The Impact of Sanitation on Child Health in Vulnerable Populations: a Multicountry Analysis across Income Levels

by

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For my brother, Gabriel Contreras,

who ensured that I could be here today.

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PREFACE

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ABSTRACT

The separation of humans from fecal waste through sanitation is a crucial element of public health that has prevented countless deaths throughout history. However, health improvements from sanitation are not shared equally across populations. Almost 500,000 children under five die from diarrhea each year, mostly in low-income countries that depend on low-cost sanitation technologies that may not effectively prevent disease. Those diseases have been virtually eliminated in high-income countries through widespread coverage with sewerage and wastewater treatment, but many populations within wealthy countries, including rural communities, racial/ethnic minorities, and other marginalized groups, do not share equitable access to sanitation and experience poor health as a result. Furthermore, sewerage requires copious amounts of water and is not sustainable in an increasingly water-stressed world. One existing solution is the reuse of wastewater for irrigation, but without adequate treatment the practice poses health risks to exposed communities. Achieving global access to sanitation that protects health requires understanding the true health benefits of different sanitation solutions, improved safety and sustainability of waste management practices, and efforts to reach vulnerable populations. In this dissertation, I present three research aims on these topics with the goal of improving our understanding of sanitation and health across national income levels.

In Aim 1, we conducted a literature review and meta-analysis of studies on sanitation and diarrhea. Three of four recent major trials on low-cost sanitation interventions found no effect on diarrhea, while historical average estimates have found strong effects. We evaluated literature reviews on sanitation and diarrhea to understand this discordance and found that consensus estimates included numerous flawed studies and inappropriately averaged across widely heterogeneous interventions and contexts. Our meta-analysis highlighted that average effects are largely driven by sewerage and interventions that improved more than sanitation alone. We found that there is no true overall effect of sanitation because variability between interventions and contexts is too complex to average and that the null effects of recent low-cost interventions are not surprising.

In Aim 2, we conducted a spatial analysis on households in Central Mexico to understand routes of exposure between wastewater reuse and diarrhea. To test if these exposures have a spatial dependency, we estimated the association between diarrheal disease in children living where wastewater is reused and household proximity to wastewater canals. We constructed a multilevel logistic regression model accounting for spatial autocorrelation and found that children living closer to wastewater canals had substantially higher odds of diarrhea compared to children living farther away. This finding suggests that spatially dependent exposure routes, such as spread by domestic animals or through aerosolization, affect communities that reuse wastewater.

In Aim 3, we characterized water and sanitation access among a marginalized population within a high-income country: the Bedouin of the Negev region in Israel. The Bedouin in Israel are formerly nomadic and have faced relocation, demolition, and forced sedentarization since the founding of Israel. Land disputes have resulted in some Bedouin living in historical villages that are not recognized as legal by the government. We conducted a household survey among planned, recognized, and unrecognized Bedouin communities. We found that Bedouin people, especially in unrecognized villages, face limited access to safely managed water and sanitation and have high rates of diarrhea in children. Our study emphasizes shortfalls in global sanitation access and the importance of reaching marginalized communities.

CHAPTER I

Introduction

1.1. Brief History of Sanitation

Sewage systems have been used to separate humans from their excrement since at least 2,000 BC, when some form of sewage system had been developed by the Mesopotamian Empire in modern day Iraq; in the village of Skara Brae in modern day Scotland; by the Minoan civilization on the island of Crete, who likely constructed the earliest flush toilet in history; and by the Indus civilization in South Asia [1,2]. The Roman Empire expanded and improved the concept of urban sewerage for over a millennium into the 4th century AD, including the development of greywater reuse for latrine flushing and the construction of the famous Cloaca Maxima, a massive sewer that is still in partial use today [3]. All of these civilizations had realized the benefits of separating humans from feces; however, in each of these cases wastewater was collected and conveyed to natural rivers or seas without any substantial treatment. After the collapse of the Roman Empire around 476 AD, sanitation practices regressed to cesspits and open sewers across the former empire, and the development of sanitation technology hit a standstill that lasted for over a thousand years and has been called the Sanitary Dark Ages [1,3,4].

Recognition of the importance of waste management reemerged throughout the 18th and 19th centuries, largely in response to exponential population growth and numerous outbreaks of cholera across the world [5]. During this period, sewerage was expanded in cities across Europe, John Snow closed the Broad Street pump, and governments took more direct responsibility for health and waste management, such as through Britain's Public Health Act of 1848 in response to a report on sanitary living by Edwin Chadwick [1,3]. The first comprehensively planned sewerage system was constructed in Hamburg, Germany in 1843 after a fire had destroyed much of the city [1,5]. Into the late 19th century, most cities that collected wastewater still disposed of it into natural water bodies or onto land for nutrient recycling [5]. As sustained population growth overwhelmed these processes, pollution became recognized as a public health threat. An explosion of treatment technologies occurred over the next century, including chemical treatment with lime (1846), chlorine (1893), and ozone (1906); horizontal (1850s) and radial-flow (1905) settling tanks for primary treatment; two chamber septic tanks (1906), which are still widely used today; filtration through soil (1870) and artificial filters (1885); and secondary treatment with activated sludge (1913) [3,4]. In high-income countries, investment in municipal plants that apply primary and secondary treatment to wastewater has all but solved the immediate challenges of fecal management. Remaining challenges include reducing the water and energy required for waste management, updating aging sewer systems, and preparing for more population growth and urbanization [1]. Still, high-income countries have demonstrated that solutions for sanitation exist and successfully separate populations from their waste. However, as I will demonstrate in this dissertation, these successes are not universally shared. Many lower-income countries, and even some populations within higher-income countries, still struggle to achieve adequate coverage with sanitation technology that has existed for over one hundred years.

1.2. Health Effects of Fecal Exposure

Where it has been achieved, the successful separation of humans from their feces has prevented immeasurable death and disease throughout history. This is because feces and sewage are full of microbiological and chemical contaminants that can negatively impact human health. Many infectious diseases are spread through the fecal-oral route, in which enteric pathogens are discharged in the feces of an infected individual and then transferred to the mouth of a susceptible individual through one of many routes of transmission. Some of the most common routes of transmission for fecal-oral pathogens include hand contact, spread by insects, contamination of drinking water sources, and through food preparation or contaminated crops [6]. Recently, other pathways have received additional attention as contributors to fecal-oral transmission, such as spread through animal feces [7]. Microbiological agents that are spread through the fecal-oral route include many species of bacteria, viruses, protozoa, and helminth worms. Some of the most important pathogens for human health are pathogenic *E. coli*, *Campylobacter jejuni*, *Salmonella typhi*, *Shigella* spp., *Vibrio cholerae*, norovirus, rotavirus, *Cryptosporidium parvum*, *Giardia lamblia*, *Ascaris lumbricoides*, and hookworm [6,8]. While many other microorganisms are spread through human feces, these pathogenic agents are particularly dangerous due to the diarrheal symptoms they cause.

In 1982, the U.S. Center for Disease Control and Prevention (CDC) and the World Health Organization (WHO) estimated that there were 4.6 million deaths due to diarrheal disease annually among children under five years old living in Africa, Asia (excluding China), and Latin America [9]. An updated estimate from the WHO in 1992 found that around 3.3 million children under five died from diarrhea each year worldwide [10]. The number of deaths caused by diarrhea continued to decline over the following years to an estimated 1.5 million deaths in 2012 [11]. In 2016, childhood mortality associated with diarrhea had dropped tremendously to an estimated 446,000 deaths per year [12]. Diarrhea still was the fifth leading cause of death among children under five in 2016, and the eighth leading cause of death among all age groups, resulting in over 1.5 million total deaths per year. These deaths generally are due to dehydration associated with fluid and electrolyte loss occurring with diarrhea [13]. Modern interest in diarrhea is focused on children under five, who are at the highest risk of diarrheal morbidity and mortality. In earlier history, diarrhea was a large contributor to morbidity and mortality in all age groups during repeated outbreaks of cholera. Six cholera pandemics affected the world between 1817 and 1923; the seventh cholera pandemic started in 1961 and is still active today [14]. In recent years, an estimated 2.86 million cases of cholera occur annually, resulting in about 95,000 deaths [15].

The morbidity and mortality associated with diarrheal disease alone make up a significant global health burden, but other possible health consequences of acute and repeated enteric infections have been identified. Environmental enteric dysfunction (EED) is a general condition of intestinal inflammation and malabsorption of nutrients that was first described in the 1960s [16,17]. While its etiology is not well understood or defined, EED is thought to be caused by repeated infections with fecal-oral pathogens [16]. Repeated infections with these pathogens result in recurring attacks on enteric cells that cause chronic inflammation and decreased gut function and nutrient absorption. In addition, foreign microbes can cause compositional changes to the natural and beneficial populations of microorganisms that live in our digestive and excretory system, the gut microbiome, further decreasing gut health and resilience [16]. Researchers have hypothesized that damage caused by EED to gut health in children can lead to further developmental issues, including cognitive delays and decreased linear growth [16–18]. Furthermore, the gut health of a child is not only dependent on the child's exposures but also is affected by the gut health of the mother in utero, underlining the importance of environmental sanitation at the population level [19].

1.3. Sanitation Access Across Income Levels

In an estimate using data from 2012, 280,000 out of 1.5 million (19%) diarrhea-related deaths among children under five were caused by inadequate access to sanitation [11]. These values were calculated using an average estimate for the effect of sanitation on diarrhea from a systematic review and meta-analysis that found sanitation access reduced diarrhea by an average of 28% [20]. In the second chapter of this dissertation, I will describe the critical limitations of using that estimate and other average estimates that combine different sanitation technologies, resulting in overstated benefits of cheaper forms of sanitation. Nevertheless, the near elimination of diarrhea-related mortality in high-income countries associated with expanded sewerage demonstrates the health benefits of successfully separating people from their waste. But sewerage generally is considered too expensive for widespread use in low-income countries [21,22]. Many communities in lower-income countries, especially in rural settings, instead depend on pit latrines that are designed to separate people from their waste but keep the waste on-site until emptying, which do not have a clear impact on reducing diarrheal disease or environmental contamination compared to sewerage access [23–25].

There are additional non-health benefits of increasing coverage with basic sanitation facilities, including dignity, safety, and school attendance, especially for women and girls. Still, access to even basic sanitation facilities is not universal. Goal Six of the United Nation's (UN) Sustainable Development Goals (SDGs) includes a target to reach complete coverage with safely managed sanitation services worldwide by 2030 [26]. In 2017, only an estimated 45% of the global population had access to safely managed sanitation services, which is defined by the use of improved facilities, not shared between households, and the safe disposal of waste [27]. An additional 29% were estimated to have access to basic sanitation, defined by improved facilities not shared between households, but without safe disposal of waste [28]. The same estimates across global regions demonstrate immense disparities faced by the Global South. Seventy-six percent of people in Europe and Northern America (the U.S. and Canada) had access to safely managed sanitation in 2017, compared to 38% in Northern Africa and Western Asia, 31% in Latin America and the Caribbean, and only 18% of people in sub-Saharan Africa [27]. Progress on improving access to safe sanitation over the past two decades has also varied substantially by region. Between 2000 and 2017, the proportion of people with access to safely managed sanitation services rose by 19 percentage points (from 12% to 31%) in Latin America and the Caribbean, by 12 percentage points (from 26% to 38%) in Northern Africa and Western Asia, and by only three percentage points (from 15% to 18%) in sub-Saharan Africa [27].

Regional and national estimates reported by the Joint Monitorring Programme (JMP) of the UN show how national wealth influences access to sanitation services, but additional disparities within each of those estimates reveal populations with the worst access to sanitation. In 2017, 76% of people in Europe and Northern America had access to safely managed sanitation, but only 48% of the rural population in this region had access compared to 85% of the urban population [27]. In many countries, the poorest households have the worst access to sanitation. In 2017, 93% of Guatemalans in the richest quintile of households had access to at least basic sanitation services compared to 45% of those in the poorest quintile of households [27]. The same disparity when comparing the richest households to the poorest can be found in many countries, such as 88% vs. 10% in India; 51% vs. 11% in Kenya; 58% vs. 2% in Liberia; 75% vs. 8% in Mozambique; 93% vs. 25% in Pakistan; 98% vs. 48% in Vietnam; and 95% vs. 59% in the Republic of Moldova, among many others [27]. The JMP did not report these data for high-income countries, but several examples of groups that face poor access to sanitation within high-income countries demonstrate how these challenges persist even in wealthy countries.

In 2019, the University of North Carolina at Chapel Hill's (UNC) Water Institute published a Policy Research Digest on persistent inequalities in access to water, sanitation, and hygiene (WASH) for vulnerable minority groups within wealthy countries [29]. This report highlighted three minority populations in high-income countries that face poor access to WASH services: 1) Roma communities throughout Europe, who are characterized by low coverage with piped drinking water, open defecation, and dependence on public toilets, 2) black and Latino minorities in the United States who live in peri-urban communities that are excluded from nearby municipal water and sanitation services with "racially obvious" boundaries, and 3) indigenous people of Canada, many of whom were historically relocated to lands with poor water access and still struggle to receive adequate federal support and representation [29]. Two additional groups that face poor access to sanitation services despite living in high-income countries include Mexican Americans and immigrants living in colonias along the U.S.-Mexico border and individuals experiencing homelessness. These examples will be discussed more in Chapter IV of this dissertation, along with the results of my work to measure WASH access among the Bedouin people of the Negev Desert in Israel, a high-income country.

1.4. Further Challenges in Sanitation

The availability of basic sanitation facilities at the household level is an important step in achieving universal coverage, but provision of those facilities alone is not a complete solution to global sanitation challenges. Behavior change is not achieved by simply supplying a household with improved facilities, and substantial research is devoted to facilitating changes in WASH behaviors, including the exclusive use and maintenance of sanitation facilities [30]. Many strategies for achieving sanitation-related behavior change through interventions have been developed, including the popular community-led total sanitation (CLTS) strategy, which attempts to create a sense of "shame" and "disgust" in communities to trigger interest in increasing the use of sanitation facilities [31]. Randomized trials of CLTS interventions have resulted in increased construction of latrines, but in general they have had almost no effect on child health [32]. In addition to issues related to behavior change and household access, there are numerous challenges to achieving sanitation access everywhere people need it, such as at work, at school, and in healthcare facilities. In 2016, only 66% of schools worldwide had access to a functional single-sex bathroom, and 23% of schools had no sanitation facility at all [33]. The same year, only 23% of healthcare facilities in sub-Saharan Africa had basic services, including a facility for staff, one functioning single-sex facility, and a facility for those with limited mobility; 21% of healthcare facilities globally had no sanitation service at all [34].

Adequate sanitation facilities in households, schools, and hospitals can separate people from their fecal waste, but safely managing that waste throughout its lifecycle is another challenge in sanitation. Before the development of the SDGs, the UN's primary goal in sanitation was to increase access to improved facilities, defined by the technology of the facility constructed. Improved facilities include pit latrines if they are constructed with a concrete slab to separate people from their waste, as well as toilets that flush away feces as wastewater [28]. With the development of the SDGs, the JMP added the category of safely managed sanitation to indicate the use of improved facilities plus the safe disposal and/or treatment of waste after collection. With this new indicator, the JMP emphasized the importance of managing waste from generation through treatment. In addition, the SDGs included a target within Goal Six to improve water quality by "reducing pollution, eliminating dumping and minimizing release of hazardous chemicals and materials, halving the proportion of untreated wastewater and substantially increasing recycling and safe reuse globally" [26].

In the baseline report for that target from 2018, the UN estimated that 59% of domestic wastewater was collected and safely treated, although the only available estimates were mostly from high- and middle-income countries and excluded much of Africa and Asia [35]. The true global estimate for wastewater treatment is likely much lower, and some available estimates have found that less than 10% of wastewater generated in low-income countries is safely treated [36,37]. The fate of wastewater is of growing concern as more and more nations face water scarcity, an issue that is exacerbated by continued climate change. Over half of water withdrawn for human use is eventually discharged as wastewater, including greywater and sewage [38]. One growing solution to meeting water demands without accelerating water stress is the reuse of wastewater for agricultural irrigation. Wastewater has a high concentration of nutrients due to human fecal waste, and humans have irrigated with wastewater to recapture these nutrients since as early as 3,000 BC [39]. Today, wastewater reuse for agriculture is practiced in over 50 countries and is used to irrigate an estimated 10% of all irrigated lands [40]. However, as most wastewater generated is never treated, especially in lower-income countries, this practice creates substantial risk to environmental and human health. One estimate suggests that the land irrigated with untreated wastewater is probably ten times as large as the land irrigated with treated wastewater [41]. The WHO has released guidelines for the safe reuse of wastewater in agriculture, most recently updated in 2006, but the epidemiological evidence on the public health risks associated with reuse is limited [42]. In Chapter III of this dissertation, I will present the results of a research project conducted in Mexico that adds additional evidence to our understanding of those risks.

1.5. Dissertation Objectives

In this dissertation, I will present the results from three research aims on the health effects of sanitation across multiple countries with varying levels of national wealth. In Chapter II, I discuss the results of a systematic review and meta-regression that aimed to build a more nuanced understanding of the historical literature on what types of sanitation interventions work to prevent childhood diarrheal disease in lower-income countries, and to situate the results from recent latrine-based interventions within that historical context. In Chapter III, I present a spatial analysis on wastewater reuse for agricultural irrigation in Central Mexico, an upper-middle income country, that provides a better understanding of the routes of exposure between wastewater and people that contribute to enteric infections in children. In Chapter IV, I present the results of a household survey conducted among the Bedouin people in the Negev region of Israel and discuss how legal battles over land rights have resulted in marginalization of the Bedouin and extreme disparities in sanitation access and diarrheal disease within a high-income country.

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CHAPTER II

Does Basic Sanitation Prevent Diarrhea? Contextualizing Recent Intervention Trials through a Historical Lens

2.1. Introduction

Three recent and rigorously conducted intervention trials found that basic improvements to household sanitation had no effect on diarrhea among young children in Kenya (WASH-Benefits Kenya [1]), Zimbabwe (Sanitation, Hygiene, Infant Nutrition Efficacy trial (SHINE) [2]), and Mozambique (Maputo Sanitation trial (MapSan) [3]). A similar sanitation intervention did lead to a 39% decrease in the prevalence of childhood diarrhea in Bangladesh, from 5.7% to 3.5% per week (WASH-Benefits Bangladesh [4]). None of these interventions had an impact on child growth two years after the intervention.

These studies successfully tested specific hypotheses: providing or improving latrines at the household level prevents diarrhea and improves child growth among children in that household. However, as is true for all intervention trials, generalizability of these results to other interventions and settings is limited [5–7]. For example, these household-level trials did not test the effect of sanitation at high community coverage, which has been shown to be an important predictor of intervention effectiveness [8–10]. Due to this question of generalizability, it is important to assess how these results fit into the history of sanitation evidence, while acknowledging that these studies reflect some of the most thorough examinations of sanitation and diarrhea ever conducted. In 1991, a literature review found that sanitation interventions reduced diarrhea by 36% on average, a number widely cited over the following years [11]. The most recent systematic review of sanitation interventions found an overall diarrheal reduction of 25% [8]. Thus, it is useful to consider how the results of recent trials fit into the entire body of evidence. Before these trials, there was an evidence-based consensus that sanitation interventions prevented diarrhea. These recent data points do not negate years of experience; however, their relative high quality raises important questions. Why do the results from three of four of these trials disagree with previous estimates? Which effects should inform interventions and policy decisions?

One common feature of previous meta-analyses is that the average effect of sanitation has been estimated across widely heterogeneous groups of studies. Summarizing studies that measured different forms of sanitation, in different settings, and with different contextual factors obfuscates details on what is required to affect health. Some of these nuances have been noted, such as the stronger effect of sewerage interventions and interventions achieving high community coverage [8], but still questions remain on additional study features that characterize successful sanitation interventions.

To help answer these questions, we conducted a review of the historical evidence of sanitation effects on diarrhea, as well as a series of meta-regression analyses on intervention studies. Specifically, this review has two aims: (1) describe the historical evidence on the relationship between sanitation access and diarrhea by reexamining the history of literature reviews on the topic, and (2) characterize heterogeneity across results from all existing intervention studies to place more recent trials within a historical context and to identify features of successful interventions.

2.2. Methods

In the first aim, we evaluated the history of literature reviews on the relationship between sanitation and diarrhea from the earliest review identified (1983) to the latest (2018). We describe the group of studies included in each review, its conclusions and limitations, and conclude with a summary of how the prevailing estimate of the overall effect of sanitation on diarrhea has changed over the last three decades. For the second aim, we conducted sub-group meta-regression analyses on intervention studies identified in the most recent systematic review [8]. We categorized this list of studies on several factors, such as intervention type and coverage level, and included these as study-level covariates to demonstrate their effects on intervention success [12]. We describe features that may modify intervention effectiveness to a greater degree than previous reviews and identify the types of studies that drive historical expectations of an effect of sanitation on diarrhea.

2.2.1. History of Literature Reviews

To review past literature on sanitation and diarrheal disease, we conducted a systematic search to identify all literature reviews on the topic. We searched

PubMed and Embase using the following search terms: (diarrhea OR diarrhoea) AND (sanitation OR latrine OR sewer*). Each search term was restricted to the title, abstract, or author keywords. The search results from each database were restricted to reviews. We assessed the titles and abstracts from each search to identify reviews on the relationship between sanitation and diarrhea. Articles were excluded if they were specific to a country, region, population (e.g., HIV patients), or infectious agent (e.g., cholera). Reviews were not included if they descriptively discussed the issue of diarrhea and/or sanitation without adding new information on their relationship. The references of each identified review were checked for additional reviews that were not identified by our initial search. Each identified review was assessed in detail to determine the types of studies reviewed and its conclusions. In addition, the cited references of each review were evaluated to better assess the strength of evidence included and to uncover caveats to its conclusions. We present a short description of our findings for each review in chronological order, along with a brief history of how the consensus estimate for the overall effect of sanitation on diarrhea changed over time (Table 2.1).

2.2.2. Sub-Group Meta-Regression Analyses

Heterogeneity among sanitation intervention trials was characterized through meta-regression analyses of studies identified in the latest systematic review (Table 2.2). Eligible studies were those that tested sanitation interventions, including randomized, quasi-randomized, and non-randomized controlled trials; case-control and cohort studies if they were related to a specific intervention; time-series studies; and cross-sectional household survey studies if they used an appropriate causal matching method (e.g., propensity score matching) [8]. The authors searched Pubmed, Embase, Scopus, and Cochrane Library for eligible studies between 1970 and 2016 and followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We created a list of studies reviewed by Wolf et al. (2018) from the article text and Supplementary Materials. The WASH-Benefits Bangladesh, WASH-Benefits Kenya, and SHINE trials were added to the final study list. The results of the MapSan trial were not included, as these were not publicly available during the completion of this review.

The text of each article was reviewed to understand the type of sanitation intervention, study design, and results of each study. After this initial review, we constructed a set of variables to extract from each study. The variables we selected were trial features that varied between studies and that could potentially modify the effect of sanitation interventions on diarrhea. The list of variables included (1) sanitation intervention type, (2) use of the community-led total sanitation (CLTS) model, (3) sanitation access initiation (i.e., whether the household made the decision to obtain sanitation or if the intervention was provided to households by the study team directly), and (4) community coverage.

We classified studies into categories of intervention type defined by four indicator variables: (i) latrine interventions, (ii) interventions that included more than sanitation (e.g., social capital or water quality interventions; but excluding hygiene promotion), (iii) sewerage interventions, and (iv) no intervention, which comprised causal analyses of national surveys or Demographic and Health Surveys (DHS).

Studies that employed CLTS methods were indicated with a binary variable. Two final indicator variables were created for household-initiated sanitation access and study-initiated interventions. Household-initiated sanitation access included interventions that promoted sanitation construction and offered free or subsidized facilities if the household was motivated to receive them without direct study contact, along with studies on existing sanitation access, such as from DHS and national survey data. Study-initiated intervention studies were those in which households were asked to participate with the knowledge that a sanitation facility would be constructed by the study team upon agreement. Sewerage studies were excluded from both groups.

Community coverage with the intervention was extracted from studies that measured total sanitation coverage among intervention communities after the intervention occurred, per the definition of sanitation used in the study. Coverage was extracted only if it was measured for the entire community. For example, if a study randomly selected a subset of households to receive the intervention and only reported that 100% of the sampled households received the intervention, no coverage value would be extracted. After extracting reported community sanitation coverage, this value was used to create additional indicator variables for various coverage thresholds. Wolf et al. showed a stronger effect of interventions that achieved ≥75% coverage compared to those that reached <75% of households, but this was the only threshold reported. To observe the range of potential threshold values, we created three indicator variables for coverage at or above 60%, 75%, and 90%, respectively. We chose 60% because it resulted in an even number of studies above and below the threshold while lower thresholds led to few studies below the threshold. We chose 90% in order to observe the effects of very high coverage. Because sewerage interventions inherently reach 100% coverage, we repeated the sub-group analyses by coverage after excluding sewerage studies to determine the impact of coverage on toilet or latrine-based interventions specifically.

Each of these indicator variables represent a potential modifier of the effect of sanitation interventions on diarrhea. To test the impact of these effect modifiers, meta-regression models were constructed to estimate a pooled effect of interventions within each category. For example, an average effect was calculated for the subset of studies that had a value of 1 for the sewerage indicator variable. These sub-group estimates were compared to each other and to the overall effect of all studies to assess which variables modify intervention effectiveness. But because average effects can conceal important differences between studies, we described the characteristics of individual studies in Table 2.2 and constructed a forest plot to show their individual effects. We further describe key differences within some sub-groups in the closing discussion.

Study estimates and 95% confidence intervals (CIs) were extracted from the Supplementary Materials of Wolf et al. (2018) to take advantage of the conversion to risk ratios (RRs) the authors already completed. Meta-regression models were fit using the *metafor* package in R [12]. For all models, study estimates were weighted by their inverse standard error, which was calculated as

$$1/[(RR_{upper} - RR)/1.96],$$

where RR_{upper} is the upper RR of the 95% CI and 1.96 represents the critical z-score at the 95% confidence level.. Models were fit with random effects in order to match the methods used by Wolf et al.

2.3. Results

The systematic search for literature reviews on sanitation and diarrhea resulted in 199 possible reviews. After reviewing the titles and abstracts of these 199 results, 164 articles were deemed not relevant to the relationship between sanitation and diarrhea or were focused on a specific population. Of the remaining 35 articles, 10 literature reviews were identified on the relationship between sanitation and diarrhea [8,11,15,25,26,40,41,47,54,72]. Fifteen articles were excluded because they did not review primary literature; these articles or book chapters described the topic of sanitation and/or diarrhea broadly and cited other reviews if numeric estimates were present. Another eight articles were excluded because they did not specifically review sanitation and diarrhea together, e.g., if the outcome of interest was enteric dysfunction or the review focused on clinical care. One likely relevant study was excluded because it was published in Portuguese [91]. One eligible review found only one study [55]; we did not include this article in our analysis as it is not clear why the authors did not find a number of eligible studies that were found in earlier reviews [92]. After searching the references of the 10 identified literature reviews, three additional reviews were identified resulting in a total of 13 literature reviews on the relationship between sanitation and diarrhea [13,14,18].

2.3.1. History of Literature Reviews

2.3.1.1. Blum and Feachem, 1983

The first literature review we describe was published by Blum and Feachem in 1983. This review referenced one earlier review conducted by a scientific working group of the WHO in 1979, but the text available online omits the relevant pages describing evidence on health outcomes [93]. Blum and Feachem identified studies that assessed the relationship between water supply and/or excreta disposal facilities on any health outcome. Health outcomes included diarrhea and/or dysentery, enteric infection, nutritional status, eye or skin infection, and mortality. But instead of summarizing the health effects of these studies, Blum and Feachem focused on the severe methodological limitations they found in the literature. The authors found that even though most studies claimed to show health improvements, methodological problems raised “serious doubts as to the validity of their conclusions” [13].

The authors focused on 44 published studies of water supply or sanitation and diarrhea or diarrhea-related infection. They found seven primary methodological problems: lack of adequate control (having no control group or a non-comparable control), the one to one comparison (comparing only one exposed village to another unexposed village), confounding variables, health indicator recall (they considered any recall period over 48 h as a methodological problem), health indicator definition, failure to analyze by age, and failure to record facility usage. Fourteen of the 44 studies measured diarrhea as an outcome and included sanitation in their exposure assessment, including three studies conducted in the United States in the 1950s and 1960s. The review does not separate studies that measured sanitation in isolation from those that studied water supply and sanitation together.

Additional study details are not described here, as the focus of the review by Blum and Feachem was on the severe limitations of these studies. Only one study out of the 44 was found to have none of the seven major methodology problems: a cross-sectional analysis of sanitation and helminth infections in Tennessee [94]. The remaining 43 studies had at least one severe limitation, and most had multiple methodology problems. The most common problem was the lack of an "explicit effort" to control for important confounding variables [13]. Only seven studies were found to have adequate control for confounding variables, including three on sanitation and diarrhea [95–97]. Overall, the authors concluded that there was little confidence on the health effects of sanitation, despite the number of studies conducted on the topic. They emphasized the importance of understanding the health benefits of improved water and sanitation access by the end of the International Drinking Water Supply and Sanitation Decade (1981–1990).

2.3.1.2. Esrey and Habicht, 1986

The first of two reviews led by Esrey aimed to evaluate the effect of water and sanitation interventions on diarrheal disease, infection, nutritional status, and childhood mortality from studies conducted after 1950. The authors note the importance of randomly allocating WASH (water, sanitation, and hygiene) interventions but did not limit the review to randomized trials or even intervention studies. The review included any study that compared two or more groups with different water and/or sanitation conditions. Eight studies were identified that examined water and sanitation together without estimating their individual effects. Six of the eight found that sanitation was associated with improved health, although three were described as having serious study flaws.

Twenty-three other studies measured the association between sanitation access and disease, infection, or mortality. Eighteen of these studies reported an association between sanitation and improved health. Three of the 18 studies that found health improvements were described as having significant methodological flaws. Of the remaining 15 studies, only three could be confirmed as including the relationship between diarrheal morbidity and sanitation [98–100]; most of the remaining studies measured infant mortality. Only one of the three studies on diarrheal morbidity and sanitation found an association when comparing families with a pit toilet to families with no toilet [98], although none of the three studies controlled for any potential confounders. Esrey and Habicht concluded that sanitation interventions could help improve child health, especially when interventions are tailored to the local community, but did not attempt to estimate an overall effect of sanitation.

2.3.1.3. Esrey et al. 1991

In 1991, Esrey and colleagues published another review that estimated the effect of drinking water and sanitation interventions on diarrheal disease, nutritional status, mortality, and infection with *Ascaris lumbricoides*, *Dracunculus medinensis*, hookworm, *Schistosoma haematobium*, *S. mansoni*, and trachoma. For diarrheal disease, the authors only searched for studies published after the previous review. An estimate of the overall reduction of diarrheal disease morbidity associated with sanitation improvements was calculated as the median value for all studies considered, rather than the mean.

Thirty studies on sanitation were included in this review, but the total number of studies that measured diarrhea as the outcome is not stated. Eleven studies that measured diarrhea and had an extractable effect estimate were included in an overall estimate for sanitation and diarrhea. The median reduction in diarrheal morbidity from these 11 studies was 22%. Five of these 11 studies were described as “rigorous” studies, indicating that they did not have serious methodological flaws. A separate overall estimate was calculated for “rigorous” studies. The five studies had a median diarrhea reduction of 36%. However, the studies considered “rigorous” or “flawed” were not defined in this review. Knowing which studies were included in the overall estimate is necessary to understand its limitations. Since the authors chose to summarize the studies with the median effect, which provides less information than a pooled estimate with a confidence interval, it is especially important to see the range of effects and determine how well the median represents this range. As we will discuss, the importance of these limitations is underlined by the persistence of this estimate over the next two decades.

2.3.1.4. Fewtrell et al. 2005

Acknowledging the earlier reviews by Esrey and colleagues, Fewtrell et al. sought to create the first systematic review of water, sanitation, and hygiene interventions and their relative effects on diarrheal disease. This review was the first to focus specifically on studies assessing interventions and the first to model an overall effect through meta-regression. The authors searched for studies published before 26 June 2003 and used Esrey et al.'s previous reviews to identify additional eligible studies.

Only four studies were deemed eligible from the authors' search. Two of these presented data that could be used to conduct a meta-analysis [16,17]. The other two studies are not identified in the text or any supplemental material. One study by Azurin and Alvero was an evaluation of communal latrines combined with improved water supply and their effect on the risk of cholera for people of any age (RR = 0.32, 95% CI 0.24, 0.42). The authors did not measure diarrhea as an outcome and did not control for potential confounders. Fewtrell and colleagues graded the study as "poor quality". The other study by Daniels et al. measured the impact of a government latrine construction program on diarrheal disease using a hospital-based case-control study design (OR = 0.76, 95% CI 0.58, 1.01). Neither of these studies is a strong examination of the effect of sanitation on diarrhea. Despite identifying only two eligible studies, one of "poor" quality that measured cholera as its outcome, the authors calculated a pooled estimate and reported a 32% overall reduction in diarrhea associated with sanitation interventions (RR = 0.68, 95% CI 0.53, 0.87).

2.3.1.5. Waddington et al. 2009

Waddington, Fewtrell, and colleagues updated their previous systematic review [15] a few years after its release and searched for studies published after 26 June 2003. Eligible studies were RCTs or those employing quasi-experimental designs, including matched analysis of survey data. Risk ratios, rate ratios, odds ratios, and prevalence ratios were recorded and used to calculate an overall estimate without conversion to a single ratio type. The authors instead ignore the potential overestimation of odds ratios and report the estimate from each study as its "effect size (ES)". An overall ES was calculated as a weighted mean of each study's ES without conversion.

The authors identified six studies that estimated the impact of sanitation on diarrheal disease [19–21,23,24]. None of these studies appeared in the previous review. One of the six studies was a large national survey of "poor" quality that used a diarrheal recall period greater than two weeks [22]. One study was deemed poor because the comparability between treatment groups was not clear in the text [23]. Another study that measured the effect of a large national latrine project in

Honduras was described as poor because it used a one-month recall period and had unclear comparability between treatment groups [24]. The three high quality studies included a propensity score matched analysis of DHS data in Nepal [19] and two non-randomized studies of urban sewerage [20,21]. Using all six identified studies, the authors estimated an overall reduction in diarrheal disease of 37% (ES = 0.63, 95% CI 0.43, 0.93). This estimate was similar to their previous estimate (32%) and nearly identical to the 1991 estimate from Esrey et al. (36%), although the limitations of each already have been described.

2.3.1.6. Clasen et al. 2010

In 2010, Clasen et al. published a new systematic review on sanitation interventions and diarrhea [25]. Their review described the four reviews that preceded it and aimed to apply a more rigorous search strategy using the methodology defined by the Cochrane Collaboration for systematic reviews. Clasen et al. included randomized, quasi-randomized, and non-randomized controlled trials of sanitation interventions. The authors found 13 studies that met these criteria, including seven studies published in Chinese [101–107], five published in English [49,58,108–110], and one in French [48]. There was no overlap in the studies identified in Fewtrell et al. (2005) or Waddington et al. (2009) and this review. Clasen et al. thoroughly described the types of interventions studied, potential sources of bias, and other characteristics of each study. The types of interventions varied, including unimproved latrines, shared latrines, improved latrines, biogas reactors, septic tanks, and relocating toilets “away from water sources”. Some information could not be extracted from many studies, especially from the eight non-English studies, such as baseline sanitation access, the type of water supply, intervention coverage, and risk of bias.

All of the identified studies were non-randomized controlled trials. Eleven out of the thirteen studies reviewed found that the sanitation intervention reduced diarrhea, but confidence intervals were only calculated for two studies [58,104]. Clasen et al. did not calculate confidence intervals for the other eleven studies due to insufficient number of intervention clusters (i.e., villages, communities, or schools). RRs for the effect of the intervention on diarrhea ranged from 0.20 [102] to 1.03 [108]. The authors concluded that sanitation interventions are effective at preventing diarrhea, but they did not estimate an overall effect of sanitation due to limited evidence. Clasen et al. described substantial heterogeneity in the existing literature that limited study comparability. They also note that only five of the 13 studies studied interventions of sanitation alone, without drinking water or other improvements, and that these five studies included limited geography. Four took place in China, and one was conducted in the United States [109].

Of the five English studies, two were later included in the most recent systematic review by Wolf et al. (2018) [49,58], along with the French language study [48]. Of the three English studies excluded from the most recent review, one was likely excluded due to measuring diarrhea from healthcare records [110] and one may have been excluded for its use of a borehole latrine intervention [109]. The other may have been excluded due to the authors reporting issues in implementation leading to low compliance [108]. None of the Chinese studies were included in the most recent review.

Clasen et al. (2010) conducted the most methodologically rigorous review between, at least, 1983 and 2014. However, they did not extract confidence intervals from 11 studies that included 1–3 clusters (e.g., villages) per intervention arm, instead only extracting point estimates. This decision limited the review's analysis of intervention effects and impedes a clear understanding of each study's results.

2.3.1.7. Norman et al. 2010

Another review published in 2010 focused on the effects of sewerage on diarrhea [26]. This review was not limited to interventions, including both observational and intervention studies. Norman et al. found 25 studies that met these criteria, including six cohort studies, four case-control studies, one non-randomized intervention study, and fourteen cross-sectional studies. Fourteen of the 25 studies were conducted in Brazil, three took place in Mexico, and the remaining came from Nicaragua, Honduras, Peru, the United States, Iran, Syria, Saudi Arabia, and Australia. Diarrhea was the primary outcome of 17 studies, with the remaining eight studies measuring enteric infection [20–22,24,27–39]. Norman et al. estimated a pooled effect of sanitation on all outcomes from 25 studies (RR = 0.70, 95% CI 0.61, 0.79) and on diarrhea from 17 studies (RR = 0.70, 95% CI 0.58, 0.85). The authors noted that confounding is a potential issue with the inclusion of mostly observational studies. However, they showed that the effect of sewerage was even stronger for studies that included multivariate regression (RR = 0.64, 95% CI

0.53, 0.77) compared to studies that did not (RR = 0.78, 95% CI 0.63, 0.97). They also conducted a sensitivity analysis to show that even if there were a very strong unidentified confounder (RR with disease = 0.65; RR with exposure = 2.00), the RR for sewerage on diarrhea would still be 0.78. The types of studies included in this review were varied, and the study designs are not ideal for measuring a causal relationship. But the relationship between sewerage and diarrhea was consistent across all subgroup and sensitivity analyses, providing additional strength to the conclusions of Norman et al. that sewerage is associated with reduced diarrhea.

2.3.1.8. Cairncross et al. 2010

Cairncross et al. sought to provide more information to the "consensus view on the impacts of health of improved water quality, water quantity and sanitation" established by Esrey and colleagues in their earlier reviews [11,14]. The authors again searched for intervention studies that measured the effect of sanitation on diarrheal disease. The search included articles published any time before April 2007. Cairncross et al. initially identified seven quasi-randomized intervention studies, but all of these included water quality interventions that precluded estimating the effect of sanitation alone. An additional search was conducted to identify more studies, and that search resulted in four new studies that were conducted in China and published in Chinese [101,103–105]. These were included in the seven Chinese studies reviewed by Clasen et al. (2010). The four studies estimated diarrheal reductions of 63%, 51%, 20%, and 8%, but confidence intervals were not shown. Finally, the scope of the review was widened to include before and after studies of sanitation, and one additional study was identified [34]. In this last study, diarrheal disease was measured before and after expansion of sewerage in Salvador, Brazil. The study found positive effects, as diarrheal disease was reduced citywide by 21% (95% CI 19%–26%) and by 43% (95% CI 39%–46%) in high-risk areas.

The authors decided not to calculate an overall estimate of sanitation interventions on diarrheal disease due to high variability in the types of interventions tested in the five studies. However, the authors still noted the "striking consistency between the reductions found in various reviews of 36% [11], 32% [15], 20%–51% (the four Chinese studies) and 22%–43% [34]".

But there are several issues with this statement. The comparison excluded two of the four Chinese studies, which had reductions of 8% and 63%. This was likely to show the median effect of the four studies, but still obscures the wide range of estimated values and assumes the true value lies somewhere in the middle. In addition, the authors failed to note that one estimate is a single before and after analysis of urban sewerage [34] and that another estimate comes from only two studies [15]. The authors concluded that "there is not enough evidence to justify a departure from the prevailing consensus, published nearly two decades ago and widely cited with approval since then, that sanitation reduces diarrhoea risk by about 36%".

Thus, our understanding of the impact of sanitation on diarrhea did not improve much between 1983 and 2010. A median estimate from 1991, based on five studies that we could not identify, remained the consensus. Other reviews were conducted, but these also were based on few studies and were indiscriminate on study quality and sanitation definition.

2.3.1.9. Heijnen et al. 2014

A review published in 2014 by Heijnen et al. examined how shared sanitation compares to individual household latrines in preventing a number of health outcomes, including diarrhea, helminth infections, enteric fevers, other fecal-oral diseases, trachoma, and adverse maternal or birth outcomes [41]. Eligible studies compared these outcomes between individuals using shared sanitation and those using household latrines, with no limits placed on study design. Nine studies were found that compared this effect on diarrheal disease, and six had effect estimates available for inclusion in a meta-analysis. All six studies employed a case-control design and enrolled cases from health clinics, emergency departments, or hospital records. One of these studies was a multi-country analysis and contributed seven effect estimates to the meta-analysis, resulting in 12 total estimates ref. [45]. Compared to individual household latrines, shared sanitation was associated with a 44% average increase in the odds of diarrhea (OR = 1.44, 95% CI 1.18, 1.76). The types of shared sanitation included both communal latrines and household latrines that were shared between two or more families. Heijnen et al. completed a thorough review of the existing literature, but their analysis highlights the limited evidence on shared sanitation. The authors note that the underlying evidence allows for only weak causal inference and call for more research to determine if circumstances exist in which shared sanitation can be an effective tool for improving health.

2.3.1.10. Wolf et al. 2014

The number of articles on sanitation interventions grew rapidly after 2010. In 2013, the WHO convened a meeting of experts to agree on protocols for new systematic reviews on WASH interventions and health outcomes. As a result of that meeting, Wolf et al. estimated the impact of drinking water and sanitation interventions on diarrheal disease [47]. This review included RCTs, quasi-randomized and non-randomized control trials with baseline data, case-control and cohort studies when they were related to an intervention, time-series studies, and observational studies using specific matching methods (e.g., propensity score matching). Studies were excluded if they were targeted to institutions, such as schools and workplaces, if they were conducted in non-representative populations, such as HIV patients, or if they had very low compliance (<20%). The search was limited to interventions occurring in low- and middle-income countries and studies published between 1970 and May 2013.

Eleven eligible sanitation studies were identified. Overall, sanitation interventions reduced diarrhea risk by 28% (RR = 0.72, 95% CI 0.59, 0.88). The effects of sewerage interventions were found to be substantially higher at 69% and 63%, but there were only two sewerage studies to compare [21,22]. The authors noted that this sample size is extremely limited and that the estimates should be treated with caution. Studies that measured a non-sewerage sanitation intervention led to a more modest, but significant, reduction in diarrheal disease of 16% (RR = 0.84, 95% CI 0.77, 0.91). This marks the first review that distinguished between the large effects of sewerage from the effects of other sanitation interventions, although all studies were included in the overall estimate of a 28% reduction.

2.3.1.11. Jung et al. 2017

The role of neighborhood level sanitation in preventing diarrhea was reviewed by Jung et al. in 2017 [54]. Importantly, this review was not on neighborhood level coverage with household sanitation. Instead, the authors defined neighborhood sanitation as “the removal of exposed fecal matter or wastewater from the neighborhood”. This definition includes studies on sewerage or drainage access, the elimination of open defecation, or observations of neighborhood fecal contamination (e.g., presence of wastewater or fecal matter). In contrast, household sanitation was defined as “the presence of any type of household sanitation facility within the subject’s residence, or the disposal method of child feces”. The authors did not exclude any study designs. Studies were excluded if they reported an aggregate measure of neighborhood or household sanitation but did not control for sanitation at the other level, e.g., studies on sewerage that did not separate the effect of improved household sanitation. Thirteen studies were excluded for this reason, but the authors did not identify the excluded studies.

Twenty-two eligible studies were identified, including five studies on neighborhood sanitation, 16 studies on household sanitation, and one study that included estimates of both. Only five of these studies have been included in other reviews that we describe in this article [17,21,49,55,58]. The remaining studies all employed a case-control or cross-sectional design. Six studies on neighborhood sanitation found that the exposure was associated with 44% lower odds of diarrhea on average (OR = 0.56, 95% CI 0.40, 0.79), including significant effects in five of the six studies. The exposures of interest included "no sewage spillage around house", "no observable feces in the neighborhood yard", "no open sewage ditch nearby", "no rubbish and fecal material lying around, blocked open drains around home and nearby streets", "no wastewater in street", and "communities with simplified sewerage and surface drainage vs. surface drainage only". Household level sanitation was associated with 36% lower odds of diarrhea on average (OR = 0.64, 95% CI 0.55, 0.75). This association was nearly identical when divided between studies on the presence of sanitation and studies on children's usage of sanitation facilities.

Jung et al. concluded that both neighborhood and household level sanitation is associated with decreased diarrhea, and that the magnitudes of each association are comparable. The article is limited in including almost exclusively observational research, but a review of observational evidence is a useful addition to other reviews that focus on intervention studies alone. The review is unable to assess whether the underlying associations were due to confounding, which is particularly important as the authors reported that eight studies did not adjust for likely confounders. The neighborhood level analysis is further limited by the definition of neighborhood sanitation. The exposures used in these studies, mostly relying on visual inspection for fecal matter, were not strong indicators of neighborhood sanitation. In addition, the strongest effect in this group was associated with a sewerage intervention and is not comparable to the other neighborhood level studies [21].

2.3.1.12. Freeman et al. 2017

Freeman and colleagues conducted another WHO commissioned review of sanitation interventions and their effect on diarrheal disease, as well as helminth infections, trachoma, schistosomiasis, and nutritional status. Freeman and colleagues also aimed to update other reviews on soil-transmitted helminth (STH) infection, trachoma, schistosomiasis, and nutritional status. It is not clearly stated which eligibility requirements were employed for the review of diarrheal disease. Freeman et al. included most of the same studies as Wolf et al.; however, this review also included some non-intervention studies and school-based interventions that would have been ineligible in Wolf et al. 2014.

A total of 33 eligible studies were identified, and 27 were included in a meta-analysis. Of these 27 studies, 11 were included in Wolf et al. 2014. Three were studies on sewerage. Effect estimates were converted to ORs for meta-analysis. Using all 27 studies, Freeman et al. estimated that sanitation improvements reduce diarrhea by an average of 12% (OR = 0.88, 95% CI 0.83, 0.92). This estimate demonstrates a considerably smaller effect compared to previous reviews. However, this overall estimate included non-interventions that were previously ineligible, such as hospital-based case-control studies [84–86]. Sixteen studies were found that measured the effect of a sanitation intervention [21,22,24,49,50,55,73–82]. In a subanalysis, these intervention studies were found to reduce diarrheal disease by 23% (OR = 0.77, 95% CI 0.66, 0.91). This estimate includes three studies (with five total effect estimates) on school-based sanitation interventions [75,76,82].

Freeman et al. also described the impact of sanitation coverage on intervention effectiveness. Of the 16 intervention studies, nine were described as reporting on latrine coverage or latrine use. Three of those nine studies found that the intervention reduced diarrhea. However, two of these studies were actually sewerage interventions [21,34]. The other study found that the intervention did not lead to increased latrine coverage, suggesting that latrine access did not reduce diarrhea. Instead, the authors attributed the reduction in diarrhea to drinking water and handwashing behavior [73] Thus, only sewerage studies appeared to have effects at high coverage.

Freeman et al. estimated an overall diarrheal reduction of 12%, but this estimate included a number of studies with non-generalizable designs, such as hospital-based case-control studies. Their estimate for the 16 intervention studies, a 23% reduction, is more in line with the results of previous reviews. However, this estimate still includes school-based interventions, which likely follow unique transmission dynamics, and three sewerage studies that possibly drive the observed overall effect of sanitation interventions.

2.3.1.13. Wolf et al. 2018

While Freeman et al. focused specifically on sanitation and included several infection-related outcomes, Wolf et al. again reviewed the evidence on the impact of drinking water and sanitation interventions on diarrheal disease, with a new review on the effect of handwashing interventions [8]. This review was a direct update to Wolf et al. 2014 and used the same protocol. Unlike in Freeman et al. 2017, only intervention-based studies were eligible for inclusion. Observational study designs were allowed if they were conducted around an intervention. The search for new studies included articles published between January 2012 and February 2016, bringing the total range of studies to between 1970 and 2016.

In this update, eight new eligible sanitation studies were identified and added to the 11 studies from Wolf et al. 2014 [19,21,22,24,48–53,55,58,77–79,87–90]. Four estimates were extracted from Capuno et al. 2011, resulting in 22 total effect estimates from 19 studies. Using all 22 estimates, the overall effect of sanitation was estimated as a 25% reduction in diarrhea risk (RR = 0.75, 95% CI 0.63, 0.88). The authors again estimated the effects of sewerage interventions and non-sewerage studies separately. Two studies compared a sewerage intervention to a baseline of unimproved sanitation (RR = 0.60, 95% CI 0.39, 0.92) and two studies compared sewerage interventions to a baseline of improved sanitation (RR = 0.71, 95% CI 0.47, 1.07). Using 15 studies, the overall effect of non-sewerage interventions was a 16% reduction in diarrheal disease (RR = 0.84, 95% CI 0.73, 0.98), which is the same point estimate as found in Wolf et al. 2014.

The authors examined the impact of several study factors on the effect of sanitation interventions by including covariates in meta-regression models. The effect of sanitation interventions was not different when baseline access was unimproved sanitation versus open defecation. Access to an improved vs. unimproved water source, provision of a latrine vs. promotion only, survey data analyses, and follow-up time were found to be not associated with the effect of sanitation interventions on diarrheal disease. Combined interventions were found to be more successful than single interventions (RR = 0.59, 95% CI 0.43, 0.81). The authors then examined the effects of community coverage on intervention effectiveness. Twelve studies had available data on coverage after the intervention. Interventions that led to sanitation coverage of <75% reduced diarrhea by an average of 24% (RR = 0.76, 95% CI = 0.51, 1.13), and those that led to coverage >75% reduced diarrhea by 45% (RR = 0.55, 95% CI 0.34, 0.91).

Wolf and colleagues have provided the most thorough understanding of the evidence on sanitation and diarrheal disease to date. Unlike earlier reviews, the authors spend considerable attention to the unique study characteristics that lead to successful sanitation interventions. The review highlights that sewerage studies and studies that achieve high levels of sanitation coverage are much more successful at preventing diarrheal disease. However, the authors do not acknowledge that only five studies achieved coverage greater than 75%, and three of these were sewerage studies. The other two studies included a water, sanitation, and hygiene intervention [49] and a national sanitation intervention deemed poor quality in Waddington et al. 2009 [24]. Both found that the intervention resulted in lower diarrhea, but evidence on the effect of non-sewerage sanitation interventions at high coverage is limited. In addition, studies testing an intervention that included more than only sanitation reduced diarrheal disease 41% more (95% CI 19%, 57%) than studies with sanitation alone. This suggests that non-sanitation components of combined interventions could be driving the overall estimate of the effectiveness of sanitation, but these effects were not separated by Wolf et al. For their primary result, the authors chose to report the overall effect of sanitation interventions using all eligible studies: a 25% reduction.

2.3.1.14. Updates to the Overall Effect of Sanitation over Time

For many of these historical reviews, estimating an overall effect of sanitation on diarrhea was the primary aim. It is useful to have a simple number to use in advocating for sanitation interventions, but the resulting effect estimates have obscured the fact that different sanitation interventions lead to different results. Realistic expectations for the success of WASH interventions should be based on more nuanced estimates for that type of intervention and, when possible, for specific contextual and study factors that apply to the intervention in question.

Despite the limitations of using one overall estimate to describe the effect of sanitation interventions, our understanding of these effects has clearly grown over time. The estimate from Esrey et al. in 1991 was “widely cited” and carried through to 2014 despite its limited conclusiveness as a median effect from only five unidentified studies. Two additional reviews were conducted but found very little new information [15,40]. One other review found six new studies, but graded half of these as poor quality [18]. The three high-quality studies included a national survey and two non-randomized sewerage studies. The overall effect estimate calculated in this review was very similar to the prevailing consensus, with an average reduction in diarrhea of 37%. Three reviews on specific components of sanitation found protective effects of sewerage, household latrines compared to shared sanitation, and neighborhood sanitation [26,41,54].

In 2014, Wolf and colleagues conducted a thorough review after a sizable growth in the number of available studies. Eleven intervention studies were reviewed and found an average reduction in diarrheal disease of 28% (RR = 0.72, 95% CI 0.59, 0.88). For the first time, the authors noted that two sewerage studies led to drastically larger reductions in diarrheal disease (69% and 63%) compared to the 16% reduction seen in non-sewerage studies (RR = 0.84, 95% CI 0.77 0.91). With a broader set of eligibility criteria, Freeman et al. updated the overall estimate of sanitation studies. They found a 12% average reduction in diarrheal disease (OR = 0.88, 95% CI 0.83, 0.92). When limited to only intervention studies, the authors found a more comparable reduction of 23% (OR = 0.77, 95% CI 0.66, 0.91).

Currently, the best estimate for the overall effect of sanitation comes from the latest review: Wolf et al. 2018. In this review, the authors found a similar reduction of diarrheal disease from sanitation interventions of 25% (RR = 0.75, 95% CI 0.63, 0.88). However, the authors again noted that the effect among non-sewerage studies was a more modest 16% (RR = 0.84, 95% CI 0.73, 0.98). Sewerage provision is still largely considered infeasible or unaffordable to achieve universal access to sanitation [26,111,112]. For more common interventions, mostly latrines, a 16% reduction can be considered the best estimate for the effect of sanitation on diarrhea. However, as the second aim of our review shows, the best average effect still covers a wide range of sanitation interventions and requires a deeper examination to reveal the nuanced effects of sanitation on diarrhea.

2.3.2. Sub-Group Meta-Regression Analyses

2.3.2.1. Recreating the Overall Estimate from Wolf et al. 2018

Our analysis of the *History of Literature Reviews* demonstrates that sanitation interventions are too varied to describe with a single average estimate. We estimated an average effect across heterogeneous studies, but only to confirm that our meta-regression models were similar to those fit by Wolf et al. We aimed to recreate their overall estimate of a 25% average reduction (RR = 0.75, 95% CI 0.63, 0.88). While excluding the WASH-Benefits and SHINE trial results, we estimated an overall effect that is slightly attenuated (RR = 0.77, 95% CI 0.64, 0.90). We refit this model with fixed effects and various random effects estimators to test if the observed difference was due to model specifications, but the result was consistent across estimators. The disagreement could be due to the use of different weighting calculations, statistical programs, or subtle changes between the RRs reported in the text of Wolf et al. (2018) and those used in final analyses. Despite the small discrepancy, we assumed that our model results are similar to those that would be obtained directly by Wolf et al. using the same criteria. Due to the high degree of heterogeneity within these studies, the effect we estimated is not meaningful and only serves to test our methods against the original source.

2.3.2.2. Intervention Type

Average estimates and confidence intervals for the effect of sanitation were calculated for the four intervention types described above: (i) latrine interventions, (ii) interventions that included more than sanitation alone (e.g., social capital or water quality interventions; but excluding hygiene promotion), (iii) sewerage interventions, and (iv) no intervention (causal analyses of national DHS surveys (Table 2.3).

Including WASH-Benefits Kenya and Bangladesh, eight latrine interventions had no statistically significant average effect on diarrhea risk (RR = 0.90, 95% CI 0.67, 1.12; [1,4,24,55,78,79,87,90]; Figure 2.1). The pooled effect of the six non-WASH-Benefits latrine interventions was about the same (RR = 0.90, 95% CI 0.61, 1.18). There were five studies that intervened on more than sanitation alone, including the SHINE trial. These studies reduced diarrhea by an average of 26% (RR = 0.73, 95% CI 0.46, 1.02). This result was almost identical when excluding the results from the SHINE trial. Nine causal estimates from national survey or DHS analyses resulted in an average diarrheal reduction of 15% (RR = 0.85, 95% CI 0.66, 1.04). Lastly, three interventions on sewerage access led to a 64% average reduction in diarrhea (RR = 0.36, 95% 0.00, 0.76). But one study with a small confidence interval around a large effect magnitude (RR = 0.31, 95% CI 0.28, 0.34) appears to drive this estimate [21]. The other two sewerage interventions found no effect on diarrhea, but their interpretations are limited by sample size (23 children in the intervention group of Pradhan et al. 2002 [22]) and study design (Klasen et al.

estimated the effect of sewerage by comparing a water plus sewerage intervention to a water intervention, in two geographic regions that had opposite results [77]).

The studies that found the largest effect of sanitation on diarrhea were on sewerage (64% reduction), followed by those on interventions including more than sanitation alone (26%), and national survey or DHS data (15%) (Figure 2.1). Latrine interventions, whether considering the most recent trial results or not, did not have a significant effect on diarrhea on average. The studies included in each of these groups are similar on intervention type, but they still are characterized by a high degree of heterogeneity. Our pooled estimates help demonstrate broad differences between interventions and the severe limitations of estimating a single effect of sanitation, but these estimates still average effects across widely different contexts and require a more nuanced understanding of the studies described.

2.3.2.3. Community-Led Total Sanitation

Four studies employed a CLTS model, each employing an RCT design [78,79,87,90]. These studies did not impact the risk of diarrhea in children on average (RR = 0.91, 95% CI 0.55, 1.28; Table 2.3).

2.3.2.4. Initiation of Sanitation Access

Studies on sanitation access that was household-initiated had a stronger effect on diarrhea compared to study-initiated interventions (Table 2.3). Fifteen estimates from 12 studies on household--initiated sanitation led to a 16% average reduction in diarrhea (RR = 0.84, 95% CI 0.68, 1.00), while four study-initiated interventions did not have an effect on diarrhea on average (RR = 0.95, 95% CI 0.67, 1.24 [1,2,4,55]).

2.3.2.5. Community Coverage

Thirteen studies in this analysis had available sanitation coverage data. The WASH-Benefits and SHINE trials intervened in a subset of houses within a community and did not measure total coverage. Studies with higher community coverage had a larger effect on diarrhea using cutoffs of 60%, 75%, and 90% (Table 2.4; Figure 2.2). Studies that did not reach 60% coverage found no average effect (5 studies; RR = 0.85, 95% CI 0.54, 1.17). Studies that reached coverage over 60% reduced diarrhea by an average of 35% (8 studies; RR = 0.65, 95% CI 0.42, 0.88). Studies with a final community coverage under 75% had no significant effect overall (8 studies; RR = 0.88, 95% CI 0.61, 1.15), while studies with coverage over 75% reduced diarrhea by 44% on average (5 studies; RR = 0.56, 95% CI 0.30, 0.82). Lastly, studies that did not achieve 90% coverage again did not significantly impact diarrhea on average (9 studies; RR = 0.88, 95% CI 0.62, 1.14), but the strongest effect was found among studies that achieved coverage over 90%, with a 45% reduction in diarrhea risk (4 studies; RR = 0.55, 95% CI 0.28, 0.82). Only one study reached coverage above 75% but below 90% (85% coverage [77]), resulting in nearly identical results using the two cutoffs.

After excluding three sewerage interventions, only two remaining studies resulted in coverage over 75% [24,49]. Both studies also reached coverage over 90%, so models for the two cutoff values are the same. Eight studies that did not achieve

75% coverage again had no effect on diarrhea, while the two studies that achieved coverage at or above 90% resulted in a non-significant 28% average reduction in diarrhea (RR = 0.72, 95% CI 0.37, 1.07). The effect of coverage among non-sewerage interventions nearly disappeared at the 60% threshold. Five studies that did not reach 60% coverage led to a non-significant 15% average reduction (RR = 0.85, 95% CI 0.54, 1.17). The remaining five studies that did reach coverage over 60% resulted in a non-significant effect that was almost of the same magnitude (RR = 0.80, 95% CI 0.51, 1.08).

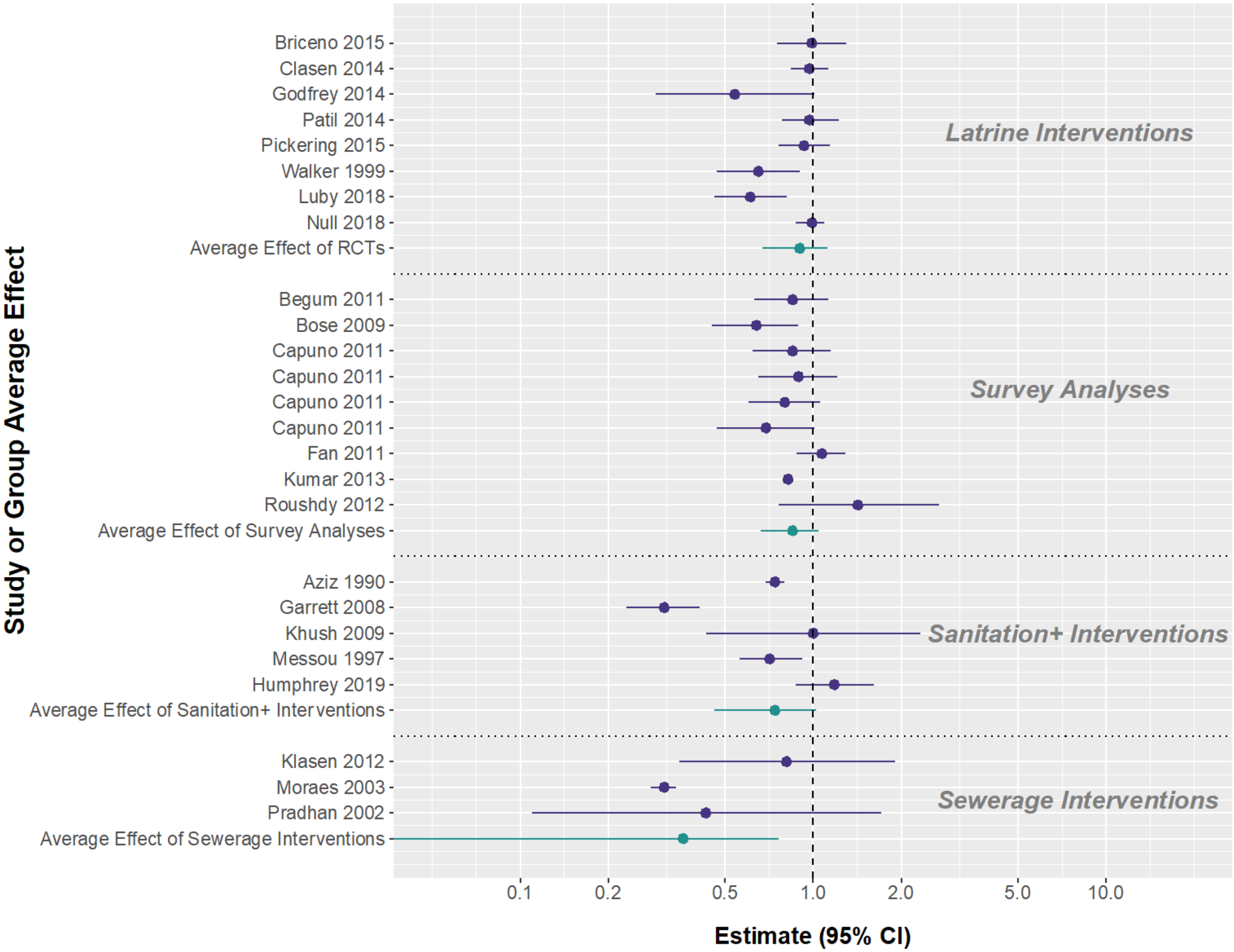

Figure 2.1. Forest plot of sanitation studies included in meta-analysis by intervention type. Effect estimate and 95% confidence intervals are plotted for each study (purple) and for the pooled estimate of four intervention types (green). The four intervention types are latrine interventions (Latrine Interventions), no intervention: causal analyses of national survey data (Survey Analyses), interventions that improved more than sanitation alone (Sanitation + Interventions), and interventions on sewerage access (Sewerage Interventions).

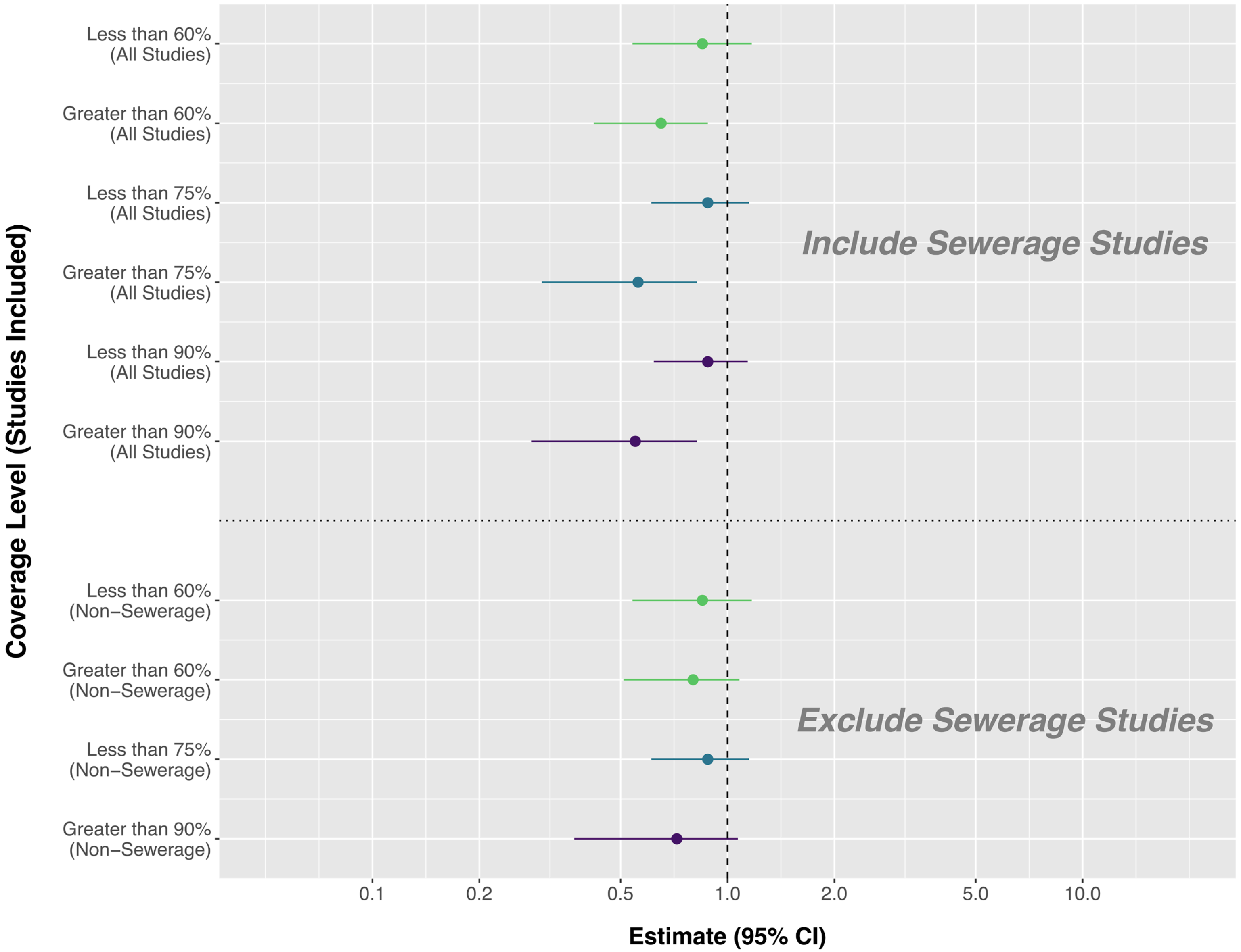

Figure 2.2. Forest plot of sanitation studies by community coverage with the intervention for (top) all studies and (bottom) non-sewerage studies. Effect estimate and 95% confidence intervals are plotted for three coverage thresholds: 60% (green), 75% (blue), and 90% (purple). No non-sewerage studies reached coverage between 75% and 90%.

2.4. Discussion

Recently conducted sanitation intervention trials had no impact on child growth and most had no effect on diarrhea. The lack of an effect on diarrhea was particularly surprising against a backdrop of historical evidence that seemingly suggested sanitation is highly effective in its prevention. The WASH-Benefits trials aimed to assess whether combined interventions were “more effective than single interventions”, highlighting the prevailing expectation that water, sanitation, and hygiene alone would have an effect on diarrhea [113]. In the first part of this review, we showed that the null effects of sanitation on diarrhea found in Kenya, Zimbabwe, and Mozambique should not be as surprising as they first seemed (Figure 2.1). Instead, the strong effect of sanitation found in WASH-Benefits Bangladesh is the more surprising result. We found that prior estimates that sanitation reduces diarrhea by 23%–37% were based on averages that inappropriately included poorly conducted studies and combined widely different types of interventions, including latrines, sewerage, and those that included more than sanitation alone. These overall estimates have obfuscated the true effects of different sanitation interventions by masking the high degree of heterogeneity among studies. Some of the review authors attempted to describe these nuances, but the study features considered were limited and the authors still chose to report an overall effect of all study types as the primary result.

In the second part of this review, we more thoroughly disentangled this nuance in the current body of evidence and showed the limitations of summarizing the literature with a pooled estimate. We found that sewerage interventions drove the protective effect of sanitation estimated in the most recent systematic review, as did interventions that included more than sanitation improvements alone. Latrine interventions did not affect diarrhea on average. But a high degree of heterogeneity remains within each of these groups. Although most latrine interventions did not show an impact, three latrine-based interventions did reduce diarrhea. Even between the two recently conducted trials, discordant results were found. Sanitation had no effect on diarrhea in WASH-Benefits Kenya, while there was a 39% relative reduction found in WASH-Benefits Bangladesh.

Along with these large differences by intervention type, we found that two additional study features are important in predicting the effectiveness of a sanitation intervention: intervention coverage and household motivation to achieve sanitation access. Previous estimates have shown that high coverage with a sanitation intervention leads to larger reductions in diarrhea, but we found that this difference is substantially diminished after excluding sewerage interventions (Figure 2.2). For latrine interventions, reaching very high coverage (over 90%) may improve effectiveness, but this is only supported by one combined WASH intervention and one latrine estimate that is likely confounded [24,49]. Nonetheless, some prior observational studies do support a herd protection effect. There is stronger evidence within this review to support the increased effectiveness of sanitation when the household, rather than a study team, initiates access. Below, we discuss in detail the influence of: (1) sewerage decoupled from other types of sanitation interventions (2) latrine interventions, highlighting further heterogeneity and the limitations of average effect estimates, (3) intervention coverage and the potential for herd protection, and (4) the source of sanitation initiation, which might partially explain why many sanitation interventions fail to prevent diarrhea.

2.4.1. Sewerage Interventions

We found that the overall effect of sanitation was strongly influenced by sewerage interventions, which led to a 64% average reduction in diarrhea. However, these results are mostly based on one study in Brazil [21]. The other two sewerage studies do not provide clear information on how the intervention affected diarrhea. In Nicaragua, a complex social investment project did not find an effect [22]. However, not all households in the intervention area were connected to the sewer system, and only 23 children under six were measured in the intervention group. Two of those children were reported to have diarrhea. Another intervention expanded sewerage and piped water access in mountain and coastal regions of Yemen [77]. The control group for the sanitation intervention comprised households that received only the piped water intervention, limiting the reliability of the sewerage estimate. The effect of sanitation on diarrhea was negative in the coastal region and positive in the mountain region, but only the coastal effect was included in the latest systematic review. Thus, the effect of sewerage found in our meta-analysis was largely based on one study in Brazil, which greatly limits the generalizability of its conclusion. Additional support for an effect of sewerage on diarrhea was found in a sewerage-specific literature review, which found a 30% overall reduction in diarrhea associated with sewer access [26]. Sustainability and affordability are important limitations in expanding sewerage to achieve universal sanitation access. But its strong association with health, although from limited evidence, supports considering the example of sewerage when designing and implementing new sanitation interventions.

If connections are accessible, sewerage can reach universal coverage in the population and achieve the potential health benefits of herd protection. Functional sewerage infrastructure completely separates users from fecal waste without risk of exposure during pit emptying or from flies around pit latrines. These benefits underscore the utility of sewerage in reaching the Joint Monitoring Programme's (JMP) definition of safely managed sanitation: the use of improved sanitation facilities that are not shared with other households and where excreta are safely disposed of in situ or transported and treated off-site [114]. However, sewerage may not be the best sanitation option in all settings, such as very rural communities or water-stressed regions. For these communities, new strategies are needed to safely manage sanitation without the same resource requirements.

2.4.2. Latrine Interventions

Eight latrine interventions (without additional intervention components) had no average effect on diarrhea. Three latrine interventions, including WASH-Benefits Bangladesh, did demonstrate an effect on diarrhea. One was a large-scale national sanitation campaign conducted in Honduras in the 1990s that measured diarrhea occurrence in all age groups using a one-month recall [24]. The intervention involved provision of World Bank funds to local municipalities, which were asked to choose a social investment project to have implemented. The options included items such as a new school, drinking water projects, or latrine construction, and were provided by local contractors. It is not clear if municipalities could only choose one project or if they could choose multiple projects within their budget. Waddington et al. rated this study as poor quality due to its use of a one-month recall period for diarrhea and because the “comparability of treatment and control groups [was] not sufficiently clear”. Control households in this analysis were “pipeline controls” that had not received the intervention, but would soon receive the intervention. The manuscript text does not explain if controls for the latrine analysis were those who had elected to receive the latrine project, or those that had not yet selected their project. The authors showed that the control group was more rural, less educated, had poorer access to baseline sanitation, and had less income compared to intervention communities. Walker et al. conducted multivariate regression to account for some of these differences, but that estimate was not used in the latest systematic review. Compared to households with a “washable toilet”, households with no access to sanitation facilities had higher odds of diarrhea (Odds Ratio (OR) = 2.68, $p = 0.05$). The definition of a washable toilet was not provided, but we believe it indicates a porcelain toilet as opposed to an in-ground latrine. Access to a project latrine was not associated with additional decreases in diarrhea compared to the “washable toilet”. It is unclear why this group was chosen as the reference group, but its selection precludes understanding how project latrines affected diarrhea compared to no sanitation when adjusting for confounders. Wolf et al. were restrained to report the unadjusted OR with a hand-calculated confidence interval. Due to the differences between intervention and control communities described above, this unadjusted effect estimate has a high risk of bias due to confounding and must be considered with caution.

The other successful latrine intervention was another large-scale national WASH campaign that employed a CLTS-like intervention in rural Mozambique (the One Million Initiative) [90]. The study outcome was self-reported water-related disease for any member of the household, and it was reported with six-month and two-week recall periods. It is not clear how the two recall periods were used in the analysis or which resulted in the estimate reported in the latest review. The control group comprised communities that were located in districts where the intervention was implemented, but control villages themselves were not included in the intervention. Wolf et al. were able to obtain additional information from the authors, but the quantitative effect of the intervention on diarrhea is not shown in the manuscript text and is not readily available in the literature. Thus, we are unable to determine if there are potential limitations to the validity or generalizability of the estimated effect, as we did for the intervention in Honduras. One potential design limitation is the use of pipeline controls, which does not guarantee equal covariates on average, as does randomization. The likely confounding described above in Honduras emphasizes the potential for bias introduced by this method [24].

Both of these trials tested the effectiveness of a national sanitation campaign, whereas the WASH-Benefits trials tested a latrine intervention at the household level. The two arms of this trial found different results, possibly demonstrating that sanitation can prevent diarrhea under the right circumstances. In Bangladesh, a 39% relative reduction in diarrhea might have been achieved in part due to the local population's receptiveness to behavior change, which possibly lead to higher compliance than in Kenya. That the other effective latrine intervention with trustworthy results was a large national campaign supports the need for intensive efforts to successfully achieve community buy-in and behavior change. Another potential explanation for the discordant results of WASH-Benefits is the lower diarrheal prevalence found in Bangladesh during the study period, which was around 5% in the control group compared to 27% in Kenya [1,4]. Household-level sanitation interventions likely do not effectively prevent transmission from the outside environment. If a setting with lower diarrheal prevalence is also characterized by lower environmental transmission, household-level sanitation may have better success in further reducing diarrhea. A final explanation for these mixed results is that unmeasurable contextual differences between settings, interventions, implementations, and studies critically influence effectiveness. The importance of context further underscores the difficulties in describing the multifaceted research body on sanitation with a single average effect.

The majority of studies ever conducted on sanitation interventions found that latrine interventions do not prevent diarrhea. In light of our review of historical average estimates, this result is not as surprising as it first appears. Instead, the more unique result is that WASH-Benefits Bangladesh, using a latrine intervention, without attempting to achieve high coverage, and employing a study-initiated access model, led to a successful reduction in the prevalence of diarrhea.

2.4.3. Intervention Coverage

Wolf et al. (2018) previously showed that interventions that reach 75% coverage or more in the intended population have a stronger effect on diarrhea than studies reaching lower coverage. We found that excluding sewerage interventions, which inherently reach very high coverage and also have the strongest effects on diarrhea, diminishes this effect. After excluding sewerage interventions, we found no difference between studies above or below 60% coverage. Non-sewerage interventions that achieved very high coverage (above 90%) did have a marginally significant effect on diarrhea (we were unable to use a separate 75% threshold for non-sewerage studies because no study reached coverage between 75% and 90%). But only two studies reached 90% coverage, including a complete water, sanitation, and hygiene intervention conducted in Bangladesh [49] and the likely confounded analysis of a social investment campaign in Honduras [24]. These two studies do not provide strong evidence for the effect of reaching high coverage with a latrine intervention on diarrhea. Observational research has found that community sanitation coverage is related to child height and stunting in Mali and Ecuador

[9,10]. One observational study from national survey data in India found that community coverage was related to diarrhea [115], but another observational study found no effect of community coverage on diarrhea in Mali [9]. Additional theoretical model analysis has suggested that all benefits from sanitation interventions come from the indirect effects due to community coverage [116]. There is not enough evidence to know if these latrine interventions could have had a stronger effect at higher coverage, but it is possible that not approaching herd protection was a factor in the observed results of the WASH-Benefits Kenya and SHINE trials.

2.4.4. Study-Initiated vs. Household-Initiated Access

WASH-Benefits Kenya, WASH-Benefits Bangladesh, SHINE, and another trial in India [55] employed a sanitation intervention that was study-initiated, meaning that households were asked to participate in the study with the knowledge that a latrine would be constructed if they agreed. Of these, only WASH-Benefits Bangladesh led to a decrease in diarrhea. In contrast, 12 studies on sanitation access that was household-initiated, meaning members of the household made the decision to obtain sanitation without direct study contact, led to a statistically significant 16% overall reduction in diarrhea. These studies include community interventions in which a sanitation-promoting environment was created, as well as analyses of DHS or national survey data in which households had existing access to sanitation. These results suggest that there is an important difference between households that are self-motivated to obtain sanitation access and households that obtain sanitation access only because it was offered directly.

Survey analyses measure the effect of existing sanitation access on diarrhea, which could be confounded by other household characteristics, such as wealth or education. However, the studies included here all employed some causal-based analysis, such as propensity score matching. These methods reduced the likelihood of bias from analyzing observational data, but it is possible that residual confounding remained. Fundamental differences between self-motivated sanitation access and access provided in randomized trials also could explain why observational studies on sanitation often show an association with diarrhea, while we have found that most RCTs of sanitation interventions do not impact diarrhea. Some of these differences could be due to residual confounding, as pointed out in an observational re-analysis of the WASH-Benefits control groups that found latrine access was associated with improved child growth but credited the association to confounding [117]. Another potential explanation is effect modification due to different levels of motivation to obtain sanitation access. This effect modification could explain why our analysis found a stronger effect for survey analyses and household-initiated access compared to RCTs and study-initiated access, and could be related to the difficulties of achieving behavior change in intervention trials. This modification also could explain the association between baseline latrine access and child growth in the WASH-Benefits re-analysis. Rather than discounting the results of many observational studies, further work should be done to understand the different motivational drivers identified by these studies.

2.5. Conclusions

The results of this review support the message that new forms of transformative WASH must be developed in order to improve health [6]. We found that sanitation interventions have rarely been shown to prevent diarrhea, but this fact was obscured by numerous average estimates that were not limited to studies on sanitation alone and that failed to adequately consider which forms of sanitation were driving results. Given the complexity of any environmental intervention, context matters in its success or failure, and average effects across studies mask those crucial contextual differences. We showed the implications of this for diarrhea. These results likely apply to other health outcomes, including child growth and sub-clinical infection, but an understanding of outcome-specific nuances warrants more attention. We also did not assess the importance of sanitation access for social outcomes potentially related to sanitation, such as dignity, safety, and educational attainment. These factors alone may justify the implementation of basic sanitation improvements in some settings.

This review uncovers important limitations in the existing literature on sanitation and diarrhea, along with opportunities to improve interventions. Transformative sanitation, and WASH more broadly, is not yet defined; but the important study features identified here, including complete separation of waste from the home, high community coverage, and sufficient household motivation, are likely prerequisite characteristics of future transformative sanitation interventions. More work is needed to understand how each of the factors we described is specifically related to transmission and disease. Future research on transformative sanitation must depend on rigorously conducted trials, as well as thorough and carefully controlled observational studies on prevalent sanitation behaviors. Some of this work will require rigorous inquiry from social science disciplines to better understand the interplay between social and environmental contexts. With strengthened foundational research, new forms of transformative sanitation interventions can be developed to prevent diarrhea and achieve better health worldwide.

Table 2.1. History of Literature Reviews on Sanitation and Diarrhea.

Review	Scope of Review	Eligibility Criteria	Number of Studies on Sanitation and Diarrhea	Number of Studies Included in Overall Estimate	Overall Estimate of the Effect of Sanitation on Diarrhea	Conclusions	Limitations
Blum and Feachem, 1983 [13]	Studies on water supply and/or excreta disposal facilities and any health outcome	None	14 studies on excreta disposal (alone or with water supply) and diarrhea	N/A	N/A	Severe methodological limitations in almost all studies raises doubts to the validity of their conclusions	Water supply and excreta disposal were not assessed separately; a health recall period greater than 48 h was considered a methodology problem
Esrey and Habicht, 1986 [14]	Effect of water and sanitation interventions on diarrhea, infection, nutritional status, and childhood mortality	Any study that compared groups with different water and/or sanitation conditions	8 studies on sanitation and water together; 23 other studies on sanitation and some health outcome; 3 studies confirmed to measure sanitation and diarrhea morbidity	N/A	N/A	Sanitation interventions can improve child health, especially when tailored to local communities	Did not clearly distinguish between studies on different health outcomes
Esrey et al. 1991 [11]	Effect of drinking water and sanitation interventions on diarrhea, nutritional status, mortality, and various infections	Studies published after the previous review (1986)	30 studies on sanitation alone; 18 "rigorous" studies did not have severe flaws	11 for all studies; 5 for "rigorous" studies (studies not identified in text)	Median effect of all 11 studies: 22% reduction Median effect of 5 "rigorous" studies: 36% reduction	Despite the poor quality of existing studies, it can be inferred that sanitation improvements lead to better health	The authors do not indicate which studies were "rigorous", and it is not clear from reviewing the references separately Using the median value hides the potentially wide range of effects, especially for only 5 "rigorous" studies
Fewtrell et al. 2005 [15]	First systematic review of water, sanitation, and hygiene interventions on diarrhea	Studies that measured the effect of a water, sanitation, hygiene, or combined intervention	4 eligible studies	2 [16,17]	32% reduction (RR = 0.68 ,95% CI 0.53, 0.87)	Sanitation interventions are effective at reducing diarrhea, although the evidence is limited Few differences between these results and those from Esrey et al. 1991	The two studies used to calculate an overall effect were (i) a sanitation and water supply intervention and their effects on cholera and (ii) a hospital-based case-control study; the two studies not used for the estimate are not identified in the study

Waddington et al. 2009 [18]	Update to Fewtrell et al. 2005	RCTs or studies employing quasi-experimental designs, including matched analysis of survey data	6 studies; 3 high-quality studies	6 studies [19–24]	37% reduction (Effect Size (ES) = 0.63, 95% CI 0.43, 0.93)	Sanitation interventions are highly effective at reducing diarrhea, but few studies have been conducted on the topic	The overall "effect estimate" did not attempt to convert effects from different studies to the same ratio (e.g., RR or OR) The estimate included 3 studies of "poor quality"; the three high quality studies included an analysis of DHS data and two studies on sewerage
Clasen et al. 2010 [25]	Systematic review of sanitation interventions on diarrhea using the Cochrane methodology	Randomized, quasi-randomized, or non-randomized controlled trials	13 studies; 7 in Chinese, 5 in English, 1 in French	N/A	N/A	The heterogeneity in type and quality of sanitation interventions is high and does not allow for estimation of an overall effect; but there is evidence that sanitation interventions prevent diarrhea	Confidence intervals were not extracted or reported from 11 studies due to insufficient number of clusters (e.g., a one-to-one village comparison); only point estimates were reported for those studies
Norman et al. 2010 [26]	Systematic review on the effects of sewerage access on diarrhea and enteric infection	Any trial, cohort, case-control, or cross-sectional study	25 total studies; 17 on diarrhea	17 studies on diarrhea [20–22,24,27–39]	30% reduction (RR = 0.70, 95% CI 0.58, 0.85)	Sewerage is associated with reduced diarrhea in all age groups; confounding from observational studies is a potential issue, but sensitivity analyses suggest it is not a major limitation	Depends on observational studies, but the authors attempted to accounted for potential confounding through sensitivity analyses
Cairncross et al. 2010 [40]	The impact of improved water quality, water quantity, and sanitation on diarrhea	First, intervention studies on sanitation and diarrhea After only four studies in Chinese were found, the criteria expanded to include before and after studies	4 quasi-randomized studies published in Chinese and 1 before and after sewerage study	N/A	No overall effect was calculated	The authors noted the consistency of diarrhea reductions found in various reviews of 36% (Esrey et al. 1991), 32% (Fewtrell et al. 2005), 20-51% (the median values of the four Chinese studies), and 22–43% (the one sewerage study, Barreto et al. 2007), although there is a serious lack of evidence on the subject There is not enough evidence to support moving past the consensus estimate of 36% (Esrey et al. 1991)	In finding no studies that fit their original criteria, the authors showed the striking lack of evidence on sanitation and diarrhea The comparison between different effect estimates did not note that one estimate was a single sewerage study, another came from only two studies (Fewtrell et al. 2005), and results from the four Chinese studies ranged from 8 to 63%

Heijnen et al. 2014 [41]	Comparison of shared sanitation vs. household latrine access on diarrhea, infection, enteric fevers, adverse birth outcomes, trachoma, and other fecal-oral diseases	Any study that compared health outcomes of populations using shared sanitation to those using household latrines	9 studies with diarrhea as an outcome measure	12 estimates from 6 studies [27,42–46]	44% increased odds of diarrhea when sharing sanitation (OR = 1.44, 95% CI 1.18, 1.76)	Those relying on shared sanitation are at higher risk of diarrhea and other health outcomes, although the conclusions are limited by methodological concerns, not knowing actual latrine use, and study heterogeneity	The authors acknowledged several limitations of their results, including that none of the studies followed an experimental design and not all studies adjusted for confounding. All studies were hospital- or clinic-based case-control studies
Wolf et al. 2014 [47]	Impact of drinking water and sanitation interventions on diarrhea	RCTs, quasi-randomized and non-randomized control trials, observational studies when based on an intervention, time-series studies, and survey data with causal matching methods	11 total studies; 2 sewerage studies	11 for total effect; 9 for non-sewerage effect [17,19,21,22,24,48–53]	All studies: 28% reduction (RR = 0.72, 95% CI 0.59, 0.88) Non-Sewerage Studies: 16% reduction (RR = 0.84, 95% CI 0.77 0.91)	Sanitation interventions can lead to reductions in diarrhea Sewerage interventions might be even more effective, but there were only two studies to reach a conclusion on	Mostly limited by underlying evidence Sewerage was the only factor assessed as a potential effect modifier
Jung et al. 2017 [54]	Comparison of neighborhood and household sanitation access on diarrheal morbidity	Studies that estimated the association between sanitation at the household and/or neighborhood level and diarrhea; excluded studies that aggregated the effect of both levels	22 total studies; 5 neighborhood level; 16 household level; 1 study measured both levels	6 for the effect of neighborhood level; 17 for household level [17,21,38,39,49,55–71]	Neighborhood Sanitation: 44% reduction (OR = 0.56, 95% CI 0.40, 0.79) Household Sanitation: 36% reduction (OR = 0.64, 95% CI 0.55, 0.75)	Both neighborhood level and household level sanitation are independently, and nearly equally, associated with reduced risk of diarrhea	This article reviewed mostly observational research, making it harder to compare to other reviews Neighborhood sanitation effect was partially driven by one sewerage study [21]; the other neighborhood exposures relied on visual inspection for fecal matter or wastewater and were not strong indicators of sanitation

Freeman et al. 2017 [72]	The effect of sanitation interventions on diarrhea, various infections, and nutritional status	Excluded cross-sectional studies with no matching methods	33 studies	27 total studies; 16 intervention studies [17,19,21,22,24,48–52,55,73–86] (could not find a citation for a study listed as Castro 2015)	All studies: 12% reduction (OR = 0.88, 95% CI 0.83, 0.92) Intervention studies: 23% reduction (OR = 0.77, 95% CI 0.66, 0.91)	The studies reviewed were of low quality, but the results indicate an association between sanitation and diarrhea	Studies that went into the total estimate used a wider variety of study designs, including three hospital-based case-control studies Other studies in the overall estimates were unique, including five effect estimates from school-based sanitation interventions
Wolf et al. 2018 [8]	Update to Wolf et al. 2014	RCTs, quasi-randomized and non-randomized control trials, observational studies when based on an intervention, time-series studies, and survey data with causal matching methods	19 studies	22 effect estimates from 19 total studies; 15 non-sewerage studies; 4 sewerage studies [19,21,22,24,48–53,55,58,77–79,87–90]	All studies: 25% reduction (RR = 0.75, 95% CI 0.6, 0.88) Non-sewerage studies: 16% reduction (RR = 0.84, 95% CI 0.73, 0.98) Studies with > = 75% coverage: 45% reduction (RR = 0.55, 95% CI 0.34, 0.91) Studies with < 75% coverage: 24% reduction (RR = 0.76, 95% CI 0.51, 1.13)	Evidence is limited, but sanitation is associated with reduced diarrhea, especially with high coverage	Only one coverage threshold was assessed The authors did not note that three out of five studies that achieved coverage over 75% are sewerage studies and may not reflect latrine coverage Studies testing an intervention that included more than sanitation alone were not separated from the overall estimate

Table 2.2. Studies on Sanitation Interventions Included in Sub-Group Meta-Regression Analyses.

	Type of Intervention	Community Coverage	Community-Led Total Sanitation Model	Initiation of Sanitation Access	Effect on Diarrhea (95% CI)	Notes
Aziz et al. 1990 [49]	Interventions of More Than Sanitation Alone	92%	No	NA or Unknown	0.74 (0.69, 0.80)	A community-based water, sanitation, and hygiene intervention was associated with a 26% reduction in diarrheal disease in children in rural Bangladesh.
Begum et al. 2011 [50]	None: Analysis of National Survey or DHS Data	Not Reported	No	Household	0.85 (0.63, 1.13)	An analysis of DHS and MICS survey data from Bangladesh found that sanitation had no association with diarrheal disease in children, unless the household had both improved sanitation and improved water access.
Bose 2009 [19]	None: Analysis of National Survey or DHS Data	Not Reported	No	Household	0.64 (0.45, 0.89)	A propensity score matched analysis of DHS data from 2006 in Nepal found that access to improved sanitation reduced childhood diarrhea by 46%.
Briceño et al. 2015 [87]	Latrine Intervention	56%	Yes	Household	0.99 (0.75, 1.30)	An RCT of a large-scale, government-led, community-based handwashing and sanitation campaign found no effect on diarrhea in rural Tanzania. There was a statistically significant reduction in diarrhea only among communities that received both interventions, and only at the 10% confidence level.
Capuno et al. 2012 [51]	None: Analysis of National Survey or DHS Data	Not Reported	No	Household	1993: 0.85 (0.62, 1.15) 1998: 0.89 (0.65, 1.21) 2003: 0.80 (0.60, 1.06) 2008: 0.69 (0.45, 1.01)	A propensity score analysis of four years of DHS data in the Philippines reported a 10 percentage point decrease in diarrheal incidence associated with access to a flush toilet. But this value is the maximum difference in one of the four years (2008) from six different matching methods. It is not clear which matching method was recorded for Wolf et al. (2018).
Clasen et al. 2014 [55]	Latrine Intervention	38%	No	Study	0.97 (0.84, 1.13)	An RCT of a community-based sanitation promotion and construction intervention found no association with diarrheal disease in Odisha (Orissa), India.
Fan and Mahal 2011 [52]	None: Analysis of National Survey or DHS Data	Not Reported	No	Household	1.07 (0.88, 1.29)	Several matched analyses were conducted using 1994 survey data from India. Improved toilets were associated with an 8.5 percentage point reduction in diarrhea using exact matching, but no association was found using two other matching methods.
Garrett et al. 2008 [58]	Interventions of More Than Sanitation Alone	49%	No	Household	0.31 (0.23, 0.41)	A village-level RCT on a combined water access, water treatment, latrine promotion, and behavior change intervention found that living in an intervention village was associated with a 69% reduction in diarrhea. This is the value reported by Wolf et. al., but includes all of the interventions together. Latrine presence was independently associated with diarrhea (RR = 0.71, 95% CI 0.54, 0.92).

Godfrey et al. 2014 [90]	Latrine Intervention	62%	Yes	Household	0.54 (0.29, 1.01)	An RCT was implemented to test the effect of a large-scale government WASH program in Mozambique (The One Million Initiative). A water intervention, a CLTS intervention, and a water + CLTS intervention group were compared to controls. Controls were from districts where the government had begun implementing the intervention, but it was not implemented in the control communities themselves. The intervention was implemented in communities and in schools. The outcome, "self-reported water-related disease", was measured for all age groups. This outcome was measured with 6-month and 2-week recall in a household questionnaire. Water-related disease decreased in all groups, including the control group, and decreased the most in the CLTS-only group. Outcome rates are not presented in the available text; rates on only presented graphically. Wolf et al. received additional information from the author.
Khush and London 2009 [88]	Interventions of More Than Sanitation Alone	57%	No	Household	1.00 (0.43, 2.32)	A non-randomized CLTS and drinking water improvement campaign in India did not result in changes to diarrheal disease, but the prevalence of diarrhea in all groups was low (2%).
Klasen et al. 2012 [77]	Sewerage Intervention	85%	No	NA or Unknown	0.81 (0.35, 1.90)	The effect of extending access to piped water and sewerage in urban Yemen was estimated in two regions: a costal region and a mountain region. Diarrheal risk increased in the mountain region after the intervention, while risk decreased in the coastal region. The intervention is a drinking water and sewerage intervention, compared to a control group that only received the drinking water intervention.
Kumar and Vollmer 2012 [53]	None: Analysis of National Survey or DHS Data	Not Reported	No	Household	0.82 (0.79 0.85)	A propensity score analysis of survey data in India found no effect of improved sanitation among low- and middle-income households or for girls; there were effects for high income households and boys. The statistically significant effects are each 2–3 percentage point reductions.
Messou et al. 1997 [48]	Interventions of More Than Sanitation Alone	Not Reported	No	NA or Unknown	0.71 (0.56, 0.92)	Study was published in French. The intervention was a shared (public) double pit latrine, designed to be shared by 10 people, along with improved water supply, hygiene promotion, and oral hydration therapy (this information was extracted from Clasen et al. 2010)
Moraes et al. 2003 [21]	Sewerage Intervention	91%	No	NA or Unknown	0.31 (0.28, 0.34)	Neighborhoods that received government expanded sewerage access had almost 70% fewer episodes of diarrhea compared to control neighborhoods. Analysis was adjusted for child's age, gender and birth order, number of children aged < 5 years in the household, crowding, mother's education, monthly per capita income, exclusive use of kitchen, animals in the house, presence of a washstand, water usage and house floor material.
Patil et al. 2014 [78]	Latrine Intervention	41%	Yes	Household	0.97 (0.78, 1.22)	An RCT of a community-based sanitation intervention (TSC) in rural India found no health benefits, including diarrheal disease.
Pickering et al. 2015 [79]	Latrine Intervention	65%	Yes	Household	0.93 (0.76, 1.14)	An RCT of a community-based sanitation intervention (CLTS) in rural Mali found no differences between intervention and control villages on diarrheal disease. Intervention children were taller and less likely to be stunted.

Pradhan and Rawlings 2002 [22]	Sewerage Intervention	100%	No	NA or Unknown	0.43 (0.11, 1.71)	An analysis of a multi-faceted social investment project in Nicaragua found no association between sewerage promotion and diarrhea in children under six. Not all households in the intervention area were connected to the sewer network. There were only 23 children under six in the intervention group; two of the 23 were reported to have diarrhea. The effect estimate differs from that recorded in a review of sewerage studies, (Norman et al. 2010), where RR = 0.37 (95% CI 0.20, 0.66). It is not clear from either review or the article text why these numbers differ or which is a more accurate representation of the effect.
Roushdy et al. 2012 [89]	None: Analysis of National Survey or DHS Data	63%	No	Household	1.42 (0.76, 2.68)	An analysis of DHS data from 2008 in Egypt found that improved sanitation had a positive, non-significant association with diarrheal disease in children.
Walker et al. 1999 [24]	Latrine Intervention	90%	No	NA or Unknown	0.65 (0.47, 0.90)	This study evaluated a mostly World Bank/Honduran government funded social investment project in Honduras in the 1990s. Municipalities were offered projects from a “menu” of options. It is not clear if municipalities chose only one project or any projects that could be afforded by their allotted budget. The estimate reported by Wolf et al. is a crude estimate comparing intervention households to those who would soon receive the intervention (pipeline controls). In their executive summary, Walker et al. state that confounding is a large concern since pipeline controls were more rural, had worse sanitation, were less educated, and had lower incomes compared to intervention households. It is also not clear if the control group comprised municipalities that had chosen latrine projects or those that had not chosen their project(s). Full article text only found in Spanish; an executive summary is available in English.
Humphrey et al. 2019 [2]	Interventions of More Than Sanitation Alone	Not Reported	No	Study	1.18 (0.87, 1.61)	The Sanitation Hygiene Infant Nutrition Efficacy (SHINE) trial was a randomized controlled trial of a combined water, sanitation (construction of a ventilated improved pit latrine), and hygiene intervention. The intervention had no effect on diarrhea in children.
Luby et al. 2018 [4]	Latrine Intervention	Not Reported	No	Study	0.61 (0.46, 0.81)	The WASH-Benefits-Bangladesh trial was a randomized controlled trial that included a sanitation arm (compound level pour flush latrine construction). The sanitation intervention led to a reduction in diarrhea in children, from 5.7% to 3.5% using one-week recall.
Null et al. 2018 [1]	Latrine Intervention	Not Reported	No	Study	0.99 (0.88, 1.10)	The WASH-Benefits-Kenya trial was a randomized controlled trial that included a sanitation arm (compound level improved latrines). The intervention had no effect on diarrhea in children.

Table 2.3. Results of Subgroup Meta-Regression Models

Model	Risk Ratio (95% CI)	Number of Studies Included (Number of Estimates)
All Studies	0.80 (0.67, 0.92)	22 (25)
Intervention Type		
Latrine interventions	0.90 (0.67, 1.12)	8 (8)
Interventions on more than sanitation alone	0.74 (0.46, 1.02)	5 (5)
Sewerage interventions	0.36 (0.00, 0.76)	3 (3)
No Intervention: National survey or DHS analysis	0.85 (0.66, 1.04)	6 (9)
Other Sub-Groups		
Community-led total sanitation studies	0.91 (0.55, 1.28)	4 (4)
Household-initiated WASH access[a]	0.84 (0.68, 1.00)	12 (15)
Study-initiated interventions[b]	0.95 (0.67, 1.24)	4 (4)

[a] Includes studies in which the household chose to obtain access without direct contact from a study team, including some sanitation promotion interventions and cross-sectional surveys.

[b] Includes studies in which households were asked to participate knowing that a latrine would be constructed if they agreed.

Table 2.4. Effect Modification by Sanitation Coverage

Model	Risk Ratio (95% CI)	Number of Studies Included
All Studies		
Under 60% Coverage	0.85 (0.54, 1.17)	5
Over 60% Coverage	0.65 (0.42, 0.88)	8
Under 75% Coverage	0.88 (0.61, 1.15)	8
Over 75% Coverage	0.56 (0.30, 0.82)	5
Under 90% Coverage	0.88 (0.62, 1.14)	9
Over 90% Coverage	0.55 (0.28, 0.82)	4
Excluding Sewerage Intervention Studies		
Under 60% Coverage	0.85 (0.54, 1.17)	5
Over 60% Coverage	0.80 (0.51, 1.08)	5
Under 75% Coverage[a]	0.88 (0.61, 1.15)	8
Over 90% Coverage[a]	0.72 (0.37, 1.07)	2

[a] The two non-sewerage studies that reached 75% coverage also reached over 90% coverage, so the 75% threshold could not be assessed separately for these studies.

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CHAPTER III

Spatial Risk of Diarrheal Disease in Association with Household Proximity to Untreated Wastewater Used for Irrigation in the Mezquital Valley, Mexico

3.1. Introduction

The reuse of wastewater for agricultural irrigation has long provided farmers with a cheap, nutrient-rich, and dependable water source that amplifies crop yields. As climate change escalates water scarcity worldwide, wastewater reuse can help strengthen climate resiliency among farmers and improve the sustainability of global food systems. However, these benefits occur alongside considerable health risks to farmers, their families, and communities exposed to wastewater through reuse. Wastewater may be heavily contaminated with enteric pathogens from human and animal feces, antibiotic resistant bacteria, and, especially in urban wastewater, toxic or biologically disruptive chemicals and metals. Treatment before reuse can reduce contamination significantly, but most generated wastewater stays untreated, particularly in low- and middle-income countries [1,2].

Associations between wastewater reuse and adverse health outcomes have been documented in numerous studies [3–5]. Wastewater exposure has been consistently associated with enteric infections and diarrheal disease in children [4,6–8]. Yet, little information exists on the most important routes of exposure underlying these associations. Many studies have hypothesized that farmers who irrigate with wastewater are at the highest risk of infection [5]. However, three studies in Vietnam found that engaging in wastewater irrigation was not associated with diarrheal disease, potentially due to protective measures employed by farmers [9–11]. In addition, two studies in Pakistan and our previous study in Mexico found that farmers engaged in wastewater irrigation and their families do not face higher risk of diarrhea or enteric infection when compared to non-farming families within the same communities, while the entire community is at higher risk compared to other populations [4,7,12]. These results suggest that the association between wastewater reuse and poor health cannot be explained by direct exposure, and that unidentified indirect routes might be largely responsible for increased disease risk. These routes may include consumption of crops grown with wastewater, contact with domestic animals that interact with wastewater, flooding of land near canals, spread of fecal matter from canals by flies, and aerosolization of pathogens from wastewater [5,13–21].

We hypothesize that the relative importance of some indirect routes of exposure, such as aerosolization of pathogens or spread by flies and domestic animals, is related to a household's physical location within a reuse system. Households that are closer to wastewater canals have more exposure to the routes described above, and thus children living in these households are more likely to have enteric infections and resultant episodes of diarrheal disease compared to children in farther households. To test this hypothesis, and to better understand how communities are affected by wastewater reuse, we conducted a spatial analysis on diarrheal disease among children and its association with household proximity to wastewater canals in the Mezquital Valley, Mexico.

The Mezquital Valley is an agricultural area in the state of Hidalgo that receives most of the wastewater generated by Mexico City through two large underground tunnels. The wastewater is then transported throughout the Valley for use in agricultural irrigation via a system of aboveground, uncovered canals (Figure 3.1). This reuse system has operated since 1896 and presently irrigates around 900 square miles of cropland, making it the largest and one of the oldest such systems in the world [22]. By law, crops grown using wastewater irrigation are to be used only for animal fodder and are not for human consumption. However, we have learned through informal interviews with local farmers that crops grown with wastewater are consumed by humans through traditional food systems, local markets, and directly by farmers and their families. The Mezquital Valley was the site of previous studies that found associations between wastewater reuse and diarrheal disease and that influenced the development of the most recent update to the World Health Organization's (WHO) Guidelines for the Safe Use of Wastewater, Excreta, and Greywater [4,6,23,24]. The first large-scale wastewater treatment plant for the reuse system was completed in 2018 and has the capacity to treat about half of the incoming wastewater. However, the impact of the treatment plant on irrigation water quality and health is still unknown.

In 2016, we began a longitudinal study to assess changes in disease risk associated with the eventual operation of the new treatment plant. Here, we present a Bayesian spatial analysis using household survey data and global positioning system (GPS) location data for households and wastewater canals in the Mezquital Valley. We aimed to estimate the association between diarrheal disease in children and household proximity to wastewater canals in order to better understand how wastewater reuse affects community health.

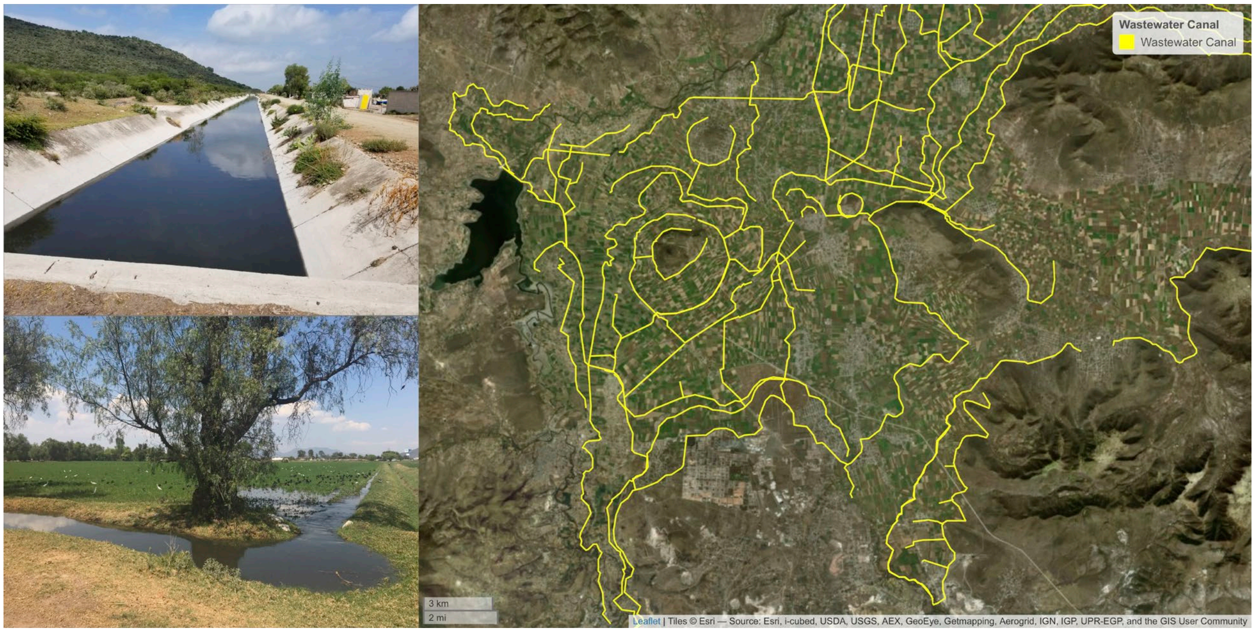

Figure 3.1. The Mexico City-Mezquital Valley wastewater reuse system: (top left) large, concrete protected segment of canal bringing wastewater from Mexico City, (bottom left) flood irrigation of cropland using temporary dug canals, (right) overview of wastewater canals throughout the Mezquital Valley, photographs used with permission from Jesse Contreras and Leon Espira, University of Michigan

3.2. Methods

3.2.1. Data Source

We conducted three rounds of surveys in the Mezquital Valley between November 2016 and November 2017 to longitudinally measure diarrheal prevalence in children. Participants were recruited and surveyed during in-home visits by trained interviewers. Households were sampled from four municipalities within the Mezquital Valley that are characterized by high levels of agricultural activity and wastewater reuse: Tula de Allende, Atitalaquia, Tetepango, and Tlahuelilpan. We sampled specific localities (towns) within those four municipalities that were known to have substantial agricultural activity based on our previous work in the area [4]. A large reservoir is located between one study locality and the wastewater canal system. Because participants in this locality do not face the same exposure to wastewater canals, they were excluded from this study before analysis. The remaining localities varied by degree of rurality, including peri-urban communities around the larger city of Tula as well as more rural communities, but each locality was located near wastewater canals and practiced agricultural activity.

Eligible households were those with at least one child under four years old in which a parent or legal guardian was present. We used the criterion of four years to ensure that children could be followed for one year while still under five, which is the age of interest for the diarrheal disease outcome, but respondents were asked to report on all children under five years old in the household. At the baseline visit, a parent or legal guardian in participating households completed a survey with questions related to sociodemographics, agricultural activities, household characteristics, hygiene practices, caregiving practices, and diarrhea in children. Follow-up surveys included questions that may change over time, including select sociodemographics and diarrhea. Diarrheal disease was recorded for children under five years old and defined as passing three or more loose stools in a day within the past seven days [25]. Survey data were recorded on cellphones using the Qualtrics offline application [26].

3.2.2. Spatial Data

At the baseline visit, interviewers logged the coordinates of each household with a handheld GPS recorder. For consistency, interviews logged coordinates while standing as close to the front door of the household as possible. Geographic Information Systems (GIS) shapefiles for the Mezquital Valley wastewater canal system were provided by the Instituto Nacional de Estadística y Geografía (INEGI) of Mexico. These files describe the entire canal system around our study communities, but exclude the smallest canals that bring water directly to fields. These excluded canals could be a missed source of exposure to households, but they are generally used only during irrigation periods and do not contain water at other times. The shortest distance between each household and any point along a wastewater canal was calculated in meters using ArcMaps and serves as the primary exposure variable [27]. This exposure variable did not consider how many canals were near a household. If households were equally close to more than one canal segment, the exposure variable remained a single value for the closest point to any canal.

3.2.3. Spatial Analysis

The outcome for our analysis, diarrheal disease within the past seven days, was recorded for each child under five in participating households at each survey round. The primary exposure, household distance to a canal, was treated as continuous in meters (m). For descriptive analyses, the prevalence of the outcome and proportions or mean values of potential covariates were calculated across quintiles of household distance. In addition, we applied a smoothing function to the prevalence of diarrhea over household distance among all observations to visualize the unadjusted relationship between diarrheal prevalence and distance (Figure 3.2). This analysis indicated that the relationship between distance from a canal and diarrheal prevalence was non-linear, with a sharp decline in prevalence over the first 250 m. The rate of decay slowed significantly after this point. We explored several model specifications to address this non-linearity, including a discontinuous changepoint model to potentially identify a single transition point at which diarrheal disease was no longer related to distance from a canal [28]. No such point was identified (results not shown). We found that the natural log of distance adequately represented the qualitative decay of diarrhea while maintaining model parsimony. Therefore, we used the natural log of distance as the primary exposure in our models.

We fit hierarchical logistic regression models via Markov chain Monte Carlo (MCMC) using RStan [29]. We estimated the change in odds associated with a single meter increase in household distance from a canal and used that model coefficient to estimate the change in odds associated with a 10-fold and 100-fold increase in distance. Random intercepts specific to each locality (town) were introduced to control for residual correlation in diarrheal prevalence within communities that is independent of the effects of distance to a canal. Due to the small number of households from certain communities, some spatially contiguous localities were combined into a single unit, resulting in nine locality groups. Random intercepts for each household also were included to account for repeated observations of households through multiple survey rounds.

Households that are close to each other, and thus share a similar distance exposure, also could share similar characteristics or exposures that are related to disease status. To account for this, we included a spatial autocorrelation model that considered potential spatial clustering of diarrheal disease risk unrelated to canal exposure. Specifically, we estimated the household random intercepts using a Gaussian process (GP) prior, specific to each locality group, that considered covariance with nearby households. The GP was a parameterized with a Matern covariance function that had a smoothness parameter fixed to 3/2, with the ratio of the length-scale (rate at which household correlation decays with distance) and signal amplitude learned from the data [30,31]. In order to ensure that the spatially structured random effect specifically captured clustering of risk between nearby households, the household GP was constrained using an informative prior for the length-scale parameter that favored a spatial correlation of 0.5 at a distance of 60 meters, declining to nearly zero at 400 meters [31]. Nevertheless, model results were robust to changes to the prior selected for length-scale. Final models were run with eight chains of 4,000 iterations each, and convergence was assessed using the Gelman-Rubin statistic [32].

3.2.4. Covariate Selection

Model covariates were potential confounders of the relationship between household distance from a canal and diarrheal disease (socioeconomic status (SES) and access to sewerage), a predictor of diarrheal disease that is not related to distance but may increase precision (ages of children), and study factors to control for potential heterogeneity between surveys (survey round and season). We selected these covariates based on prior knowledge of their causal relationships with diarrheal disease and our understanding of their possible association with household proximity to wastewater canals in the Mezquital Valley. After assessing the relationship between each covariate and the primary outcome and exposure variables through bivariate descriptive analyses, we decided to include each variable as covariates in our final model.

SES factors included caregiver education level in total years completed, a binary indicator of occupation in agricultural or pastoral fieldwork, and an overall wealth indicator comprising seven household ownership questions (presence of a refrigerator, cellular telephone, vehicle, washing machine, microwave, computer, and flat-screen television). Households were asked about three additional assets. Those three assets were not included in our analysis because they were owned by almost all households in the study (electricity and any television) or by almost no households (Internet access in the household). The remaining seven ownership questions were used to construct a wealth index using principal component analysis (PCA) [33]. The calculated PCs did not account for much variation in the questions, resulting in a wealth index that was highly correlated with the sum of the seven binary ownership variables (correlation coefficient = 0.99). Tertiles of the wealth index were calculated and used in adjusted models. Households that reported a connection to the public sewage network or to a private septic tank were considered to have access to sewerage. This assumes that private septic tanks protect household members from fecal exposure to a similar degree as the public system, although we did not confirm that the septic tanks in our study were safely constructed and emptied to protect health. The age of each child was calculated in months using the date of survey completion. After descriptive analyses indicated a non-linear association between age and diarrhea, age was modeled using a categorical variable with eight age groups (0-9 months, 10-15, 16-21, 22-27, 28-33, 34-39, 40-45, 45-59 months). The rainy season was defined as May through October based on statewide rainfall data from the National Meteorological Service (SMN) of Mexico for the years from 2004 to 2017. However, each round took place fully in either the rainy or dry seasons, resulting in complete collinearity of the two variables. The baseline survey took place during the dry season, while the first and second follow-up surveys took place during the rainy season. We included study round in adjusted models, which accounts for any potential differences between the rainy and dry season but precludes estimation of an independent effect of season.

3.2.5. Attributable Risk

After estimating the adjusted association between household distance from a canal and diarrheal disease, we next estimated the proportion of risk at each household location that was attributable to canal proximity. The attributable risk proportion was defined as the proportion of risk that would be prevented if a household were minimally exposed to a wastewater canal [34]. Minimal exposure was defined as the exposure faced at the distance of the farthest household within each locality group. We estimated the attributable risk proportion by comparing the modeled prevalence at the observed distance of a household to an estimated prevalence as though the household was at the minimal-exposure distance in its locality group, holding all else constant. The attributable risk proportion (ARP) was calculated for each household as:

$$ARP = \frac{Risk\ at\ Observed\ Distance - Risk\ at\ Counterfactual\ Distance}{Risk\ at\ Observed\ Distance}\ .$$

The population attributable risk proportion was calculated as the mean ARP across households. Population attributable risk proportions were calculated for i) all households in the study and ii) the subset of households within 100 meters of a canal. In addition, attributable risk proportions were calculated at each discrete spatial location along one canal segment to visualize the spatial decay of attributable risk.

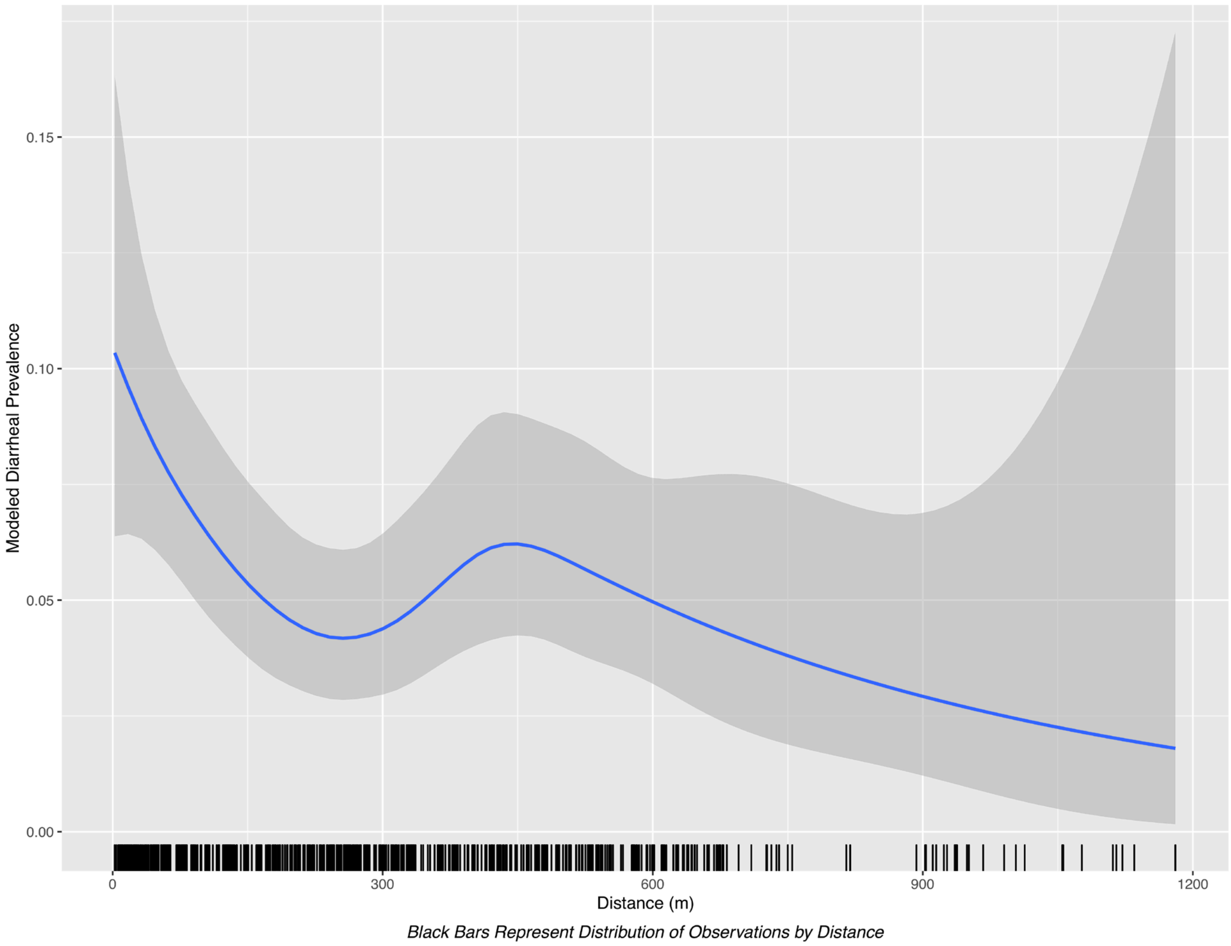

Figure 3.2. Relationship between diarrheal disease and distance between a household and the closest point on a wastewater canal: diarrheal prevalence (blue line) and 95% confidence intervals (gray area) were estimated with an unadjusted smoothing function using all 1,856 observations; black bars along the x-axis display the distance locations of all observations

3.3. Results

3.3.1. Household Characteristics

A total of 568 households completed the baseline survey. Of those, 550 (97%) completed the first follow-up and 546 (96%) completed the second follow-up survey. Four households were excluded due to missing covariates, resulting in 1,664 total interviews for analysis. Seventy-nine of these households had more than one child under five during at least one survey round. There were 646 children observed at one or more survey rounds, resulting in a total of 1,856 total child observations.

Five hundred ninety-six (92%) of those children were recorded in all three rounds, 18 (3%) were at two rounds, and 32 (5%) were at only one round, including children born between rounds. The average distance from a household to a wastewater canal was 327 m (range: 2 – 1,181 m). There were no clear trends across distance quintiles for any wealth indicator variable measured (Table 3.1). The quintile of households closest to a canal had the lowest proportion of households engaged in fieldwork (19%) and with access to sewerage (80%). The same quintile had the highest proportion of households who reported diarrheal disease at least once during the study (25%).

A total of 105 children were reported to have diarrhea during any survey round (6%). These included 46 cases (7% of 633 children measured in the baseline survey) at baseline, 37 (6% of 608 children) during the first follow-up, and 22 (4% of 615 children) during the second follow-up. Households that reported at least one case were less likely to include a field worker (19% vs. 32%) and were more likely to have a vehicle, a microwave, and a computer (Table 3.2). Children with diarrhea were younger than non-cases (21.4 vs. 27.9 months old) and fewer children had diarrhea during the rainy season compared to the dry season (56% vs. 44%; Table 3.3). The average distance from a canal was shorter for households that reported a case of diarrhea during any survey compared to those that never reported a case (mean = 278 vs. 337 m). SES indicators, household distance, and diarrheal prevalence varied between locality groups as expected given general background differences between localities (Appendix Table A.1).

3.3.2. Spatial Analysis

After considering model covariates individually and in combination, the final model was adjusted for age of the child (using eight age groups: 0-9 months, 10-15, 16-21, 22-27, 28-33, 34-39, 40-45, 45-59 months), survey round, caregiver education in total years completed, tertile of wealth based on PCA, and presence of a field worker. The adjusted posterior median odds ratio (OR) for a 10-fold increase in distance to a canal (e.g. 100 m vs. 10 m) in the adjusted model was 0.55 (95% Credible Interval (CI) 0.33, 0.91; Table 3.4). Based on the same estimate, the OR for a 100-fold increase in distance to a canal (e.g. 1,000 m vs. 10 m) was 0.30 (95% CI 0.11, 0.82; Figure 3.3). The odds of diarrhea were lower among older children and those living in households with a fieldworker.

3.3.3. Attributable Risk

The proportion of cases of diarrheal disease in all households attributable to proximity to wastewater canals was 24% (95% CI 5%, 38%). Of the 105 cases that occurred in our study, 25 (95% CI 5, 40) were potentially attributable to canal exposure using this estimate. Among diarrheal cases occurring in households within 100 m of a canal, the population attributable risk proportion was 50% (95% CI 11%, 71%), indicating that 16 (95% CI 4, 23) of the 32 cases occurring in this group were potentially attributable to canal exposure. Figure 3.4 demonstrates the spatial decay of attributable risk as household distance increases along an example canal segment.

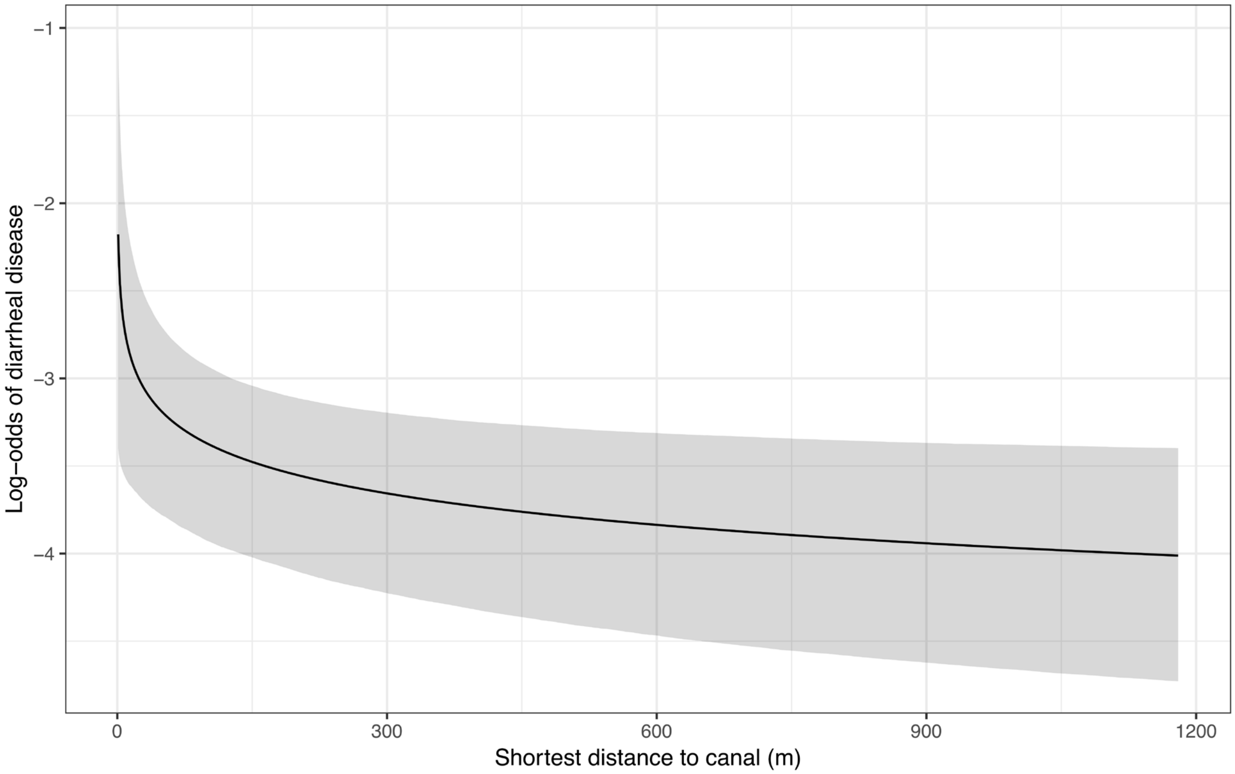

Figure 3.3. Posterior log-odds of diarrheal disease (black line) and 95% credible interval (gray area) over shortest distance between a household and a wastewater canal: model covariates (child age, wealth tertile, caregiver education level, presence of a field worker, and survey round) were set to equal their average for each child

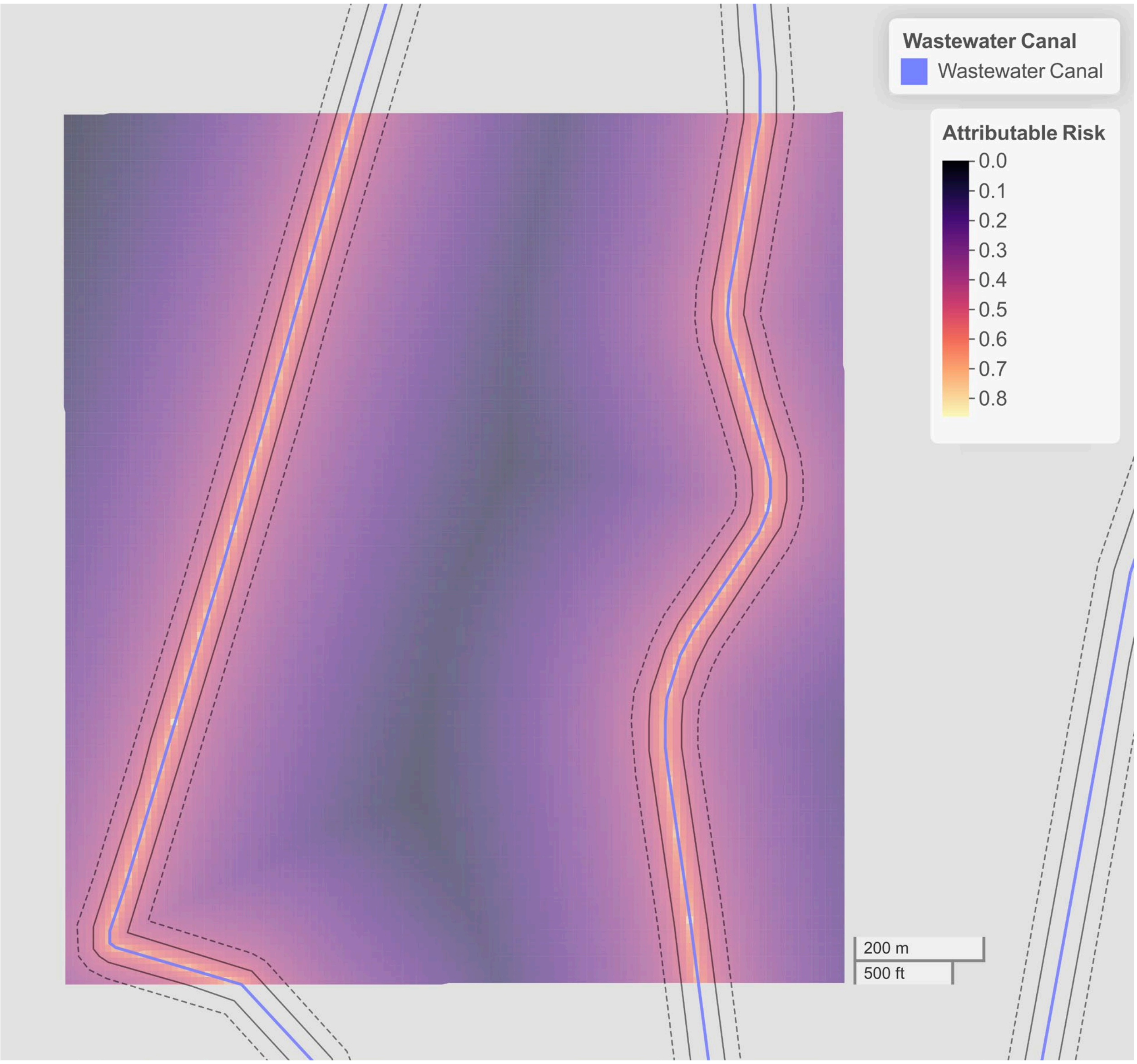

Figure 3.4. Spatial map of model results along an example wastewater canal segment: the proportion of diarrheal disease attributable to household proximity to a wastewater canal was calculated for each location within the map, with distance bands drawn at 25 m (solid line) and 50 m (dashed line); the portion of risk attributable to distance is highest at the canal (yellow) and lowest at the midpoint between the two canals shown (dark purple); proportions were calculated for a hypothetical household with average covariate values

3.4. Discussion

Wastewater reuse for irrigation is an important practice across the world that will only grow over time as a tool to alleviate water scarcity and improve climate resilience. But to maximize the benefits of increased reuse, more attention is needed to understand its accompanying health risks. This is especially true in low- and middle-income countries, where less than a quarter of wastewater generated is ever treated [2]. The health risks of wastewater reuse should be considered along the entire reuse system, including generation and transportation of waste, agricultural practices during and after wastewater application, community-wide risks where wastewater irrigation occurs, and final consumption of crops grown with wastewater. Previous work has shown that this system as a whole is associated with increased risk of diarrheal disease in children, and also that direct participation in wastewater irrigation is not a significant route of exposure for farmers' families [4,7,9–12]. Farmers working on fields that are irrigated with wastewater theoretically have a very high exposure, and could expose their own children by carrying pathogens from the field to the home on their clothes or hands. However, we found that the odds of diarrhea actually were lower for children living in households engaged in agricultural or pastoral fieldwork compared to children in households without a fieldworker, possibly due to unmeasured socioeconomic or behavioral differences. Although the reasons for their lower risk are still unknown, this result supports the conclusion that occupation is not the primary pathway for harmful wastewater exposure.

In this study, we focused on community-wide risks that are specifically related to household proximity to wastewater canals that transport untreated wastewater for irrigation in the Mezquital Valley, Mexico. We estimated that the risk of diarrheal disease in children under five decreased rapidly as distance between the household and a wastewater canal increased. Children living just 100 m away from a canal had over 45% lower odds of diarrheal disease compared to children in households 10 m from a canal. Children living 1,000 m away had 70% lower odds compared to those living 10 m away, which represents the true range of distance observed in our study. The closest 2% of households lived within 10 m of a canal and the farthest 2% of households lived over 1,000 away. The average distance between a household and a wastewater canal in our sample was 327 m. Based on these model results, a household at the average distance had 59% (95% CI 14%, 81%) lower odds of diarrhea compared to a household located 10 m away. We also found evidence that this association plays an important role in the Mezquital Valley, with 24% of all cases of diarrhea, and 50% of cases in households within 100 m of a canal, were attributable to household proximity to a wastewater canal, based on the results of our model.

Our ability to estimate this association was aided by the collection of GPS locations for households and the availability of detailed canal maps, allowing for precise calculation of the exposure variable. Our understanding of household exposure would have been improved with more detailed spatial data on elevation, canal flow and width, and barriers between canals and households. In addition, we did not account for households that potentially were exposed to multiple canals or households that had more cumulative exposure to a single canal. Because we were unable to assess how these factors may have reduced the true exposure, it is possible we misclassified the exposure level of close households by using a unidimensional measure in distance alone. Using a more nuanced exposure variable that considers these factors would provide a clearer understanding of the relationship between wastewater canals and health. We were able to control for potential confounding between diarrhea and household distance to a canal by SES, child's age, and season, although residual confounding could be present from unmeasured factors. The inclusion of multiple rounds of household surveys in this study also allowed us to observe temporal changes in the prevalence of diarrhea over one year, and the inclusion of spatially dependent random effects helped account for incidental similarities between neighboring households that have similar distance exposures.

Further research should build on these results to determine the more specific routes of exposure that could lead to spatially related disease risk where wastewater is reused. Exposure to pathogens through occupation and consumption of crops occurs, but we do not believe that these exposures are related to household location and therefore would not explain the results of this study. Aerosolization of pathogens directly from wastewater canals into nearby communities is a possible route, with potential aerosolization and transport of pathogens demonstrated at spray irrigation sites [20] and wastewater treatment plants [16,19]. Less is known about the potential for aerosolization from large, slower-moving canals. In addition, more information is needed on zoonotic transmission of pathogens between animals that interact with wastewater and humans living nearby. Based on informal discussions with local residents, people in the Mezquital Valley generally do not interact directly with wastewater canals outside of agricultural work. However, we have observed dogs, cows, sheep, and chickens swimming in and drinking wastewater directly from the canals. Flies also are common along wastewater canals. Studying pathogen spread from animals, on their bodies or in their feces, and flies could help explain the spatial gradient of pathogen transmission and disease risk. Finally, the role of space should be investigated for other health outcomes associated with wastewater reuse, such as skin diseases and the spread of antibiotic resistant bacteria, to demonstrate the full scope of spatially related health risks.

The WHO's Guidelines for the Safe Use of Wastewater describe pathogen reduction through wastewater treatment as the primary tool to improve safety of wastewater reuse. This represents the ideal form of improving health throughout the entire wastewater reuse system, as the wastewater coming into contact with farmers, crops, and nearby communities is made safer before any exposure. However, the WHO also recommends reducing pathogen exposure through agricultural practices (e.g. drip irrigation), occupational measures (e.g. protective clothing), and consumer practices (e.g. produce disinfection and cooking) [24]. While these measures already could be partially responsible for historical reductions in diarrheal prevalence in the Mezquital Valley [4], our results suggest that there are additional exposure routes related to the presence of wastewater canals that affect the entire community and would not be affected by these strategies. Wastewater treatment would be expected to reduce exposure through any of these routes. However, some communities within the Mezquital Valley still discharge sewage into the canals without treatment, potentially propagating contamination and negating some of the benefits of upstream treatment. If exposure to wastewater through the indirect routes suggested by our analysis persists despite upstream treatment, more focus on small-scale, local sewage treatment may be necessary. Other local interventions, such as covering wastewater canals or building fencing around them, could help prevent transmission from certain exposure routes. But learning which pathways truly drive disease risk is necessary to design appropriate interventions. Better understanding these routes of exposure will help to identify which health protection measures and forms of treatment would be most effective in continuing to improve the safety of wastewater reuse for agriculture.

Table 3.1. Characteristics of study households and children by quintile of household distance to a wastewater canal

	Quintile 1 (n = 113)	**Quintile 2 (n = 113)**	**Quintile 3 (n = 112)**	**Quintile 4 (n = 113)**	**Quintile 5 (n = 113)**	**Total (n = 564)**
Household Characteristics						
Distance to a Canal in Meters, Mean (Range)	41 (2 – 82)	150 (82 – 219)	276 (219 – 345)	447 (350 – 533)	717 (537 – 1,181)	Overall Mean: 327
Total Years of Caregiver Education, Mean ± SD	9.3 ± 3.2	9.5 ± 2.5	9.8 ± 2.9	9.0 ± 3.1	9.9 ± 3.0	9.5 ± 3.0
Has Refrigerator, No. (%)	94 (83)	88 (78)	88 (79)	88 (78)	89 (79)	447 (79)
Has Cellular Telephone, No. (%)	108 (96)	103 (91)	103 (92)	109 (96)	104 (92)	527 (93)
Has Vehicle, No. (%)	47 (42)	36 (32)	43 (38)	43 (38)	36 (32)	205 (36)
Has Washing Machine, No. (%)	71 (63)	60 (53)	57 (51)	61 (54)	74 (65)	323 (57)
Has Microwave, No. (%)	31 (27)	24 (21)	26 (23)	17 (15)	29 (26)	127 (23)
Has Computer, No. (%)	18 (16)	6 (5)	12 (11)	6 (5)	19 (17)	61 (11)
Has Flat Screen Television, No. (%)	68 (60)	71 (63)	63 (56)	60 (53)	74 (65)	336 (60)
Has Field Worker, No. (%)	21 (19)	35 (31)	45 (40)	39 (35)	28 (25)	168 (30)
Owns Dog, No. (%)	81 (72)	80 (71)	84 (75)	71 (63)	78 (69)	394 (70)
Has Access to Sewerage, No. (%)	90 (80)	110 (97)	110 (98)	109 (96)	109 (96)	528 (94)
Had More than One Child Under Five During at Least One Survey Round, No. (%)	6 (5)	21 (19)	17 (15)	15 (13)	20 (18)	79 (14)
Had Diarrheal Case at Any Survey Round, No. (%)	28 (25)	19 (17)	12 (11)	22 (19)	16 (14)	97 (17)
Characteristics of All Child Observations (n = 1,856)						
Child Had Diarrhea in Preceding Week, No. (%)	31 (8)	20 (5)	12 (3)	26 (7)	16 (4)	105 (6)
Age of Child in Months, Mean ± SD	27.7 ± 13.7	27.2 ± 14.5	28.4 ± 13.9	27.3 ± 13.7	26.9 ± 14.3	27.5 ± 14.0

Table 3.2. Characteristics of study households that reported diarrhea at least once during any round and households that never reported diarrhea

	Reported Diarrhea at Least Once at Any Round (n = 97)	**Never Reported Diarrhea (n = 467)**	**Total (n = 564)**
Distance to a Canal in Meters, Mean ± SD	278 ± 236	337 ± 255	327 ± 253
Total Years of Caregiver Education, Mean ± SD	9.4 ± 3.2	9.5 ± 2.9	9.5 ± 3.0
Has Refrigerator, No. (%)	76 (78)	371 (79)	447 (79)
Has Cellular Telephone, No. (%)	93 (96)	434 (93)	527 (93)
Has Vehicle, No. (%)	37 (38)	168 (36)	205 (36)
Has Washing Machine, No. (%)	57 (59)	266 (57)	323 (57)
Has Microwave, No. (%)	27 (28)	100 (21)	127 (23)
Has Computer, No. (%)	16 (16)	45 (10)	61 (11)
Has Flat Screen Television, No. (%)	59 (61)	277 (59)	336 (60)
Has Field Worker, No. (%)	18 (19)	150 (32)	168 (30)
Owns Dog, No. (%)	61 (63)	333 (71)	394 (70)
Has Access to Sewerage, No. (%)	88 (91)	440 (94)	528 (94)
Had More than One Child Under Five During at Least One Survey Round, No. (%)	17 (18)	62 (13)	79 (14)

Table 3.3. Characteristics of 1,856 survey observations of 646 children by diarrheal disease status at each observation

	Had Diarrhea (n = 105)	**Did Not Have Diarrhea (n = 1,751)**	**Total (n = 1,856)**
Baseline Survey, No. (%)	46 (44)	587 (34)	633 (34)
First Follow-Up, No. (%)	37 (35)	571 (33)	608 (33)
Second Follow-Up, No. (%)	22 (21)	593 (34)	615 (33)
Rainy Season, No. (%)	59 (56)	1,164 (66)	1,223 (66)
Age of Child in Months, Mean ± SD	21.4 ± 11.1	27.9 ± 14.1	27.5 ± 14.0

Table 3.4. Results of Bayesian logistic models on the association between household distance to a wastewater canal and diarrheal disease in children with random intercepts for locality and spatially correlated household intercepts for repeated observations

	Crude Model OR (95% CI)	**Adjusted Model OR (95% CI)**
10-fold increase in distance from a canal (e.g. 100 m vs. 10 m away)[a]	0.58 (0.36, 0.96)	0.55 (0.33, 0.91)
100-fold increase in distance from a canal (e.g. 1,000 m vs. 10 m away)[a]	0.34 (0.13, 0.93)	0.30 (0.11, 0.82)
Child aged 10-15 months vs. 0-9 months	--	2.20 (1.05, 4.49)
Child aged 16-21 months vs. 0-9 months	--	1.84 (0.86, 4.07)
Child aged 22-27 months vs. 0-9 months	--	1.20 (0.52, 2.83)
Child aged 28-33 months vs. 0-9 months	--	0.73 (0.28, 1.81)
Child aged 34-39 months vs. 0-9 months	--	1.15 (0.49, 2.78)
Child aged 40-45 months vs. 0-9 months	--	0.15 (0.03, 0.58)
Child aged 46-59 months vs. 0-9 months	--	0.27 (0.06, 0.94)
Middle vs. Lowest Tertile of Wealth Indicator	--	0.69 (0.38, 1.23)
Highest vs. Lowest Tertile of Wealth Indicator	--	1.04 (0.59, 1.85)
One year increase in education completed by caregiver	--	0.97 (0.90, 1.05)
Field worker in the household vs. no field worker	--	0.52 (0.26, 0.96)
First Follow-Up Survey vs. Baseline Survey	--	0.86 (0.53, 1.40)
Second Follow-Up Survey vs. Baseline Survey	-	0.48 (0.27, 0.84)

[a] Both results are based on the same model estimate for a one meter increase

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CHAPTER IV

Water and Sanitation Access and Childhood Diarrhea among the Bedouin of Southern Israel: Global Health Disparities Within a High-income Country

4.1. Introduction

In recent decades, substantial progress has been made in increasing access to drinking water, sanitation, and hygiene (WASH). However, stark inequalities remain between higher- and lower-income countries, as well as for disadvantaged or marginalized groups within individual countries [1]. These disparities are highlighted in the Sustainable Development Goals (SDGs), which include an aim to achieve universal access to safely managed WASH services by 2030 [2]. In this manuscript, we present an example of WASH disparities that persist within a high-income country among Bedouin communities that reside in the Negev region of southern Israel.

Estimates of WASH coverage by global region highlight the deep disparities that exist between countries. In 2017, the proportion of households with access to basic drinking water and sanitation services was over 98% in Europe and North America [3]. In sub-Saharan Africa, only 61% of households had access to basic drinking water and only 31% of households had access to basic sanitation services [3]. However, focus on national or regional coverage estimates masks additional disparities within countries by wealth and urbanicity. Among the wealthiest quintile of households in Mexico and Georgia, both upper-middle income countries, over 99% had access to at least basic sanitation services in 2017 (data not available for individual high-income countries). In the poorest quintile, 80% and 65% of households had access to basic services in Mexico and Georgia, respectively [3]. Regionally, less than one percent of all households in Europe and North America lacked access to basic sanitation services in 2017, but still 6% of rural populations lacked basic services [3].

SDG Goal Six is intended to provide impetus for governments and agencies to extend WASH access to historically hard-to-reach populations, with focus on those that lack access due to socioeconomic status (SES) or because they live in rural settings [1]. Other marginalized communities within high-income countries lack basic WASH access due to their racial, ethnic, or cultural backgrounds. Some of those groups include black and Latino communities in the United States (U.S.), indigenous Canadians, and Roma communities throughout Europe [4,5]. In this paper, we focus on another population that faces health and socioeconomic disparities related to their cultural history and ongoing legal battles for land rights: the Bedouin people of the Negev region in Israel, a high-income country.

4.1.1. The Bedouin of Southern Israel

The Bedouin are a group of Arab peoples living throughout desert regions in the Middle East and North Africa and have lived in Israel’s Negev Desert since the 18th century. Historically the Bedouin have led a nomadic, pastoral lifestyle, and have generally opposed requirements for legal proof of ownership of their lands. Following the Israeli War of Independence in 1948, many Bedouin living in the Negev fled or were expelled from Israel. The Israeli government claimed ownership of the land left behind by the Bedouin who fled, and most of those who remained behind were relocated to the Syag region east of Be'er Sheva (Figure 4.1). Over the next two decades, Bedouin landowners attempted to reclaim their land, but Israeli courts ruled that land occupied without legal proof of ownership was forfeited to the government [6]. The Israeli government then began a process to resettle Bedouin people, who are legal citizens of Israel, to free these government-owned lands for Jewish development [7]. The government continued relocation to the Syag region, which encompasses a small portion of the land previously occupied by Bedouin tribes [8].

The Israeli government constructed seven planned towns for the Bedouin in the Syag between 1968 and 1989. An estimated 146,700 out of 224,200 (65%) Bedouins currently living in the Negev live in these planned towns. Another 15,100 (7%) live on traditional tribal lands that have gained status as recognized villages by the Israeli government after negotiations through local regional councils. An additional 55,700 (25%) live on traditional tribal lands that have not received formal recognition or legal status [8]. We refer to these as unrecognized villages, although the government considers them "illegal" settlements. Legal permits to construct new buildings are not accessible in unrecognized villages, so construction or cultivation of cropland is frequently met with the threat or act of demolition by the government. Unrecognized villages face limited access to government services, including education, healthcare, sewerage, roads, and transportation [9,10]. Although government services are more available in recognized villages and planned towns, all Bedouin settlements in the Negev have lower municipal budgets and less access to public goods and services compared to Jewish settlements in the Negev or Arab groups in other parts of Israel. Bedouin people face the highest rates of poverty in Israel, especially in unrecognized villages where almost 80% of residents live in poverty [11]. Bedouin adults face numerous health disparities, such as high rates of depressive symptoms, respiratory diseases associated with proximity to an industrial park, and biological stress and depression related to threat of demolition [12–15]. Health disparities affect Bedouin children as well, including three times higher rates of infant mortality compared to Jewish populations in the Negev, high proportions of underweight and vitamin deficiency, and increased hospitalization due to diarrhea [16–18].

4.1.2. WASH Access among the Negev Bedouin

In 2011, the Israeli Supreme Court recognized that all citizens have a right to water in a case brought forth by residents of an unrecognized Bedouin village [19]. While recognizing that unrecognized villages have a right to water, the Court upheld the government's policy of requiring Bedouin from unrecognized villages to collect water from water centers only located near recognized villages [19]. Thus, all Bedouin citizens of Israel have a legal right to water, but access to safe water when it is needed is not guaranteed. Households in unrecognized villages can apply for “private” connections to a government source, which consists of a roadside pipe constructed by the government to serve multiple families (Figure 4.2) [19]. The households are responsible for connecting their home to the pipe after it is constructed. Some Bedouin attach their own connections to these pipes without obtaining permission. In many of these cases, potable water is transported through thin plastic tubes that sit on top of the desert sand, resulting in very hot water that must be cooled before use (Figure 4.2). Unlike for drinking water, there is no legal right to sanitation services for the Bedouin, who generally do not have the same access to public sewerage as other groups [9]. Sewerage exists in planned towns, but unrecognized and even some recognized villages lack similar access. In some cases, sewage is transported directly into the environment without collection or treatment, but little is known about the extent of sanitation coverage in Bedouin communities (Figure 4.3).

To better understand WASH access among Israel’s Bedouin people, we conducted a household survey to measure access to drinking water and sanitation services in five Bedouin communities in the Negev region. We also measured childhood diarrheal disease to estimate the impact of WASH on health in these communities. The survey was competed in one planned Bedouin town, two recognized villages, and two unrecognized villages in order to assess how the legal status of some Bedouin communities has impacted the health and wellbeing of their people.

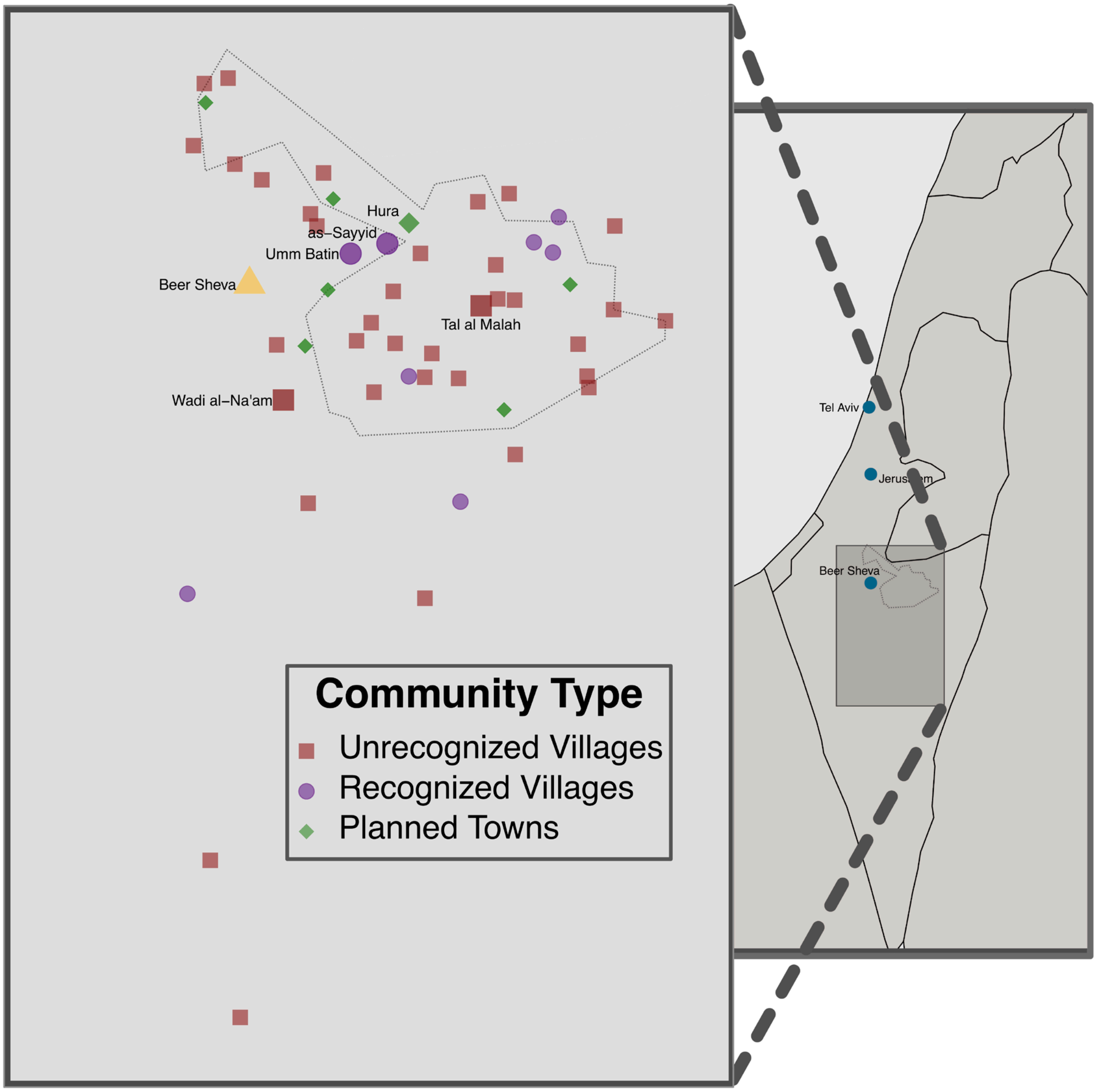

Figure 4.1. Bedouin villages in the Negev region of Israel: Bedouin villages include unrecognized villages (red squares), recognized villages (purple circles), and planned towns (green diamonds); the five communities included in our survey and Be'er Sheva are labeled by name; the approximate area of the Syag region is indicated with a dotted line

Figure 4.2. Examples of drinking water access for the Negev Bedouin: (left) “private” standpipe allowing connections to the public water source; (right) plastic tubes transporting water from a public source to Bedouin households; both photographs taken by Grace Christensen, Emory University

Figure 4.3. Examples of sanitation facilities for the Negev Bedouin: two examples of sanitation facilities transmitting sewage directly into the environment

4.2. Methods

4.2.1. Study Population

Households were sampled from five Bedouin communities in the Negev region of southern Israel (Figure 4.1; Table 4.1). These included 1) Hura, a planned town with about 20,000 residents; 2) as-Sayyid, a village of about 5,500 people that was recognized in 2003; 3) Umm Batin, a village with around 4,000 inhabitants that was recognized in 2004; 4) Wadi al-Na’am, the largest unrecognized Bedouin village of about 13,000 people; and 5) Tal al-Malah, an unrecognized village with around

1,500 residents [20,21]. Both recognized villages, as-Sayyid and Umm Batin, are part of the al-Kasom Regional Council.

4.2.2. Household Sampling and Survey Methods

Data were collected through a cross-sectional household survey that took place between August 2019 and January 2020. To be eligible for the study, households needed to include at least one child under five years old and a woman over 18 years old to act as the key informant. Households were defined as people living in the same household unit and sharing food or expenses. Some Bedouin families follow a polygamous structure, in which two or more women are married to the same man. Under our definition of a household, women in polygamous families could be part of the same household if they live together and share food or expenses, or they could be in separate eligible households if they do not.

Interviewers were local Bedouin women who completed training by research staff on obtaining informed consent and conducting interviews. Interviewers were trained to choose a street and household at random at the start of each day to begin sampling. Where neighborhoods were comprised of defined streets and blocks, interviewers skipped two households between successful interviews. Where neighborhoods did not have well defined streets, no households were skipped.

The survey instrument included sections on household demographics, household characteristics including access to water and sanitation, observations by interviewers of water and sanitation infrastructure, household finances, healthcare access, child health and nutrition, immunizations, child sanitation behaviors, and recent travel patterns. Many survey questions, including demographics, water and sanitation access, and interviewer observations, were adapted from Demographic and Health Surveys (DHS) conducted in rural communities in Jordan and Egypt [22]. The survey was piloted with Bedouin women and edited to ensure questions were appropriately phrased and translated for Bedouin culture. Surveys were conducted in person using Qualtrics' offline software [23]. The key informant gave written, informed consent before any participation or collection of data.

4.2.3. Health and Socioeconomic Variables

The primary outcomes were diarrheal disease in children under five, access to safely managed drinking water, and access to safely managed sanitation. Diarrheal disease was defined as having three or more loose or watery stools in a day and was measured for each child under five in the household [24]. Safely managed drinking water is defined by the United Nation's (UN) Joint Monitoring Programme (JMP) as water from an improved source located on premises, available when needed, and free from fecal and chemical contamination [3]. Improved sources are those with the potential to deliver safe water based on design and construction, and include piped water, boreholes or tubewells, protected dug wells, protected springs, rainwater, and packed or delivered water. Based on three survey questions, we defined safely managed drinking water as water that 1) comes from an improved source, 2) is located in the home or yard, and 3) was available for at least part of each day in the last week. We considered piped water from the public supply as an improved source whether the connection was provided by the government or illegally constructed.

We did not include a measure of fecal or chemical contamination to fully meet the definition of safely managed drinking water.

Safely managed sanitation is defined by the JMP as the use of improved facilities that are not shared with other households and where excreta are safely disposed in situ or transported and treated off-site [3]. Improved sanitation facilities are designed to safely separate excreta from human contact and include flush/pour toilets to a piped sewer system, septic tank, or pit latrine; ventilated pit latrines; composting toilets; and pit latrines with slabs. Based on two survey questions, we defined safely managed sanitation as 1) improved facilities that safely dispose of excreta that 2) are not shared with other households. We did not confirm safe disposal of excreta beyond self-report by the household. Interviewers also recorded observations of sanitation facilities to assess use, maintenance, and cleanliness.

Secondary outcomes included access to healthcare, immunization status of children under five, and socioeconomic indicators. We asked participating women questions about healthcare access including where they seek care, reasons for not seeking care when sick, and cultural barriers to healthcare access. Interviewers recorded the immunization status of children under five directly from vaccination booklets, if available, for fecal-oral viruses. The immunizations recorded were inactivated polio vaccine (IPV 1, IPV 2, and IPV 3), oral polio vaccine (bOPV 1, bOPV 2), and rotavirus vaccine (rotavirus 1 and rotavirus 2). Indicator variables were created for children who were up to date on each immunization dose based on their age and national immunization recommendations [25]. Numerous socioeconomic indicators were measured in the survey, including education of the respondent and her husband, employment and sources of income, land and livestock ownership, and ownership of assets to indicate wealth. The list of potential assets was adapted from previous DHS surveys in similar rural communities. An overall variable for household wealth was created by counting the number of assets owned by the household from a total of six: electricity, solar panels, refrigerator, air conditioner, washing machine, computer, and internet. These assets were selected based on our judgment of which assets are meaningful within Bedouin communities, input from Bedouins during survey piloting, and because these assets were not uniformly distributed among households in our sample.

4.2.4. Data Analysis

Data analysis included descriptive summaries of the count and prevalence or mean of each variable. We measured each of those values for all five communities to assess variability between communities and by village legal status. Variables measured at the household-level included safely managed drinking water and sanitation, socioeconomic indicators, and demographic and respondent characteristics. Child-level variables were measured for each child under five years old separately and included diarrheal disease, treatment for diarrhea, recent fever, and immunization status. For child-level variables, the age of each child was measured through their reported birthdate and the date of survey completion. If only a birth year was provided, the midpoint of that year (July 1st) was used for the birthdate. Children were excluded from child-level analyses if their birthdate-confirmed age was over 60 months or if the respondent did not provide a birthdate. Households that did not have birthdate-confirmed children under five, i.e. if they gave no birthdates for their children, were still included in all household-level analyses. Due to a limited sample size, we did not estimate statistical significance for any differences in variables across villages or by legal status. For our primary outcomes (diarrheal disease, safely managed drinking water, and safely managed sanitation) we estimated 95% confidence intervals around prevalence estimates to assess the uncertainty around each estimate. Confidence intervals were estimated as $p \pm 1.96 * \sqrt{\frac{p*(1-p)}{n}}$, where p is the prevalence estimate and n is the sample size. All data analysis was completed using R software [26].

4.3. Results

4.3.1. Socioeconomic Characteristics

We sampled between 33 and 40 households from each Bedouin community, resulting in a total of 190 household surveys completed (Table 4.2). Overall, SES indicators were highest in Hura, as-Sayyid, and Tal al Malah. In Tal al Malah, an unrecognized village, respondent education, employment, and household assets were much higher than expected, possibly indicating sampling bias in that community. Women from Tal al Malah in our sample had the highest education, as 55% had completed university or technical college and 53% were currently employed. Households from Wadi al-Na'am, the other unrecognized community, had the lowest SES overall. Sixty-five percent of women from Wadi al-Na'am in our sample had less than a high school education, and their households had the lowest access to wealth assets.

4.3.2. Household WASH Access

Most households (97%) reported that their primary source of drinking water is piped to their home or yard (Table 4.2). However, only 51% of households were provided a connection to piped water by the government, including just 5% of households in Wadi al-Na'am and 30% of households in Tal al Malah. Another 46% of households, mostly in the unrecognized villages, reported piped drinking water that was not provided by the government, i.e. the household constructed their own piping to connect their household to a government water line. Intermittency of water supply was high, as 41% of households reported that their primary drinking water source was unavailable for at least one full day in the past week, including 73% of households in Tal al Malah. Thus, despite high access to piped water, only 57% (95% CI 50%, 64%) of households had access to a drinking water source that met our definition of safely managed (75% in Hura, 51% in as-Sayyid, 61% in Umm Batin, 71% in Wadi al-Na'am, and 24% in Tal al Malah).

All households in Hura, as-Sayyid, Umm Batin, and Tal al Malah and 68% of households in Wadi al-Na'am reported a flush toilet or pour flush latrine as their primary sanitation facility (Table 4.2). The remaining households in Wadi al-Na'am reported access to a pit latrine. Despite high access to flush toilets, only 39% of households in the total sample with a flush toilet or latrine reported that their flushed waste goes to a piped sewer system (75% in Hura, 41% in as-Sayyid, 30% in

Umm Batin, zero in Wadi al-Na'am, and 23% in Tal al Malah). In 30% of those households, sewage was flushed directly into the environment outside or near the home (23% in Hura, zero in as-Sayyid, 42% in Umm Batin, 4% in Wadi al-Na'am, and 78% in Tal al Malah). The remaining households flushed their waste into a pit latrine (30%), septic tank (2%), or cesspit (2%). Overall, 63% (95% CI 56%, 70%) of households had access to sanitation facilities that met our definition of safely managed (75% in Hura, 86% in as-Sayyid, 50% in Umm Batin, 88% in Wadi al-Na'am, and 15% in Tal al Malah). In total, 44% (95% CI 37%, 51%) of households had access to both a safely managed drinking water source and safely managed sanitation (60% in Hura, 43% in as-Sayyid, 35% in Umm Batin, 63% in Wadi al-Na'am, and 15% in Tal al Malah).

4.3.3. Children's Health

Across all five communities, there were 264 children under five years old confirmed by their birthdate from 168 households (Table 4.3). Caregivers reported that 57 of those children had diarrhea in the previous week, resulting in an overall prevalence of 22% (95% CI 17%, 27%). The prevalence of caregiver-reported diarrhea was highly variable by village including zero cases in as-Sayyid, 9% of children in Hura, 68% in Umm Batin, 18% in Wadi al-Na'am, and 24% of children in Tal al Malah. Caregivers reported giving the child less to drink than usual for 26% of diarrheal cases and less to eat than usual for 39% of cases. The prevalence of fever followed a similar pattern as diarrhea but was lower overall (12% of children) and less variable (13% in Hura, 4% in as-Sayyid, 10% in Umm Batin, 14% in Wadi al-Na'am, and 12% in Tal al Malah).

Coverage with immunizations against polio was higher than against rotavirus. Among children old enough for the vaccine, 92% received the first dose of IPV and 83% received the third dose. Eighty-four percent of eligible children received each dose of OPV. In contrast, only 61% and 56% of eligible children received the first two doses of rotavirus vaccine, respectively. Immunization coverage varied substantially between communities but was lowest in Wadi al-Na'am. No children in Wadi al-Na'am had received any dose of rotavirus vaccine and only 13% of eligible children had received the second or third dose of IPV.

4.4. Discussion

4.4.1. Household WASH Access

Our sample from five Bedouin communities in the Negev was characterized by poor access to WASH services. Water is a recognized human right in Israel and the government is obligated to provide Bedouin citizens with drinking water, even in unrecognized communities. That responsibility appears to be met in these five communities, as almost all households in our sample had access to piped drinking water. However, the government did not provide connections for about half of all households and for a majority of those in the two unrecognized villages. The remaining households either have access to a public source but were required to construct their own connection, or they constructed an illegal connection to the public source. We did not ask households to report the legality of their connection, but the potential dependency for some households on illegal connections that could be disconnected by the government suggests that the presence of piped water is not necessarily a secure source.

Another issue with piped water in Bedouin communities is availability of water when needed. For legal and illegal connections alike, water is piped to many Bedouin households through plastic tubes that sit on top of the desert sand and are directly exposed to the sun (Figure 4.2). Water that reaches households during the day is extremely hot and not drinkable or usable without cooling. Especially for households without refrigeration, including 47% of our sample in Wadi al-Na'am, this hot water is not available for use when needed. In addition, almost half of all households and three quarters of those in the unrecognized village of Tal al Malah reported that their primary drinking water source was unavailable for 24 hours or more during the last week, possibly due to low pressure through the plastic pipes used to transport water to Bedouin households over large distances. The JMP defines safely managed drinking water as available when needed due to the social and health consequences of intermittent supply [27]. Piped water that is not continuously pressured is more likely to be contaminated with microbial organisms [28]. Households with intermittent supplies face adverse health outcomes due to compromised water quality, recontamination of water that is stored for later use, and restriction of intake when water is unavailable [27,29–32]. More research is needed to understand the specific causes of water intermittency among Bedouin households and their resulting health consequences.

For sanitation, despite almost all households reporting using a toilet or latrine that flushes, waste goes to a piped sewer for only 39% of those households. For a third of those households, flushed waste goes directly into the environment. In the unrecognized community of Tal al Malah, this is true for 78% of households. Even in Hura, a planned town with the best infrastructure and most government support, about one quarter of households reported that their waste goes directly into the environment without collection. Waste is flushed directly outside of the home for some households, creating a direct point of exposure to enteric pathogens (Figure 4.3). For other households, waste is flushed to nearby wadis (dry streams that fill during winter) coming from the seasonal Be'er Sheva and Hebron Rivers. Dumping untreated wastewater into wadis from urban areas has resulted in contamination of groundwater and seasonal rivers in Israel, the West Bank, and Saudi Arabia [33–35]. In addition, the presence of fecal waste in dry wadis enables potential human contact with contaminants, such as through children playing, or spread of pathogens by animals or flies [36].

Notably, households in Tal al Malah had the worst access to water and sanitation despite having much higher than expected SES, which might overstate the true SES level of the village. About one quarter of households sampled in Tal al Malah had access to safely managed drinking water, and only 15% had access to safely managed sanitation services. These results suggest that even wealthy, highly educated households within some unrecognized villages are not able to access safe

WASH services, and that the legal status of Bedouin villages is a substantial barrier to achieving access.

4.4.2. Children's Health

Bedouin children in our sample faced a high prevalence of diarrheal disease (22% overall). Coverage with immunizations against fecal-borne pathogens was mixed, including over 80% coverage with the third of three doses of IPV but just over 50% coverage with the second of three doses of the rotavirus vaccine. Coverage also was uneven between villages, as few children received these immunizations in Tal al Malah, which possibly explains a portion of the high diarrheal burden among Bedouin children. The large proportion of households depending on intermittent water supplies and with poor or no fecal waste management might further explain this high morbidity. Poor WASH access among Bedouin communities also might help to understand a 2013 silent outbreak of poliovirus that occurred in Israel, which resulted in zero cases of paralysis but had sustained transmission in the planned Bedouin town of Rahat [37]. The results of our survey in Hura demonstrate that even in planned Bedouin towns households struggle with intermittent drinking water supply and resort to dumping sewage into the environment without collection. The potential for fecal-borne diseases to spread between Bedouin communities and even into other regions of Israel remains high due to poor WASH access. As evidenced by a 20% diarrheal prevalence in the two unrecognized villages in our sample compared to 9% in the planned town, the risk of pathogen spread is exacerbated by the legal status of unrecognized Bedouin villages.

The diarrheal prevalence measured in the two other communities, as-Sayyid and Umm Batin, represent outliers that likely do not reflect the true overall prevalence in those communities. Zero cases were reported in as-Sayyid and 68% of children in Umm Batin were reported to have had diarrheal disease in the past week. This variability could reflect different understanding of the severity of diarrhea that respondents were being asked to report. Our survey asked if the child had three or more loose stools in a day, or more loose stools than usual in a day, during the last week. In as-Sayyid, participants might have viewed diarrhea under our definition as a regular occurrence and would only report a case if it were more severe diarrhea. In Umm Batin, respondents might have reported all occurrences of loose stool, which is much more common in young children, rather than true cases under our definition. Although interviewers were trained to consistently read the question as written, we are not able to rule out interviewers working in different villages using different phrasing for the question. In addition, under-reporting of diarrhea could have occurred due to social desirability, and over-reporting could have occurred among households that reported what they thought the study team wanted to hear. As a sensitivity analysis, we looked at the prevalence of caregiver-reported fever among the same children. If respondents were under- or over-reporting disease, rates of fever might be similarly reported. We found that the general pattern held, with as-Sayyid reporting the fewest cases (4%) and Umm Batin reporting the most (20%), but the reported prevalences were much less variable (12% overall) (Table 4.3). This comparison moderately supports that diarrhea was not intentionally over- or under-reported and that the extreme ends of those estimates came from different understanding of the question or true differences in our sample. Lastly, these results might reflect the limitations of our sample size. By random occurrence, we might have sampled healthy children in as-Sayyid and more children with diarrhea in Umm Batin, such as those infected with a common pathogen in a hypothetical local outbreak occurring during the study period.

4.4.3. Disparities in High-Income Countries

Our results underscore that global health inequities are not limited to those between high- and low-income countries. Within high-income countries, marginalized groups face health and environmental challenges that are inharmonious with the wealth of the country overall, including Bedouin people in Israel. In 2017, 35% of households in the 47 “least developed countries” as defined by the UN had access to safely managed drinking water, and 34% had access to basic sanitation services [3,38]. In Tal al Malah, we measured the coverage with safely managed drinking water and sanitation as 24% and 15%, respectively. Israel is a high-income country, with a gross domestic product (GDP) per capita that is just above that of France and Japan [39]. Despite the high economic production of Israel, only 44% of Bedouin households in our study had access to drinking water and sanitation services that met our definition of safely managed. Those that did meet the definition of safely managed still face additional challenges to true WASH access, such as intermittency and relying on illegal connections. As another example, the unrecognized village of Wadi al-Na'am had high coverage with safely managed sanitation, but only because its population primarily relies on pit latrines that may not truly be safely managed when emptied and cleaned, especially without access to government services. The Bedouin in the Negev of Israel are a clear example of global WASH disparities occurring within high-income countries, and they are not the only case [5].

We highlight two of several other examples of groups in wealthy countries that face disparities in WASH access: Mexican Americans and immigrants living in Texas colonias and individuals and families experiencing homelessness. Colonias are defined as residential areas along the U.S.-Mexico border that lack some basic living needs and were often developed as settlements for migrant workers located outside of city jurisdictions where building codes were not enforced [40]. In Texas, approximately 18% of colonias in the six counties where colonias are most common do not have access to safe drinking water, wastewater disposal, or were located on illegally plotted land (data not disaggregated), representing almost 40,000 people [4]. Individuals experiencing homelessness also face challenges to access WASH services and often depend on housed friends or public sources for those needs [41,42]. In the U.S., variable access to public toilets, feelings of being unwelcome, and physical and mental illness lead many individuals experiencing homelessness to engage in open defecation [43]. The presence of enteric pathogens has been found in feces from open defecation sites, and poor access to and utilization of sanitation facilities has contributed to outbreaks of hepatitis A among persons experiencing homelessness in multiple U.S. states in recent years [44–46].

To further demonstrate how inequalities affect the Bedouin of Israel, we compared the prevalence of diarrhea reported in our sample to the results of DHS surveys that took place in low-income countries [22]. DHS surveys measured two-week diarrheal prevalence, and thus captured more cases than our one-week prevalence. Ignoring that difference in recall periods, the prevalence we estimated in two unrecognized villages combined (20%) is about the same as that measured by DHS surveys in Burkina Faso (1992 & 1999), Ghana (1993 & 2008), Cambodia (2005), Bolivia (1998), and Nigeria (2003), among others (Fuller et al. 2015). Even Hura, which had a reported prevalence of 9%, is more comparable to Madagascar (2004), Guyana (2009) Bangladesh (2007), Philippines (2008), and India (1992 & 2006) than to populations in high-income countries, where the combined average incidence of diarrhea among children under five was just 1% per week in 2016 [47].

4.5. Conclusions

Our study found that the Bedouin of the Negev region in Israel have poor access to safely managed drinking water and sanitation, and Bedouin children face a high burden of diarrheal disease. Many Bedouin households rely on a drinking water source that is not readily available when needed, and for many others fecal waste is flushed away directly to the environment without collection. In one unrecognized village, access to safely managed water and sanitation was worse than reported by the world's poorest countries. The prevalence of childhood diarrheal disease in unrecognized villages was also more comparable to the poorest populations than to the prevalence in other high-income countries. The Bedouin of Israel are an example of stark disparities in health and WASH access that persist within high-income countries across the world. For the Bedouin, an ongoing legal fight over land rights compounds those inequalities and prevents expanded government support in unrecognized villages to solve these issues. Increased effort and novel solutions for reaching vulnerable groups are necessary to improve health and expand WASH access for the Bedouin in Israel and for other marginalized populations worldwide.

Table 4.1. Five Bedouin communities sampled for this study

Village Name in English	Type of Community	Year of Founding or Recognition	Estimated Population	Additional Information
Hura	Planned Town	Founded in 1989	20,000	One of seven planned towns constructed by the Israeli government to promote sedentarization of the Bedouin and movement into the Syag region of the Negev
as-Sayyid	Recognized Village	Settled before the founding of Israel; Recognized in 2004	5,500	as-Sayyid is inhabited primarily by a Bedouin tribe of the same name with a distinct culture; originally intended to be recognized as part of Hura, opposition due to cultural differences led to recognition as an independent village
Umm Batin	Recognized Village	Settled before the founding of Israel; Recognized in 2004	4,000	Despite recognition, Umm Batin does not have a formal master plan and is subject to the government's policy for demolition of newly constructed homes
Wadi al-Na'am	Unrecognized Village	Settled in the 1950s	13,000	The largest unrecognized village; Bedouin comprised of families settled here after being removed from their lands following the war of 1948; located near an industrial zone and toxic waste disposal site
Tal al Malah	Unrecognized Village	Settled before the founding of Israel	1,500	Located just north of Israel's Nevatim air base, which was constructed partially on lands expropriated from the village's inhabitants [48]

Table 4.2. Socioeconomic characteristics and WASH access among Bedouin households

	Planned Town	**Recognized Villages**		**Unrecognized Villages**		**Total**
	Hura	**as-Sayyid**	**Umm Batin**	**Wadi al-Na'am**	**Tal al Malah**	**–**
Households surveyed, No.	40	37	33	40	40	190
Range of dates for survey completion	Nov 14, 2019 – Jan 3, 2020	Jul 24 – Dec 10, 2019	Aug 24 – Dec 28, 2019	Jul 24 – Jul 25, 2019	Aug 18 – Oct 3, 2019	Jul 24, 2019 – Jan 3, 2020
Demographics and Socioeconomics						
Highest level of education completed by respondent: university or technical college, No. (%)	22 (55)	6 (16)	9 (27)	3 (8)	22 (55)	62 (33)
Highest level of education completed by respondent: high school, No. (%)	11 (28)	22 (59)	20 (61)	11 (28)	10 (25)	74 (39)
Highest level of education completed by respondent: less than high school, No. (%)	7 (18)	9 (24)	4 (12)	26 (65)	8 (20)	54 (28)
Respondent is employed, No. (%)	11 (28)	7 (19)	7 (21)	8 (21)	21 (53)	54 (29)
Household owns livestock, No. (%)	9 (23)	7 (19)	12 (36)	9 (23)	10 (25)	47 (25)
Household has access to:						
electricity, No. (%)	31 (78)	32 (86)	14 (42)	0	11 (28)	88 (46)
solar panels, No. (%)	19 (48)	22 (59)	25 (76)	38 (95)	40 (100)	144 (76)
refrigerator, No. (%)	39 (98)	34 (92)	30 (91)	21 (53)	36 (90)	160 (84)
air conditioner, No. (%)	29 (73)	20 (54)	12 (36)	0	20 (50)	81 (43)
washing machine, No. (%)	24 (60)	35 (95)	14 (42)	5 (13)	8 (20)	86 (45)
computer, No. (%)	16 (40)	15 (41)	9 (27)	17 (43)	20 (50)	77 (41)
internet, No. (%)	16 (40)	16 (43)	8 (24)	3 (8)	7 (18)	50 (26)
Number of household assets out of six: *electricity, refrigerator, air conditioner, washing machine, computer, and internet*, mean (SD)	3.9 (1.7)	4.1 (1.2)	2.6 (1.6)	1.2 (1.0)	2.6 (1.6)	2.9 (1.8)
Husband has more than one wife, No. (%)	8 (21)	6 (17)	7 (24)	14 (36)	10 (26)	45 (25)
Female respondent required to be accompanied to go to the doctor, No. (%)	12 (30)	5 (14)	14 (42)	14 (35)	33 (83)	78 (41)
Water and sanitation access						
Drinking water piped to home or yard; provided by government, No. (%)	31 (78)	35 (95)	16 (48)	2 (5)	12 (30)	96 (51)
Drinking water piped to home or yard; not provided by government, No. (%)	9 (23)	1 (3)	16 (48)	33 (83)	28 (70)	87 (46)
Drinking water collected from public source, No. (%)	0	0	0	5 (13)	0	5 (3)
Drinking water comes from well, No. (%)	0	1 (3)	1 (3)	0	0	2 (1)

Drinking water unavailable from primary source for >= 24 hours in last week, No. (%)	10 (25)	17 (46)	12 (36)	9 (23)	29 (73)	77 (41)
Makes drinking water safer, e.g. boils water, No. (%)	22 (55)	7 (19)	11 (34)	2 (5)	37 (93)	79 (42)
Number of households with safely managed drinking water source, No.	30	18	19	27	9	103
Proportion of households with safely managed drinking water source, % (95% CI)	75 (62, 88)	51 (35, 67)	61 (44, 78)	71 (57, 85)	24 (11, 37)	57 (50, 64)
Sanitation facility: toilet that flushes or a pour flush latrine, No. (%)	40 (100)	37 (100)	33 (100)	27 (68)	40 (100)	165 (87)
Sanitation facility: ventilated improved pit latrine, No. (%)	0	0	0	1 (3)	0	1 (1)
Sanitation facility: pit latrine with slab, No. (%)	0	0	0	11 (28)	0	11 (6)
Sanitation facility: pit latrine without slab, No. (%)	0	0	0	1 (3)	0	1 (1)
Sanitation facility shared between two or more households, No. (%)	1 (3)	4 (11)	4 (13)	2 (5)	4 (10)	15 (8)
Sewage goes to piped sewer system (if flush toilet/latrine), No. (%)	30 (75)	15 (41)	10 (30)	0	9 (23)	64 (39)
Sewage goes to septic tank or cesspit (if flush toilet/latrine), No. (%)	1 (3)	3 (8)	4 (12)	0	0	8 (5)
Sewage goes to pit latrine (if flush toilet/latrine), No. (%)	0	19 (51)	5 (15)	25 (93)	0	49 (30)
Sewage goes into environment (if flush toilet/latrine), e.g. yard or ravine, No. (%)	9 (23)	0	14 (42)	1 (4)	31 (78)	55 (33)
Number of households with safely managed sanitation facilities, No.	30	32	16	35	6	119
Proportion of households with safely managed sanitation facility, % (95% CI)	75 (62, 88)	86 (75, 97)	50 (33, 67)	88 (78, 98)	15 (4, 26)	63 (56, 70)
Number of households with safely managed drinking water and safely managed sanitation, No.	24	15	11	24	6	80
Proportion of households with safely managed drinking water and safely managed sanitation, % (95% CI)	60 (45, 75)	43 (27, 59)	35 (19, 51)	63 (48, 78)	15 (4, 26)	44 (37, 51)
Interviewer observed soap available at the primary handwashing location if permitted access, No. (%)	31 (78)	30 (97)	18 (62)	23 (62)	20 (65)	122 (73)

Table 4.3. Health and immunization status of children under five years old in sampled Bedouin households

	Planned Town	Recognized Villages		Unrecognized Villages		Total
	Hura	**as-Sayyid**	**Umm Batin**	**Wadi al-Na'am**	**Tal al Malah**	**--**
Total number of children under five confirmed by birthdate, No.	56	46	41	58	63	264
Households with children confirmed under five, No.	37	27	30	34	40	168
Average number of children under five per household, mean	1.5	1.7	1.4	1.7	1.6	1.6
Number of children with diarrhea in last week, No.	5	0	28	9	15	57
Proportion of children with diarrhea in last week, % (95% CI)	9 (2, 16)	--	68 (54, 82)	18 (8, 28)	24 (13, 35)	22 (17, 27)
Child with diarrhea given more to drink than usual, No. (%)	3 (60)	--	9 (32)	3 (33)	3 (20)	18 (32)
Child with diarrhea given less to drink than usual, No. (%)	1 (20)	--	11 (39)	0	3 (20)	15 (26)
Child with diarrhea given more to eat than usual, No. (%)	0	--	5 (18)	0	1 (7)	6 (11)
Child with diarrhea given less to eat than usual, No. (%)	3 (60)	--	18 (64)	1 (11)	0	22 (39)
Healthcare sought for child's case of diarrhea, No. (%)	4 (80)	--	5 (18)	4 (44)	9 (60)	22 (39)
Child received oral rehydration liquid or packet for their diarrhea, No. (%)	2 (40)	--	1 (4)	0	7 (47)	10 (18)
Child received antibiotic pill or syrup for their diarrhea, No. (%)	1 (20)	--	4 (14)	0	1 (7)	6 (11)
Number of children with fever in last week, No. (%)	7 (13)	2 (4)	8 (20)	6 (10)	9 (14)	32 (12)
Children over two months old with documented receipt of the first dose of Rotavirus vaccine[a], No. (%)	23 (59)	15 (60)	35 (90)	0	34 (67)	111 (61)
Children over four months old with documented receipt of the second dose of Rotavirus vaccine, No. (%)	20 (51)	15 (65)	28 (72)	0	34 (68)	97 (56)
Children over two months old with documented receipt of the first dose of inactivated polio vaccine (IPV 1)[b], No. (%)	38 (97)	22 (88)	38 (97)	13 (57)	51 (100)	162 (92)
Children over four months old with documented receipt of the second dose of inactivated polio vaccine (IPV 2), No. (%)	38 (97)	20 (87)	38 (97)	3 (13)	50 (100)	149 (86)
Children over six months old with documented receipt of the third dose of inactivated polio vaccine (IPV 3), No. (%)	34 (92)	17 (77)	37 (97)	3 (13)	46 (100)	137 (83)
Children over six months old with documented receipt of the first dose of oral polio vaccine (OPV 1)[c], No. (%)	34 (92)	17 (77)	29 (76)	17 (74)	42 (91)	139 (84)
Children over 18 months old with documented receipt of the second dose of oral polio vaccine (OPV 2), No. (%)	30 (97)	14 (78)	28 (85)	8 (42)	36 (97)	116 (84)

[a] Rotavirus schedule: 1st dose at two months, 2nd dose at four months, 3rd dose at six months (not included in our survey)

[b] IPV schedule: 1st dose at two months, 2nd dose at four months, 3rd dose at six months

[c] OPV schedule: 1st dose at six months, 2nd dose at 18 months (recommended that children receive both IPV and OPV)

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CHAPTER V

Conclusion

Despite decades of progress in improving access to sanitation globally, and in reducing diarrheal disease mortality in children from almost five million deaths occurring annually in 1982 to fewer than 500,000 today, significant barriers remain in achieving universal sanitation coverage and eliminating the burden of enteric infections [1,2]. The research presented in this dissertation highlights three challenges for sanitation and health that remain to be solved: i) understanding the true health effects of latrines and other low-cost sanitation solutions, ii) safely managing fecal waste and wastewater throughout its lifecycle, from generation to disposal or reuse, and iii) reaching the most vulnerable populations to end inequalities in sanitation access, including marginalized groups within wealthy countries.

Chapter II of this dissertation was motivated by four recently conducted randomized controlled trials (RCTs) that tested the effects of latrine interventions on children's health [3–6]. Surprisingly, three out of the four trials found no effect of sanitation (or other WASH interventions) on diarrhea, and, unsurprisingly, none found an effect of any WASH intervention on child growth. The trials are considered to be among the most robust tests of WASH interventions to date, and researchers are still grappling with what these results mean for the role of WASH in public health [7–9]. We added to this discussion by reviewing the history of epidemiological evidence on the relationship between sanitation access and diarrheal disease. We found that the null results of these recent sanitation trials are not as surprising as they first appear. Numerous systematic reviews and meta-analyses across three decades estimated a substantial reduction in diarrheal disease associated with sanitation interventions, but those analyses inappropriately averaged over widely heterogeneous studies. In particular, most reviews combined all types of sanitation interventions, including sewerage, sanitation plus microloan programs, and simple latrines. By analyzing those studies separately, we showed that latrine-based interventions did not have an independent average effect on diarrhea. On that point, our analysis agrees with three out of four of those recently conducted intervention trials.

Most latrine interventions, as they have been historically delivered, do not reduce diarrhea. This null effect could be due to residual fecal contamination coming into the home from other households that do not have access to sanitation, or from other routes of exposure that are not solved by simple latrines, such as from contaminated food or exposure to animal feces [10–13]. Sewerage, on the other hand, has been shown to prevent diarrhea and has helped wealthy countries reduce the burden of fecal-oral infections to almost zero. But sewerage is not considered affordable for widespread use in most low-income countries. Increasing the availability of funding for expanding sewerage access is one potential solution to provide sanitation to the global majority. Alternatively, latrines and other simple technology might be improved if more attention is placed on reaching high coverage within a community and closing all potential routes of fecal exposure. Nevertheless, our analysis shows that continuing to provide the lowest cost sanitation options at the household level is not sufficient to protect population health in low-income countries.

While Chapter II of this dissertation addressed the impact of a household's sanitation access on the health of its inhabitants, Chapter III focused on large-scale fecal waste management and the population health effects of wastewater reuse for agriculture. We conducted a study in the Mezquital Valley, Mexico, where most of the wastewater generated by Mexico City is reused for agricultural irrigation. Previous research in that area, including our own, and across the world has consistently found that populations living where wastewater is reused face higher risk of numerous health outcomes, including childhood diarrheal disease [14]. However, much less is known about the routes of exposure between wastewater reuse and the local community that results in disease [15].

In Chapter III, we added to that knowledge through a spatial analysis among households in the Mezquital Valley. We estimated the association between household proximity to a wastewater canal and childhood diarrhea to test for the existence of spatially dependent routes of exposure between health and wastewater where it is reused. We found that living closer to a canal was significantly associated with higher odds of diarrhea for children compared to living farther away from a canal. We found no evidence that this association could be explained by agricultural occupation or consumption of crops irrigated with wastewater, which suggests the existence of other spatially dependent routes of exposure, such as aerosolization of pathogens from wastewater canals or spread of pathogens by animals and flies. These exposure routes appear to impact the entire community where wastewater is reused, rather than only those engaged in irrigation or consumers of contaminated crops. This finding is notable considering the World Health Organization's (WHO) current recommendations for the safe reuse of wastewater in agriculture, which suggest that personal protective equipment for farmers and sanitizing crops before consumption are the next best methods to reduce exposure to pathogens after wastewater treatment [16].

Our results suggest that those practices would not be sufficient to prevent adverse health outcomes where wastewater is reused, since the entire community is exposed to wastewater contaminants regardless of their occupation or consumption. Some interventions that could reduce community exposure to wastewater from canals used for transport include constructing barriers around canals to prevent animal exposure and moving canals underground to prevent almost all routes of exposure. Wastewater treatment remains the best solution for preventing adverse health throughout the lifecycle of fecal waste, but in practice most wastewater generated worldwide is never treated [17,18]. Our analysis underscores the importance of expanding wastewater treatment and ensuring the safe management of fecal waste from generation to reuse.

Chapter IV of this dissertation presented an example of a marginalized population within a high-income country that struggles with poor access to drinking water and sanitation despite the overall wealth of the country. We conducted a household survey in five Bedouin communities in the Negev region of southern Israel and found that Bedouin households face significant issues with drinking water availability, access to fecal waste management, and a high prevalence of diarrheal disease among children. In our sample of unrecognized villages, considered illegal by the government, the low availability of safely managed water and sanitation and high prevalence of diarrhea are comparable to levels in the world's poorest countries. The marginalization of Israel's Bedouin people is related to decades of struggle over land rights and government relocation off of traditional lands. Across the world, other marginalized communities within high-income countries similarly struggle with poor access to water and sanitation, resulting in high rates of preventable diseases [19–23]. Improving access to sanitation is mostly framed as an issue for low- and middle-income countries [24]. However, our analysis demonstrates that sanitation access is a global challenge that spans across all levels of wealth and income.

Overall, this dissertation provides new information for old challenges. Significant progress has been made in achieving access to sanitation over recent decades, but more work is needed to reach the most vulnerable populations. This dissertation work provides relevant knowledge to the topic, and can, ultimately, improve our ability to reach universal sanitation access and improve global health.

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APPENDIX

Table A.1. Characteristics of study households and children in the Mezquital Valley by quintile of household distance to a wastewater canal

	Group A1 (n = 109)	Group A2 (n = 87)	Group A3 (n = 52)	Group A4 (n = 32)	Group B1 (n = 67)	Group B2 (n = 39)	Group B3 (n = 93)	Group B4 (n = 40)	Group B5 (n = 45)
Household Characteristics									
Distance to a Canal in Meters, Mean (Range)	290 (8 – 1,135)	279 (14 – 507)	512 (208 – 990)	174 (27 – 281)	267 (24 – 937)	151 (7 – 402)	563 (155 – 1,181)	126 (2 – 391)	332 (23 – 949)
Total Years of Caregiver Education, Mean ± SD	9.7 ± 3.7	9.9 ± 2.9	9.2 ± 3.3	9.3 ± 1.7	9.0 ± 2.3	9.1 ± 2.6	9.5 ± 2.8	9.3 ± 3.2	9.8 ± 2.6
Has Refrigerator, No. (%)	92 (84)	72 (83)	31 (60)	19 (59)	57 (85)	33 (85)	78 (84)	29 (73)	36 (80)
Has Cellular Telephone, No. (%)	105 (96)	85 (98)	44 (85)	25 (78)	64 (96)	36 (92)	89 (96)	37 (93)	42 (93)
Has Vehicle, No. (%)	53 (49)	30 (34)	9 (17)	13 (41)	22 (32)	11 (28)	32 (34)	15 (38)	20 (44)
Has Washing Machine, No. (%)	71 (65)	46 (53)	17 (33)	13 (41)	46 (69)	12 (31)	67 (72)	25 (63)	26 (58)
Has Microwave, No. (%)	35 (32)	13 (15)	3 (6)	7 (22)	20 (30)	9 (23)	17 (18)	8 (20)	15 (33)

Has Computer, No. (%)	22 (20)	2 (2)	3 (6)	2 (6)	4 (6)	4 (10)	13 (14)	4 (10)	7 (16)
Has Flat Screen Television, No. (%)	59 (54)	60 (69)	26 (50)	17 (53)	36 (54)	21 (54)	58 (62)	27 (68)	32 (71)
Has Field Worker, No. (%)	15 (14)	63 (72)	28 (54)	17 (53)	15 (22)	11 (28)	10 (11)	2 (5)	7 (16)
Owns Dog, No. (%)	75 (69)	59 (68)	39 (75)	23 (72)	61 (91)	24 (62)	51 (55)	23 (58)	39 (87)
Has Access to Sewerage, No. (%)	94 (86)	86 (99)	45 (87)	32 (100)	65 (97)	37 (95)	93 (100)	33 (83)	44 (98)
Had Diarrheal Case at Any Survey Round, No. (%)	26 (24)	12 (14)	11 (21)	4 (13)	10 (15)	2 (5)	16 (17)	12 (30)	15 (33)
Had More than One Child Under Five During at Least One Survey Round, No. (%)	4 (6)	6 (15)	10 (11)	2 (5)	13 (29)	10 (9)	14 (16)	15 (29)	5 (16)
Characteristics of All Child Observations (n = 1,856)									
Child Had Diarrhea in Preceding Week, No. (%)	24 (7)	13 (5)	10 (5)	4 (4)	10 (5)	2 (2)	15 (5)	13 (10)	14 (8)
Rainy Season, No. (%)	229 (66)	188 (66)	120 (65)	66 (64)	137 (66)	88 (67)	199 (66)	84 (67)	112 (66)
Age of Child in Months, Mean ± SD	25.0 ± 14.5	28.7 ± 14.5	27.9 ± 13.2	30.7 ± 13.6	26.8 ± 14.3	30.1 ± 14.3	28.3 ± 13.9	26.5 ± 12.8	26.4 ± 13.2