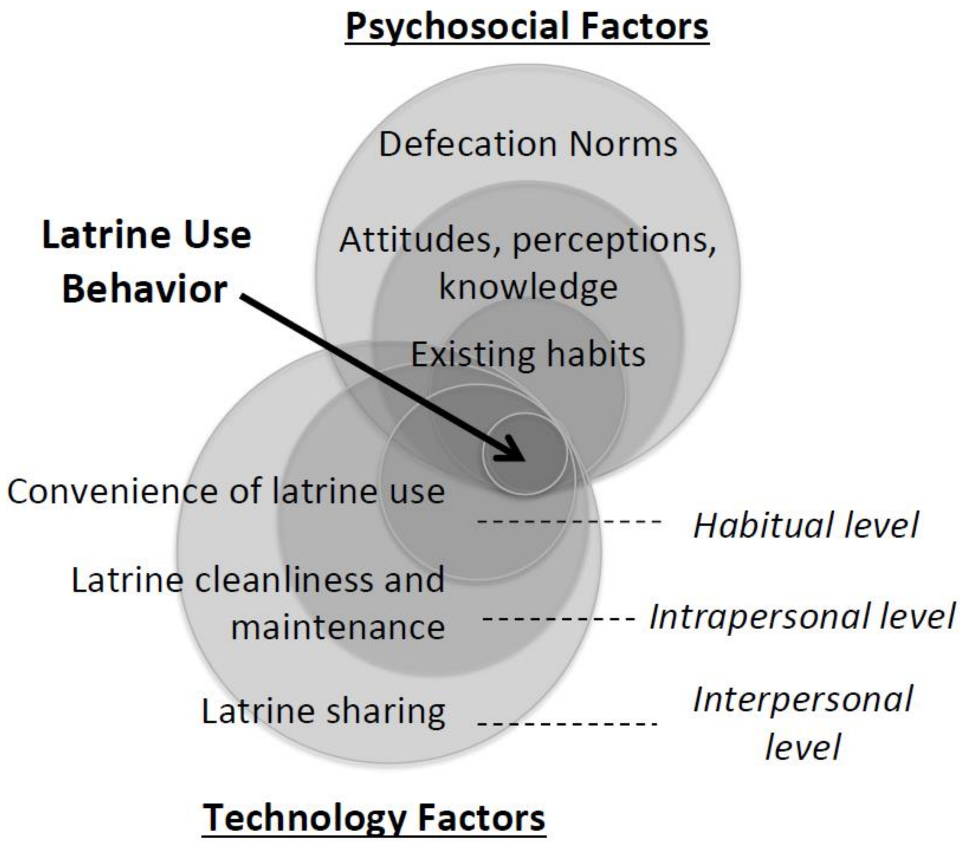


Table 2.1. Classification of survey questions and corresponding number of survey questions within each category

Classification of Survey Question	Number of Survey Questions within Category	Number of Survey Questions Remaining for Analyses
Attitudes towards open defecation and latrine use	14	9
Descriptive norms (i.e., one's perceptions of other's actual behaviors, related to open defecation/latrine use) *	20	13
Injunctive norms (i.e., one's perceptions of how others should behave, related to open defecation/latrine use)	6	1
Perceptions of community benefits resulting from latrine use	3	0
Attitude towards shared sanitation	6	5
Perceived attributes of latrine construction	12	10
Perceived convenience of household latrines	9	7

**Questions within this category are time-scale dependent so as to reflect the influence of seasonality on behavior*

Table 2.2. Percent Distribution of the Study Population and Percent Individuals that Use a Latrine by Background Characteristics

Background Characteristics	**Percent distribution of population**	**Percent latrine users**	**Number of people in each category**
Gender			
Female	50%	78%	77
Male	50%	74%	77
Age			
18-30 years	47%	79%	72
31-40 years	15%	78%	23
41-50 years	16%	72%	25
51-60 years	15%	70%	23
61+ years	7%	72%	11
Race/Ethnicity			
Afro-Ecuadorian	81%	78%	124
Chachi	20%	67%	30
Total Population	100%	76%	154

Table 2.3. Data Reduction: Logistic regression models derived from SPCA and Adaptive ENET approaches. Both models present the list of estimated beta coefficients, standard errors (SE), and p-values for variables predictive of self-reported latrine use. The predictive mean squared error (PMSE) is shown below the results of each respective model. Variables selected by both modeling approaches are in bold.

SPCA Model

Response to corresponding question	**Beta Estimate**	**SE**	**p-value**
*****Yes to, "The latrine is clean enough to use."***	2.4	0.62	0.0001
*****Yes to, "I use the latrine everyday."***	2.5	0.62	< 0.0001
****No to, "During the dry season, I think that majority of the elderly men in my village regularly use a latrine."***	-1.6	0.78	0.04
***Yes to, "The cabin of the latrine is too small for me to use."*	-0.81	0.56	0.15
**Yes, to "It is more convenient to use the latrine at night than to defecate in a container within my household."*	0.61	0.63	0.33
***Yes to, "The walls of the latrine are too small to provide enough privacy while using the latrine."*	0.57	0.59	0.33
PMSE		0.13	

**Referent group is 'Don't Know'*

***Referent group is 'No'*

Adaptive ENET Model

Response to corresponding question	**Beta Estimate**	**SE**	**p-value**
*****Yes to, "The latrine is clean enough to use."***	1.2	0.18	< 0.0001
*****Yes to, "I use the latrine everyday."***	1.4	0.17	< 0.0001
****No to, "During the dry season, I think that majority of the elderly men in my village regularly use a latrine."***	-0.15	0.23	0.51
**No to, "For the type of work I do, it is more convenient to defecate outside of the house."*	0.10	0.12	0.40
***Yes, to "There are too many people in this household for one latrine."*	0.14	0.12	0.23
PMSE		0.14	

2.7 Appendix

Appendix 2.1. Survey Questions

Below is a list of all the psychosocial-related survey questions that were included in the study. Bolded questions were removed during the data cleaning process.

1. *Open defecation gives the opportunity to get out of the house.*
2. *Defecating in the open at the night is opportunity to defecate in peace.*
3. *Elderly people are used to open defecation, they cannot adopt latrine use.*
4. *I dislike the feeling of confinement when I defecate in a latrine.*
5. *It is unhygienic to store feces in a latrine pit close to the home.*
6. *Latrine use is part of my everyday activities.*
7. ***Open defecation is more convenient than using a latrine**.*
8. ***Practicing open defecation is cleaner than using my latrine.***
9. *Defecating in a river removes feces from my community.*
10. ***Defecation should be practiced in a way that does not soil my community.***
11. ***Defecation should be practiced in a way that does not soil my household**.*
12. *I do not use the latrine when it is raining because I do not want to get wet.*
13. ***I prefer to use a latrine rather than defecate in the open**.*
14. *I prefer to defecate on the ground rather than in the water.*
15. *During the rainy season, I think that most of the men in my village regularly use a latrine.*
16. ***During the rainy season, my relatives all use a latrine when they go to defecate.***
17. *During the rainy season, I think all of my neighbors regularly use a latrine.*
18. *During the rainy season, I think that most of the women in my village regularly use a latrine.*
19. ***During the rainy season, I think that most of the male adolescents in my village regularly use a latrine.***
20. ***During the rainy season, I think that most of the female adolescents in my village regularly use a latrine.***
21. *During the rainy season, I think that most of the children in my village regularly use a latrine.*

22. *During the rainy season, I think that most of the elderly men in my village regularly use a latrine.*
23. *During the rainy season, I think that most of the elderly women in my village regularly use a latrine.*
24. *During the dry season, I think that most of the men in my village regularly use a latrine.*
25. ***During the dry season, my relatives all use a latrine when they go to defecate.***
26. *During the dry season, I think all of my neighbors regularly use a latrine.*
27. ***During the dry season, I think that most of the women in my village regularly use a latrine.***
28. *During the dry season, I think that most of the male adolescents in my village regularly use a latrine.*
29. ***During the dry season, I think that most of the female adolescents in my village regularly use a latrine.***
30. *During the dry season, I think that most of the children in my village regularly use a latrine.*
31. *During the dry season, I think that most of the elderly men in my village regularly use a latrine.*
32. ***During the dry season, I think that most of the elderly women in my village regularly use a latrine.***
33. *Young children are taught not to defecate in the open.*
34. *Feces from infants will not cause illness*
35. ***I would be embarrassed if someone found me going for open defecation during the rainy season***
36. ***It is okay if some people in the village do not use a latrine when they go for defecation.***
37. ***All adults in this village should use a latrine***
38. ***All adolescents in this village should use a latrine.***
39. ***All children in this village should use a latrine.***
40. *If a person has diarrhea, and is very ill, she or he should use the latrine.*
41. ***Using a latrine contributes to the community's development.***
42. ***Using a latrine contributes to my community's health.***
43. ***When I use a latrine, it contributes to my child's health.***

44. *There are too many people in this household for one latrine.*

45. *I have to wait for too long in the morning before it is my turn to use the latrine.*

46. *In the morning, if the latrine is in use by another member, I go for open defecation.*

47. *I don't have issues if my neighbor uses our latrine to defecate.*

48. ***Members of my community use the public latrines on a daily basis.***

49. *If my household did not have its own latrine, I would use my neighbor's latrine.*

50. *The pit is small and would fill too quickly if everyone used the latrine every day.*

51. ***It is too much work to get water to use the latrine at night.***

52. *The cabin of the latrine is too small for me to use.*

53. *There is a bad gas / odor that comes from the latrine.*

54. *The walls of the latrine are too small to provide enough privacy while using the latrine.*

55. *I am pleased with how the latrine looks.*

56. ***Access to water for hand washing after latrine use is difficult.***

57. *The latrine basin is strong enough to hold my weight.*

58. *The walls protect me from insects while I am using the latrine.*

59. *The latrine is clean enough to use.*

60. *A poorly maintained latrine should not be used.*

61. *I am satisfied with the type of latrine my household has.*

62. *By regular use of the latrine, I miss the opportunity to go out of the house.*

63. *For the type of work I do, it is more convenient to defecate outside of the house.*

64. *In the morning, it is more convenient to use the latrine than going for open defecation.*

65. *It is more convenient to defecate outside than to return home to use the latrine.*

66. *My morning routine is not suited for using the latrine to defecate.*

67. *It is more convenient to use the latrine at night than to go to within a container in my dwelling.*

68. ***It is difficult to use the latrine because there is no water source nearby.***

69. ***It is dangerous to use the latrine at night**.*

70. *There are times when it is dangerous to use the latrine because animals may be in the pit.*

Appendix 2.2 Background Characteristics of Selected Communities

The three communities enrolled in this study were selected from the EcoDeSS sample of 24 rural communities in Esmeraldas, Ecuador (Eisenberg, 2006). They were selected for inclusion in this study based on size, racial/ethnic makeup of the population, and representativeness of the study region in terms of access to clean water and improved sanitation facilities and sanitation practices. In 2013, the final year of data collection for the EcoDeSS study, Community A, a remote Afro-Ecuadorian river village, was comprised of 36 households and 201 individuals. Community B, a remote Chachi village geographically located on a river, had 22 households and 150 people living in the community. In contrast, Community C, which is located near a road and main town, had 164 households and 720 individuals when censused in 2013. Appendix Table 2.4 presents additional demographic information and WASH characteristics for these communities.

Appendix Table 2.4. Demographic characteristics of each community, including the percent of the population under 5 years of age, the median age of the population (and interquartile range), and the percent of the population that is female. WASH characteristics include the percent of the distribution of sanitation facility by type, the percent distribution of drinking water source, and whether the household respondent reported treating the water in the last week; these indicators at the household level.

Community Demographics			
	Community A	**Community B**	**Community C**
5 years of age and younger	16%	15%	16%
Age	15.8 (27.8)	15.7 (28.7)	19.0 (28.4)
Female	46%	50%	50%
Household WASH Characteristics			
	Community A	**Community B**	**Community C**
Sanitation Facility			
Toilet or latrine with a septic tank	63%	0%	63%
Latrine without a septic tank (Private)	16%	17%	5%
Latrine without a septic tank (Shared)	19%	17%	9%
Latrine without an enclosed pit	0%	22%	2%
No facility	3%	39%	0%
Missing	0%	4%	22%
Total	100%	100%	100%
Drinking Water Source			
Purchased Water	28%	0%	3%
Piped Water	0%	0%	60%
Rainwater	9%	0%	3%
River/Surface water	59%	92%	2%
Missing	3%	8%	32%
Total	100%	100%	100%
Water Treatment in last Week			
Yes	45%	4%	17%
No	55%	91%	50%
Missing	0%	4%	33%
Total	100%	100%	100%

Appendix 2.3 Assessment of Correlation

Initial exploration of correlation in the survey included basic logistic regression models examining the association between each of the categorical predictors and the outcome, latrine use, in the full dataset. We planned to assess variable inflation factors, however, the initial model failed to converge and we received error messages noting that some of the fitted probabilities were numerically exactly equal to 0 or 1. These error messages seemed to indicate that the dataset exhibited highly correlated variables. As a second step, we estimated Spearman's rank correlation coefficient for each combination of the 45 categorical variables. A correlation coefficient of 0.6 or greater was identified between 13 variable pairs, indicating at least a moderate correlation between the following variables pairs:

- *During the rainy season, I think that most of the women in my village regularly use a latrine* and *During the rainy season, I think that most of the female adolescents in my village regularly use a latrine*
- *During the rainy season, I think that most of the women in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly men in my village regularly use a latrine*
- *During the rainy season, I think that most of the women in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly women in my village regularly use a latrine*
- *During the rainy season, I think that most of the female adolescents in my village regularly use a latrine* and *During the rainy season, I think that most of the children in my village regularly use a latrine*
- *During the rainy season, I think that most of the female adolescents in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly men in my village regularly use a latrine*
- *During the rainy season, I think that most of the female adolescents in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly women in my village regularly use a latrine*
- *During the rainy season, I think that most of the children in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly women in my village regularly use a latrine*

- *During the rainy season, I think that most of the children in my village regularly use a latrine* and *During the dry season, I think that most of the children in my village regularly use a latrine*
- *During the rainy season, I think that most of the elderly men in my village regularly use a latrine* and *During the rainy season, I think that most of the elderly women in my village regularly use a latrine*
- *During the dry season, I think that most of the male adolescents in my village regularly use a latrine* and *During the dry season, I think that most of the children in my village regularly use a latrine*
- *During the dry season, I think that most of the children in my village regularly use a latrine* and *During the dry season, I think that most of the elderly men in my village regularly use a latrine*
- *The cabin of the latrine is too small for me to use* and *The walls of the latrine are too small to provide enough privacy while using the latrine*
- *I am pleased with how the latrine looks* and *I am satisfied with the type of latrine my household has.*

Given evidence of correlation in the dataset, analysis techniques should incorporate methods for reducing correlation between the independent variables of study.

Appendix 2.4 Overview of SPCA and Adaptive ENET

Supervised Principal Component Analysis

Application of Principal Component Analysis (PCA) is common in questionnaire development as the method identifies redundancy of questions and underlying correlations between constructs [1,2] by ranking components in terms of their variance contribution through use of an orthogonal linear transformation [3]. Here, use of SPCA accounts for the correlation between each factor and the outcome of interest via estimation of univariate standard regression

[1] Ferguson E, Cox T. Exploratory factor analysis: A users' guide. International Journal of Selection and Assessment. 1993 Apr 1;1(2):84-94.

[2] Oppenheim AN *Questionnaire Design, Interviewing and Attitude Measurement*. 1992. Pinter, London

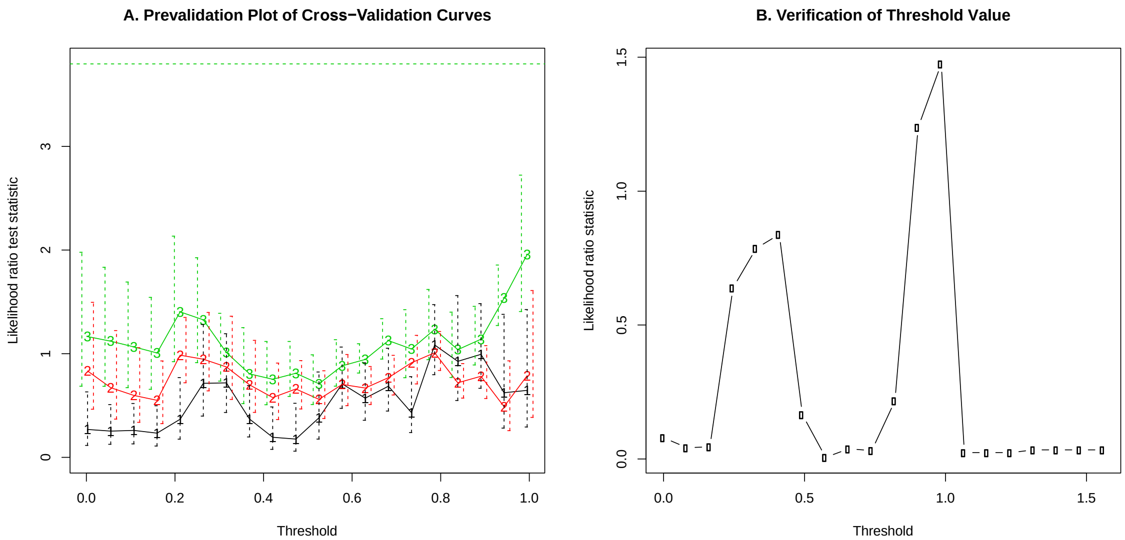
[3] Jolliffe IT. Principal component analysis and factor analysis. Principal component analysis. 2002:150-66.

coefficients or feature score for each feature [4]; here, we use feature scores. Only variables with a univariate feature score exceeding in absolute value a threshold θ are included in a reduced data matrix for PCA. PCA techniques are then run to develop a fixed ordering of features.

The θ value was determined by performing a cross-validation of the log-likelihood ratio test statistic utilizing training data and test data. Initial explorations of k-fold cross-validation showed overfitting when a standard 5-fold approach was used. Thus, we used an 8-fold cross-validation. To determine a θ value, first individual feature scores were generated for each variable. Next, a PCA was run on the entire dataset, then, simultaneously, multiple PCAs were run on datasets with variables limited to those meeting various θ thresholds. To select the most appropriate θ value to use, we conducted a likelihood ratio test (LRT). The goal of LRT is to compare how a logistic regression model that used the PCA results corresponding to each limited dataset fit the data relative to a logistic regression model that used the PCA results from the entire dataset. Appendix Figure 4.1 A shows the cross-validation curves for estimating the best θ threshold, where symbols “1”, “2”, and “3” denote the number of principal components used - one, two, and three, respectively. These cross-validation curves use the training data. The best value of a threshold for θ is defined as the value that correspond to the highest LRT statistic, the latter being a value between zero and infinity. A θ threshold of 0.98 was selected and was used to identify variables that comprised the reduced dataset, which was used for the remainder of the SPCA. Following the selection of the θ threshold, a confirmatory analysis was performed by applying the various threshold values to the test data and computing the LRT statistic. Appendix Figure 4.1 B shows this verification; the LRT statistic is indeed highest when the θ threshold value is equal to approximately 1.0. Finally, with the θ threshold selected, we performed PCA using variables meeting this threshold, and the results of the PCA were used in a logistic regression where the goal was to predict the outcome of interest (consistent latrine use behavior).

[4] Bair E, Hastie T, Paul D, Tibshirani R. Prediction by supervised principal components. Journal of the American Statistical Association. 2006 Mar 1;101(473):119-37

Appendix Figure 2.2. Selection of θ Threshold Value. A. Prevalidation Plot of Cross-Validation Curves and B. Verification of Threshold Value



Adaptive Elastic NET

To account for the possible presence of highly correlated variables among the set of predictors in a linear or logistic regression model, Adaptive ENET selects variable by adding to the squared loss function two weighted penalty terms (λ_1 and λ_2) that tune the squared error loss in the model. The λ_1 term, applied to the vector of regression predictors, that is β, allows for variable shrinkage and selection, while the λ_2 term, applied to the squared absolute value of β, stabilizes solution pathways to address correlation of variables and improve prediction [5]:

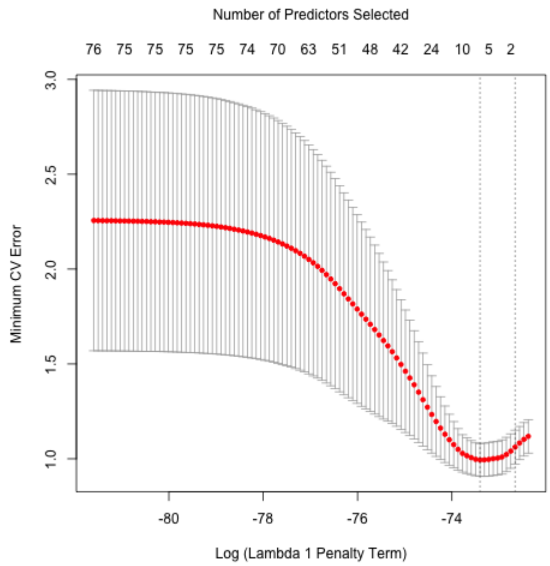
$$\hat{\beta} = \underset{\beta}{\operatorname{argmin}} |y - X\beta|^2 + \lambda_2 |\beta|^2 + \lambda_1 |\beta|_1$$

We use a 5-fold cross-validation to estimate both penalty terms. First, the λ_2 penalty term is set at a value that results in minimum cross-validation error, estimated at 0.01. Given this value, the λ_1 optimal penalty term is then determined. The λ_1 term is selected by accounting for λ_2 and the minimum error produced by the model, while being aware of the number of predictors that will be selected by the model. Appendix Figure 4.2 shows that minimum error will be achieved when log λ_1 is equal to of -73.3. This corresponds to a model with twelve predictors,

[5] Zou H, Zhang HH. On the adaptive elastic-net with a diverging number of parameters. Annals of statistics. 2009;37(4):1733

given the determined λ_2 term and k-fold validation.

Appendix Figure 2.3. Selection of λ_1 Penalty Term



Appendix 2.5 Limited Out-of-Sample Analysis and Clustered Data

Eight psychosocial variables were selected from either the SPCA or Adaptive ENET models; we have data from another study within the same geographical region for six of these variables. These additional data, referred to in subsequent text as the 'out-of-sample data', includes the three communities sampled for this project, as well as seventeen other communities within the geographical region. Using both the original and the out-of-sample datasets, we examined the association between the six common psychosocial variables and self-reported latrine use in two separate regression models. To ease comparison between the two datasets, observations with definitive "yes" (coded as 1) or "no" (coded as 2) responses to all survey questions were included in the analysis while "don't know" responses were excluded. Model 1 uses data from the primary study and model 2 uses the out-of-sample data. Model 2 accounts for household-level clustering via an exchangeable correlation matrix within a generalized estimating equations (GEE) approach, which is further discussed below (see *Household-Level Clustering of Latrine Use* section). The confidence intervals surrounding the β estimates in Model 2 were derived using robust standard errors. Given these difference in modeling approaches, the specific *beta* estimates should not be compared; rather, the overall model results are of interest. These sensitivity analyses were conducted using R (version 3.0.2), using the base program and the *geepack* package.

Out-of-Sample Data: Following the primary study, a larger population-based child cohort study was rolled out in the same geographical region. The objective of the cohort study was to assess the relationship between latrine use behaviors in the population and individual child growth. Thus, households were selected for study enrollment if an infant less than 12 months of age was living in the household at the baseline visit (June 2016). Among enrolled households, all members were interviewed and questioned about their defecation practices and psychosocial norms, attitudes, and beliefs related to latrine use. In total 193 adult household members (18 years or older) participated in the baseline survey. For the purposes of this analysis, the out-of-sample data was limited to participants with "yes" or "no" responses to the survey questions and contained 186 adults living in 96 households in 20 communities. It should be noted that there is a difference in latrine use among those excluded from this analysis and those included (Fisher exact test = 6.4, 95% CI =1.0-69, p=0.02), with the seven excluded individuals having a greater likelihood of being inconsistent latrine users.

Out-of-Sample Validation: The objective of comparing the regression models across datasets that assess the associations between the common psychosocial variables and latrine use is to gauge whether these variables have an overall consistent relationship across datasets. A crude assessment of the validity of the study findings can be achieved by comparing the predicted mean squared error (PMSE) for each model. The PMSE is a metric of model accuracy which reflects the squared difference between the fitted values of predicted outcomes and the observed values (i.e., from the dataset). Specifically, examination of the PMSE for these out-of-sample predictions will allow us to assess how well the variables selected from the primary analysis predict latrine use in a different population sample.

Two logistic regression models presenting the association between six psychosocial variables and self-reported latrine use are presented in Appendix Table 2.5. The PMSE value corresponding to each model is also presented.

Appendix Table 2.5 Logistic regression models derived from the primary study and the out-of-sample data. Both models test the association between six common psychosocial variables and latrine use. Presented for each model are estimated beta coefficients, the lower and upper bounds for these estimates, p-value, and the model PMSE.

	Model 1: Logistic regression model using the primary study data (N=174 people)				**Model 2**: Logistic regression implementing GEE with the out-of-sample data (N=186 people)			
Variable *("no" responses)*	**Beta Estimate**	**Beta Estimate: Lower Limit**	**Beta Estimate: Upper Limit**	**p-value**	**Beta Estimate**	**Beta Estimate: Lower Limit**	**Beta Estimate: Upper Limit**	**p-value**
I use the latrine everyday.	-2.6	-4.0	-1.3	< 0.001	-0.24	-1.34	0.87	0.68
There are too many people in this household for one latrine	-1.7	-2.8	-0.54	0.004	-0.35	-1.02	0.33	0.31
The cabin of the latrine is too small for me to use	0.51	-0.39	1.4	0.27	-0.88	-1.52	-0.24	0.01
The latrine is clean enough to use.	-2.5	-3.7	-1.2	< 0.001	0.08	-0.98	1.1	0.88
For the type of work I do, it is more convenient to defecate outside of the house	0.79	-0.14	1.7	0.10	0.39	-0.30	1.1	0.27
It is more convenient to use the latrine at night than to defecate in a container within my household	-1.4	-2.6	-0.21	0.02	-0.04	-0.98	0.90	0.93
PMSE	0.12				0.19			

The PMSE values for both models are low and do not greatly differ. Model 1 generated a PMSE of 0.12 and Model 2 yielded a PMSE of 0.19. The low values suggest that the six psychosocial norm variables present reasonable proxies of latrine use in both populations, with slightly greater error in the out-of-sample dataset. This comparison acts as limited validation and provides some evidence that variables selected by the main study findings have some degree of external validity.

Household-Level Clustering of Latrine Use: We can gain insight into the likelihood of clustering effects within our study by examining the influence of household-level clustering in the analysis above. For Model 1, it was not possible to include household clustering within our analyses as these data were not available. In contrast, the out-of-sample data did contain information on household membership. Model 2 accounts for clustering of data at the household-level using a GEE approach. Within this model, we assume that the correlation structure is the same within each household, but unknown, and hence, use an exchangeable correlation matrix. We estimated the strength of clustering within each household to be -0.003 (95% confidence interval= -0.17, 0.16), with a maximum cluster size of six interviewed people living in the same household. This value indicates no clustering within the data. Thus, based on this analysis, we conclude that if clustering of latrine use behavior was present within a household, it would likely have little effect on the main results of our study where this nested aspect of the data was ignored.

Chapter 3

Latent variable modeling to develop a robust proxy for sensitive behaviors: application to latrine use behavior and its association with sanitation access in a Middle-Income Country

3.1 Abstract

Globally, diarrhea is a leading cause of child morbidity and mortality. Although latrines are an established intervention, several studies have shown no effect on child health when a household owns a latrine. One explanation for this result is that latrine access does not equate to latrine use. Latrine use, however, is difficult to accurately ascertain, as defecation behavior is often stigmatized. To address this measurement issue, we measure latrine use as a latent variable, predicted by a suite of psychosocial indicators. We administered a survey of 16 defecation-related psychosocial questions to 251 individuals living in rural Ecuador. We apply latent class analysis (LCA) to these data to model the probability of latrine use as a latent variable. To account for uncertainty in predicted latent class membership, we used a pseudo-class approach to impute five different probabilities of latrine use for each respondent. Via regression modeling, we tested the association between household sanitation and each imputed latrine use variable. The optimal model presented strong evidence of two latent classes (entropy=0.86): consistent users (78%) and inconsistent users (22%). There was no association between the probability of latrine use, predicted from the LCA, and household access to basic sanitation (OR=1.1, 95% CI=0.6-2.1). Effective implementation and evaluation of sanitation programs requires accurate measurement of latrine use. Psychosocial variables, such as norms, perceptions, and attitudes may provide robust proxy-measures. While longitudinal studies are needed to further assess these surrogate measures, broadly our approach can be adapted to measure other sensitive behaviors.

3.2 Introduction

Diarrheal disease, which is both preventable and treatable, is a persistent leading cause of morbidity and mortality for children under five years of age throughout the globe. Diarrhea-related mortality accounts for nearly 500,000 child deaths per year, which are concentrated in resource-limited settings (1). Millions of children worldwide are undernourished (2), and while malnutrition has a host of causes, enteric pathogen exposure is associated with both acute and chronic malnutrition (3,4). Water, sanitation, and hygiene (WASH) interventions reduce exposure to enteric pathogens that cause illness (5) and it is estimated that diarrheal-related child mortality could be reduced by more than one-third in low and middle-income countries (LMICs) if sanitation interventions were implemented at full-scale (6). Sanitation blocks multiple transmission routes of enteric pathogens, reducing individual-level exposures as well as community-level exposures (7,8). Indeed, latrine construction programs are viewed as fundamental for achieving Sustainable Development Goal (SDG) 6.2, which seeks to end open defecation and provide universal access to adequate and equitable sanitation (9). Yet, results from two recent randomized control trials of latrine construction interventions have shown no effect on child health, largely due to limited uptake of latrine use (10,11). Moreover, an analysis of Demographic and Health Survey data has shown a null association between access to improved sanitation facilities and prevalence of diarrhea in children throughout much of the globe (12). These results suggest there is a need to re-evaluate the assumption used in sanitation interventions that access to latrines ensures their use. We suggest that WASH program success can be better evaluated if behavior is incorporated as an indicator of WASH success rather than simply the presence of sanitation hardware.

Historically, sanitation intervention success has been measured as a household's access to a sanitation facility rather than sanitation practices at the individual level (13). One reason that access has been the accepted exposure variable is that it is easy to measure. Latrine use, however, is difficult to measure and no gold standard of measurement exists. A limited number of intervention studies include a metric of defecation behavior, and the methods used to capture latrine use behavior vary across studies (14). The most commonly used measure is self-reported defecation practices; however, outside social contexts where report of open defecation is not stigmatized, such as in India (15), survey questions asking about a respondent's sanitation behaviors present challenges, such as social desirability bias due to the sensitivity of the topic

(16,17). Beyond self-report, hygiene behavior is commonly captured through direct observation (18,19), which is a time-consuming effort subject to the Hawthorne effect (20). Other measures of behavior include use of sensors inside a latrine to quantify the number of times a latrine was entered (21) and observations of the latrine to assess whether it appears to have been used (22). While sensors may supply a more objective estimate of overall latrine use than self-report (23), neither sensors nor observations provide information necessary for assessing individual-level latrine use, or the proportion of users on the household or community levels. Such details are important drivers of enteric pathogen transmission and are integral in exposure risk of developing negative health outcomes.

This measurement conundrum for latrine use behavior is not unique to the sanitation field. Rather, many sub-fields of public health that rely on self-report of sensitive behaviors face similar issues of misclassification and measurement error. For example, epidemiology studies focusing on sexually transmitted infections have long been challenged by measurement of behavior (24), with self-reported condom use, a key intervention, presenting misclassification within the study (25,26). Here, we take a latent variable approach to capturing latrine use in a LMIC population with high latrine access, variable latrine use, and stigmatized self-report of defecation practices. Our approach is rooted in health behavior theory that recognizes both demographic factors and social processes as determinates of individual-level behavior (27). Using psychosocial indicators of latrine use behavior, we first apply latent variable modeling to create a proxy-indicator of latrine use at the individual level. Latent class modeling specifically refers to a group of techniques that identify one's underlying propensities to respond to particular questions and classifies a person into a group given their responses (28); thus, it lends itself well to measuring sensitive concepts that may not be easily captured by one direct question. We hypothesize that individuals in this population will generally belong to one of three classes: those who always use a latrine, those who sometimes use a latrine, and those who never use a latrine. With an assigned likelihood of latrine use, we next test the association between the latent variable measure of latrine use and household-level access to an improved, non-shared sanitation facility.

3.3 Methods

Data

The data are from a cross-sectional sample, collected between July and August 2016 as part of a longitudinal study examining the relationship between latrine use and child health. We surveyed 251 individuals 13 years and older living in 20 rural communities in Esmeraldas, Ecuador (see Table 1 for demographics). The communities selected for enrollment participated in previous enteric pathogen transmission studies (29). Eligibility for household enrollment was based on whether a child 12 month of age or younger lived in the home. Within each selected community, a household census was conducted to determine if eligibility criteria was met; if so, the household was approached for participation. Of eligible households, 94% were contacted and of these, 94% participated. Each individual 13 years or older living in an enrolled household was also approached for participation. Ninety-two percent of eligible individuals were present during the field team's visits and 81% of them consented to interview. The study communities are heterogeneous in terms of race/ethnicity; there are Afro-Ecuadorians, Chachi (an indigenous groups), and *mestizos*. Moreover, individuals practice a variety of sanitation behaviors, ranging from latrine use in private, household latrines to use of community latrines, to open defecation (Chapter 2).

Measures

Study participants were interviewed face-to-face by a local, trained survey team within the participant's home. The interviews focused on the psychosocial determinants of latrine use behavior and sociodemographic information. The survey tool was designed using the Integrated Behavior Model of Water Sanitation and Hygiene (IBM-WASH), a health behavior framework that presents behavior as a byproduct of intersecting dimensions of technology, context, and psychosocial factors that operate through ecological levels (30). We used 16 indicators, each measured by a specific question, to assess psychosocial determinants of latrine use (Table 2). Some of these indicators reflect descriptive social norms of defecation behavior in the communities; for example, whether a respondent agrees or disagrees that men in their village use a latrine during the dry season. Other indicators reflect themes of personal safety, convenience, and anxiety related to latrine use, as well as attitudes towards sharing a latrine with others. We also asked about perceptions of the latrine cleanliness and maintenance, and about habitual latrine use. The items were derived from ethnographic data from the study site as well as their demonstrated association with consistent latrine use in the communities of study (Chapter 2). Each survey question had three possible responses: *yes*, *no*, or *don't know*.

The survey team documented the presence of a sanitation facility following WHO/UNICEF Joint-Monitoring Programme definitions. A sanitation facility is considered improved if it separates human excreta from contact with the facility user (31). Improved sanitation facilities that are not shared with other households are defined as basic sanitation, whereas an improved facility that is shared with at least two household is considered limited sanitation. An unimproved facility does not provide hygienic separation of fecal matter from latrine users.

There are a number of important covariates for the analysis. Education and wealth, metrics of socioeconomic position (32), are associated with latrine access and the desire to own a latrine (33,34). Distinct patterns of defecation as well as the sanitation facility used vary by race/ethnicity within the study site. Women and men display distinct patterns of latrine use that may not be captured by the other covariates (35,36). Because wealth ascertainment in LMIC research often reflects asset ownership, which proxies one's access to resources (37), we measured asset ownership and whether one's household walls were constructed with cement. Asset deprivation is a composite indicator considered within the Standard of Living component in the Multidimensional Poverty Index that accounts for access to three different types of assets: information, mobility, and livelihood (38). Sociodemographic and asset covariates were measured via self-report; trained field staff observed household construction materials.

The Institutional Review Board at the University of Michigan and the Universidad San Francisco de Quito Bioethics Committee approved the data collection methods and study procedures.

Analytical Approach

We used latent class analysis (LCA) to classify individuals according to their propensity to use a latrine. LCA is a modeling approach that enables estimation of the probability of an individual belonging to one of a small number of hypothesized latent (or unobserved) classes based on a set of measured indicators, and allows for measurement error to be explicitly accounted for when estimating the final categorical latent construct (39). To model latrine use as a latent construct, we used the 16 psychosocial determinants of latrine use behavior measured in the aforementioned survey tool, and employed full information maximum likelihood (FIML) with robust standard errors.

Model building proceeded in a sequential process by first specifying the measurement model, where the 16 measured determinants were indicators of latent class membership. We then specified the hypothesized number of latent classes, first including three classes and then including two classes. In the three-class model, we expect individuals to be grouped into the following latrine user categories: never users, occasional users, and always users. A two-class model aggregates these categories into latrine users and non-users or consistent latrine users and inconsistent latrine users. To determine the optimal class solution (that is, the number of classes within the sample), we compared the model fit between the three-class and two-class models. Good fitting models are characterized by: (1) a low Bayesian Information Criterion (BIC) value; (2) a statistically non-significant chi-square goodness-of-fit statistic that assessed the observed class distribution and expected probability distribution of classes; and (3) relative entropy above 0.80 (40–43) (see Appendix for a comparison of class assignment in each of the models tested). Once the optimal class solution was determined, we examined the latent-class conditional item probabilities for each indicator (i.e., the probability of response to each survey question given class assignment). Uninformative indicators were removed from the model (see Appendix for conditional item probabilities for all indicators). An indicator was considered uninformative if the item probability confidence interval overlapped between class assignments.

In addition to identifying latent classes of latrine users, we also described the characteristics of the individuals in each class. Because of the inherent uncertainty in predicted class membership via LCA, we employed a multiple imputation (or pseudo-class) approach (44), using five random draws from a uniform distribution to generate five simulated class memberships for each respondent (given their original predicted class probability). Demographic descriptive statistics are presented for the modal class membership for each individual from the five imputations.

Using each imputed class membership as the outcome to test the association between class membership (the dependent variable) and household-level access to a basic sanitation facility, we fit five logistic regression models. Each of the regression models was adjusted for: individual-level educational attainment (categorical), race/ethnicity (binary), and gender (binary). While it is theoretically plausible that gender acts as an effect modifier, it was not possible to explore this given the small sample size. At the household-level, the following variables were also included as proxy-indicators to control for wealth: cement household walls (binary) and whether a household is asset- deprived (binary). We accounted for household clustering when computing standard errors and planned to run multinomial logistic models if the three-class outcome was selected and binary logistic regression if the two-class outcome was chosen.

Following the regression modeling, estimates from the five models fitted to the imputed data sets were combined following rules described by Rubin (45) (see Supplement for demographic proportions for each imputation and model results for each imputation). Combining the models allows for the standard error of the association between latrine access and latrine use to be calculated.

3.4 Results

The study sample was young (median age = 23), predominately female (65%) and Afro-Ecuadorian (63%). Most participants did not complete high school (81%), and of those that worked in the last year, it was most common to receive cash remittance. Slightly more than half of respondents live in households with non-cement walls (51%) and in households with access to basic sanitation (53%). Sixty-one percent of participants were from asset-deprived homes, and overall access to improved sanitation is high in the population (86%), with half of the sample having access to basic sanitation (i.e., basic sanitation) (Table 3.1).

The responses to the 16 indicators are presented in Table 3.2. Survey questions asking about within-home latrine sharing and about convenience of latrine use while outside of the home had more evenly split responses relative to the rest of the survey questions. While most survey questions generated a *yes* or *no* response, indicators asking about descriptive norms of latrine use by men and neighbors tended to have more *don't know* responses.

Model Fit

Using all 16 indicators, the 3-class and 2-class model solutions presented similar model fit statistics and predicted class memberships (Table 3.3). Nested group profiles are evident between the models. We thus label the three-class groups as "never users" (1%), "sometimes users" (25%), and "always users" (74%) and membership in the two-class model as "inconsistent latrine users" (22%) and "consistent latrine users" (78%). Within the 3-class model it is not feasible statistically to distinguish the 1% of the sample (n = 3, i.e., the "never users") from the remainder in further multivariable analyses; thus, the 3-class solution was rejected.

After removing uninformative indicators from the two-class model, five indicators remained. The chi-squared (395) and BIC (1,527) estimates of the 5-indicator 2-class model were drastically improved relative to the initial 16-indicator model (chi-squared=2.93E+13 and BIC=4,675), while the entropy estimate (0.86) and predicted class memberships remained the same (0.78 and 0.22). The two-class model with five indicators was used in further analyses.

Overall, the final two-class model presents evidence of high conditional probabilities for four of the five indicators in the consistent latrine use class, indicating robust classification (Table 3.4). This is also reflected in the high value for the entropy estimate. The indicator for within-household latrine sharing ("*There are too many people in this household for just one latrine"*), however, has a low conditional item probability among those with assigned consistent latrine use membership. Only 52% of consistent latrine users responded *no* to this question, revealing that this indicator may not appropriately distinguish between classes.

Latent Class Membership Assignment

Based on the final 2-class model, consistent latrine use was lowest among young adults (age 18-21), and also increased with higher educational attainment (Table 3.5). Consistent latrine use was also lowest among those that were unemployed in the prior year, while access to resources at the household-level showed no differences in latrine use. Accounting for individual factors and household resources, the fully adjusted regression model results showed no association between household access to a basic sanitation facility and the probability of latrine use (Basic Sanitation OR=1.1, 95% CI=0.6-2.1 in Table 3.6).

3.5 Discussion

For latrines to reduce pathogen transmission they must be used. Thus, research and programmatic evaluation need to have accurate defecation behavior measurements. To this end, our findings reveal three important insights into the complicated relationship between latrine presence and latrine use. First, our model predicts that nearly a quarter of this population practices inconsistent latrine use behavior (22%, Table 3.2), even when access to improved sanitation is high (86%, Table 3.1). Although we do not present self-reported latrine use data, we suspect that misclassification would have been high in this variable given that less than ten percent of respondents disagreed with the statement "I use a latrine daily" (see Supplement for further comparisons). Thus, we suspect that there is high misclassification in self-reported latrine use, and we argue that psychosocial indicator variables are a potential surrogate for latrine use behavior that minimizes misclassification bias. Second, we found that basic sanitation access was not associated with latrine use. This null association is consistent with data from India, which present variable sanitation practices among individuals living in a household with a sanitation facility (15,46). Some individuals will defecate in the household's latrine, while others practice open defecation. Our null finding also provides an explanation for the null relationship between latrine access and child health observed in a number of settings (10–12). And third, we found that five simple indicators could be used as reasonable indicators of the two "latent" classes of individuals in this population, as evidenced by a high entropy value for the final model that approached one (0.86). This high entropy value indicates limited misclassification in group assignment and is also an overall reflection of the indicators' high conditional item probabilities in the consistent latrine use class (47,48). The strength of these indicators suggests that they are plausible underlying manifestations of latrine use behavior. In further examining which indicators were informative for group classification, social theories of behavior provide additional rationale for these model results.

Of the 16 indicators examined, those that were least informative asked about individual-level psychosocial determinants of behavior. In contrast, the indicators in the final model that best distinguished between class memberships asked individuals about community defecation norms (i.e., other's latrine use behavior) and latrine sharing between households. Social theories of behavior view individual factors alone as limited metrics of behavior (49). Humans often exhibit the behavior of those around them, with sociocultural factors shaping daily habits in invisible ways (50). For example, the LCA suggests that agreement with indicators asking whether others use latrines presents a very high probability that one is a consistent latrine user. Moreover, agreement with statements regarding latrine sharing between households may reflect a strong commitment to latrine use; that is, an individual implies that they would willingly face a variety of barriers to use someone else's latrine (inconvenience, distance, dirty environment, etc.) if within-household access to a latrine did not exist. The psychological literature supports commitment as an important driver to behavior (51), again providing evidence of a plausible mechanism driving latrine use behavior. Overall, if we apply traditional metrics of Hill's exposure-outcome causality criteria to the study findings, our results exhibit strength, consistency (with the body of research), plausibility, and coherence (52).

Although the indicators used in the model were plausible, consistent, and coherent, our approach does not validate that the selected psychosocial variables are robust indicators of latrine use. Given the challenges of collecting unbiased measurements of latrine use, validating the predictive power of these indicators is difficult. Nevertheless, to address this limitation, we conducted extensive fieldwork to assess drivers of latrine use behavior (Chapter 2). Beyond this initial work to define the 16 indicator variables that have potential to be surrogate indicators of latrine use, our LCA analysis suggests that community-level norms of latrine use behavior are the strongest indicators. Thus, there is good potential for these indicators to generalize to other populations. Indeed the social environment tends to influence health behaviors (53). Related to defecation, social norms and the behaviors of others in our social networks have been identified as determinants of latrine use behavior in India and Ethiopia (54–56). The Community-Led Total Sanitation Campaign, a sanitation program targeting LMICs communities that seeks to end open defecation and has received lots of attention throughout the globe, operates through levels of behavior change that include community-pressure to promote latrine use (57,58). Our research was conducted in a very specific population; determining which social norms of latrine use behavior are applicable indicators across cultures requires further research. Furthermore, because social norms surrounding defecation behavior may also be influenced by the various components of the latrine itself (such as maintenance or cleanliness), incorporating additional information on the latrine would add this exploration and further the generalizability of this research.

In studying the epidemiologic triad, we focus on human behavior at the interface of the environment and biological agent of disease. Our approach, illustrated here for latrine use behavior, follows methods commonly used to measure socially stigmatized actions, such as intimate partner violence (59), aggression and bullying (60), or substance abuse (61). We present an initial understanding of measuring a sensitive behavior within the WASH sector, which allows us to test common assumptions of how people defecate, a critical component to disease transmission. More research is needed, however, to refine latrine use indicators. Inconsistent latrine use may have a different set of determinants than consistent latrine use, as these behaviors are not strictly opposites; thus, additional work is required to determine indicators of inconsistent latrine use and whether said indicators can distinguish groups of people. Moreover, because psychosocial norms, attitudes, and beliefs may change over time, longitudinal analysis are required to determine if these indicators are temporally consistent. Finally, future research is needed to test hypotheses assessing whether latrine use measures are adequate indicators of reduced exposure to enteric pathogens. Regardless of the disease system of study, epidemiologists interested in population dynamics that lead to health and disease should include metrics of behavior and social process into their research. Development of psychosocial indicators of sensitive behaviors and application of LCA is a useful tool for measurement of sensitive behavioral risk factors, such as hygiene or sexual activity, where self-report data suffer from misclassification and no gold standard measurement exists.

3.6 References

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Table 3.1. Background characteristics of the study sample. Median (SD) is reported for age. For the other covariates, the frequency distribution (in proportions) is reported. The corresponding number of individuals (N) is also shown.

Background characteristic		**N**
Age (in years)	23 (14)	251
Sex		
Female	0.65	162
Male	0.35	89
Ethnicity		
Afro-Ecuadorian	0.63	157
Mestizo and Other	0.13	33
Chachi	0.24	61
Educational Attainment		
Less than primary school	0.25	63
Completed primary school	0.20	51
Less than secondary school	0.36	90
Completed secondary school	0.17	43
Missing	0.02	4
Payment Type Received for Employment		
Solely cash	0.47	118
Cash and kind/ solely kind	0.06	16
Not paid	0.16	41
Not employed in the previous 12 months	0.30	76
Living in Household with Cement Walls		
Yes	0.45	115
No	0.51	128
Missing	0.03	8
Living in an Asset-Deprived Household		
Yes	0.61	152
No	0.39	98
Missing	< 0.01	1
Household Sanitation Access		
Improved Access		
Basic sanitation	0.53	132
Shared sanitation	0.33	118
Unimproved Access	0.05	13
No access to a sanitation facility	0.09	22
Missing	0.01	2

Table 3.2. Descriptive statistics for latent class analysis indicators: the percent of respondents that agree, disagree, or answer don't know to each survey statement.

LCA Indicators			
Survey Questions	**Percent Agreement**	**Percent Disagreement**	**Percent Don't Know**
When I use the latrine, it causes me to feel anxious.	0.19	0.82	0.00
I use the latrine every day.	0.91	0.09	0.00
I do not use the latrine when it is raining because I do not want to get wet.	0.81	0.19	0.00
During the dry season, I think that most of the men in my village regularly use a latrine.	0.68	0.14	0.18
During the rainy season, I think all of my neighbors regularly use a latrine.	0.80	0.07	0.14
During the rainy season, I think that most of the children in my village regularly use a latrine.	0.87	0.08	0.04
There are too many people in this household for one latrine.	0.43	0.56	0.01
If my household did not have its own latrine, I would use my neighbor's latrine.	0.86	0.14	0.00
The cabin of the latrine is too small for me to use.	0.26	0.73	0.01
I am pleased with how the latrine looks.	0.64	0.35	0.01
The latrine's basin is strong enough to hold my weight.	0.92	0.06	0.01
The latrine is clean enough to use.	0.87	0.10	0.03
It is more convenient to defecate outside than to return home to use the latrine.	0.44	0.55	0.00
My morning routine is not suited for using the latrine to defecate.	0.33	0.66	0.01
It is more convenient to use the latrine at night than to defecate in a container within my household.	0.85	0.15	0.01
It is dangerous to use the latrine at night.	0.36	0.64	0.00

Table 3.3. Model fit information and distribution of predicted classes probabilities using all 16 indicators.

Number of classes	BIC	X2	Relative entropy	Predicted class probabilities
2	4676	3.4E+13	0.86	0.22; 0.78
3	4675	2.3E+06	0.85	0.01; 0.25; 0.74

Table 3.4. The parameter estimates for the final 2-class model that included 5 indicators: item conditional probability, standard error (SE), and response to the survey question. The overall probability of assignment into the consistent latrine use membership class is 0.78 while assignment into the inconsistent latrine use class was 0.22. The model fit statistics include BIC = 1,527; X2 = 395; and relative entropy = 0.86.

Indicator	Consistent Latrine Use		Inconsistent Latrine Use	
	Question Response	**Item Probability (SE)**	**Question Response**	**Item Probability (SE)**
During the dry season, I think that most of the men in my village regularly use a latrine.	Yes	0.85 (0.03)	Don't Know	0.53 (0.11)
During the rainy season, I think all of my neighbors regularly use a latrine.	Yes	1.00 (0.00)	Don't Know	0.57 (0.11)
During the rainy season, I think that most of the children in my village regularly use a latrine.	Yes	0.96 (0.02)	Yes	0.60 (0.08)
There are too many people in this household for one latrine.	No	0.52 (0.03)	No	0.70 (0.07)
If my household did not have its own latrine, I would use my neighbor’s latrine.	Yes	0.90 (0.02)	Yes	0.71 (0.07)

Table 3.5. The proportion of the population that are classified as consistent latrine users, by background characteristics. Standard error (SE) and the total sample size for each demographic group are also presented.

Demographic Variable	**Consistent Latrine Use Class (SE)**	**N**
Age		
Age 13-17	0.80 (0.05)	58
Age 18-21	0.64 (0.08)	48
Age 22-26	0.80 (0.06)	49
Age 27-36	0.80 (0.06)	46
Age 37-83	0.81 (0.06)	50
Sex		
Females	0.75 (0.04)	162
Males	0.81 (0.04)	89
Ethnicity		
Afro-Ecuadorian	0.76 (0.04)	157
Mestizo and Other	0.78 (0.07)	33
Chachi	0.79 (0.06)	61
Educational Attainment		
Less than primary school	0.71 (0.06)	63
Completed primary school	0.75 (0.06)	51
Less than secondary school	0.80 (0.07)	90
Completed secondary school	0.81 (0.10)	43
Payment Type Received for Employment		
Solely cash	0.81 (0.04)	118
Cash and kind/ solely kind	0.88 (0.10)	16
Not paid	0.76 (0.07)	41
Not employed in the previous 12 months	0.70 (0.05)	76
Living in Household with Cement Walls		
Yes	0.74 (0.04)	115
No	0.78 (0.05)	128
Living in an Asset-Deprived Household		
Yes	0.74 (0.04)	152
No	0.80 (0.06)	98

Table 3.6. Overall association between access to basic sanitation and latrine use (combined from each model using imputed latrine use as the outcome). The odd ratios (OR) and 95% confidence intervals (CI) is presented for relevant variables in the unadjusted and the adjusted models.

Model Covariate	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Less than basic sanitation *(referent group)*	1 (-)	1 (-)
Basic sanitation	1.1 (0.6-2.2)	1.1 (0.6-2.1)
Less than primary school *(referent group)*	-	1 (-)
Completed primary school	-	1.4 (0.6-3.3)
Less than secondary school	-	2.1 (0.9-4.9)
Completed secondary school	-	2.4 (0.8-6.8)
Chachi, Mestizo, or Other Ethnicity (*referent group*)	-	1 (-)
Afro-Ecuadorian	-	1.0 (0.5-2.0)
Male *(referent group)*	-	1 (-)
Female	-	1.5 (0.8-3.2)
Household walls constructed of other material (*referent group*)	-	1 (-)
Household constructed of cement	-	0.6 (0.3-1.2)
Asset Deprived Household (*referent group*)	-	1 (-)
Non-asset Deprived Household	-	0.5 (0.3-1.0)

3.7 Appendix

Appendix 3.1 Conditional item probabilities for all 16 indicators

Final group assignment in LCA is conditional outcome probabilities of response to each indicator included in the model. Mathematically, this is represented in the following formula, which uses an indicator function so that the probability of 1 is:

$$P(Y = y) = \sum_{c=1}^{C} \gamma_c \prod_{j=1}^{J} \prod_{r_j=1}^{R_j} \rho_{(j, r_j|c)}^{I(y_j = r_j)}$$

In this formula, j represents each item and r_j represent the response to the specific item; c is the total number of classes. The γ parameter is a vector of latent class membership probabilities, which sum to 1, and ρ parameter, therefore, is a matrix of item-response probabilities conditional on latent class membership. Overall, the response pattern is y (Lanza et al, 2013)[6].

Hence, examination of the conditional item response probability provides insight into how each indicator was used to distinguish between classes. Appendix Table 3.7 presents the class-conditional outcome probabilities for each of the 16 items in the 2-class model

[6] Lanza, S. T., & Rhoades, B. L. (2013). Latent class analysis: An alternative perspective on subgroup analysis in prevention and treatment. *Prevention Science*, *14*(2), 157-168.

Appendix Table 3.7. Parameter estimates for the 2-class model, where the probability of membership in the consistent latrine use class is 0.78 and the probability of membership in the inconsistent latrine use class is 0.22. The item conditional probability and standard error (SE) are presented alongside the corresponding response to the survey question, disaggregated by class membership.

Indicator	Consistent Latrine Use		Inconsistent Latrine Use	
	Question Response	**Item Probability (SE)**	**Question Response**	**Item Probability (SE)**
When I use the latrine, it causes me to feel anxious.*	No	0.80 (0.03)	No	0.84 (0.07)
I use the latrine every day.*	Yes	0.93 (0.02)	Yes	0.86 (0.08)
I do not use the latrine when it is raining because I do not want to get wet.*	Yes	0.82 (0.03)	Yes	0.76 (0.09)
During the dry season, I think that most of the men in my village regularly use a latrine.	Yes	0.85 (0.03)	Don't Know	0.56 (0.14)
During the rainy season, I think all of my neighbors regularly use a latrine.	Yes	0.98 (0.02)	Don't Know	0.61 (0.14)
During the rainy season, I think that most of the children in my village regularly use a latrine.	Yes	0.95 (0.02)	Yes	0.61 (0.09)
There are too many people in this household for one latrine.	No	0.52 (0.02)	No	0.71 (0.07)
If my household did not have its own latrine, I would use my neighbor’s latrine.	Yes	0.90 (0.02)	Yes	0.72 (0.07)
The cabin of the latrine is too small for me to use.*	No	0.70 (0.04)	No	0.81 (0.07)
I am pleased with how the latrine looks.*	Yes	0.62 (0.04)	Yes	0.71 (0.07)
The latrine's basin is strong enough to hold my weight.*	Yes	0.93 (0.02)	Yes	0.89 (0.04)
The latrine is clean enough to use.*	Yes	0.87 (0.03)	Yes	0.86 (0.07)
It is more convenient to defecate outside than to return home to use the latrine.*	No	0.54 (0.04)	No	0.55 (0.10)
My morning routine is not suited for using the latrine to defecate.*	No	0.64 (0.04)	No	0.72 (0.09)
It is more convenient to use the latrine at night than to defecate in a container within my household.*	Yes	0.87 (0.03)	Yes	0.77 (0.08)
It is dangerous to use the latrine at night.*	No	0.66 (0.04)	No	0.57 (0.10)

*Uninformative indicator, based on item probability and standard error value for each class

Appendix 3.2 Class assignment in each model

As presented in the main study, the 3-class and 2-class models with all sixteen indicators had comparable predicted class memberships. The class memberships for the 3-class model were "never users" (1%), "sometimes users" (25%), and "always users" (74%) while membership in the 2-class model was "inconsistent latrine users" (22%) or "consistent latrine users" (78%). Using these profile labels, we assume that "never users" and "sometimes users" have the same assignment as "inconsistent users" in the 2-class model. Hence, we aggregated the "never users" and "inconsistent users" into one group so that the model results consisted of two classifications: 26% of the population and 74% of the population. We then compared the assigned classification across the models. Of the 251 people in the study sample, 11 individuals (or 4% of the overall sample) had differing assignments between these models. Those with different assignment were classified as "sometimes users" in the 3-class model, but "consistent users" in the 2-class model. Nevertheless, latrine use assignment was comparable between the models (Cohen's kappa =0.88).

The 16-indicator 2-class model and the 5-indicator 2-class model had identical overall proportions of predicated class membership (22% vs. 78%). Agreement between models was very high (Cohen's kappa =0.97), with only three individuals having a different predicted class membership between the two models.

Appendix 3.3 Imputed latrine use assignment

As described in the main study text, a pseudo-class approach was used to limit any uncertainty that latrine use classification would add to additional statistical analysis. Uncertainty is inherent in the predicted assignments because the true underlying probability distribution of latrine use classes is unknown. In pseudo-class approach, five probabilities of latrine use assignment were imputed. Appendix Table 3.8 provides the percent distribution of consistent latrine user by sociodemographic characteristics for each of the five imputations.

Appendix Table 3.8. Population demographics by imputed consistent latrine use assignment. For each imputation, the proportion of the population that are classified as consistent latrine users, by background characteristics, and standard error (SE).

Demographic Variable	Consistent Latrine Use Class (SE)				
	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5
Age					
Age 13-17	0.79 (0.05)	0.81 (0.05)	0.79 (0.05)	0.81 (0.05)	0.79 (0.05)
Age 18-21	0.63 (0.07)	0.64 (0.07)	0.63 (0.07)	0.63 (0.07)	0.69 (0.07)
Age 22-26	0.82 (0.06)	0.80 (0.06)	0.80 (0.06)	0.80 (0.06)	0.80 (0.06)
Age 27-36	0.80 (0.06)	0.80 (0.06)	0.80 (0.06)	0.78 (0.06)	0.80 (0.06)
Age 37-83	0.80 (0.06)	0.82 (0.06)	0.80 (0.06)	0.82 (0.06)	0.80 (0.06)
Sex					
Females	0.75 (0.04)	0.75 (0.04)	0.74 (0.04)	0.75 (0.04)	0.75 (0.04)
Males	0.80 (0.04)	0.82 (0.06)	0.81 (0.04)	0.81 (0.04)	0.82 (0.06)
Ethnicity					
Afro-Ecuadorian	0.76 (0.03)	0.77 (0.03)	0.75 (0.03)	0.76 (0.03)	0.76 (0.03)
Mestizo and Other	0.79 (0.07)	0.79 (0.07)	0.79 (0.07)	0.76 (0.07)	0.79 (0.07)
Chachi	0.77 (0.05)	0.79 (0.05)	0.79 (0.05)	0.80 (0.05)	0.82 (0.05)
Educational Attainment					
Less than primary school	0.70 (0.06)	0.71 (0.06)	0.70 (0.06)	0.71 (0.06)	0.70 (0.06)
Completed primary school	0.76 (0.06)	0.75 (0.06)	0.75 (0.06)	0.75 (0.06)	0.76 (0.06)
Less than secondary school	0.78 (0.04)	0.80 (0.04)	0.79 (0.04)	0.80 (0.04)	0.82 (0.04)
Completed secondary school	0.84 (0.06)	0.84 (0.06)	0.81 (0.06)	0.79 (0.06)	0.79 (0.06)
Payment Type Received for Employment					
Solely cash	0.81 (0.04)	0.81 (0.04)	0.81 (0.04)	0.81 (0.04)	0.80 (0.04)
Cash and kind/ solely kind	0.88 (0.08)	0.88 (0.08)	0.81 (0.10)	0.88 (0.08)	0.94 (0.06)
Not paid	0.73 (0.07)	0.76 (0.07)	0.78 (0.06)	0.76 (0.07)	0.78 (0.06)
Not employed in the previous 12 months	0.71 (0.05)	0.71 (0.05)	0.68 (0.05)	0.70 (0.05)	0.71 (0.05)
Living in Household with Cement Walls					
Yes	0.74 (0.04)	0.74 (0.04)	0.73 (0.04)	0.74 (0.04)	0.74 (0.04)
No	0.82 (0.04)	0.83 (0.04)	0.82 (0.04)	0.73 (0.04)	0.83 (0.04)
Living in an Asset-Deprived Household					
Yes	0.72 (0.04)	0.75 (0.04)	0.74 (0.04)	0.74 (0.04)	0.73 (0.04)
No	0.80 (0.04)	0.80 (0.04)	0.77 (0.04)	0.79 (0.04)	0.74 (0.04)

The regression model results for each imputed outcome are presented in Appendix Tables 3.9 (unadjusted) and 3.10 (adjusted). Of note, overall results reflect combination of each of these model following Rubin’s rules.

Appendix Table 3.9. Unadjusted association between access to basic sanitation and latrine use. Each of the five models uses imputed latrine use as the outcome. The odds ratio (OR) for basic sanitation access, along with the 95% confidence intervals (CI), is presented. The combined odds ratio between household access to basic sanitation and consistent latrine use is 1.1 (95% CI = 0.56-2.2, *within-model variance = 0.092, **between model variance = 0.024)

Individual models	**OR**	**Lower Boundary**	**Upper Boundary**
Model 1: Basic Sanitation	1.1	0.6	1.9
Model 2: Basic Sanitation	1.1	0.6	1.9
Model 3: Basic Sanitation	1.2	0.7	2.2
Model 4: Basic Sanitation	1.2	0.6	2.1
Model 5: Basic Sanitation	1.1	0.6	1.9

*an average of the variance across imputations

**[1/(m-1]*(imputed model coefficient-average coefficient)^2; m= number of imputations

Appendix Table 3.10. Adjusted association between access to basic sanitation and latrine use. Each of the five models uses imputed latrine use as the outcome. The odds ratio (OR) for each variable included in the model, along with the 95% confidence intervals (CI), is presented. The summary within-model and between-model variance is also presented.

	Adjusted Models with Imputed Latrine Use Outcomes						
Model Covariate	**1. OR (95% CI)**	**2. OR (95% CI)**	**3. OR (95% CI)**	**4. OR (95% CI)**	**5. OR (95% CI)**	***Within-Model Variance**	****Between-Model Variance**
Less than basic sanitation *(referent group)*	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Basic sanitation	1.0 (0.55-2.0)	0.95 (0.51-1.8)	1.1 (0.60-2.2)	1.2 (0.62-2.3)	1.0 (0.55-1.9)	0.11	0.01
Less than primary school *(referent group)*	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Completed primary school	1.6 (0.68-3.6)	1.3 (0.54-3.0)	1.3 (0.59-3.0)	1.3 (0.57-2.9)	1.5 (0.64-3.7)	0.18	0.01
Less than secondary school	1.9 (0.86-4.0)	2.1 (0.94-4.8)	1.9 (0.90-4.2)	2.1 (0.93-4.8)	2.5 (1.1-5.8)	0.17	0.01
Completed secondary school	3.1 (1.1-8.9)	2.6 (0.98-7.0)	2.3 (0.92-5.9)	1.9 (0.74-4.8)	2.1 (0.84-5.5)	0.24	0.04
Chachi, Mestizo, or Other Ethnicity (*referent group*)	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Afro-Ecuadorian	1.2 (0.65-2.2)	1.0 (0.54-1.9)	0.94 (0.50-1.8)	1.0 (0.56-1.9)	0.91 (0.48-1.7)	0.10	0.01
Male *(referent group)*	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Female	1.3 (0.68-2.5)	1.7 (0.82-3.4)	1.5 (0.79-3.0)	1.6 (0.84-3.2)	1.6 (0.79-3.3)	0.12	0.01
Household walls constructed of other material (*referent group*)	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Household constructed of cement	0.49 (0.24-1.0)	0.63 (0.32-1.2)	0.68 (0.35-1.3)	0.63 (0.32-1.2)	0.56 (0.28-1.1)	0.12	0.02
Asset Deprived Household (*referent group*)	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)	-	-
Non-asset Deprived Household	0.48 (0.24-1.0)	0.47 (0.24-0.91)	0.50 (0.26-1.0)	0.54 (0.27-1.1)	0.46 0.24-0.89)	0.12	0.004

*an average of the variance across imputations

**[1/(m-1]*(imputed model coefficient-average coefficient)^2; m= number of imputations

Appendix 3.4 Comparison of Latrine Use Metrics and LCA Model Consistency

While it is not possible to validate the latent variable classification, we can gain insight into the difficulty of measuring latrine use by comparing three different measurement approaches: frequency of latrine use, calculated latrine use (from self-report of all defecation practices within the last week), and latent variable classification. Frequency of latrine use was measured by asking one survey question, with three possible response options (always, sometimes, or never): How frequently do you use a latrine? Calculated latrine use was measured through responses to a series of 20 survey questions. First, each respondent was asked about 10 common defecation behaviors and whether anyone in the community practiced each defecation behavior (response was binary, yes/no). Then, the respondent was asked how many times in the last week they individually practiced each of these 10 defecation practices, with probing included for defecation in the morning, afternoon, evening, and night for each specific behavior. If a respondent reported at least one defecation behavior that was not latrine use in the past week, we classified them as "inconsistent" latrine use. Otherwise, they were considered an "always" latrine user. Appendix Table 3.11 presented the percent of the total population that is a latrine user according to each of these different calculations.

Appendix Table 3.11. Percentage of the Population Reporting Latrine Use via Two Different Survey Approaches

Latrine Use Variable	Total Sample (n=251)	Women (n=162)	Men (n=89)
Frequency of Latrine Use			
Always	0.89	0.91	0.87
Frequently	0.10	0.08	0.12
Never	0.01	0.01	0.01
Calculated Latrine Use			
Consistent	0.72	0.82	0.53
Inconsistent	0.28	0.18	0.47

As evident in Table Appendix Table 3.11, even though both variables were estimated by self-report responses to questions about personal defecation practices, there are notable differences between those that reported always using a latrine. A greater proportion of the sample self-reported always using a latrine use in the frequency-style survey question relative to the calculated approach. While these differences were evident in the total population, greater difference appear among men, where approximately half of men interviewed reported only use a latrine for defecation in the previous week (and nearly 9 in 10 reported always using a latrine). The overall distinction in response patterns provides additional evidence of likely over-reporting of latrine use behavior.

In addition to observing the overall distribution of latrine use via each different measurement approach, we can also assess the agreement between each of the three variables - frequency of latrine use, calculated latrine use, and latent variable classification (Appendix Table 3.12). By using Fleiss' kappa statistic to assess agreement, the three variables exhibit slight agreement in the total sample as well as in women and men. No more than slight agreement was observed between all combinations of the variables, with the kappa statistic ranging from 0.07 to 0.15. Overall, the women included in the sample showed marginally better agreement between the variables relative to men and women. The slight agreement between the three variables provides further rationale that validation with self-reported latrine use should be not conducted.

Appendix Table 3.12. Agreement between each approach to measuring latrine use

Agreement between the following variables (kappa statistics)	Total Sample	Women	Men
Frequency of latrine use, calculated latrine use, and latent variable classification*	0.08	0.1	0.03
Frequency of latrine use and calculated latrine use	0.15	0.17	0.11
Frequency of latrine use and latent variable classification	0.06	0.17	0.16
Calculated latrine use and latent variable classification	0.07	0.15	0.02

*Fleiss' kappa where all other comparisons are calculated with Cohen's kappa

The agreement comparison suggests that each of that while these variables may be measuring the same constructs; they are each subject to different types of error. The error generated from the latent variable classification of latrine use is reflected in the model entropy value (0.86), while the error in self-reported latrine use cannot be quantified. If the latent classification was free of measurement error, the entropy value would be 1.0, which is unrealistic in any survey-based research. Nonetheless, we are interested in providing additional evidence that the latent classifications are reliable and overall not driven by certain observations within the dataset. To assess the extent to which the latent classifications are robust, we compared the model results from the full sample to the same model run in 10 randomly selected subsamples of the dataset (Appendix Table 3.13). Overall, the models run in the randomly selected subsamples showed little variability (for example, entropy ranged from 0.84 to 0.92). The average fit statistics from the subsample models were very comparable to the model with the full dataset.

Appendix Table 3.13. LCA models in 10 subsamples of the overall dataset (n=225 in each sample). The average fit statistics for each of these 10 models are: BIC =1365; X2=381; entropy=0.87. Overall, the 10 subsamples have an average predicted class membership of 0.78 and 0.22.

Subsample	**BIC**	**X^2**	**Relative entropy**	**Predicted class probabilities**
Sample 1	1392	395	0.86	0.75; 0.25
Sample 2	1354	363	0.86	0.78; 0.22
Sample 3	1368	465	0.92	0.78; 0.22
Sample 4	1361	240	0.85	0.78; 0.22
Sample 5	1363	370	0.88	0.78; 0.22
Sample 6	1338	353	0.85	0.77; 0.23
Sample 7	1332	457	0.88	0.80; 0.20
Sample 8	1378	372	0.84	0.78; 0.22
Sample 9	1378	411	0.87	0.77; 0.23
Sample 10	1389	382	0.88	0.77; 0.23

In aggregate, these sensitivity analyses (Appendix Tables 3.11-3.13), add to our conclusions that the LCA model adequately distinguished the underlying probability of latrine use through use of psychosocial variables. With the ability to assess error in the final latent variable classifications, we also suggest that our model models are minimally biased relative to the bias that would be included in self-report.

Chapter 4

Enteric Pathogen Transmission and Child Undernutrition: Use of Mathematical Modeling to Identify Intervention Opportunities

4.1 Abstract

There is growing concern that environmental exposure to enteric pathogens influences long-term malnutrition-related morbidities (such as growth faltering) among preschool age children in low-resource settings. Environmental exposure to pathogens may exacerbate the feedback between infection and nutrition, which is influenced by interacting transmission pathways: nutritional status impacts susceptibility to infection, and diarrheal disease impacts absorption of nutrients to influence overall nutritional status. We use a staged Susceptible-Infectious-Susceptible compartmental model to understand the mechanisms through which environmental-mediated enteric pathogen transmission is influenced by one's nutritional status. Each staged stratum represents a subset of the population defined by nutritional status, and movement between strata reflects increased infections and greater susceptibility to pathogens as a result of nutritional status. Model parameters were identified using enteric pathogen transmission rates from the literature. To incorporate parameter uncertainty, we used Latin hypercube sampling with 1,000 simulations to draw a stratified random sample of parameter sets across plausible ranges gathered through literature review. We implemented sanitation and nutritional interventions to test the counterfactual effects of reducing overall pathogen transmission as well as the number of undernourished children. The simulations show that sanitation most effectively reduces pathogen transmission in both single and combined intervention scenarios; while treatment of undernutrition provides the largest gains in reducing the number of undernourished children. We also show that the reductions in the number of undernourished children are driven by nutritional treatment, even when nutrition and sanitation interventions are combined. These results suggest that sanitation promotes child growth only under certain conditions. Through accounting for interdependencies, we present a holistic understanding of mechanisms by which enteropathogens

may be causing undernutrition at the community-level, highlighting potential opportunities for improving child health.

4.2 Introduction

Formative research from Scrimshaw and colleagues (1) identified the synergistic relationship between infectious disease and nutrition among young children. This early research mostly focused on manifestations of clinical disease, weight loss, and growth retardation, drawing heavily from research in rural Latin American communities (2,3). While any infection results in worse nutritional status, special note was given to enteric infections (4). Children with diarrheal disease were observed to have reduced dietary intake, intestinal absorption (5,6), and increased catabolism (i.e., the breakdown of large molecules) (7). With poorer nutritional status, immune system processes did not function as well as in well-nourished children (8), leaving undernourished children with a decreased resistance to additional infections. Subsequently, an infection-malnutrition cycle ensues whereby infection influences undernutrition and undernutrition affects susceptibility to infection. Over time, this cycle can impair growth, as suggested by several early studies providing evidence that repeated clinical diarrhea result in growth faltering (3,9–11). Our knowledge of this cycle, however, comes from studies that examine infection and growth as independent processes, which limits our ability to understand how to best intervene on this system. Here, we develop a mathematical model to explore the dynamic properties of the cyclical relationship between enteric pathogens and undernutrition responsible for diarrheal disease.

The current understanding of the relationship between diarrheal disease and undernutrition is more nuanced as we now have a better mechanistic understanding. It is hypothesized that both repeated episodes of diarrhea and persistent subclinical enteropathogen infections result in long-term undernutrition, a condition termed ‘environmental enteric dysfunction’ (12,13). Enteric infection reduces absorption of nutrients and causes inflammation that influences overall nutritional status (14,15). In turn, nutritional status modifies one’s susceptibility to new infections. Being malnourished is associated with reduced intestinal barrier function (16), which increases the likelihood of infection, while also modifying the immune response (17) (i.e., T-cells (18), cytokines, (19), and the ability of lymphocytes to respond appropriately to cytokines (20)). Moreover, undernutrition is an important risk factor for mortality among children suffering from enteric infection (21,22). The probability of mortality increases with increasing severity of undernourishment, and in some cases, severely malnourished children with diarrheal disease have more than a 20 times higher likelihood of death relative to children with a healthy nutritional status (23,24).

Given this infection-malnutrition cycle, multipronged interventions that incorporate nutrition specific components (such as improving diet adequacy) as well as components that target indirect pathways leading to malnutrition (i.e., nutrition-sensitive programs) are central for promoting child nutrition. Among nutrition-sensitive programs, which encompass the agricultural, educational, health, and social sectors (25), emphasis has been given to improving access to water, sanitation, and hygiene (WASH) so as to reduce enteric infections, and, subsequently, improve child growth (26). Generally, there is scientific consensus that improving WASH improves child growth (27), however, the null results of recent sanitation trials on child growth (28–31) suggest a need to further examine the underlying processes connecting sanitation and nutrition, as well as consider the joint programmatic effects of improving diet adequacy and reducing enteric transmission. From the biological perspective, undernutrition and enteric infection are interconnected by immune system processes (32,33). Hence, it is plausible that persistent and repeated infection may inhibit the positive effects of nutritional interventions, although little population-based research is available to support this hypothesis (34). Likewise, improved nutrition may reduce the negative effects of infection on growth by: 1) strengthening the immune system, 2) providing nutrients to both compensate for nutrient loss due to malabsorption and to stimulate growth catch-up, and 3) promoting the growth of commensal gut organisms that enhance the immune system and gut functioning (34). Dewey's hypotheses are supported by evidence suggesting that food and micronutrient supplementation results in improved child growth when accounting for infection in certain settings (35–37). Additionally, recent results from the WASH Benefits study (38) — a trial that compares child health outcomes under WASH, nutrition, and combined WASH-nutrition interventions — showed improved growth in Kenyan and Bangladeshi children that were enrolled in the nutrition trial arm. However, additional growth was not observed when WASH was combined with nutrition (39,40). Furthermore, reduction in diarrheal disease was not observed in any of the study trial arms in Kenya (39), while in Bangladesh, diarrhea reductions were observed in all trial arms except the improved water group (40). Notwithstanding the WASH Benefits Kenya trial, population-level data examining the interactions between enteric pathogen infection and child nutrition are sparse.

To improve our understanding of the infection-malnutrition cycle and to provide guidance for the development of effective interventions that promote child growth, we developed a systems-based dynamic model. An inherent property of this cyclical system is that infection events are dependent on nutritional status and nutrition status is dependent on prior infection status. Standard public health analytical tools rely on assumptions of independence between variables (41); because enteric infection and undernutrition exhibit dependencies, such standard tools (i.e., regression) have limited use in studying this cyclic relationship (42). To appropriately assess the interconnectedness of infection and nutrition pathways on the population-level, a systems-based analysis is required (43). Such an approach is useful in answering the following types of questions:

- *How can child nutrition and immune system processes be incorporated into a community-level pathogen transmission model?*
- *Do nutritional interventions reduce pathogen transmission within this system?*
- *Do sanitation interventions reduce child undernutrition within this system?*
- *What is the impact of combined nutritional and sanitation interventions on child growth?*

To answer these questions, we developed an enteropathogen transmission model that includes repeated infections and accounts for the impact of undernutrition on both transmission and recovery rates. We simulated a group of children from birth to two-years of age, a critical time for child growth and development (44). Sanitation and nutrition programs were then incorporated individually as well as combined into the model simulations to test their impact.

4.3 Methods

Model Structure

Pathogen Transmission: Drawing from Pitzer's rotavirus model in (45), an endemic pathogen in the population with limited immunity against it, we use a modified Susceptible-Infectious-Susceptible (SIS) type framework to reflect all-cause diarrhea enteric pathogen transmission among a group of children (i.e., a closed population). The infectious state variables include both subclinical and clinical infection. Children less than 2 years of age are the primary focus of the model, as they are at greatest risk of stunting resulting from pathogen exposure.

We incorporate repeated infections into the framework through staging (see Figure 4.1) similar in fashion to Van Effelterre et al. (46). Once infected (in the first stage), there is a probability of moving to the next stage where one has a greater susceptibility to reinfection (state S_{1+i}). There is little scientific knowledge regarding the timescale at which this happens and the actual likelihood; thus, we initially assume that 5% of infections will transition to the next strata as a baseline value (ω parameter; see Table 4.1 for parameter definitions). However, given the uncertainty surrounding this likelihood, we tested over the full range from 0 to 100% in our sensitivity and uncertainty analysis (discussed below). The proportion of those moving to the next strata can be calculated by ω= rate of progression/(rate of progression + rate of same-stratum recovery). We created four models, where each model ranges from 2 to 5 strata. We assume that the proportion of infected children who transition (ω parameter) to the next strata is constant, regardless of the number of strata tested. Because little data exist, we assumed that transmission rates (parameter β_i) increase and recovery rates (parameter γ_i) decrease by 50%, respectively, between the first and last strata in each model. In each of the models, the transmission parameters are multiplied by a factor to maintain the difference of 0.50 between the first and last strata parameters, so that models with different numbers of strata will have different factors between their transmission parameters at each level. For example, in the three strata model, $\beta_2=1.25*\beta_1$ and $\beta_3=1.5*\beta_1$, while in the four strata model $\beta_2=1.17*\beta_1$, $\beta_3=1.33*\beta_1$, $\beta_4=1.5*\beta_1$.

In addition to disease-susceptibility strata, our framework also includes an environmental compartment to reflect environmental mediation of enteric pathogens in many low- and middle-income countries. We modeled concentration of pathogens in the environment rather than number of pathogens as described in Li et al. (47). Susceptible individuals receive a low pathogen-dose in order to become infected, thus, we assume a linear approximation for the dose-response (48). To account for pathogen shedding by individuals older than two years of age, we included a constant number of infectious adults (I_A parameter) and a constant shedding rate (α_A) (not depicted in Figure 4.1).

Within this framework, pathogen transmission occurs only through contact with the environment, and person-to-person transmission is not explicitly considered. To estimate the transmission rate (β_i) we first found the formula for the model reproductive number (R_0) as a function of β via the next-generation method. Then we assumed that R_0=1.9, which is the upper limit from a *Shigella* transmission model estimated by Joh et al., 2013 (49). Using the other model parameters, we back-calculated an estimate of β (See Appendix for example of 2-stage model calculation of β). When considering parameter uncertainty (details given below), we used wide boundaries for the transmission parameter. Disease severity and seasonality is not accounted for in the model.

Finally, given the established associations between weight at birth and susceptibility to infections (50,51), we place children into different stratum based on their initial birth weight. We assume that those with low birth weight (less than 2,500 grams, defined by WHO (52) have a greater susceptibility to infection relative to children of adequate birth weight. Thus, low birth weight children enter the system at state S_{1+i} and all other children enter at state S_1. When the model has 3 strata or greater, children with very low birth weight (less than 1500 grams), will enter at the third level, low birth weight children at the second stratum, and normal birth weight children at the first level.

Undernutrition: Child undernutrition is an outcome of longitudinal biological processes. For example, acute undernutrition is often measured as low weight given a child's age, while chronic undernutrition is measured as short height/length given a child's age (53). We theorize that each staged stratum (the dashed-line boxes in Figure 4.1) represents a subset of the population defined by nutritional status to reflect the role of repeated and asymptomatic infection (54) in growth retardation. Thus, as a child moves through the system, their risk of exhibiting measureable signs of undernutrition increases, and children in the last stratum are conceptually comparable to chronically undernourished children in sanitaiton/nutrition trials

Base Model Equations

$$\frac{dS_1}{dt} = -\beta_1 S_1 E + (1-\omega)\gamma_1 I_1$$

$$\frac{dI_1}{dt} = \beta_1 S_1 E - \gamma_1 I_1$$

$$\frac{dS_i}{dt} = -\beta_i S_i E + (1-\omega)\gamma_i I_i + \omega_{i-1}\gamma_{i-1} I_{i-1}$$

$$\frac{dI_i}{dt} = \beta_i S_i E - \gamma_i I_i$$

$$\frac{dS_n}{dt} = -\beta_n S_n E + \gamma_n I_n + \omega_{n-1}\gamma_{n-1} I_{n-1}$$

$$\frac{dI_n}{dt} = \beta_n S_n E - \gamma_n I_n$$

$$\frac{dE}{dt} = \sum_{i=1}^{n} \left({}^{\alpha_i I_i}/_{V}\right) + {}^{\alpha_A I_A}/_{V} - \xi E$$

Base Model Parameters and Uncertainty Analysis

Values for pathogen transmission parameters reflect estimates used in the broader literature and are presented in Table 4.1 (parameters σ and I_A are discussed in the "Initial Conditions" subsection).

To incorporate parameter uncertainty in the transmission modeling, we used Latin hypercube sampling (LHS) with 1,000 simulations to draw a stratified random sample of parameter sets across plausible ranges gathered through literature review. Because this range of parameters generated large variability, we reduced the range to +/- 10% of the parameter values when assessing intervention impact on undernutrition.

LHS and all simulations were conducted using R (version 3.4.1) packages *lhs* and *deSolve*.

Literature Review: We conducted a literature review to establish feasible ranges of values for several transmission parameters. Because our model reflects generic enteric pathogen transmission, we searched for common pathogens primarily responsible for under-five diarrheal disease - *Cryptosporidium*, rotavirus, *Shigella*, and enterotoxigenic *Escherichia coli* (ETEC) (55). For each pathogen, four different searches were conducted in MEDLINE. For pathogen transmission parameters, we used search terms that included the name of each pathogen and (transmission dynamics OR mathematical OR differential equation OR compartmental OR reproduction number) MeSH terms. These searches were limited to English-language publications and children under five years of age or younger. In addition, we also conducted literature searchers to determine parameters values related to pathogen decay; shedding rate; and minimum infective dose. A summary of the observed and estimated parameters is provided in the Appendix.

Initial Conditions

We modeled 500 children. The parameter, σ, reflects the global estimated proportion of children born with low birth weight (16%) (56), which was used in the two-stage model. When accounting for very low birth weight in models with three strata or more, we set σ to the global estimate of preterm small for gestational age births (approximately 6%) (57), and thus, the low birth weight parameter to 10%.

We also assumed that community-level diarrhea prevalence was 10% in a population of 2,000 people (the I_A parameter). Enteric pathogen transmission exhibits epidemic properties for newborn children, however, all-cause diarrhea is endemic in the remainder of the population (i.e., at steady state). Thus, we seeded the environment with a concentration of 24 pathogens per unit environment to reflect the number of sick community members. We assume that the size of the environmental reservoir is 1.00 E+6 volume of water.

Interventions

Following the simulation with baseline parameter values, we examined different intervention strategies and assess their impact on pathogen transmission. Sanitation and nutritional interventions were tested in isolation as well as in combination. Within our modeling framework, we incorporated each of these interventions by adjusting the model parameters in Table 4.2 (see model equations modified for interventions and Figure 4.2).

To assess whether intervention studies reduced infections from occurring, the preventable fraction of total infections (PF) was estimated using a counterfactual approach detailed in Eisenberg et al. (58). Briefly, to describe this preventable fraction estimate in terms of causal inference, we consider the situation in which an investigator could observe outcomes under different treatment regimens for the same individual (i.e., the counterfactual) (59). Specifically, the PF estimated the efficacy of a sanitation or nutrition interventions designed to limit pathogen transmission. This statistic is defined by $PF=(I_1 - I_0) / I_1$, where I_0 and I_1 represent either the total number of infections that occurred from the scenarios in which there is no intervention and individuals are exposed to pathogens, and when an intervention is implemented to partially protect the population from exposure to enteric pathogens, respectively.

To examine undernutrition, first we present the distribution of children across the strata after two years in each intervention scenario. Then, we present the ratio of children in the first stratum (who have the lowest risk of undernutrition) or last stratum (who have the greatest risk of undernutrition) under combined intervention scenarios relative to non-intervention scenarios for each LHS sample. In this analysis, we limited the range of all transmission-related parameter values to +/- 10 percent in order to reduce uncertainty that might mask relationships between variables. This comparison provides insight into whether the combined interventions reduce the number of children that ultimately end up in the very last stratum

Sanitation Interventions: Sanitation interventions (the δ parameter) are designed to reduce pathogen exposure at both the individual-level and the community-level (60). Adequate sanitation reduces the likelihood of contamination in water source(s) and soil, while also reducing the presence of flies, a vector for transmitting pathogens. We included sanitation interventions within this framework by attenuating the concentration of pathogens available for pickup. We set the attenuation to 19% (0%-100%), reflecting the estimates of diarrheal disease attributable to sanitation as per Pruss-Ustun and colleagues (61).

Nutrition Interventions: In simulating nutritional interventions, we hypothesize that it is plausible for the immune system to rebound through two different mechanisms: treatment of undernutrition and prevention of inflammation, permeability, and nutrient malabsorption. We simulated nutritional interventions along both of these pathways, starting at six months after the initial starting point.

Here, we examine treatment of undernutrition through a complementary feeding program (the ρ parameter) implemented at the community level. We find it plausible that an adequate diet would impact susceptibility to reinfection by bolstering immune system functioning through multiple mechanisms (62–64).

While complementary feeding programs are important for treating acute undernutrition (65), use of lipid-based nutritional supplements (LNS)—usually produced in a food base from local ingredients and designed to provide energy, protein, essential fatty acids, and micronutrients—is now being explored as a preventative measure for chronic undernutrition (66). Trials of home-fortification with LNS in various low-resource settings have tested improvement to child development (physiologic, cognitive, motor, and social) that results from receiving LNS supplementation. Thus far, trial results in Burkina Faso (67,68), Bangladesh (69), Ghana (70), Haiti (71), and Indonesia (72) yielded positive effects on child growth, while children in the Malawian (73) and Peruvian (74) trials did not have improved growth after receiving LNS. Beyond linear growth, other outcomes including fat-free mass, anemia, or markers of inflammation have been studied in only a few of these trials. For example, LNS trials in Burkina Faso included C-reactive protein, (CRP; a marker of inflammation) (67) and report of clinical infections (75). Their results showed that Burkinabe children that received LNS did not experience fewer clinical infections, but had reductions in elevated CRP and increased growth. We hypothesize that immunological markers would have been enhanced had they been measured in other studies; thus, we conceptualize that an intervention like LNS would be provided to the entire community for the duration of 18 months and affect our model structure by allowing a certain proportion of children to return to their prior susceptibility rate. Because there is not scientific consensus on the appropriate rate, we set the immune function recovery rate to 0.008 per day to reflect the nine-month time period and 13% difference observed in the Hess et al. 2015 trial (67).

To prevent undernutrition related to repeated infections, we use data from an intervention that may improve gut health — zinc supplementation. Although the mechanisms of zinc supplementation on enteric infection are not fully understood, for the purposes of this simulation, we assumed that zinc supplementation improves gut health via reducing inflammation (76) and immune system process (77,78). We believe this to be a reasonable assumption as zinc supplementation has been observed to improve immune markers in children with *Shigella* (79,80). A 10-20 milligram dose (depending on child's age) of zinc daily for 10-14 days is recommended for treatment of acute diarrhea by the WHO (81), as it has been shown to reduce the diarrhea incidence by 13% (82). Additionally, children that received zinc while presenting with diarrhea had a two or three-month delay in re-infection relative to children that did not receive supplementation (83), and have also shown reduced duration and severity of diarrhea attributable to zinc (84), particularly in children older than six months of age (85). Because our model accounts for both clinical and asymptomatic enteric infection, we chose to simulate the effects of zinc supplementation (the ϕ parameter) by reducing the likelihood of moving to the next strata by 13% (0%-100%). The effects of zinc supplementation likely last longer than the course of treatment duration, and because our model reflects population-level averages of progression into the next strata, we run the zinc intervention from six months to 24 months.

Combined Interventions: We also simulated the combination of the above interventions in the following scenarios: sanitation and complementary feeding (δ and ρ parameters); sanitation and treatment of diarrhea (δ and ϕ parameters); complementary feeding and treatment of diarrhea (ρ and ϕ parameters); and sanitation, complementary feeding, and treatment of diarrhea (δ, ρ, and ϕ parameters). In these simulations, we are interested in mirroring large-scale trials (the WASH Benefits study (38) and ongoing SHINE trial (86)), which hypothesize that inclusion of complementary feeding alongside WASH will have additive effects for child health. Of note, both studies have included LNS complementary feeding into the interventions.

Model Equations: Modified for Interventions*:* The following equations incorporate additional parameters for the simulated interventions, which are bold.

$$\frac{dS_1}{dt} = -\beta_1 S_1 E + 1 - [(1-\boldsymbol{\phi})\omega\gamma_1 I_1] + \rho S_i$$

$$\frac{dI_1}{dt} = \beta_1 S_1 E - \gamma_1 I_1$$

$$\frac{dS_i}{dt} = -\beta_i S_i E + 1 - [(1-\boldsymbol{\phi})\omega\gamma_i I_i] + (1-\boldsymbol{\phi})\omega_{i-1}\gamma_{i-1}I_{i-1} + \boldsymbol{\rho} S_{i-1} - \boldsymbol{\rho} S_i$$

$$\frac{dI_i}{dt} = \beta_i S_i E - \gamma_i I_i$$

$$\frac{dS_n}{dt} = -\beta_n S_n E + \gamma_n I_n + (1-\boldsymbol{\phi})\omega_{n-1}\gamma_{n-1}I_{n-1} - \boldsymbol{\rho} S_n$$

$$\frac{dI_n}{dt} = \beta_n S_n E - \gamma_n I_n$$

$$\frac{dE}{dt} = \sum_{i=1}^{n}(1-\boldsymbol{\delta})({}^{\alpha_i I_i}/_{V}) + (1-\boldsymbol{\delta})({}^{\alpha_A I_A}/_{V}) - \xi E$$

4.4 Results

Model Structure

The timescale of transmission exhibits a negative relationship with the number of increasing strata included in the model (see Appendix for models run to steady-state conditions and simulations that account for parameter uncertainty). For example, pathogen transmission is fastest in the two-stage model and slowest in the five-stage model (Figure 4.3). Since nutritional status is a continuous variable, the possible number of strata is infinite; thus, we chose to further examine transmission dynamics in the model with the greatest number of strata, the five-stage model. Figure 4.3 shows the parameter uncertainty within the five-stage model under all LHS samples.

Intervention Scenarios

Effect on Overall Pathogen Transmission: The sanitation intervention showed large reductions in pathogen transmission early in the time period and overall 10 percent of total infections were reduced (PF = 0.1; Figure 5A and C). The two nutrition interventions did not impact enteric infection transmission (Zinc PF=0.00 and LNS PF=0.00) and transmission dynamics within these interventions are similar to those of the non-intervention scenario (Figure 4.5E and 4.5D, compared to 5B). The LNS intervention slightly reduced the total current infections across strata (Figure 4.5A).

All of the combined interventions that included sanitation also reduced community-level pathogen transmission (Figure 6). The largest reductions in total infections were observed in simulations that combined all three interventions (PF = 0.10; Figure 4.6A), however, gains made in combining all three interventions did not greatly differ from the combined sanitation and zinc intervention (PF = 0.10; Figure 4.6C) or the combined sanitation and LNS interventions (PF = 0.10 ; Figure 4.6D). The combined nutritional intervention (Figure 4.6E) did not reduce enteric infections among children (PF = 0.00).

Effect on Child Nutrition: To assess the intervention effects on undernutrition, we examined the distribution of children across each model stratum. Of the single interventions, treatment of undernutrition (i.e., complementary feeding using LNS), had the greatest impact on shifting the distribution of the children (Figure 4.7). Within the LNS intervention, more children remained in the first stratum and less children in the last stratum. Relative to the non-intervention scenario, where there were 20 children in stratum 1 and 164 children in stratum 5, the LNS intervention scenario had 3.8 times as many children in the first stratum and 47 percent less children in the last stratum. There were some increases in the number of children in the first stratum under the sanitation and zinc interventions, but these gains were small. For example, the sanitation intervention had nine more children in stratum 1 and 33 fewer children in stratum 5 relative to the no intervention distribution of children, while the zinc intervention had 8 additional children in stratum 1 and 30 fewer children in stratum 5 compared to the non-intervention scenarios.

The combined interventions showed additive effects, with each combination resulting in more children in strata 1 and less children in stratum 5 relative to the single interventions (Figure 4.8). For example, in stratum 1, there were 162 children in the combined sanitation, LNS, and zinc intervention; 138 children in the combined sanitation and LNS intervention, 121 children in the combined nutrition intervention, and 39 children in the sanitation and zinc intervention. The effects of complementary feeding drove these patterns in the increase of children in stratum 1. Gains in the combined LNS and sanitation intervention (5.6 times more children in stratum 1 relative to the non-intervention), as well as LNS and zinc (4.8 times increase), are slightly more than additive from the single interventions (LNS = 3.8 times increase; zinc = 0.4 times increase, and sanitation = 0.4 times increase).

When accounting for parameter uncertainty in the combined intervention scenarios, greater gains in the number of children in stratum 1 and reductions in the number of children in stratum 5 were observed, respectively, as the intervention parameters increased (Figure 4.9). This suggests that under certain conditions, the interventions may prove more efficacious as intervention coverage increases.

4.5 Discussion

Scrimshaw and colleagues initially put forth the theory that symptomatic infection and undernutrition were linked. They highlighted the underlying role of diet in immune system functioning with their observation that well-nourished children recovered quicker while malnourished children were susceptible to additional infections. Scientists are just beginning to move beyond clinical infection to understand the mechanistic pathways linking exposure to enteropathogens and undernutrition. In parallel there is growing interest in assessing multi-sectoral interventions that interrupt different pathways leading to chronic undernutrition. Mechanistic models can help bridge the exploration of exposure pathways and intervention trials. Our initial look at the fundamental dynamic properties of the infection-nutrition feedback cycle and its impact on intervention efficacy, provided the following insights: 1) effectiveness of interventions on reducing the infections was primarily attributable to reductions of pathogens in the environment (Figure 4.5), and; 2) treatment of undernutrition more effectively reduced the number of undernourished children than any of the other interventions (Figures 4.7 and 4.8). Regarding reduction in infections, we found that the sanitation had the largest impact and neither nutrition intervention affected the overall total of infections experience by children. These findings imply that bolstering the immune system has little direct impact on community's level susceptibility to pathogens; however, further research is required to better understand these relationships. Regarding intervention effects, we found little impact of sanitation on undernutrition. These modeling results provide a means to interpret prior sanitation and nutrition intervention trials that that use child growth and enteric infections as outcome variables.

An estimated 7.2 million cases of child stunting are attributable to unimproved sanitation (87). However, evidence from sanitation intervention trials shows mixed results on improved child growth (88). For example, regarding single-interventions, recent results from the WASH Benefits studies have suggested that sanitation alone did not improve child growth outcomes in either Kenya or Bangladesh (39,40), while in a Malian trial improvements in child growth were attributable to increased sanitation coverage (89). Latrine coverage in all three of these trials was high, which suggests that the transmission dynamics as well as the dependences between enteric infection and undernutrition may play a role in explaining these differences. Within our simulations, we observed changes to the distribution of child nutritional status under the sanitation intervention scenario (Figure 4.7), suggesting some protection against undernutrition: these reductions, however, were small relative to all of the other interventions (only 9 more children in stratum 1 and 33 fewer children in stratum 5). Identification of such modest effects would require intervention trials to be sufficiently powered. Additionally, they are reflective of the baseline transmission parameters we included in the simulations. There is wide variability the infectiousness of pathogens and environmental contamination (see the Appendix for heterogeneity of parameters and intervention effects), which should also be considered when comparing our results to those of intervention trials. Finally, it should be noted that our simulation findings reflect an upper limit of what could happen in a trial that was implemented under ideal design and implementation, with complete intervention uptake. Given the heterogeneity of sanitation and child growth trial results, additional research is required to assess under which conditions sanitation improves child development and under which conditions it does not.

Contrary to the small effect of sanitation on undernutrition, we observed that treatment-based nutritional interventions had a strong impact on altering child growth patterns, a pattern that persisted in both single and combined intervention simulations. In contrast, prevention-based nutritional interventions had a smaller impact (only 8 additional children in the first stratum and 30 children fewer in the last), similar to those of sanitation. The difference we observed in nutritional prevention vs. treatment may reflect the inconsistent impact of different types of feeding programs (micronutrient fortification, breastfeeding education, increased energy density, etc.) on child growth that has been observed in nutritional intervention trials (90). Furthermore, the effect of nutrition interventions on child health depends on a variety of underlying determinants, such as baseline food insecurity (91), poverty, access to resources, and even WASH (25). It is theorized that stand-alone nutrition interventions could be more effective if subclinical enteric infections were also reduced (92) with combined sanitation and nutrition having synergistic effects. Our results suggest that relative to single interventions, combined interventions have additive effects on child undernutrition (Figure 4.8). The additional gained protections of combined interventions, however, seem to be driven by nutritional treatment. Again, the outcome of these simulations parallel to the WASH Benefits trial results where combined WASH and nutrition provided a similar magnitude of effect on improving child growth as the nutrition alone intervention (39,40). While the comparison caveats between the simulation results and trial outcomes are nuanced, overall, our simulations, alongside randomized control trials highlight the possibility that sanitation is a sufficient, not necessary, factor for improving child growth under conditions of high pathogen exposure.

The model structure, which is uniquely suited to capture repeated infections, and the implementation of the model have a few limitations. First, we used a homogenous model to examine the effects of any enteric pathogen infection, as most programmatic interventions do not target specific pathogens. When studying pathogen transmission and the underlying immune pathways connected to gut health, large variability between people, for example, due to diet (93) or genetics (94), exists. It is possible that an individual-based and potentially stochastic approach might better capture this type of heterogeneity. Additionally, the model structure makes it challenging to assess transmission of specific pathogens, which exhibit varying transmission patterns (95). While we attempted to capture this by accounting for pathogen uncertainty, we did not explicitly model individual pathogens. Enteric pathogen burden differs by geographical region (96) and by seasonality, and thus overall transmission dynamics may vary, but likely remain qualitatively the same. To address these limitations, future work could provide examples of low dose and high dose pathogen transmission models while accounting for seasonal variation in pathogen spread. Additionally, we did not account for adult pathogen shedding into the environment when estimating the model reproduction number, which resulted in higher transmission parameters than might be realistic.

Second, we did not incorporate an explicit age structure into the framework. Rather, we modeled enteropathogen infection so that children were exposed to pathogens from birth, so that simulation time is equivalent to age in the model. The aging process, particularly in young children, is important factor for growth (97). Age also marks the onset of new behaviors that affect the risk of infection. Pathogen transmission in young children and the interacting effects on health are often byproducts of these processes. For example, while there is evidence that enteric infection can begin within the first week of life (3), high pathogen burden tends to peak during weaning (98), a time that also correlates with the age at which a child begins to crawl (environmental exposures, such as soil pathogens, are increased). Caulfield et al., 2017 (54) noted an increase in pathogen detection in non-diarrheal stools with a child’s age (mean 0.5 pathogens/stool for children age 0–2 months vs. 1.3 pathogens/stool for children age 18–24 months). Our model shows increasing pathogen transmission as children in the model age, however, the initial peak of infected children in stage one occurs at 45 days. Our model also does not include breastfeeding, which would delay transmission and likely result in transmission curves that are more reflective of the data collected by Caulfield and colleagues. Further modeling should incorporate an age structure to better capture the risk of pathogen exposure that occurs as a child grows.

Our modeling approach presents a dynamic understanding of complicated, interdependent processes. The exact biological mechanisms underlying these processes in our model are unknown. It is possible that nutritional interventions reduce susceptibility to pathogens through either of the pathways tested, both pathways, and even pathways that were not included. While there are ample opportunities for improving this model, we suggest that improved data in the on intestinal health and the immune system would greatly further research. In our model, we assumed that rate of movement down strata is constant. In reality, it is likely that the rate increases as the number of strata increases. Evidence suggests that elevated fecal markers of inflammation, which are associated with reduction in linear growth (99), as well as overall pathogen burden (100), change over time. Kosek et al.'s research delineated changes overtime in neopterin (NEO), alpha-anti-trypsin (AAT), and myeloperoxidase (MPO) in three month intervals, whereas McCromick showed age trends where samples were collected monthly. The time trends differ by each marker of inflammation, however, making it challenging to determine either a time scale or functional form of this increase. We also assumed that pathogen transmission rates increased as children moved through various strata levels. Again, this reflects patterns observed in the literature — more malnourished children have reduced immune function — nevertheless, the functional form of the increased transmission rate is unknown. More granular details are needed to determine the rate of increased susceptibility to enteric pathogen infection as a result of overall gut health. With better data, much of the uncertainty included in our model would be minimized.

Environmental contamination is common in many low resource settings. High levels of enteric pathogens have been found in soil (101,102), hands of children's caregivers (103,104), children's toys (105,106), and in prepared food (107–109). It is through pervasive exposure to a host of pathogens that repeated enteric infections occur, one hypothesized pathway leading to growth faltering. Furthermore, evidence is building that environmental conditions —geophagia (110), animal feces (111,112), and overall contaminated household environments (poor water quality, unimproved sanitation, and unhygienic handwashing conditions) (113) — are associated with markers of environmental entropy. Interventions that seek to reduce environmental exposure of pathogens and improve child growth should account for the dependencies in pathogen exposure routes and biological processes. Through exploring enteric infection and undernutrition as a dynamic system, we present a first-step towards understanding this system. We were able to highlight mechanisms that require additional study, and suggest places where additional data would provide greater insight into this system. We also highlighted how the dependencies between enteric infection and undernutrition may account for varying intervention results observed in the literature. Although a first step, this approach provides a roadmap for aligning further research priorities with current recommendations for child health programs.

4.6 References

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Figure 4.1. Base model schematic. Solid lines represent people; dashed lines represent pathogens; dashed boxes represented each stage. Variables and parameters are defined in Table 4.1.

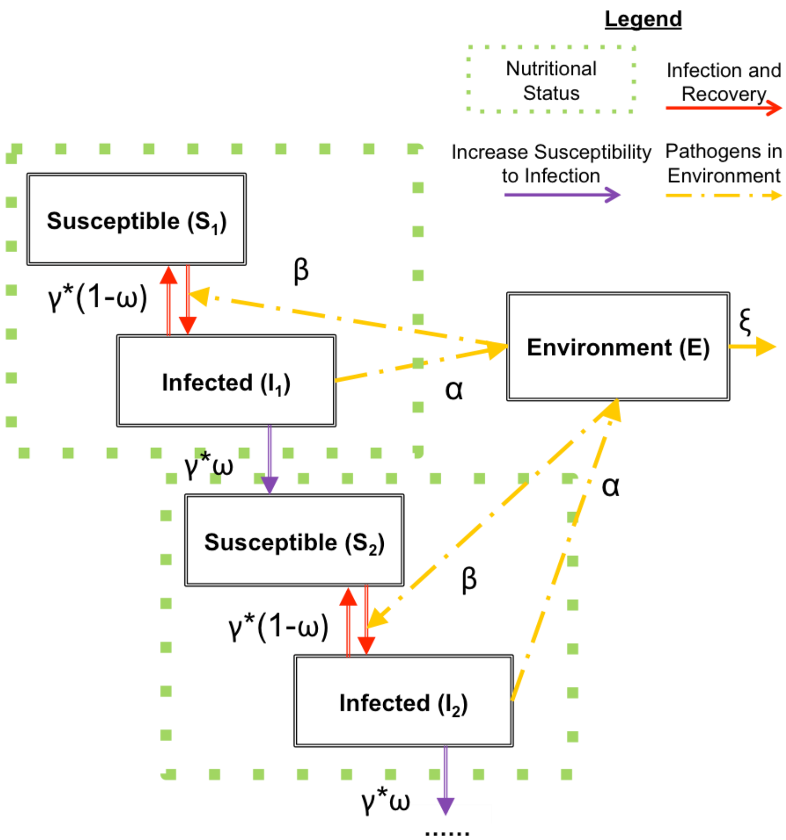


Table 4.1. Model Parameters used in the base model and its definition

Parameter	Definition	Value used	Units	Range tested	Value determined from
β_i	Child's rate of infection	1.15E-07	probability of infection / (pathogen*day)	7.88E-8 - 1.82E-7	(49)
γ_i	Child's recovery rate from compartment I	0.14	per day	0.10-0.25	(48,49,113–116)
ω	Proportion of children entering next infection stratum	0.05	n/a	0.00-1.00	Assumed
α_i	Child's shedding rate during first infection	0.12	concentration of pathogens in stool / (person * day of illness)	3.76E+06 - 3.38E+09	(91,94,117–121)
ξ	Pathogen die off rate	0.12	per day	0.04-0.27	(48,122,123)
σ	Proportion of children born with low birth weight	0.16	n/a	n/a	(56)
I_A	Steady-state adult infected population	200	people	n/a	Assumed
V	Size of environmental reservoir	1.00E+06	volume	1.00E+05 - 1.00E+07	Assumed

Table 4.2. Effect of Interventions on Model Parameters

Intervention type	Parameter affected	Intervention effect	Value (range)	Reference
Sanitation	δ	Shedding of pathogens into the environment will attenuate due to community-level sanitation.	0.19 (0.0-1.0)	(61)
Nutrition	ρ	Rate of immune function rebound	0.008 per day (0.0-0.02)	(67)
Nutrition	φ	Reduction in likelihood of entering next infection stratum due to supplementation	0.13 (0.0-1.0)	(82)

Figure 4.2. Model schematic with interventions. Solid lines represent people; dashed lines represent pathogens; dashed boxes represented each stage. Variables and parameters are defined in Tables 4.1 and 4.2.

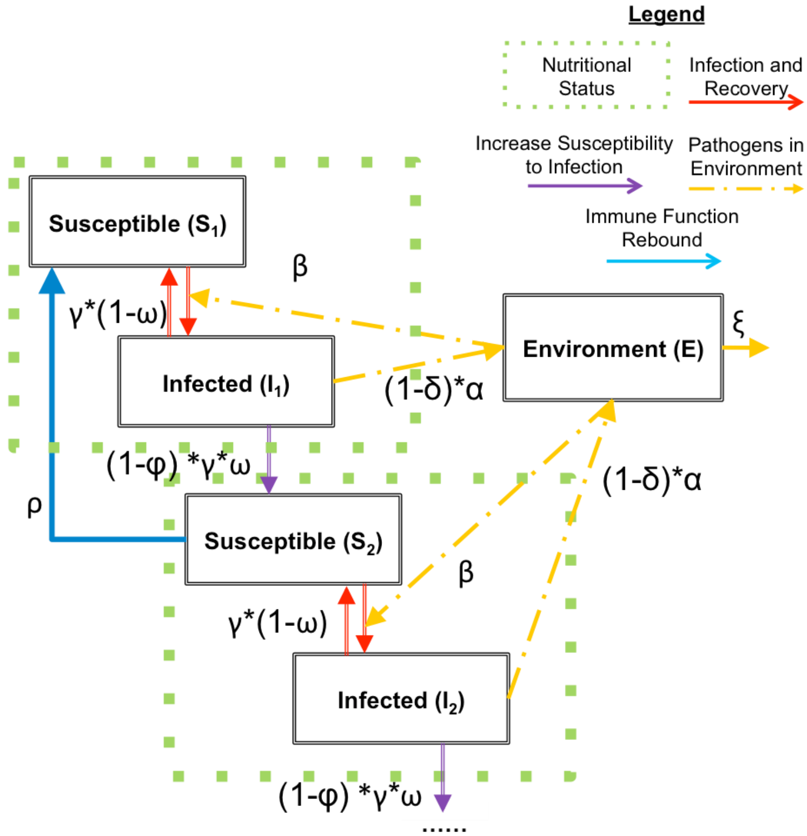


Figure 4.3. Transmission Dynamics Between Models. A. The total number of infected children over time in each model. B-E. The total number of children in each infection compartment across time for each respective model.

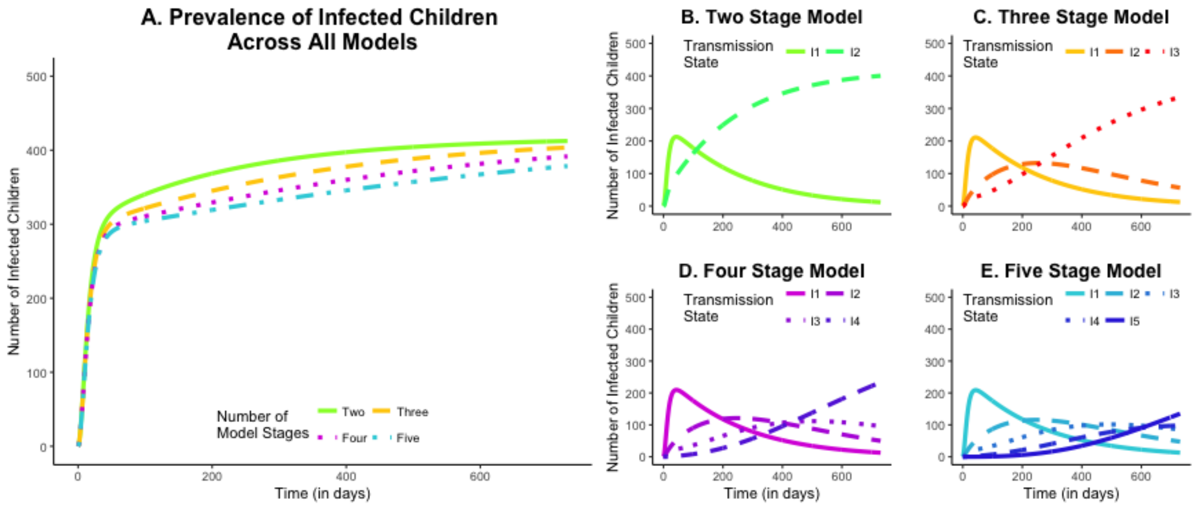


Figure 4.4. The total number of children in each infection compartment across time, accounting for parameter uncertainty. The shaded area represents the 25%-75% quantile of values from the 1000 model simulation across the parameter ranges. The blue line is the 50% quantile from these simulations.

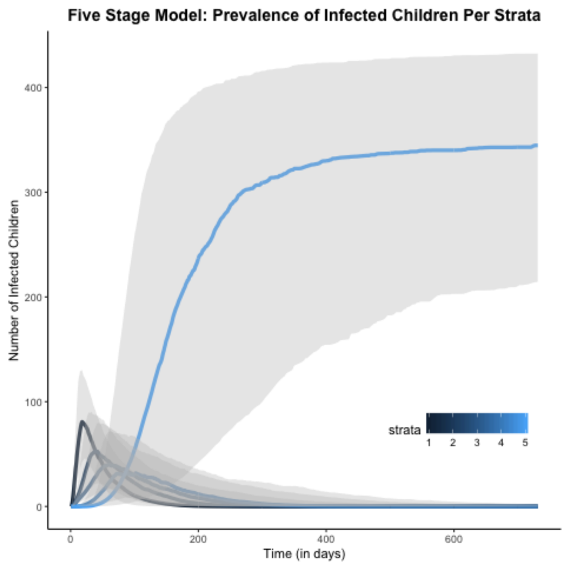


Figure 4.5. Transmission Dynamics Between Models Under Single Intervention Scenarios. A. The total number of children infected over time in each simulated intervention scenario. B. The total number of children infected over time under no-intervention conditions. C. The total number of children infected over time in the sanitation intervention scenario, with total infection PF=0.10. D. The total number of children infected over time in the zinc intervention scenario, with total infection PF=0.00. E. The total number of children infected over time in the LNS intervention scenario, with total infection PF=0.00.

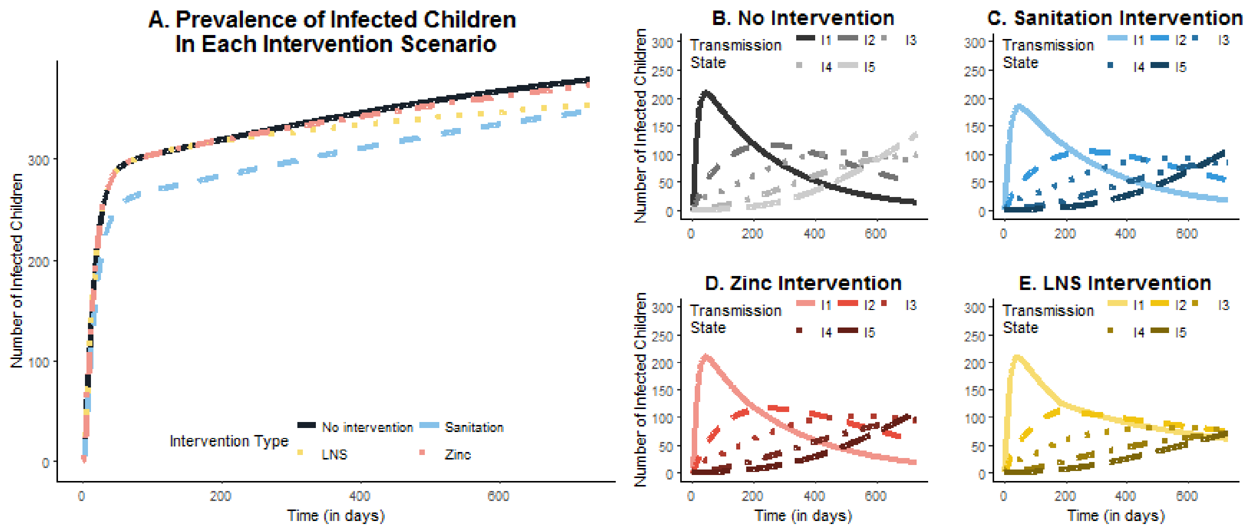


Figure 4.6. Transmission Dynamics Between Models Under Combined Intervention Scenarios. A. The total number of children infected over time in each simulated intervention scenario. B. The total number of children infected over time under all three interventions, with total infection PF=0.10. C. The total number of children infected over time in the sanitation and zinc intervention scenario, with total infection PF=0.10. D. The total number of children infected over time in the sanitation and LNS intervention scenario, with total infection PF=0.10. E. The total number of children infected over time in the zinc and LNS intervention scenario, with total infection PF=0.00.

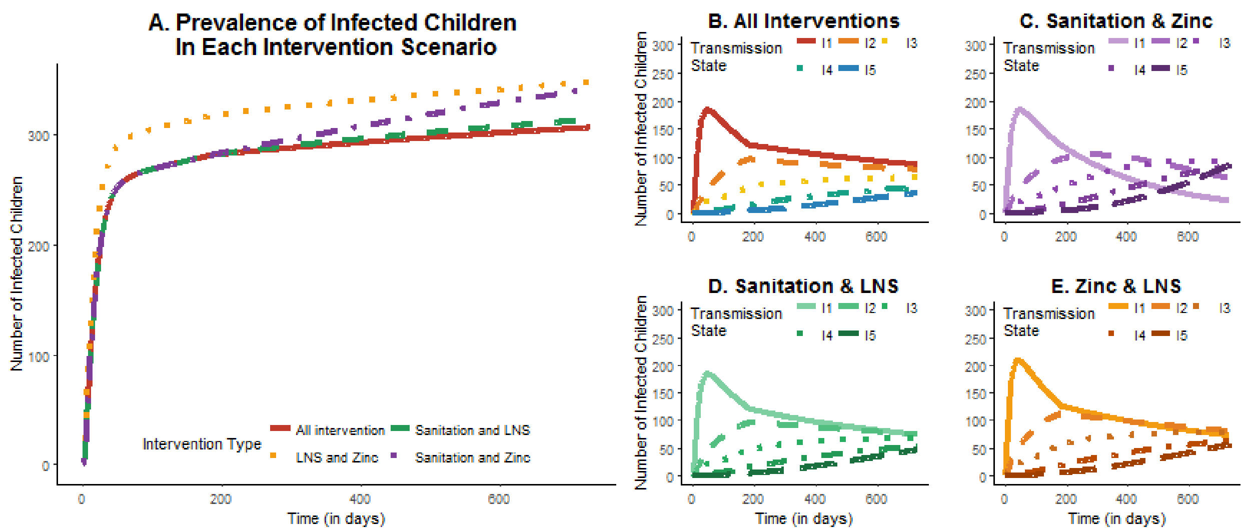


Figure 4.7. The Distribution of Children across each Modeled Stratum Under Single Interventions Scenarios. Children in the first stratum present the lowest risk of undernutrition, while those in the highest stratum have the greatest risk of undernutrition.

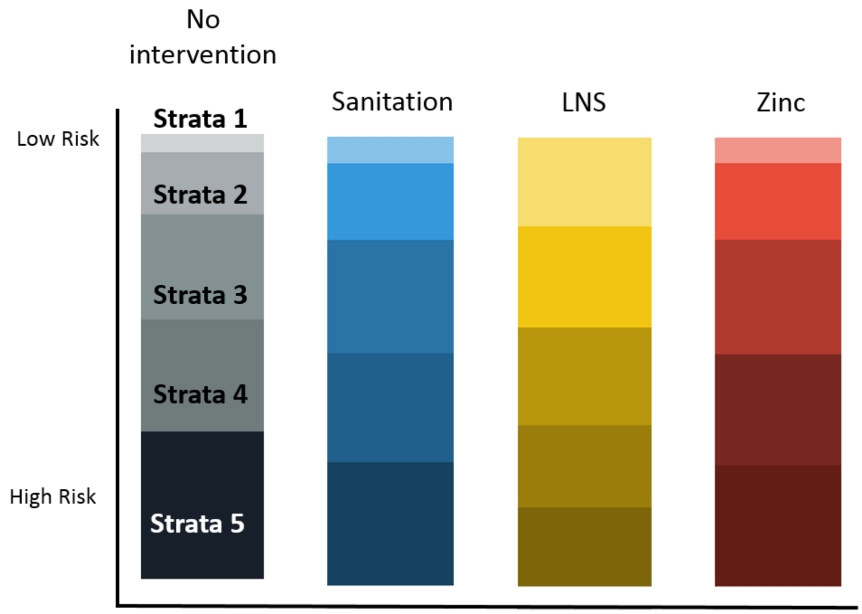


Figure 4.8. The Distribution of Children across each Modeled Stratum Under Combined Interventions Scenarios. Children in the first stratum present the lowest risk of undernutrition, while those in the highest stratum have the greatest risk of undernutrition.

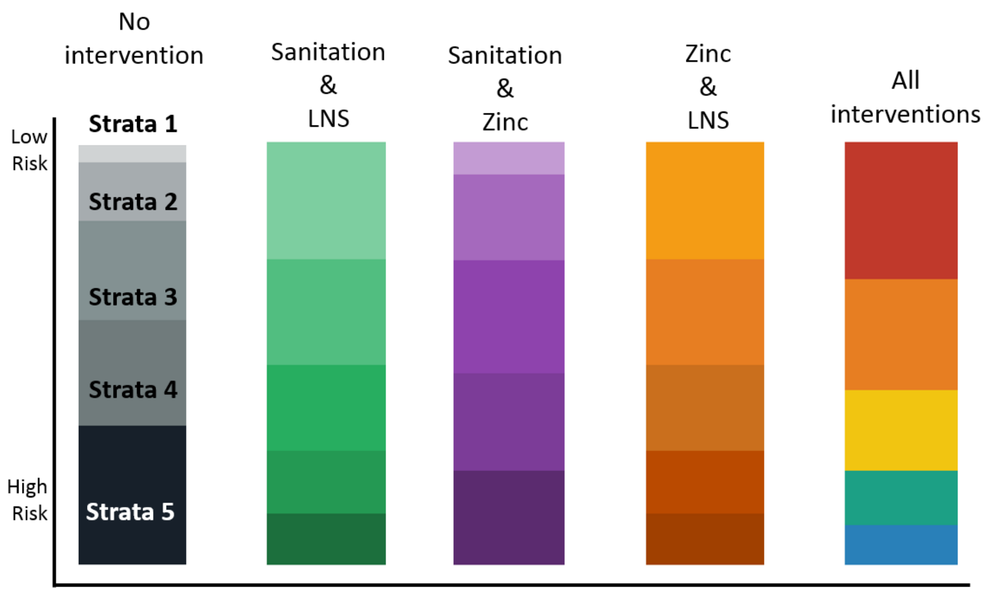
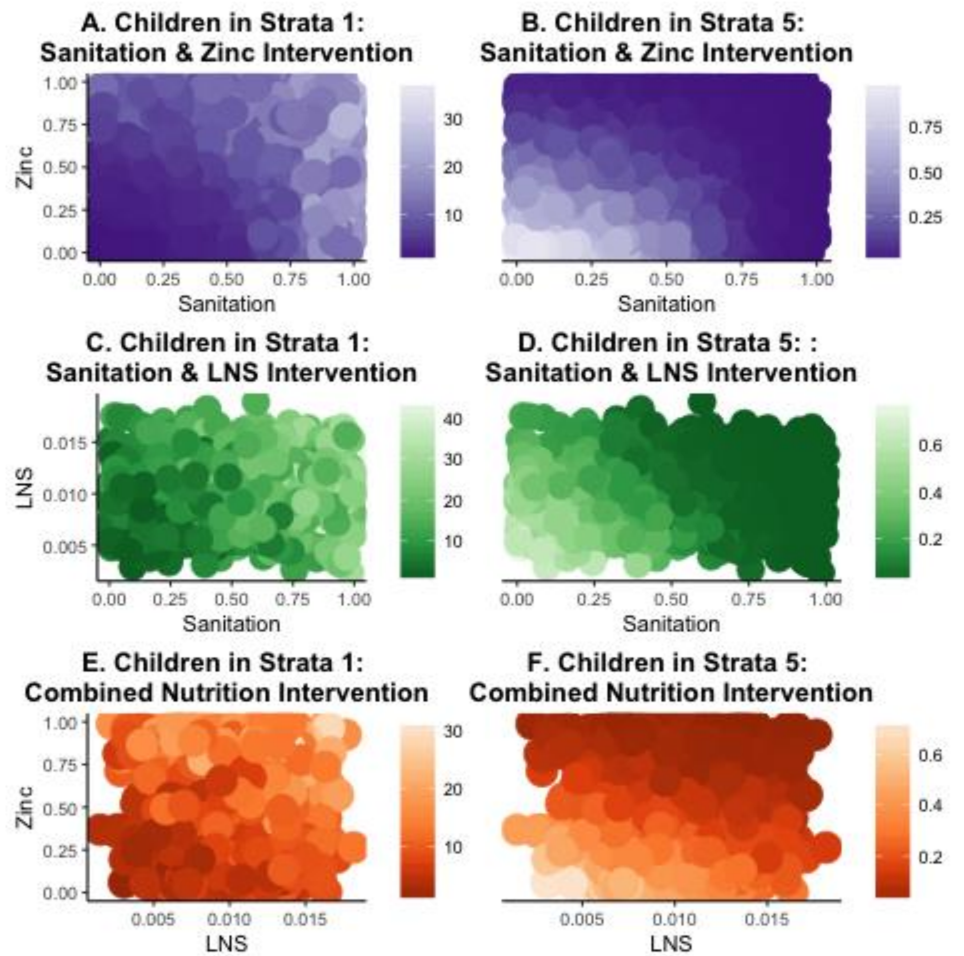


Figure 4.9. The Ratio of Children Under Combined Intervention Scenarios to No Intervention in each LHS Sample by Increasing Intervention Parameter Value. Panels A and B present children in stratum 1 and stratum 5, respectively, in simulations that included sanitation and zinc interventions. Panels C and D show children in simulations that included sanitation and LNS interventions, while panels E and F show children in the combined nutrition intervention simulations.



4.7 Appendix

Appendix 4.1 Parameter Values

We conducted a literature review to establish feasible ranges of values for several transmission parameters. We searched for the following pathogens: *Cryptosporidium*, rotavirus, *Shigella*, and enterotoxigenic *Escherichia coli* (ETEC). Each reference used, corresponding parameter value and calculations are presented in the following tables: Appendix Table 4.3 (pathogen decay); Appendix Table 4.4 (recovery rate); Appendix Table 4.5 (shedding rate).

Appendix Table 4.3. Pathogen Decay

Reference	Pathogen	Decay rate	Units	Mean Decay Rate (per day)	Lower boundary Decay rate	Upper boundary Decay rate
Toze et al., 2010	Rotavirus	0.03	per day			
Brouwer et al., 2017	Cryptosporidium	0.04	per day			
Yamahara et al. 2012	E. coli	0.27	per day			
ALL PATHOGENS				**0.115**	**0.034**	**0.27**

Appendix Table 4.4. Recovery Rates

Reference	Pathogen	Recovery rate	Units	Mean Recovery Rate (per day)	Lower boundary recovery rate	Upper boundary recovery rate
Young et al, 2014	Rotavirus	0.125	per day			
Young et al, 2014	Rotavirus	0.25	per day			
Bilcke et al, 2015	Rotavirus	0.125	per day	0.175	0.125	0.25
Pitzer et al., 2011	Rotavirus	0.125	per day			
Pitzer et al., 2011	Rotavirus	0.25	per day			
Brower et al., 2017	Cryptosporidium	0.1	per day	0.1		
Jose and Bobadilla, 1994	ETEC	0.143	per day	0.143		
Joh et al. 2013	Shigella	0.143	per day	0.143		
ALL PATHOGENS				**0.14**	**0.1**	**0.25**

Appendix Table 4.5. Pathogen Shedding

Reference	Pathogen	Data	Value	Units	Mean Shedding (pathogens/stool/day)	Lower bound shedding (smallest value/longest duration)	Upper bound shedding (largest concentration/shortest duration)
Julian 2016	Shigella	Shedding (lower)	1.00E+05	#/g feces	1.53E+09	3.57E+03	1.43E+10
Julian 2016	Shigella	Shedding (upper)	1.00E+06	#/g feces			
Julian 2016	Shigella	Shedding (lower)	1.00E+07	#/g feces			
Julian 2016	Shigella	Shedding (upper)	1.00E+11	#/g feces			
Julian 2016	Shigella	Duration (lower)	7	days			
Julian 2016	Shigella	Duration (upper)	14	days			
Dupont HL. 2005	Shigella	Duration	28	days			
Chappell et al., 1996	Cryptosporidium	Shedding (lower)	5.20E+04	oocytes/day	4.05E+08	5.20E+04	8.10E+08
Chappell et al., 1996	Cryptosporidium	Shedding (upper)	8.10E+08	oocytes/day			
Julian 2016	ETEC	Duration (lower)	3	days	9.79E+07	1.50E+07	3.33E+08
Julian 2016	ETEC	Duration (upper)	5	days			
Julian 2016	ETEC	Shedding (lower)	1.00E+08	#/g feces			
Julian 2016	ETEC	Shedding (upper)	1.00E+09	#/g feces			
Harro et al. 2011	ETEC	Shedding	7.50E+07	CFU/gram of stool			
Julian 2016	Rotavirus	Duration	24	days	2.50E+04	4.17E+03	5.56E+04
Julian 2016	Rotavirus	Shedding (lower)	1.00E+05	#/g feces			
Julian 2016:	Rotavirus	Shedding (upper)	1.00E+06	#/g feces			
Mukhopadhya et al., 2013	Rotavirus	Duration (symptomatic)	24	days			
Mukhopadhya et al., 2013	Rotavirus	Duration (asymptomatic)	18	days			
ALL PATHOGENS					**5.08E+08**	**3.76E+06**	**3.86E+09**

Appendix 4.2 Estimation of R_0

Using the two-stage model as an example, we estimated the transmission rate (β_i) by back-calculating from the model reproductive number (R_0). We estimated R_0 formula via the next-generation method:

$$R_0 = \frac{(\sigma\ \alpha_2\ 1.5\ \beta_1\ \gamma_1\ N) + (1\text{-}\sigma)\ \alpha_1\ \beta_1\ \gamma_2\ N)}{\gamma_1 0.5\ \gamma_2\ \xi}$$

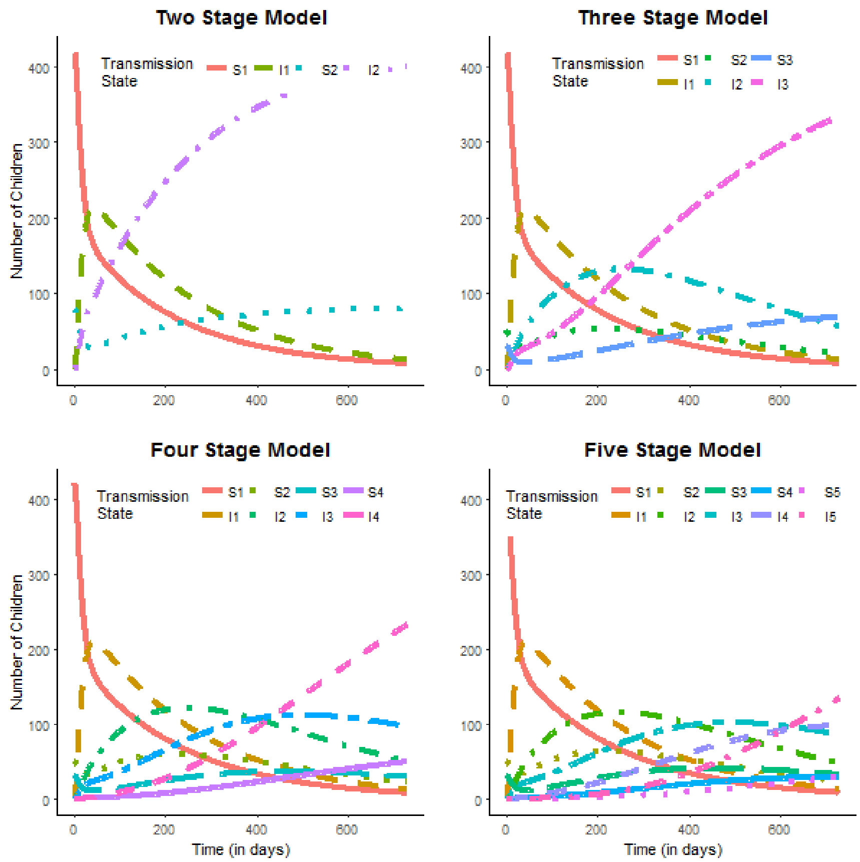
Using the model parameters, we then calculated an estimate of β:

$$\beta_1 = \frac{R_0\ \gamma_1\ \gamma_2\ \xi}{N(1.5{*}\sigma{*}\alpha_2{*}\gamma_1 + (1\text{-}\sigma){*}\alpha_1\ 0.5\ \gamma_2)}$$

Appendix 4.3 Steady State Conditions

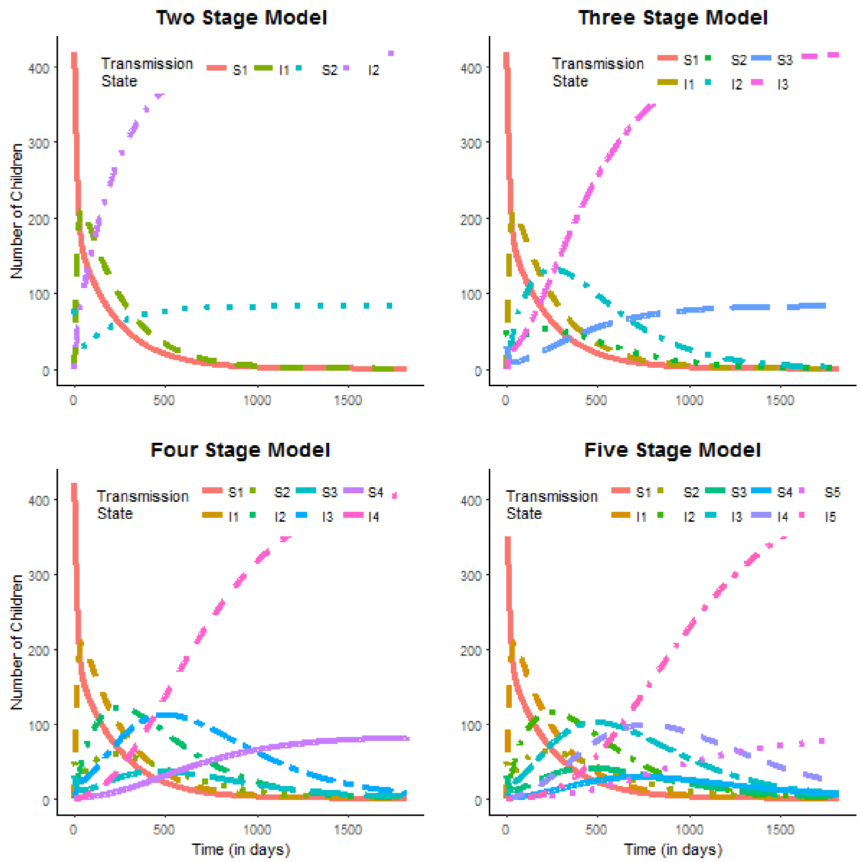
In developing the model structure, we simulated four models with an increasing number of strata over a two-year period (see Appendix Figure 4.10).

Appendix Figure 4.10 Simulations with base model parameters run over 2 years, where additional strata were added to each model



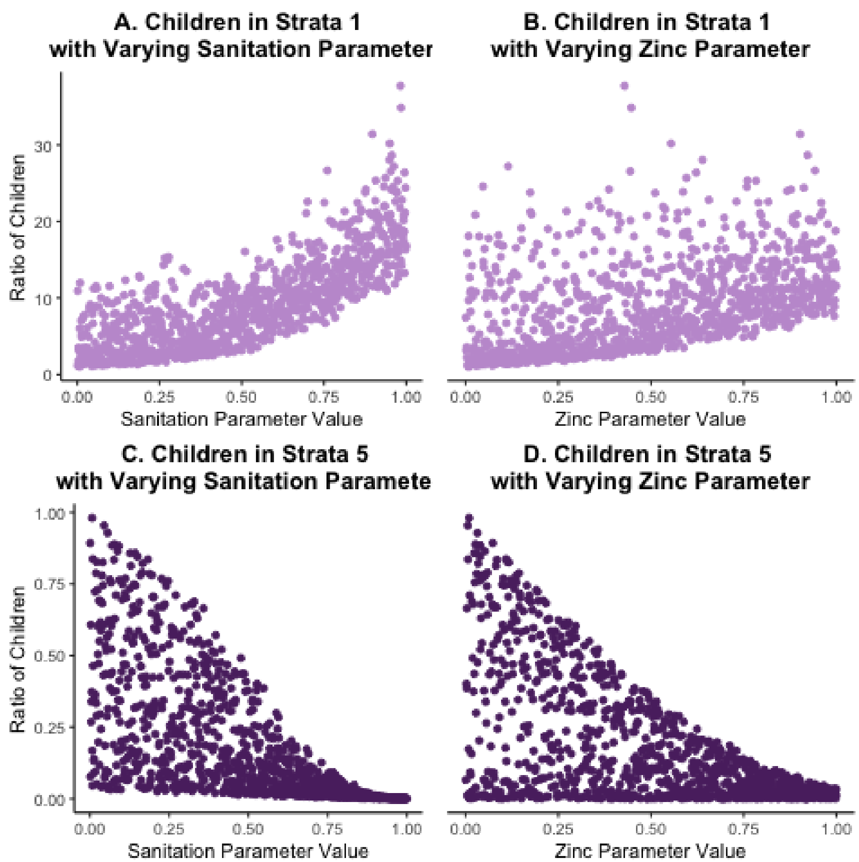
As described in the main study, with additional strata, the model transmission dynamics slow down. We ran the models until they reached steady-state conditions, and observed that in the five-stage model, steady-state was approached in the fifth stage until approximately 5 years (Appendix Figure 4.11).

Appendix Figure 4.11 Simulations with base model parameters run over 5 years, where additional strata were added to each model

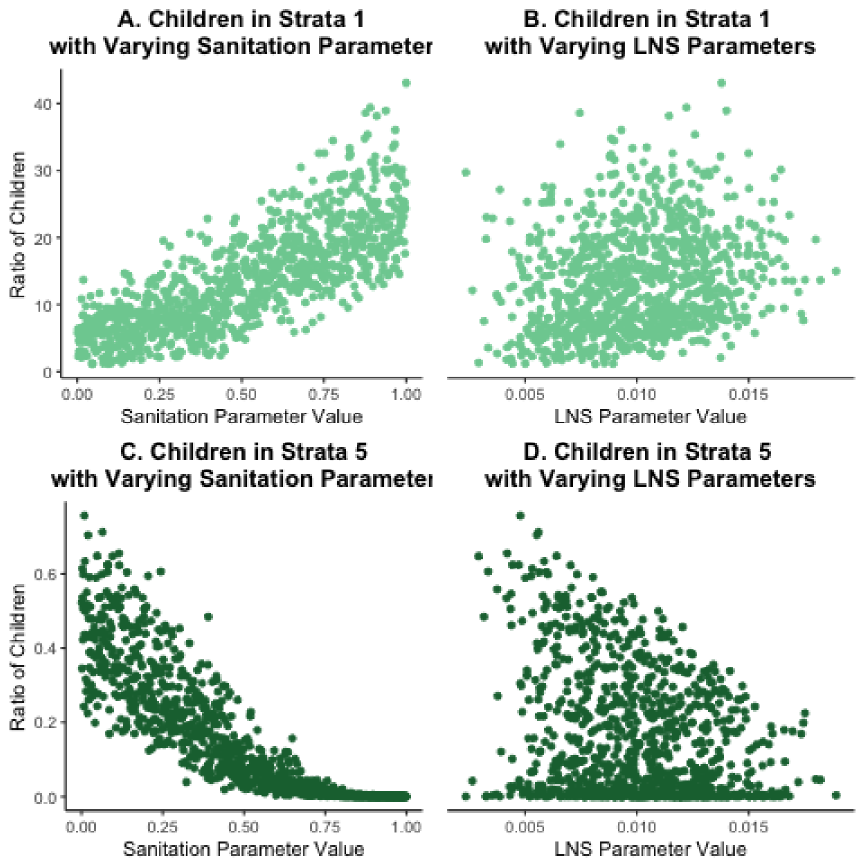


Appendix 4.4 Ratio of Children in Each Combined Intervention Scenario and No Intervention Simulations

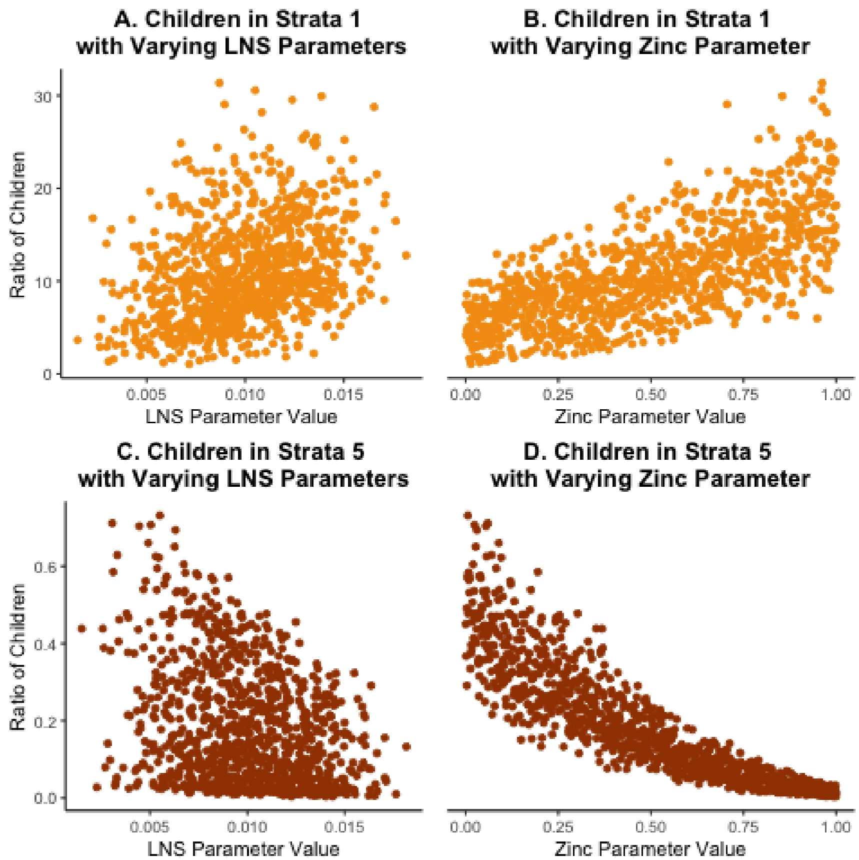
Appendix Figure 4.12. Ratio of Children in the Strata 1 and 5, respectively, Under Sanitation and Zinc Interventions Relative to No Interventions LHS Simulations. Panels A and C show the ratio of children as the sanitation parameter increases, while panel B and D show the ratio of children as the zinc parameter increases.



Appendix Figure 4.13. Ratio of Children in the Strata 1 and 5, respectively, Under Sanitation and LNS Interventions Relative to No Interventions LHS Simulations. Panels A and C show the ratio of children as the sanitation parameter increases, while panel B and D show the ratio of children as the LNS parameters increase.



Appendix Figure 4.14. Ratio of Children in the Strata 1 and 5, respectively, Under LNS and Zinc Interventions Relative to No Interventions LHS Simulations. Panels A and C show the ratio of children as the LNS parameters increase, while panel B and D show the ratio of children as the zinc parameter increases.



Chapter 5
Conclusion

The introduction of sanitation is a primary strategy for limiting community-transmission of enteric pathogens and reducing individual-level exposure (1). Thus, within the global health priorities for improving child health, emphasis has been given to expanding sanitation access. For example, globally, an estimated 2.1 billion people gained access to improved sanitation between 1990 and 2015 (a 26 percent increase in household coverage of improved sanitation) (2). These gains, however, were approximately 10 percent shy of reaching the 2015 sanitation coverage goal proposed by United Nations (UN) member-states. Additionally, inequities in sanitation access exist (3,4). While sanitation coverage is an essential element of reducing the burden of diarrheal disease morbidity and mortality in young children, we argue that sanitation coverage is a limited proxy of protection against pathogens. The goal of Chapters 2 and 3 were to assess the link between behavior and sanitation access as a potential explanation for the null findings of recent sanitation interventions. The goal of Chapter 4 was to assess multiple pathways of enteric transmission that lead to child undernutrition and infection and specifically test the effects of sanitation. Using a variety of analytical tools that prioritize improved measurement techniques and identification of causal pathways, the studies in this dissertation generate two hypotheses for why sanitation interventions may not be as effective at reducing pathogen transmission as we would expect: 1) variable use of sanitation facilities and 2) interacting biological processes that affect susceptibility to pathogens. Overall, the results from this dissertation suggest that the assumptions about use of sanitation facilities and access require further analyses and that sanitation may be a sufficient, but not necessary factor for improving child health.

The studies included in this dissertation are exploratory and sought to understand the interconnectedness between sanitation access, use, and protection latrines confer against pathogen exposure. To gain insight into processes of underlying latrine use, we first conducted formative research on defecation practices (Chapter 2). Our approach built on previous research studies conducted in India that used social theories to identify the household determinants of defecation behavior (5). We extended the study of defecation behavior into the Latin American region and assessed population determinants by using an individual data. Thus, we were able to identify individual-level determinants of latrine use in an understudied region, and also added to the broader literature more information on generalizable determinants of latrine use behavior. An important limitation of this analysis is the inclusion of self-reported latrine use, a biased metric. Nevertheless, we furthered this analysis of examining alternative means of measuring exposure in Chapter 2 by modeling latrine use as a latent variable in Chapter 3. As a latent variable, we were able to estimate the bias in the latrine use metric, which allowed us to test the association between sanitation access and individual behavior. Collectively, innovative techniques were applied in Chapters 2 and 3 to examine the relationship between sanitation access and use through novel approaches. Finally, to assess the relationship between sanitation access and protection, we developed a dynamic model to examine the implications of sanitation interventions (Chapter 4). Our simulations showed that sanitation interventions might not promote child growth under certain conditions. We also showed that due to biological dependencies in environmentally mediated transmission of pathogens, treating children for undernutrition might have a larger impact on health than mitigating pathogen exposure. These simulations parallel the results of recent sanitation intervention trials, and may provide rationale for unexpected trial outcomes. Collectively, these studies have contributed to the field of sanitation and global health by laying fundamental groundwork to further study the influence of exposure to pathogens on child health within a systems framework.

Broadly, these studies provide plausible rationale for the null results of recent sanitation interventions on child health. These studies, nonetheless, are first steps towards disentangling assumptions surrounding sanitation access. Many knowledge gaps remain and future work is needed to further understand the dynamics underlying human behavior and the effectiveness of sanitation intervention. For example, we focused our studies on the access to a latrine, using UN-based definitions. We know, however, that the quality (i.e., cleanliness, maintenance) of improved sanitation varies in our study site. Additional studies are required to disentangle whether latrine quality is a population-level determinant of latrine use. Likewise, further examination of latrine use determinants is needed for subsets of the population, such as women and girls and users of shared sanitation facilities. Women and girls require latrines to be built in a manner keeps them safe from violence (6), provides privacy during use (7), and is appropriate for menstrual hygiene management (8,9). Patriarchal norms greatly influence gendered-patterns of latrine use as well as how latrines are built, and thus, specific studies examining the women and sanitation are needed. Regarding users of shared sanitation facilities, these individuals may also exhibit different latrine use patterns (and thus determinants) relative to the entire population, as their sanitation access is not constant. In each of these population subsets, as well in the overall study site, auxiliary research regarding determinants of inconsistent latrine use would also greatly contribute to the field of sanitation. Knowledge gained from each of these sub-research areas would be greatly enhanced through longitudinal analyses, which will build upon our use of cross-sectional analysis. Finally, beyond latrine use, future work testing the direct effects of latrine use on pathogen exposure would strengthen the connections we studied within this dissertation.

Much of the work presented in the dissertation uses primary data provided graciously from individuals living in remote Ecuadorian communities in the Esmeraldas province. Esmeraldas is a province undergoing economic development, and was originally chosen by our research group to study the effects of road construction on health (10). Although Ecuador is a middle-income country (11), the communities of study are a microcosm of the development throughout the globe. The people of Esmeraldas experience overall poorer health and wellbeing relative to Ecuadorians living in other parts of the country, which is likely due in part to their marginalized social position as black and indigenous rural populations. For example, the UN estimates that 57 percent of rural Ecuadorian households have access to safely managed sanitation[7] (12); none of the households in our study sample have access to a sanitation facility that treats human waste. We also know the communities in our study experience disparities in child health outcomes — episodes of diarrhea are common in young children and undernutrition is high. The prevalence of mother-reported recent diarrhea is 16 percent for children 12 months of age or younger, an estimate that greatly varies by community, but is lower than the observed diarrhea rate in Kenyan children (27 percent; (13)) and higher than that in Bangladeshi children (nine percent; (14) (of note, national estimates of child diarrhea rate are unavailable for the country of Ecuador). Additionally, our fieldwork shows that chronic undernutrition rate among child under five living

[7] an improved, non-shared, sanitation facility where excreta are safely disposed in situ or transported and treated off-site

in Afro-Ecuadorian communities was approximately 12 percent in 2013, however, during the same year, one in every two Chachi children was stunted (15). In contrast, a recent nationally-representative nutrition and health study estimates that the proportion of child stunting was 20 to 30 percent among children living in rural, coastal communities (16).

Given the health disparities in the communities of study, there is great need to understand how enteric pathogen transmission leads to these health outcomes, and under what conditions sanitation reduces pathogen exposure. Sanitation is an important barrier to environmental contamination in the study site communities. Inconsistent latrine use behavior increases the number of pathogens in the environment. Furthermore, the concentration of pathogens in the environment is increased by annual flooding (17) and even minimal rain (18). The greater the environmental contamination, the greater the risk of both enteric infections and overall undernourishment in children. In developing interventions that seek to minimize environmental contamination, it is insufficient to focus on changing social norms of defecation or improving a child's diet without also addressing latrine functionality or the yearly flooding that results in overflow from latrines. Certainly the connections between sanitation and health are complex. While we are hopeful that our research adds to health program design by highlighting some of these complexities, we also recognize the limitations of this work to make concrete policy recommendations.

Conceptually, we view risk of pathogen exposure as a component of a complex system: our approach examined the behavioral, biological, and environmental processes underlying this risk. Traditionally, the public health sector primarily focuses on preventing enteric infections by installing sanitation hardware. We are hopeful that these studies in aggregate will shift this current paradigm. Specifically, we hope to expand discussion from whether a household *has* a sanitation facility to include *if* and *when* sanitation facilities are used and *how* their use influences child health and development. Such a paradigm shift will be useful in meeting the Sustainable Development Goal for sanitation, which seeks to end open defecation, and also for developing child health interventions that incorporate WASH behavior change components and account for underlying biological mechanisms that lead to poor physical development.

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