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Untangling the impacts of climate change on waterborne diseases: A systematic review of relationships between diarrheal diseases and temperature, rainfall, flooding, and drought

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Abstract

Global climate change is expected to affect waterborne enteric diseases, yet to date there has been no comprehensive, systematic review of the epidemiological literature examining the relationship between meteorological conditions and diarrheal diseases. We searched PubMed, Embase, Web of Science and the Cochrane Collection for studies describing the relationship between diarrheal diseases and four meteorological conditions that are expected to increase with climate change: ambient temperature, heavy rainfall, drought, and flooding. We synthesized key areas of agreement and evaluated the biological plausibility of these findings, drawing from a diverse, multidisciplinary evidence base. We identified 141 articles that met our inclusion criteria. Key areas of agreement include a positive association between ambient temperature and diarrheal diseases, with the exception of viral diarrhea; and an increase in diarrheal disease following heavy rainfall and flooding events. Insufficient evidence was available to evaluate the effects of drought on diarrhea. There is evidence to support the biological plausibility of these associations, but publication bias is an ongoing concern. Future research evaluating whether interventions, such as improved water and/or sanitation access, modify risk would further our understanding of the potential impacts of climate change on diarrheal diseases and aid in the prioritization of adaptation measures.

Graphical Abstract

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Keywords

Climate; Weather; Diarrhea; Climate Change; Ambient Temperature; Heavy Rainfall; Flooding; Drought; Social Vulnerability

INTRODUCTION

Global climate change has the potential to severely impact human health worldwide, including diarrheal diseases,¹ which are highly affected by environmental drivers such as water availability.² The Intergovernmental Panel on Climate Change (IPCC) predicts that global surface temperature change for the end of the 21st century is likely to exceed 1.5°C relative to the period from 1850–1900, and in some scenarios is likely to exceed 2°C. Changes in the global water cycle also are expected, with increasing contrast in precipitation between wet and dry regions and between wet and dry seasons, although there may be regional exceptions.³

Because of the projected impacts of climate change on hydrological systems, waterborne enteric diseases are among the primary expected health impacts of climatic shifts.^{1, 4, 5} Understanding the impact of meteorological phenomena on enteric diseases is critical because even relatively small proportional increases in risk for diarrhea represent substantial overall impacts to the global burden of disease. Diarrheal diseases account for 10–12% of all deaths in children under five years old,^{6, 7} and an estimated 1.4–1.9 million deaths worldwide.^{7, 8} In addition to mortality, diarrheal disease can impair growth and cognitive development, and increase susceptibility to other infectious and chronic diseases,⁹ which may also exacerbate individual and community vulnerability to climate change.

Despite the importance of this topic, to date there has been no comprehensive, systematic review of the literature examining the relationship between climatic variables and patterns of diarrheal diseases. Other authors have reviewed associations between temperature and all-cause diarrhea,^{10, 11} meteorological variables and specific diarrheal pathogens,^{e.g., 12, 13–16} extreme weather events and waterborne diseases,¹⁷ and climatic influences on pathogens in the environment.¹⁸ However, these have been non-systematic reviews, focused on only one pathogen, and/or focused on specific geographical regions only. Thus, there is a need to review and synthesize the body of data that has accumulated on this topic, using rigorous

methods following established guidelines,^{19–21} to better understand and interpret the epidemiological patterns reported in the literature, inform climate change adaptation and mitigation measures, and direct future research on the topic.

In this paper, we present the results of a systematic review of epidemiological associations between diarrhea and ambient temperature, heavy rainfall, flooding, and drought. We chose these meteorological conditions because of the strong evidence that these conditions are increasing due to climate change, and because of prior publications suggesting associations with diarrheal diseases. We summarize key areas of agreement, as well as gaps in the literature. In a related paper we carried out a meta-analysis of the subset of these studies specifically related to ambient temperature and diarrhea.²² Here we also evaluate the biological plausibility of each key finding, presenting a conceptual framework that describes mechanisms to explain the observed exposure-response relationships. We conclude by providing examples of how the insights from this conceptual framework can be applied, including in the evaluation of adaptation strategies.

METHODS

Systematic Search

Articles were identified through a comprehensive search of the literature and by reviewing references from 54 review articles identified through the search process. Briefly, we searched PubMed, Embase, Web of Science, and The Cochrane Collection on 26 November 2013 for the health outcome terms “diarrhea*” or “diarrhoea*”, paired with climate or meteorological terms: “climate change”, “temperature”, “rain*”, “precipitation”, “flood*”, “drought*,” and “sea surface temperature”.

Two independent reviewers considered all articles for inclusion. Articles were deemed to meet inclusion criteria if they included: 1) human health outcome data; 2) all-cause diarrhea, pathogen-specific diarrhea, gastroenteritis, or diarrhea and vomiting as outcomes; and 3) temperature, heavy rainfall, flooding, or drought as exposures of interest related to rates of diarrheal diseases. Only English-language articles were included. Case reports were excluded. Meta-analyses and reviews were included if they provided a novel analysis of the data from the studies included. We decided *a priori* to focus on articles evaluating heavy rainfall rather than average rainfall because of previous work suggesting that this is the primary rainfall exposure influencing rates of diarrheal diseases.^{23–25} While our search originally included sea surface temperature, we decided to exclude this category because all 16 articles identified focused on cholera, limiting the generalizability of such findings to other diarrheal diseases. Duplicate reports were handled by selecting the study with the most complete dataset and analysis. Following initial article review, the two reviewers discussed and resolved differences in inclusion decisions, consulting with the other study authors as necessary. Figure 1 shows the PRISMA diagram¹⁹ of the selection process. For each article that met our inclusion criteria, one reviewer extracted relevant data (including exposure, outcome, location of study, study duration, study population) and at least one other person verified the extracted information.

Evaluating the quality of the evidence

We used three approaches to assess the quality of the evidence: 1) evaluating the weight of evidence, including study design and strength and consistency of observed relationships; 2) evaluating risk of bias; and 3) exploring biological plausibility of the relationships.

Weight of Evidence—Studies were classified as quantitative epidemiological studies, non-quantitative epidemiological studies or outbreak reports. A study was classified as quantitative if the authors presented the results of a statistical analysis. To account for potential publication bias, we did not require studies to present actual point estimates, allowing us to include studies that reported whether or not significant associations were detected by the particular analytical method applied. When studies presented the results of multiple analyses, we followed the Cochrane guidelines²⁰ and selected the analysis that the authors indicated as the final or main analysis (typically a fully adjusted model), and did not include supplementary exploratory studies. However, when analyses were stratified by exposure, location, or another risk factor, and a single unified estimate was not presented, we included each of the stratified analyses in our summary. We limited temperature studies to those that examined associations between temperature and diarrheal diseases at a one-month or finer resolution.

Quantitative studies were classified as showing positive or negative associations if the analysis allowed rejection of the null hypothesis ($p < 0.05$ or 95% confidence interval did not include the null). Studies were classified as showing a neutral association if the null hypothesis could not be rejected. Outbreak reports were not eligible to be classified as quantitative studies because these studies generally report on single events with a noted association between a meteorological event and diarrheal disease, and therefore are subject to publication bias. Meta-analysis was conducted on a subset of studies of temperature and diarrhea that met more rigorous reporting and design criteria; this analysis has been described elsewhere.²² For studies of heavy rainfall, flooding and drought meta-analysis was not appropriate, according to the Cochrane Collaboration Handbook, because of the disparate analytical methods and exposure definitions applied in these studies.²⁰ The approach used here allows us to present a semi-quantitative summary of the studies we identified, in order to allow inclusion of the widest range of studies and to avoid selection bias that would result from restricting studies to those with a single exposure and outcome definition.

Following the recommendations of others,²¹ we evaluated the strength and consistency of reported relationships between each exposure of interest and diarrheal diseases within each study type and, subsequently, between study types. Quantitative epidemiological studies were considered stronger evidence sources than non-quantitative epidemiological studies and outbreak reports. Evidence of a dose-response relationship, consistency across study types and dissimilar populations, and large effect sizes were considered factors that increased confidence in the observed associations. Evidence of bias, imprecision in effect estimates and unexplained inconsistencies in the observed associations were considered factors that decreased confidence. We classified the body of evidence for each association as

providing high, moderate, low or very low confidence to draw conclusions, adapting previously outlined categories.^{21, 26}

Risk of bias—Publication bias was a primary concern, particularly because the evidence consisted of observational epidemiological studies and outbreak reports. Because we did not perform meta-analysis (for the reasons described above), standard methods to assess publication bias such as assessment of funnel plot asymmetry were not appropriate. Instead, we compared the findings of quantitative epidemiological studies that presented multiple analyses to those that presented a single estimate. We hypothesized that if there were a tendency to publish “significant” (or non-null) findings, we would be more likely to find non-significant findings in manuscripts that presented multiple estimates (since one “significant” finding among several analyses may be seen as sufficient for publication). We also summarized the location of studies, to examine whether some areas were over- or under-represented in the literature.

Biological plausibility—To evaluate the plausibility of associations reported in the epidemiological articles included in the review, we took advantage of the detail provided in these articles and also drew on other evidence from the literature to develop a conceptual diagram that details potential causal pathways between meteorological conditions and diarrheal disease outcomes.

RESULTS

Weight of Evidence—We identified a total of 141 articles that met our inclusion criteria. Details of each of these studies are provided by meteorological exposure in the Supplemental Material (Tables S1–4). In Table 1 we summarize the evidence of key findings on the relationship between diarrhea and each of our exposures of interest, and in Table S5 we summarize the results reported in the 67 articles that provided a statistical analysis of the association between meteorological exposures and diarrhea. The majority of studies focusing on temperature, heavy rainfall and flooding reported a significant positive association between the exposure variable and diarrhea. Below we review epidemiological patterns observed for each of the exposure categories.

Temperature

We identified 74 articles that examined the relationship between ambient temperature and diarrheal diseases (Table S1^{12–16, 27–95}), including 45 articles with a total of 82 statistical analyses. These articles included data collected between 1950–2009. Authors used a range of exposure definitions including average, maximum, and minimum temperatures over daily, weekly, biweekly, and monthly resolutions, and considered a variety of different temporal lags between exposure and outcome. These studies were conducted in a variety of settings. Despite this heterogeneity, there was consistency in the observed relationships. In most of the quantitative analyses (65%), there was a significant positive association between temperature and diarrhea, including 69% of analyses of all-cause diarrhea and 79% of analyses of bacterial pathogens. However, in most analyses of viral diarrheal pathogens (71%), primarily rotavirus, there was a negative association between ambient temperature

and diarrhea. Only five analyses in three articles considered protozoan diarrheal pathogens; three of these analyses (60%) described a positive association with temperature.

Several studies examined the impact of temperature shifts associated with El Niño events on diarrhea, allowing examination of temperature–diarrhea relationships outside the range of normal temperature variation for a particular location. Ambient temperature increases during El Niño events in Peru were associated with increased diarrhea among children in a cohort study³¹ and increased pediatric diarrhea admissions in children.^{79, 96}

Heavy Rainfall

We identified 31 articles describing the relationship between heavy rainfall and diarrhea that met our inclusion criteria, including 10 articles with a total of 14 statistical analyses, and 18 studies reporting on an outbreak following a heavy rainfall event (Tables S2a^{23–25, 39, 43, 46, 50, 81, 97–101} and S2b^{102–123}). These articles included data collected between 1910–2009. Articles used a wide variety of definitions of heavy rainfall, outcome definitions, data sources, and analytical approaches, which makes it difficult to compare results across studies. While there is heterogeneity in observed effects, some general trends are apparent. Of the articles that met our quantitative inclusion criteria, a significant positive association between heavy rainfall and diarrhea was noted in most (71%) of these (Table 1, Table S5). None of the quantitative studies evaluated viral or protozoan diarrhea.

Several long-term analyses of nationwide datasets reported significant associations between heavy rainfall and outbreaks of waterborne diseases in the USA,^{24, 124} Canada,²⁵ and the UK,¹⁰⁰ and between heavy rainfall and hospital admissions for diarrhea in Taiwan.³⁹ More location-specific studies of associations between heavy rainfall and diarrhea have found mixed results. In some cases, positive associations have been observed, such as higher observed diarrhea rates during peak monsoon rainfall months in the Philippines⁹⁷ and Bangladesh,⁴³ and increased diarrhea with increases in maximum rainfall in Ghana.⁸¹ Two studies (in Bangladesh⁴⁶ and the USA⁹⁸) observed no association between heavy rainfall and diarrhea, although the US study found that *any* rainfall four days prior was significantly associated with an 11% increase in acute gastrointestinal illness (AGI) visits. A common theme among several studies, from a range of settings (the Philippines,⁹⁷ Ecuador,²³ Swaziland,¹⁰⁹ UK,^{100, 120, 122} USA,¹²¹ and Japan¹²³), found that heavy rainfall after a dry period was associated with increased diarrhea. The study in Ecuador also found the converse, i.e., that heavy rainfall following a wet period was protective against diarrhea.

Our search also resulted in several studies reporting on outbreak investigations, ranging in size from just a few cases up to hundreds of thousands, again from a range of settings (Turkey,¹⁰² UK,^{104, 106, 120} Canada,^{105, 107, 117} USA,^{110, 111, 113, 114, 121} Japan,¹²³ Swaziland¹⁰⁹), citing heavy rainfall immediately preceding the outbreak as a presumptive cause of contamination of water supplies.

Flooding

We identified 40 articles on the relationship between flooding and diarrhea that met our inclusion criteria, including 14 articles with a total of 25 statistical analyses, and 15 studies that reported on an outbreak following a flood (Table S3a^{58, 125–148} and S3b^{149–162}). These

articles included data collected between 1985–2011. Of the articles that met our quantitative inclusion criteria, a significant positive association was noted in most (76%) of these (Table 1, Table S5). Most of the quantitative analyses evaluated all-cause diarrhea, thus it is difficult to generalize quantitative trends by taxa.

In the non-outbreak studies with a comparison group (Table S3a), several authors report higher diarrhea rates during flood periods versus pre-flood or non-flood period in the same year^{125, 132, 138, 146, 148} or versus comparable time periods in non-flood years.^{10, 127, 129, 130, 132, 133, 135, 141, 144, 148, 163} Many studies also report higher diarrhea rates in flood-affected compared to unaffected groups,^{58, 138, 139, 142, 145, 147} although two studies did not detect such a difference.^{134, 137} Some studies report exposure-response effects, with increasing contact with flood waters^{140, 146} or flood depth¹³⁹ associated with increased risk of diarrhea. In reviews of large national databases, positive associations were noted between flood days and diarrhea incidence in China,¹³¹ and in Finland the most common causes of waterborne disease outbreaks were floods and surface runoff.¹³⁶ Several articles report changes in the percentage of diarrhea cases attributable to particular pathogens during or after floods, including increased detection of pathogenic *E. coli*,^{126, 141} and *V. cholera*,^{132, 141} and both increased¹⁴¹ and decreased¹³² detection of rotavirus.

Table S3b details articles that reported on outbreaks of diarrheal diseases following floods, or rates of clinical diarrhea following flooding events. In these studies, flood-related outbreaks were reported for cholera¹⁵⁹ or acute watery diarrhea,^{161, 164} enterotoxigenic *E. coli* (ETEC),¹⁵⁹ rotavirus,^{149, 152} and norovirus.^{153, 160, 156}

Drought

Our search identified only three articles examining the relationship between drought and diarrheal diseases, only two of which met our quantitative inclusion criteria (Table 1; Table S4^{109, 165, 166}). These articles included data collected between 1978–2002.

Burr et al.¹⁶⁵ found a dose-response relationship between drought-related water restrictions (hours per day without access to municipal water) and rates of childhood diarrhea and vomiting in Wales. Effler et al.¹⁰⁹ document the first reported outbreak of *E. coli* O157 in Swaziland and South Africa, noting that the outbreak was preceded by heavy rainfall following three months of drought. The authors suggest that stress on livestock during the drought and heavy livestock use of traditionally exclusively human water sources, concentrated pathogens, facilitated human exposure, and allowed pathogens to be distributed broadly when the first heavy rains arrived. De Sherbinin¹⁶⁶ found no significant correlation between diarrhea and drought in Africa, defining drought as precipitation <75% of the median for the region occurring for at least three months between 1980–2000.

Risk of bias—We observed evidence of publication bias in our review. Studies that reported multiple estimates were approximately twice as likely to include results showing no effect or an effect in the direction contrary to the prevailing literature compared to manuscripts reporting a single analysis (16% and 32% of estimates from studies with single and multiple estimates, respectively) (Figure 2). We also observed geographic over-representation from certain areas: while studies were identified from all regions of the world

(Figure 3), of the 141 studies we reviewed, 45% were from four countries: Bangladesh (20), United States (17), the United Kingdom (13) and India (13). Additionally, smaller outbreaks were more commonly reported upon in developed countries.

Biological plausibility—Examination of biological plausibility of the observed relationships is discussed below.

DISCUSSION

Weight of Evidence—We observed a predominant trend for positive relationships between diarrhea and meteorological conditions that are expected to increase with climate change, with the exception of the relationship between ambient temperature and viral diarrhea. Confidence in these relationships ranged from very low (for the relationship between drought and all-cause diarrhea) to high (for the relationship between ambient temperature and bacterial diarrhea). Our systematic review uncovered the most articles focusing on the effect of temperature on diarrhea, perhaps because temperature can be measured continuously, whereas heavy rainfall, flooding, and drought are episodic and less predictable events. Definitions for heavy rainfall, flooding, and drought are often much less concrete than those of temperature, creating a less unified literature for those exposures, particularly where sophisticated modeling is conducted. Most of the studies of temperature effects were time-series analyses comparing long-term temperature datasets with diarrhea surveillance or hospital records datasets. For both heavy rainfall and flooding, studies could be divided into those that provided a systematically collected dataset with a robust comparison group versus those that reported on outbreaks. While we did not include the outbreak studies in our quantitative analysis because they are inherently subject to publication bias (only outbreaks with a noted association with meteorological conditions are captured), they still provide useful information, so we included them in the qualitative review.

The epidemiological literature on drought and diarrhea was particularly sparse. This may reflect difficulties in precisely defining drought, the timescale over which droughts occur, and outcomes reported for drought events (i.e., famine or malnutrition instead of diarrhea). Stanke et al. highlight the inherent difficulties in documenting the health effects of drought,¹⁶⁷ due to lack of standardized definitions,¹⁶⁸ complexity of determining when droughts begin and end, the accumulation and persistence of effects over time, and the indirect effects on health related to mediating circumstances such as loss of livelihoods.. In addition to extensive periods of extreme drought, changes in the duration and/or extent of seasonal dry conditions may also affect waterborne diseases, but our search was not designed to capture these effects.

Risk of Bias—We observed evidence of reporting bias in our review. When we restricted our summary of the quantitative studies to those with a single estimate, the proportion of studies finding a positive relationship between temperature, heavy rainfall, and flooding all increased (Figure 2). This suggests that there may be considerable reporting bias – studies that reported multiple estimates were more likely to include results showing no effect or an effect in the direction contrary to the prevailing literature. We also found evidence of over-

representation of certain geographic regions in the studies reviewed: 45% of the studies were from four countries and smaller outbreaks were more commonly reported upon in developed countries. The geographic representation of studies may be of particular concern for flooding, heavy rainfall, and drought because infrequent events may bias the geography further toward places where robust surveillance programs are already in place. Our decision to include only English language articles might have contributed to the lack of geographic representation of studies.

Biological Plausibility—In order to evaluate the plausibility of associations reported in the epidemiological articles included in the review, we developed a conceptual diagram illustrating potential causal pathways between meteorological conditions and diarrheal disease outcomes (Figure 4). This framework takes advantage of the rich detail provided in the articles included in the review and draws on other evidence from the literature, to explore potential biophysical and behavioral explanatory mechanisms for these relationships. Note that the figure focuses on the mechanisms leading to positive relationships, as a way to illustrate the overall trends observed in this review. In some cases the relationship will be negative, for example as often is observed for ambient temperature and viral diarrhea; this is not captured in the figure but is discussed in the text below. Below we describe plausible mechanisms associated with the observed patterns for each exposure category.

Temperature

The patterns observed in the relationship between temperature and diarrheal diseases highlight the importance of distinguishing between taxonomic categories of pathogens when considering the mechanisms involved in this relationship. Microorganisms differ in their rates of environmental survival and reproduction outside of the host, because of differential sensitivity to changes in heat, moisture, oxygen, light and nutrients.^{169–172}

The details of environmental conditions differentially affecting bacteria, protozoa, and virus survival outside of the host may explain the contrasting patterns observed for these different types of pathogens. Protozoans form spores, and even *E. coli* experience biphasic lifestyles, with host-independent and host-associated phases.¹⁷³ In terms of pathogen survival, increased die-off occurs with increasing temperatures outside of the host for bacteria,^{170, 173} protozoa,^{174, 175} and viruses.¹⁷⁶ However, in groundwater, the evidence that temperature affects pathogen survival is more consistent for viruses than for bacteria.¹⁷⁶ Temperature-based inactivation may be more complex for bacteria. Inactivation rates of fecal coliform bacteria, which may replicate in aquatic environments at higher temperatures given adequate nutrient levels,¹⁷⁷ may be affected by a combination of die-off, reproduction, predation by larger organisms, competition for nutrients, bacterial antagonism, enzymatic or chemical inactivation, and phage lysis.¹⁷⁶ Increased yields of bacteria from drinking water delivery systems have been recorded during warmer, summer months.¹⁷⁸ In addition, increased temperatures may increase bacterial and protozoan pathogen loads in animal reservoirs, and may prolong transmission seasons.¹⁶⁹

Temperature may also affect expression of virulence genes in bacterial pathogens. For bacterial pathogens of mammals, elevated temperature can signal successful infection of a

host, and lead to expression of bacterial virulence genes that continue as long as the bacteria remain at the elevated temperature.^{179, 180} Growth temperature is considered the most important environmental stimulus for the activation of virulence gene expression in *Shigella* spp., which have been shown to be induced at 37 °C and repressed at 30 °C.¹⁸⁰

Host factors directly or indirectly influenced by meteorological conditions may also explain the observed epidemiological patterns. For example, Pitzer et al.¹⁸¹ suggest that peaks in viruses in cooler periods may be most strongly influenced by demographics and human behavioral factors. Interestingly, some articles noted seasonal differences in observed relationships,^{30, 64, 96, 182} which supports the idea that seasonal factors not directly related to environmental conditions influence the observed patterns. Higher temperatures may also increase the probability of food spoilage,^{40, 63, 183} and concurrent temperature-related changes in food storage and consumption practices may affect disease risk. Water consumption rates may also increase during warmer times of the year, increasing probability of pathogen ingestion in regions with poor quality drinking water.

Heavy Rainfall & Flooding

While ambient temperature may impact pathogen survival and host behavior, both heavy rainfall and flooding can directly affect transport of pathogens, and can affect the existing water and sanitation infrastructure, altering human exposure patterns. Severe flooding can also lead to population displacement, with a variety of resulting health impacts.^{184, 185}

Transport of pathogens as a result of heavy rainfall occurs in multiple ways. If pathogens from human and/or animal excreta are present in soils and on environmental surfaces or subsurfaces, rainfall can mobilize these pathogens and transport them into surface waters or to other areas of a village, exposing individuals to pathogens. It is well documented that water in general and floodwaters specifically can spread pathogens within watersheds.^{186, 187} Heavy rainfall can also lead to resuspension of pathogens in sediment,¹⁸⁸ or mobilization of pathogens in soils.¹⁸⁹ Heavy rainfall events can cause contamination of groundwater,^{e.g., 112} and can lead to saturation of the subsurface,^{105, 110} which facilitates water transport of pathogens into surface or groundwater.

Several articles document increases in diarrhea or outbreaks following dry periods, suggesting an interaction between heavy rainfall events and the accumulation of pathogens in the environment.^{23, 97, 100, 109, 120, 122, 123} This is consistent with the results of Carlton et al.,²³ who found that heavy rainfall was associated with increased risk of diarrhea following dry periods but decreased risk following wet periods. Potential time-dependent mechanisms explaining these interactions have been described by Levy et al.¹⁴ and Moors et al.¹⁹⁰ The “concentration effect” occurs when dry conditions allow for the accumulation of microorganisms in the environment. Precipitation can cause a short-term “runoff effect,” via flushing of pathogens into surface water, resuspension of pathogens in sediment, and sewage overflows. When this occurs over longer time periods, the “dilution effect” may act, with higher flows diluting microbial concentrations. The dilution effect may be especially salient in the case of flooding, where heavy rainfall may initially distribute accumulated contaminants but then dilute contaminants after the initial flushing has occurred.

Evidence of dose-response effect related to explicit contact with floodwaters was noted in several studies, including flooding explicitly in the subject's house or yard,¹⁴⁶ increasing association with increasing flood depth,¹³⁹ explicit skin contact with flood water,¹⁴⁰ and direct contact with floodwaters.¹⁶⁰

Many articles discuss animal sources of contamination.^{102, 113, 115, 121, 122} Factors affecting pathogen transport in runoff, such as slope, vegetation, flow-rate, infiltration rate, and rainfall intensity have been studied in agricultural settings.¹⁸ Heavy rainfall can promote manure-borne oocyst transport of protozoan pathogens,¹⁸ and may lead to splashing of manure-amended soils onto fresh produce.¹⁹¹ Exposure to zoonotic pathogens can also cause illness through recreational exposure.¹¹⁵

An examination of relative rates of specific pathogens in flood versus non-flood periods can provide insight into which pathogens are associated with flooding. Several such analyses have been carried out in Bangladesh, with studies finding variable results: both cholera and ETEC associated with floods;¹⁵⁹ an initial peak in the incidence of rotavirus coinciding with flooding followed by a decline immediately after the flood receded;¹⁵² increases in the proportion of rotavirus diarrhea, rotavirus in older children, percentage of mixed rotavirus infection cases, and an abrupt change in epidemic strains coinciding with the spread of floods;¹⁴⁹ cholera playing a primary role in flood-related diarrhea epidemics, but rotavirus and ETEC also contributing to the epidemics;¹⁴¹ cholera as the most common cause of diarrhea during flood years, with rotavirus more common in non-flood years.¹³²

Heavy rainfall and flooding can also affect pathogen transmission via impacts on sanitation and/or drinking water treatment infrastructure. Several articles document or discuss heavy rainfall causing contamination of drinking water sources^{102, 104–107, 110, 112–114, 116, 117, 122, 123, 151} or food products.¹⁰⁸ Floods can overwhelm water systems, causing backflows that lead to contamination of groundwater and other drinking water sources.^{e.g., 156} Furthermore, several studies reported on dose-response relationships between consumption of municipal drinking water after a heavy rainfall and gastrointestinal illness.^{103, 104, 107, 117, 121} Resuspension of sediments by heavy rainfall events can lead to high turbidity levels in source waters, which can overwhelm drinking water treatment infrastructure.^{104, 111, 116, 192} High turbidity levels in source waters have been associated with elevated rates of gastrointestinal illness in the United States and elsewhere.^{193–197}

Many human factors can modify the associations between diarrheal diseases and heavy rainfall or flooding. For example, rainfall effects on diarrhea can vary by local practices such as fecal sludge application in agricultural communities.⁸¹

Beyond the effects of heavy rainfall, floods can lead to broader effects. Floods may destroy crops and kill livestock, which may lead to longer term effects associated with malnutrition.⁹ Flooding can also displace populations to temporary or permanent communities with inadequate infrastructure. For example, there were several reports of outbreaks of diarrheal diseases amongst Hurricane Katrina evacuees,^{153, 154} and this was cited as an explanation

for the elevated diarrhea and cholera rates observed in Bangladesh after a severe flood in 1998.¹³³

Drought

Despite the paucity of epidemiological data available, there are many plausible mechanisms for an association between dry conditions and/or drought and diarrheal diseases. Biophysical effects include the accumulation and concentration of fecal contamination in water sources under dry conditions,^{190, 198, 199} which may increase the probability of human contact with pathogens. As mentioned above, dry conditions may lead to a build-up of a fecal film on surfaces – causing a pulse of pathogens when rains occur, potentially increasing aerial transport of fecal material due to soil drying,¹⁹⁰ and also potentially leading to increases in fly abundance.¹⁸² On the other hand, droughts are typically periods of immobilization and inactivation of microorganisms of fecal origin, due to lack of hydrologic connection between surface soils and subsurface aquifers, as well as inactivation in the water column due to higher temperatures and irradiation.¹⁸⁸

Effects may also be associated with water supply conditions, such as the dose-response association between water restrictions and rates of childhood diarrhea observed by Burr et al.¹⁶⁵ Drought conditions may cause intermittent water supply, which can lead to intrusion into drinking water distribution system pipes.^{200, 201} Decreases in rainfall may increase the fraction of wastewater in surface water,¹⁹⁰ which can lead to consumption of lower quality water due to increases in the concentration of pathogens in both drinking and irrigation water sources. Dry conditions can also increase sharing of water sources between human and animal populations, as observed in Swaziland.¹⁰⁹ However, during dry seasons or under drought conditions, people may switch to less contaminated water sources such as bottled or well water. Pinfold et al. document shifts in drinking water sources in the rainy versus dry seasons in Thailand.⁷⁶ Water fetching distances, which have been associated with increased water contamination, diarrhea and impaired growth,^{202, 203} may increase with decreasing water availability. Hygiene can also be impaired by decreased water availability.¹⁹⁰

Indirect effects of drought include malnutrition, associated with increased susceptibility to diarrheal diseases, due to negative effects of drought on agricultural crops, livestock, and fisheries. A review on the health impacts of drought cite malnutrition and its associated implications for morbidity and mortality as “the most obvious and best recognized health impact of drought.”¹⁶⁷ Displacement of populations may also occur as a consequence of prolonged drought conditions, which may lead to an increase in the population with inadequate water, sanitation, and hygiene (WaSH) conditions.

Implications for population health in a changing climate—It is evident from our review of the literature that both biophysical and social phenomena determine the impact of meteorological conditions on diarrheal diseases. The extent to which a population experiences health impacts from climatic conditions depends not only upon the severity of the meteorological exposure, but also on factors such as water and sanitation infrastructure, healthcare access, and available resources with which to intervene to prevent increased disease burden. The IPCC recognizes this, stating that “vulnerability encompasses a variety

of concepts and elements including sensitivity or susceptibility to harm and lack of capacity to cope and adapt.”²⁰⁴

Still, our review reveals that even in developed countries that have more extensive water and sanitation infrastructure, elevated temperature, heavy rainfall, and flooding can impact risk of diarrheal diseases. In the United States, the largest documented waterborne disease outbreak was associated with water treatment plant failure during a spring runoff event,¹¹⁶ and significant associations between heavy rainfall and outbreaks of waterborne diseases have been documented.²⁴ A recent review of extreme water-related weather events and waterborne disease outbreaks found that in both developing and developed countries, the most common cause of outbreaks was contamination of the water source through heavy rainfall (55.2% of studies) and flooding (52.9% of studies). The authors of this review note that while in developing countries this was usually associated with untreated water, in developed countries, in the majority of cases, this was associated with contamination of a treated water source.¹⁷

Understanding the mechanisms involved in exposure – disease response relationships, as illustrated in Figure 4, can provide insights into where to intervene to prevent transmission of waterborne disease agents, under both present day conditions and future climate scenarios. In Figure 5 we illustrate this for the example of heavy rainfall and flooding. The effects of these events may be minimized through prevention of contamination of water systems, by controlling floods from occurring (“Flood Control Infrastructure”), or by reducing the presence of pathogens in the environment available for transport through adequate disposal of fecal material (“Sanitation/Wastewater Systems”). Should contamination of the environment and/or drinking water sources occur, prevention of human ingestion of pathogens may occur through efforts to improve hygiene (“Hygiene Education”) and/or through household drinking water treatment (“Drinking Water Treatment at the Point of Use”), as well as provision of drinking water treatment systems and adaptive management of those systems in order to prevent drawing from turbid water sources (“Drinking Water Treatment Systems & Management”).

Limitations—Different types of data and approaches to analysis limited our ability to combine quantitative estimates across the different studies included in the review. In a separate manuscript, we compiled a meta-analysis for studies considering temperature as an exposure. In that manuscript, we address issues such as timescale of analysis, treatment of lags, different exposure definitions (e.g., mean vs. maximum vs. minimum temperature), and stratify by pathogen.²² In the present analysis, we made an *a priori* decision to focus on articles reporting on the effects of heavy rainfall, so we did not capture studies reporting on the effects of rainfall defined in other ways, such as average precipitation. Similarly, we decided not to include sea surface temperature as a primary exposure of interest because this literature was exclusively focused on cholera, primarily in Bangladesh; this removed some sophisticated analyses from consideration.^{99, 205–208} We limited our review to articles published in English only, which narrows the scope of this review, and may have decreased our ability to collect the broadest possible sample of reports on these exposures. However, only 29 of 3,952 articles captured in our initial search (which was not restricted by language) were rejected on the basis of language. Many of these reports were considered

irrelevant because review of titles and abstracts determined that they did not explore the relationship between diarrhea and the meteorological exposures.

Future research needs—Our assessment of the mechanisms underlying the relationships between meteorological conditions and diarrheal diseases reveals complex causal pathways. While studies evaluating simple exposure-disease associations are a necessary first step, epidemiological studies in this area should move towards more sophisticated analyses that evaluate the proposed causal pathways and the potential impacts of interventions to reduce risk. Specifically, we identify three priority research areas. First, there is a need to evaluate the ways in which factors known to affect diarrhea risk such as demographics and water and sanitation infrastructure modify relationships between meteorological exposures and diarrhea incidence. The social factors that determine a community's ability to cope with and respond to climate variability must be made explicit in any study of climate and health. This is especially the case for waterborne diseases, where infrastructure is so clearly critical to reduction in disease burden.²⁰⁹ In addition, it may be important to evaluate the combined effects of climate change and land use change on diarrheal disease.²¹⁰ Studies that evaluate changes in climate-disease relationships by modifiable risk factors (such as access to safe drinking water or vaccination coverage), will improve our ability to identify vulnerable populations and opportunities to intervene to prevent negative consequences.

Second, there is a need to evaluate differences in the relationship between meteorological variables and diarrheal diseases by causative pathogen. Our findings here and elsewhere^{14, 22, 211} suggest that the relationship between temperature and diarrheal diseases varies by pathogen. We suspect that the relationships between diarrhea and heavy rainfall, flooding, and drought may also depend on the causative pathogen, as exposure pathways and environmental survival can vary considerably by pathogen. However, few studies examined the relationships between heavy rainfall, flooding, or drought and pathogen-specific diarrhea. Researchers should make attempts to go beyond examinations of all-cause diarrhea, and evaluate specific pathogens whenever possible. Classifying diarrhea by causative pathogen is more resource intensive than measuring all-cause diarrhea, however prior studies have demonstrated this is possible even in remote and/or low-resource settings.^{e.g., 212–214} Taxa- or even pathogen-specific estimates of the relationship between meteorological conditions and diarrheal agents would help guide public health practice with respect to climate change adaptation efforts and vaccine development prioritization.

Third, there is a need to evaluate the concurrent impacts of multiple meteorological exposures. A common theme that emerged from this review is that the effects of heavy rainfall on diarrhea were magnified after dry periods, suggesting that models should incorporate antecedent conditions. Analyses that incorporate combined effects and/or interactions between temperature and rainfall are also needed. To address these research needs, non-linear models such as threshold models may be appropriate in these cases, as may mathematical models that can evaluate mechanistic assumptions against sparse observed data.

CONCLUSION

We observed a predominant trend for positive relationships between diarrhea and temperature, heavy rainfall, flooding, and drought, meteorological conditions that are expected to increase with climate change. The exception to this trend was the relationship between ambient temperature and viral diarrhea, which was primarily negative. These trends occurred in both developing and developed countries. Our review also uncovered synergistic relationships between drought and heavy rainfall in promoting diarrheal diseases.. Epidemiological studies were limited for drought, and few studies of pathogen-specific diarrhea were observed for heavy rainfall, flooding, or drought, thereby limiting conclusions.

This review and conceptual framework underscore the importance of considering basic approaches to improving public health, including civil and environmental engineering and behavior change efforts, in climate change adaptation efforts. In 2012, an estimated 842 000 diarrhea deaths were caused by inadequate water, sanitation and hygiene in low- and middle-income settings.²¹⁵ While diarrheal disease burden has been declining globally, climate change has the potential to slow progress in reducing the burden of diarrheal diseases, particularly disease burden linked to unsafe WaSH conditions.²¹⁶ Future research to evaluate the ability of such measures to reduce the deleterious health impacts of climate change is needed. However, given the high current baseline rates of these diseases and the potential for increases in diarrheal disease risk under future climate conditions, investing in the prevention of diarrheal diseases through improvements in WaSH systems and other proven diarrhea prevention strategies should be a global priority.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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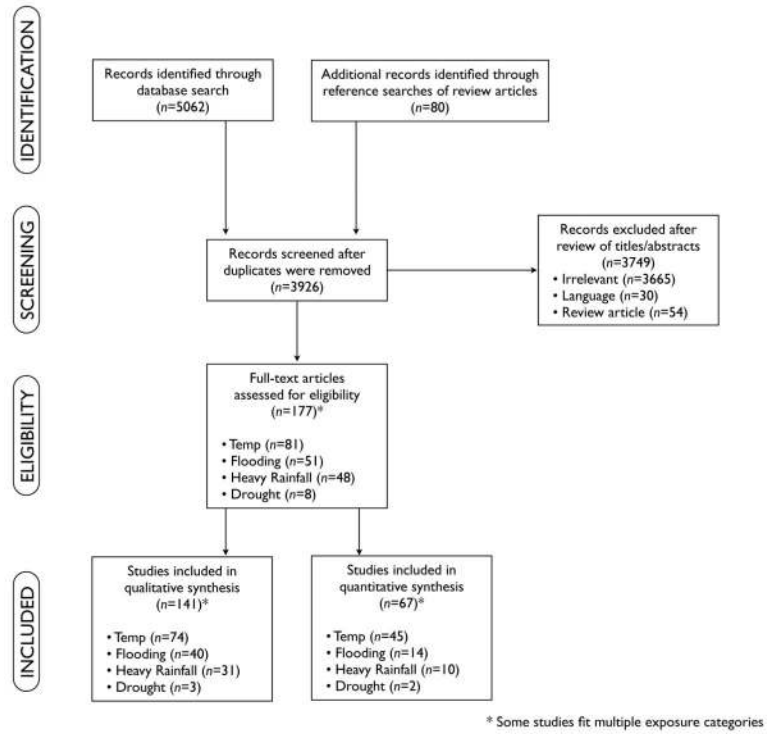
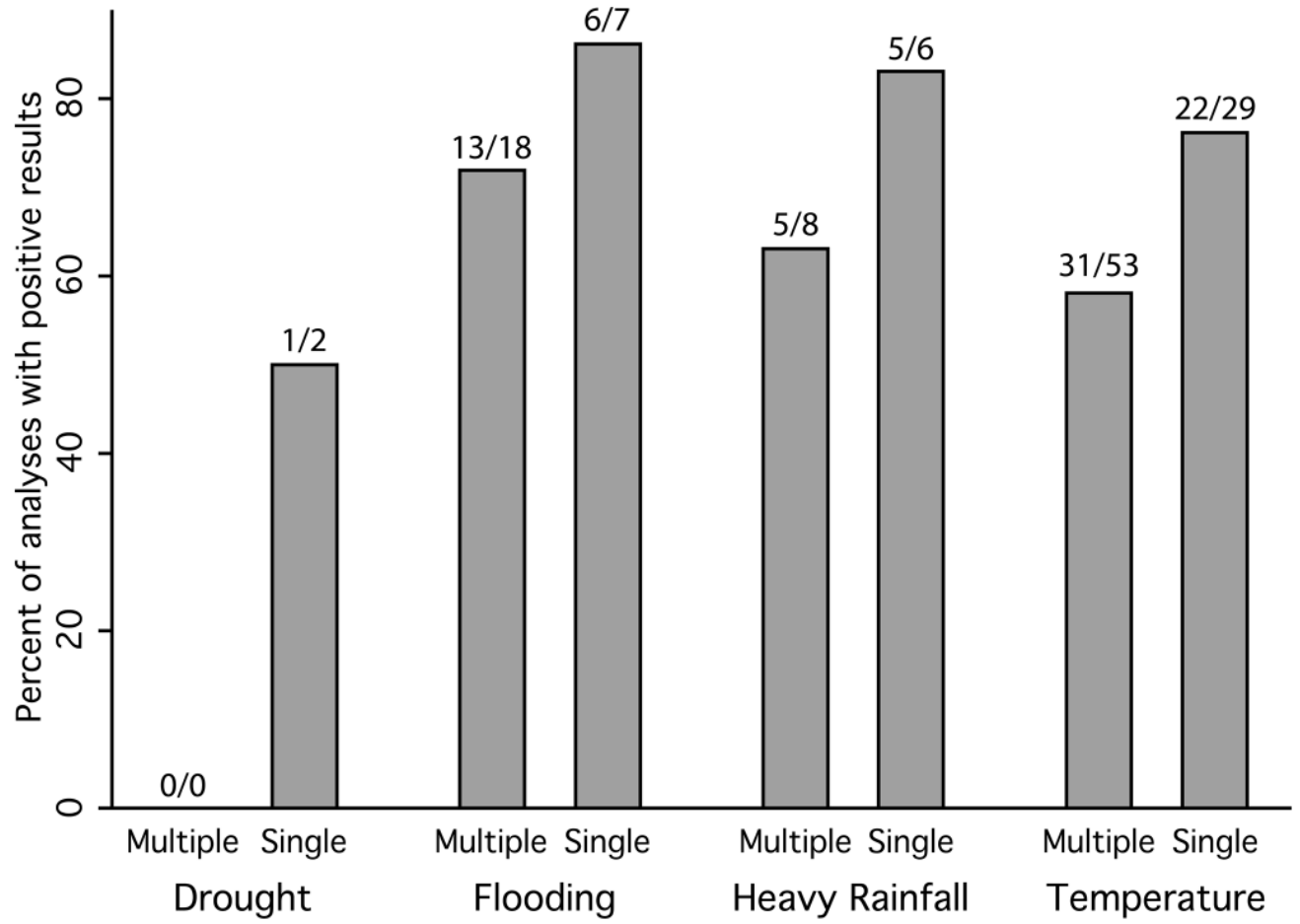


Figure 1. PRISMA diagram of the study selection process.

Figure 2a



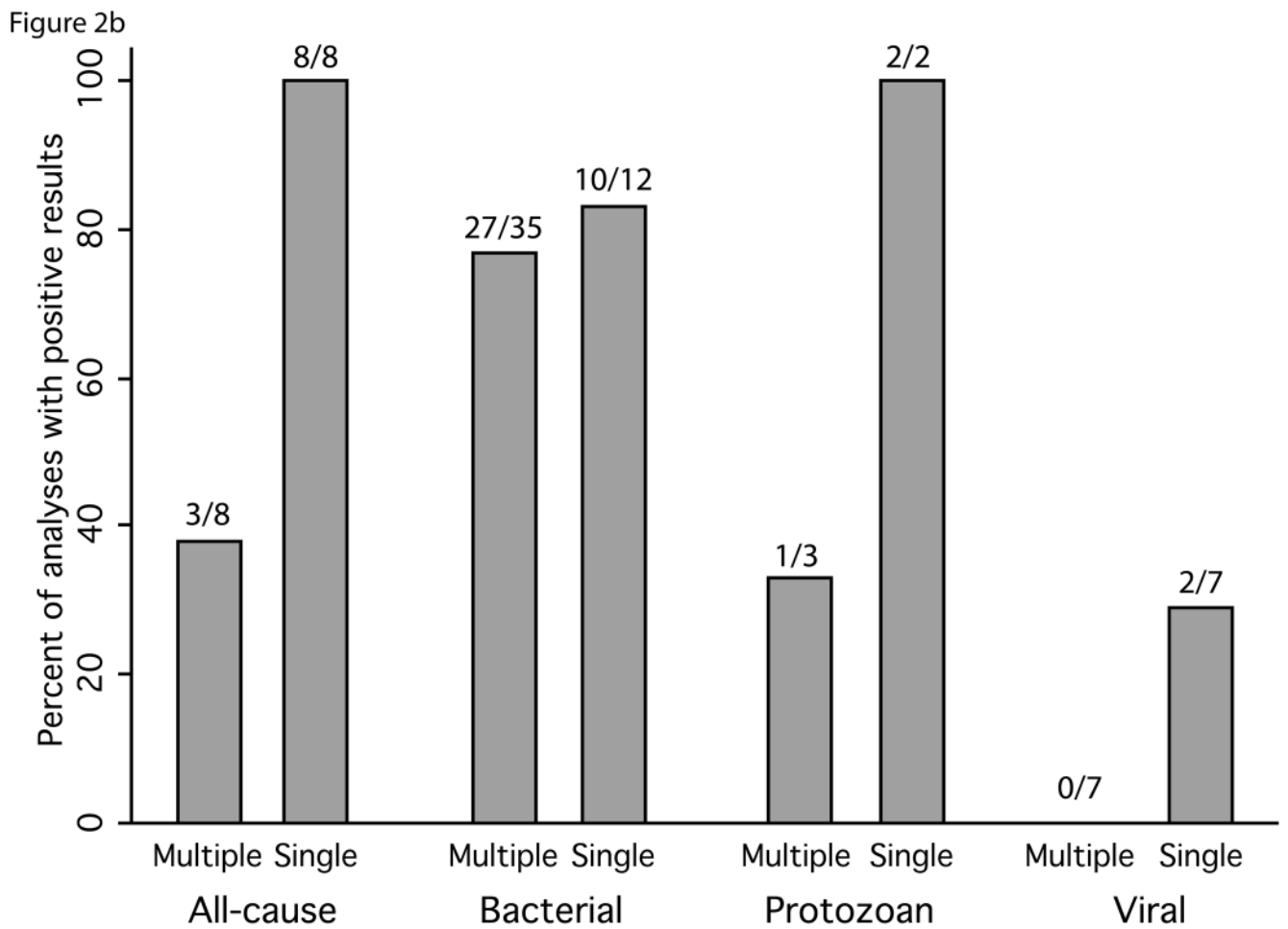


Figure 2.

Comparison of the associations between diarrhea and exposures of interest presented in manuscripts with a single quantitative analysis to manuscripts with multiple analyses. Percentage of positive results shown for a) drought, flooding, heavy rainfall and temperature; and b) for subsets of temperature papers by type of pathogen reported on in the study. Number of analyses with reported significant positive associations over the total number of analyses is shown above each bar.

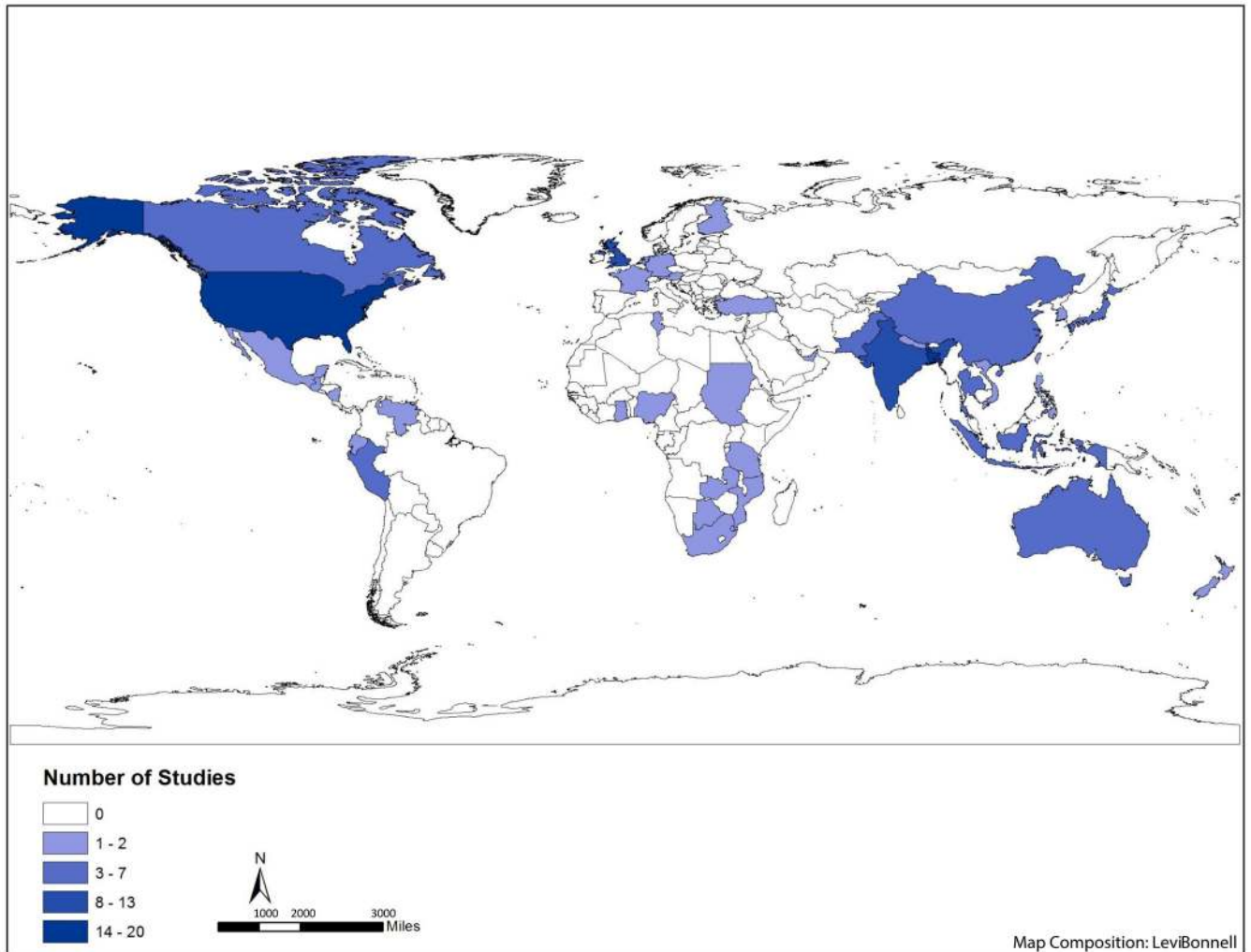


Figure 3.

Map showing all studies included in the systematic review by country. The 8 studies that included 6 or more countries were excluded from the map. This includes 3 global studies, 2 European studies, 2 African studies and 1 South Asian study. World shapefile is from the GADM database of Global Administrative Area.

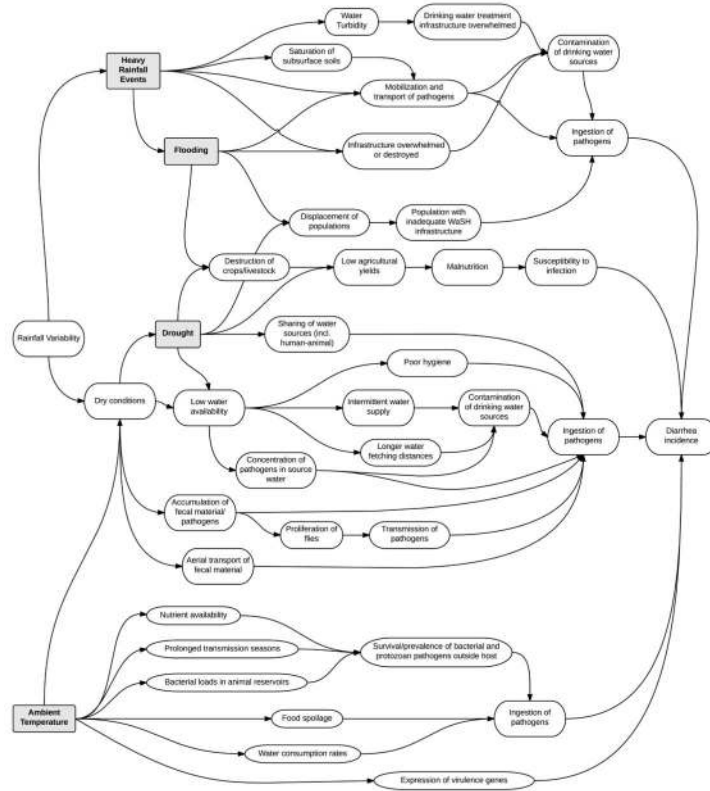


Figure 4. Conceptual diagram illustrating mechanisms by which meteorological conditions expected to be impacted by climate change could potentially increase the risk of diarrheal diseases. All arrows lead to increases in the items listed. Note that the diagram does not show possible mechanisms for how the same factors could potentially decrease the risk of diarrheal diseases.

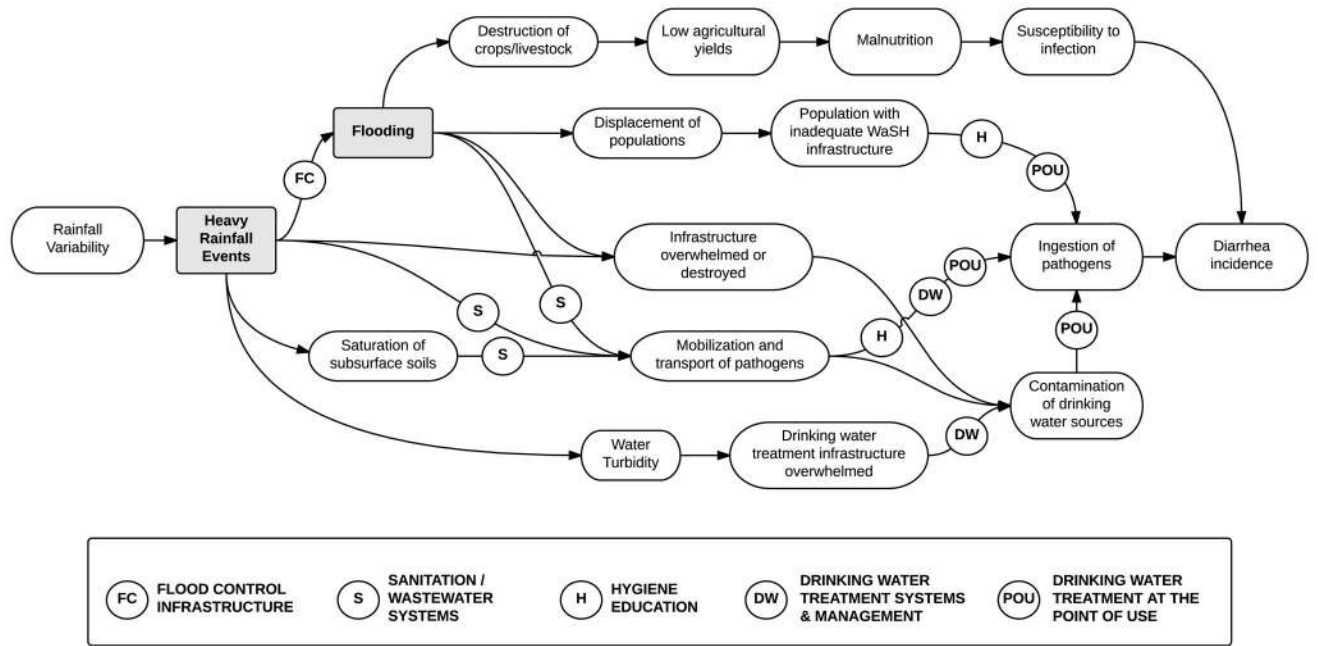


Figure 5. Conceptual diagram for heavy rainfall and flooding illustrating how interventions along the causal pathway may interrupt transmission of diarrheal pathogens.

Table 1
Summary of evidence of key findings regarding the relationship between diarrhea and ambient temperature, heavy rainfall, flooding, and drought

Confidence categories selected based on guidelines presented by Rooney et al. (2014) and Guyatt et al. (2008). High confidence: The true effect is likely to be reflected in the observed relationship. Additional research is very unlikely to change our confidence in the relationship; Moderate confidence: The true effect may be reflected in the observed relationship. Additional research may change the estimated association; Low confidence: The true effect may be different from the observed association. Additional research is likely to have an important impact on the estimated association; Very low confidence: The true effect is highly likely to be different from the observed association. Additional research is very likely to have an important impact on the estimated association.

Key findings	Weight of evidence	Notes on the quality of evidence	Confidence
AMBIENT TEMPERATURE			
Higher temperatures are associated with elevated rates of diarrhea	<ul style="list-style-type: none"> 74 relevant articles 45 studies presenting quantitative results (82 total analyses) For all quantitative analyses reported: 53 (65%) described a significant positive relationship, 16 (20%) described a significant negative relationship, and 13 (16%) showed no effect For quantitative analyses of all-cause diarrhea: 11 (69%) described a significant positive relationship, 3 (19%) described a significant negative relationship, and 2 (13%) showed no effect 	Range of exposure definitions, timescales of analyses, and analytical approaches	Moderate/High*
Associations between temperature and diarrhea vary by taxonomic category of diarrheal disease agent	<p>Of the quantitative associations reported:</p> <ul style="list-style-type: none"> Bacterial diarrhea ($n=47$): 37 analyses (79%) described a significant positive relationship; 3 (6%) described a significant negative relationship; 7 (15%) showed no effect Viral diarrhea ($n=14$): 2 analyses (14%) described a significant positive relationship; 10 analyses (71%) described a significant negative relationship; 2 (14%) showed no effect. Two meta-analyses showed a negative relationship Protozoan diarrhea ($n=5$): 3 analyses (60%) described a significant positive relationship; none described a significant negative relationship; 2 analyses showed no effect 	More evidence for bacteria and viral pathogens than for protozoan pathogens. Over-representation of certain geographic regions.	High
HEAVY RAINFALL			
Heavy rainfall events are associated with elevated rates of diarrhea	<ul style="list-style-type: none"> 31 relevant articles 10 studies presenting quantitative results (14 total analyses) For all quantitative analyses reported: 10 (71%) described a significant positive association, 3 (21%) described a significant negative association and 1 (7%) showed no effect 18 reports of an outbreak of diarrheal disease following a heavy rainfall event 	All evidence for all-cause diarrhea or bacterial diarrhea pathogens; no studies on protozoan or viral pathogens. Wide variety of exposure and outcome definitions, data sources, and analytical approaches. Implicit publication bias for outbreak reports	Moderate

Key findings	Weight of evidence	Notes on the quality of evidence	Confidence
	<ul style="list-style-type: none"> One systematic review of disease outbreaks linked to drinking water from private drinking water supplies found heavy rainfall preceded 24% of outbreaks 		
Heavy rainfall following dry periods are associated with elevated rates of diarrhea	<ul style="list-style-type: none"> 8 studies from a range of settings found that heavy rainfall after a dry period or drought was associated with increased diarrhea 	Inconsistent definitions of dry periods	Moderate
FLOODING			
Flooding is associated with elevated rates of diarrhea	<ul style="list-style-type: none"> 40 relevant articles 14 studies presenting quantitative results (25 total analyses) For all quantitative analyses reported: 19 (76%) described a significant positive association, none described a negative association, 6 (24%) showed no effect 15 reports of outbreaks of diarrhea following a flood, including outbreaks of cholera, enterotoxigenic <i>E. coli</i> (ETEC), rotavirus, norovirus and Norwalk virus 3 reports of exposure-response effects, related to direct contact with flood waters or increased flood depth 	Most quantitative evidence is for all-cause diarrhea; very few analyses of specific pathogens. Implicit publication bias for outbreak reports	Moderate
DROUGHT			
Drought is associated with an increase in diarrheal diseases	<ul style="list-style-type: none"> 3 relevant articles 2 studies presenting quantitative results (2 total analyses), 1 reporting a significant positive association and 1 showing no effect. 1 report of an outbreak of <i>E. coli</i> 0157 and cholera following a drought 1 report of a significant positive dose-response relationship between water restrictions during a drought and diarrhea 	Inadequate evidence base. Difficulties defining drought due to its prolonged nature	Very low

* Confidence in the overall positive relationship of all-cause diarrhea and ambient temperature is considered moderate due to the differential relationships observed by taxonomic category of diarrheal disease agent. However, confidence is high for the positive relationship between bacterial diarrhea and ambient temperature.

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