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Effects of climate change on the epidemiology of flood-related waterborne disease: A Systematic Literature Review

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Abstract

Natural disasters, such as flooding related to extreme precipitation, can lead to many adverse health effects (i.e. waterborne disease). Several outbreaks of waterborne disease have been linked to extreme precipitation, and gastrointestinal infection has been shown to increase after floods. Climate change is likely to lead to a higher frequency of waterborne disease through increases in extreme precipitation and associated flooding affecting water and sanitation infrastructure. This review sought to answer 2 research questions: 1. Has the epidemiology of waterborne disease related to floods changed over time? 2. Can this difference be related to climate change? A literature search was conducted in MEDLINE and Embase for studies reporting on the epidemiology of waterborne disease related to flooding. Studies were screened against inclusion and exclusion criteria, with a total of 52 publications included. Studies of campylobacter, dermatitis, pink eye, and schistosomiasis reported an association between floods and an increase in infection, adenovirus 40/41 and astrovirus showed a significant decrease in risk of disease related to flooding, and cryptosporidium, Giardia, cholera, *Escherichia coli*, leptospirosis, salmonella, shigella, hepatitis A, rotavirus, sapovirus, and dysentery had mixed evidence. Several studies reported on disease outbreaks tied to a specific flood, but the majority were from events in the past 20 years. It is difficult to draw clear conclusions regarding how waterborne disease is or is not related to floods due to the varied comparisons and outcome definitions. Additionally, most studies were of recent events precluding an analysis of any change over time. Continued research on flood-associated waterborne disease will allow for future analysis of epidemiological changes in response to alterations in climate. In the meantime, public health officials in flood-prone areas should prepare for increases in waterborne disease by educating their constituents on flood safety and implementing interventions for prevention and treatment.

Table of Contents

Overview of Tables and Figures

Abbreviations

ABBREVIATION	DEFINITION
AB,TI	Abstract, title
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
EXP	Subject explosion
HDI	Human development index
IRR	Incidence rate ratio
M-A	Meta-analysis
MESH	Medical subject headings
N/A	Not applicable
NS	Non-significant
OR	Odds ratio
SLR	Systematic literature review
TIAB	Title/abstract
UNHCR	United Nations High Commissioner for Refugees
US	United States
VS	versus
WHO	World Health Organization

Chapter 1 – Introduction

Research Question and Objectives

Natural disasters can lead to many adverse health effects, including waterborne disease. Flooding related to extreme precipitation is a particular issue when it comes to outbreaks of waterborne disease. A systematic literature review (SLR) was conducted to explore the relationship between waterborne disease outbreaks and flooding. The specific questions to be answered were:

- Has the epidemiology of waterborne disease related to floods changed over time?
- Can this difference be related to climate change?

In addition to assessing the relationship between outbreaks of waterborne disease and floods, findings of the SLR have been considered in a broader view of the association against the backdrop of climate change.

Rationale for the Review

Several outbreaks of waterborne disease have been linked to heavy rainfall, including outbreaks of *Escherichia coli* O157:H7, a pathogenic strain with high morbidity and mortality, in Walkerton, Ontario in 2000 and New York in 1999, as well as cryptosporidiosis in Wisconsin in 1993, and multiple pathogens in Ohio in 2004. These examples involved contamination of treatment plants and groundwater wells (Auld et al., 2004; Fong et al., 2007; Hoxie et al., 1997). In total, between 1948 and 1994, approximately half of waterborne disease outbreaks were found to be related to local monthly precipitation totals above the 90th percentile based on data recorded from 1948-1997 (Curriero et al., 2001).

A prior review of the health effects of storms and floods found that gastrointestinal infection increased after floods (Saulnier et al., 2017). Additionally, most of the health impacts occurred within four weeks of a flood. An assessment of one large outbreak of waterborne disease

concluded that "meteorological and climatological conditions need to be considered by water managers, public health officials, and private citizens as a significant risk factor for water contamination" (Auld et al., 2004).

Available data show that flooding is increasing over the past 50 years (Figure 1). While there have been other reviews of disease related to precipitation changes and flooding (Curriero et al., 2001; Saulnier et al., 2017), there has not been research done on whether or not disease outbreaks associated with flood events have changed over time. If there is an increase in waterborne disease related to flooding along with the changes that have been seen in the global climate, it will underscore the necessity of preparing for future events. This research may allow public health practitioners and policy-makers to proactively prepare for the possibility of waterborne disease following a flood by implementing preventative measures such as boil water orders or by increasing surveillance measures to identify problems before they become widespread. From a more long-term perspective, if this review reveals that an increase in waterborne disease has been temporally associated with an increase in flooding events, officials may find it prudent to update water supply and treatment infrastructure.
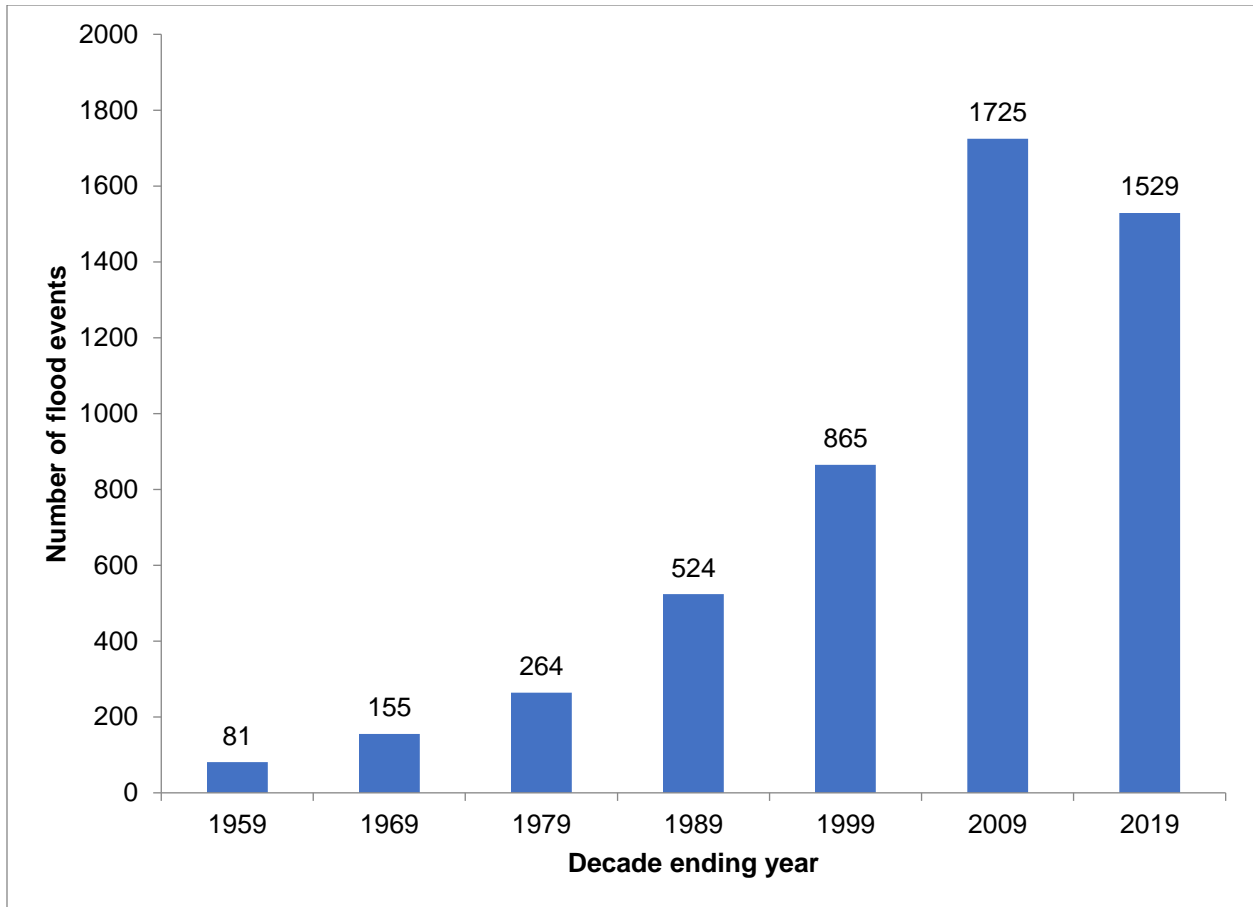
Figure 1. Number of Flood Events per Decade 1950-2019*

* Data from the International Disaster Database (Centre for Research on the Epidemiology of Disasters, N.D.)

Chapter 2 – Background

Description of the Health Problem

In October of 2009, eighteen American scientific organizations wrote to legislators emphasizing the scientific consensus of climate change (Leshner et al., 2009). This statement emphasized that climate change is anthropogenic and has and will continue to have a societal impact. These impacts include "greater threats of extreme weather events" and "disturbance of biological systems" (Leshner et al., 2009).

Climate-change related weather events include extreme precipitation events ranging from heavy rainfall to hurricanes. In the United States (US), the frequency of flooding has increased in parts of the country and decreased in others alongside a universal increase in extreme precipitation (Wehner, 2017). This increase in extreme precipitation is expected to continue, likely increasing flooding as well (Wehner, 2017).

The US Global Change Research Program released a report in 2016 on the impacts of climate change on human health that highlighted three ways climate change is likely to lead to waterborne diseases (Trtanj et al., 2016). More extreme precipitation can lead to flooding and increased runoff, causing issues with freshwater, recreation, shellfish harvesting, and drinking water sources. Additionally, increases in extreme precipitation and associated flooding will put water infrastructure in danger, leading to increased disease as water treatment facilities are damaged or wastewater overflows. Finally, rising water temperatures will allow for an increase in pathogens such as bacteria and algae that thrive in warmer conditions. While this does not seem to be an issue related to flooding at first glance, combined with an increase in runoff, oceans and rivers with these pathogens may surge and increase the chances of exposure to waterborne disease (Trtanj et al., 2016).

Worldwide, 842,000 deaths a year are due to diarrheal disease resulting from issues with water supply, sanitation, and hygiene (World Health Organization [WHO], 2019). In addition to gastrointestinal infections, waterborne pathogens can cause skin irritation or infection, respiratory infection, neurologic illness, liver and kidney damage, eye and ear infections, and sepsis (Trtanj et al., 2016). While there are numerous waterborne pathogens, the US Global Change Research Program has identified a list of those most sensitive to the effects of climate change, as seen in Table 1 (Trtanj et al., 2016).

*Table 1. Waterborne Pathogens Driven by Flooding**

Pathogen	Exposure	Outcomes
Enteric bacteria and protozoan parasites including *Salmonella enterica*, *Campylobacter*, *Escherichia coli*, *Cryptosporidium*, and *Giardia*	Drinking water Recreation Shellfish	Gastroenteritis
Enteric viruses including enteroviruses, rotaviruses, noroviruses, and hepatitis A and E	Drinking water Recreation Shellfish	Gastrointestinal illness, paralysis, infection of organs
Leptospira and *Leptonema* bacteria	Recreation	Flu-like illness, meningitis, kidney and liver failure

* ADAPTED FROM (TRTANJ ET AL., 2016)

Chapter 3 – Methods

Search Strategy

The search was conducted in MEDLINE (via PubMed) and Embase using medical subject headings (MeSH) or Emtree terms and keywords related to waterborne diseases, floods, and epidemiology outcomes. Full search strings can be found in Table 2 and Table 3.

Table 2. MEDLINE (via PubMed) Search Strings (Search Date: August 28, 2020)

	Topic	Search Terms	Hits
#1	Waterborne Diseases	"waterborne disease*"[tiab] OR giardia*[tiab] OR cryptosporidi*[tiab] OR "E. coli"[tiab] OR campylobacter*[tiab] OR norovirus[tiab] "norwalk virus"[tiab] OR "norwalk-like virus" [tiab] OR shigell*[tiab] OR vibrio*[tiab] or cholera[tiab] OR "hepatitis A"[tiab] OR leptospir*[tiab] OR legionell*[tiab] OR legionnaire*[tiab] OR salmonell*[tiab] OR typhoid[tiab] OR "small round structured virus"[tiab] OR plesiomonas[tiab] OR naegleria[tiab] OR pseudomonas[tiab] OR schistosom*[tiab] OR ameba[tiab] OR amoebae[tiab] OR "nontuberculosis mycobacter*" OR "otitis externa"[tiab] OR toxoplasmosis[tiab] OR cyclospor*[tiab]	375,117
#2	Floods	flood[tiab]	6,785
#3	Population Combined	#1 AND #2	223

	Topic	Search Terms	Hits
#4	Outcomes	"Epidemiology"[Mesh] OR incidence[tiab] OR prevalence[tiab] OR risk[tiab] OR outbreak[tiab] OR "Disease Outbreaks"[Mesh]	3,161,521
#5	Population + Outcomes	#3 AND #4	**130**

KEY: MESH – MEDICAL SUBJECT HEADING; TIAB – TITLE/ABSTRACT

Table 3. Embase Search Strings (Search Date: August 18, 2020)

	Topic	Search Terms	Hits
#1	Waterborne Diseases	'waterborne disease*':ab,ti OR giardia*:ab,ti OR cryptosporidi*:ab,ti OR 'E. coli':ab,ti OR campylobacter*:ab,ti OR norovirus:ab,ti 'norwalk virus':ab,ti OR 'norwalk-like virus':ab,ti OR shigell*:ab,ti OR vibrio*:ab,ti or cholera:ab,ti OR 'hepatitis A':ab,ti OR leptospir*:ab,ti OR legionell*:ab,ti OR legionnaire*:ab,ti OR salmonell*:ab,ti OR typhoid:ab,ti OR 'small round structured virus':ab,ti OR plesiomonas:ab,ti OR naegleria:ab,ti OR pseudomonas:ab,ti OR schistosom*:ab,ti OR ameba:ab,ti OR amoebae:ab,ti OR 'nontuberculosis mycobacter*':ab,ti OR 'otitis externa':ab,ti OR toxoplasmosis:ab,ti OR cyclospor*:ab,ti	433,156
#2	Floods	flood:ab,ti	7,815
#3	Population Combined	#1 AND #2	240
#4	Outcomes	Epidemiology/exp OR incidence:ab,ti OR prevalence:ab,ti OR risk:ab,ti OR outbreak:ab,ti OR epidemic/exp	6,254,582
#5	Population + Outcomes	#3 AND #4	**176**

KEY: AB,TI – ABSTRACT, TITLE; EXP – SUBJECT EXPLOSION

Inclusion and Exclusion Criteria

The literature identified by the search was downloaded into EndNote, and duplicates were removed. Unique citations were then uploaded to Distiller SR and screened in two phases. First, titles and abstracts were reviewed for relevance according to the inclusion and exclusion criteria described below in Table 4. No study was eliminated at this phase for a lack of information. Following title and abstract screening, the full texts of the included studies were retrieved. Full texts were screened according to the same criteria. Studies must have met all inclusion criteria and no exclusion criteria to be eligible for final inclusion.

Table 4. Inclusion and Exclusion Criteria

	Inclusion Criteria	**Exclusion Criteria**
Population	Waterborne disease outbreak or cases related to a flood	• Non-waterborne disease • Disease not related to flooding
Intervention/ Comparator	N/A	N/A
Outcomes	• Incidence and prevalence of waterborne diseases related to floods • Occurrence of waterborne disease outbreak related to flood • Risk of waterborne disease outbreak related to flood • Other epidemiology outcomes of waterborne disease related to flood	No epidemiology outcomes of waterborne disease related to flood
Study Design	• Real-world study designs • Models	• Letters, editorials, comments • Narrative reviews • SLRs/M-As*
Other Criteria	English language	Non-English language

*SLRS/M-AS WILL BE RETRIEVED AND HAND SEARCHED FOR RELEVANT LITERATURE IN THE BIBLIOGRAPHY
KEY: M-A – META-ANALYSIS; N/A – NOT APPLICABLE; SLR – SYSTEMATIC LITERATURE REVIEW

Data Extraction

After the included studies were determined, data from these studies were extracted using a form created in Distiller SR. When risk ratios or relative risks were not available in the full text, but the component data were available, these outcomes were calculated using a form designed for that purpose. Data were extracted and synthesized qualitatively for analysis.

Quality Assessment

All included studies were assessed for quality using the Johanna Briggs Institute Critical Appraisal Tool appropriate for the study design (Joanna Briggs Institute, N.D.). Tools used included Checklist for Prevalence Studies, Checklist for Case-Control Studies, Checklist for Cohort Studies, and Checklist for Analytical Cross-Sectional Studies.

Chapter 4 – Results

Search Results and Selection Process

A total of 130 citations were found from MEDLINE (via PubMed), and 176 from Embase. After removing duplicates from the database searches, 184 unique citations remained. Seventy-three studies were excluded at abstract level for being irrelevant to the study questions. One hundred eleven studies were screened in full text; 65 were excluded with reasons outlined in Figure 2. Forty-six studies were included. Additionally, 6 publications were identified through the manual checking of bibliographies of identified SLRs and meta-analyses. After all exclusion criteria, a total of 52 studies were included.
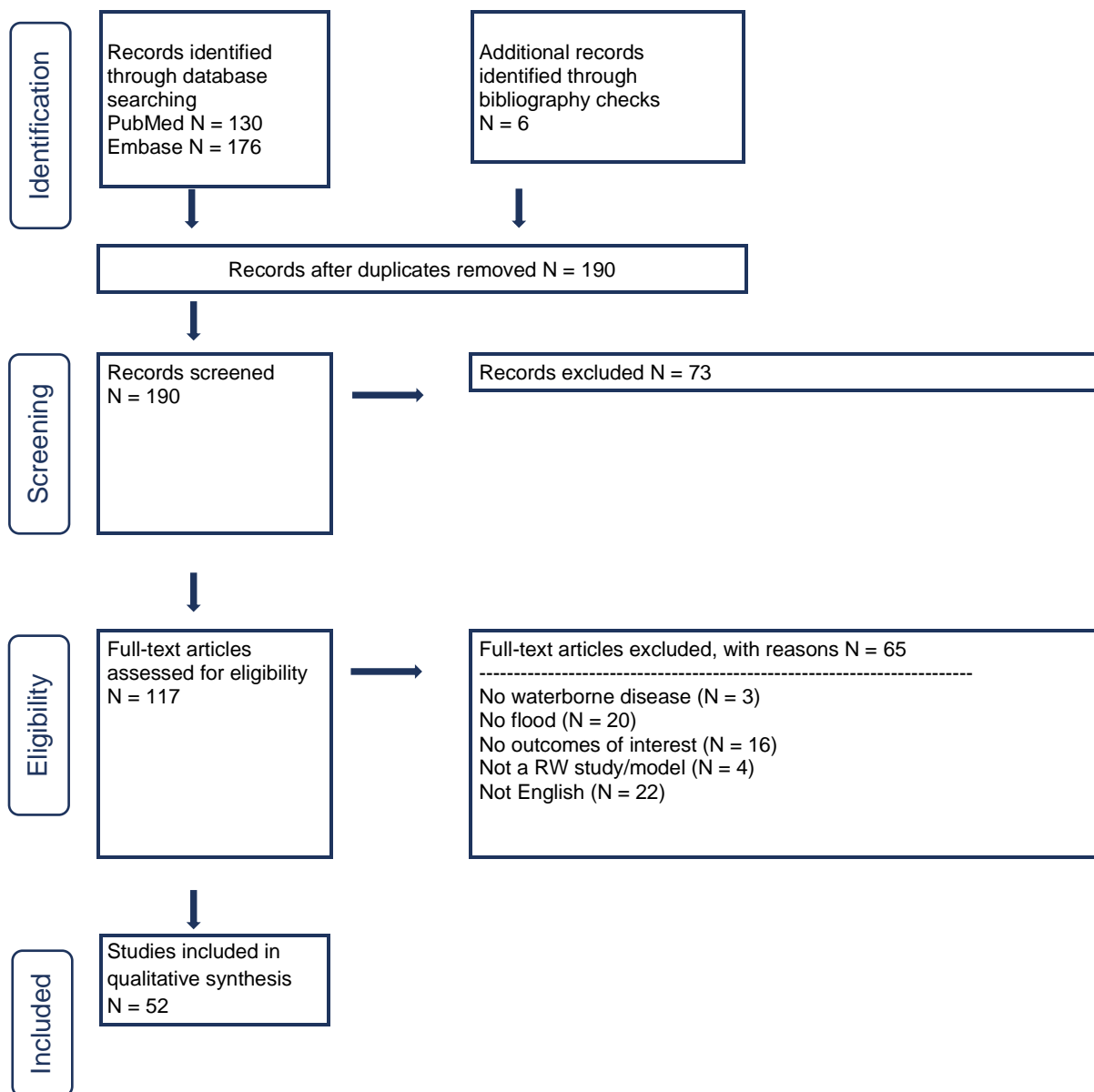
Figure 2. PRISMA Diagram Showing Study Attrition

Description of Studies

An overview of the 52 studies included can be found in Table 5. Full data extraction is available in Appendix A: Full Data Extraction. Most (31) were prevalence studies, evaluating the epidemiology of a waterborne disease, often using spatio-temporal methods. Other study designs included case-control (12), cross-sectional (5), and prospective cohort (4). Leptospirosis was the most frequently reported on condition in 27 studies. Eleven studies reported on cholera; 7 on unspecified diarrhea; 5 each on dysentery (amebic or bacillary), salmonella/typhoid/paratyphoid, and Schistosoma; 3 each on dengue, hepatitis A, and rotavirus; 2 each on cryptosporidium, *E. coli*, Giardia, and shigella; and one each on adenovirus 40/41, astrovirus, campylobacter, dermatitis, hepatitis E, pink eye, and sapovirus. Studies were primarily conducted in Asia (Figure 3). China and India were the most common countries in the identified literature, with 9 studies each. Other Asian countries represented included Bangladesh (5), Thailand (3), Philippines (2), Fiji (2) and Bangladesh and India, Cambodia, Indonesia, Lao PDR, Malaysia, Pakistan, Sri Lanka, and Vietnam (1 each). The next most common area for studies was South America, including Brazil (3), Argentina (2), Guyana (1), and Peru (1). Other countries included were Australia (2), and Germany, Mozambique, Mexico, Nigeria, Poland, and sub-Saharan Africa (1 each). Studies frequently compared time periods with and without floods (15), areas with and without floods (7), and infection status of study participants (9). Four studies reported on other types of comparisons and 17 were not comparative but contributed data about the presence of an outbreak.

Table 5. Overview of Included Studies

Citation	Study Design	Country	Country HDI^	Specific Flood Reported	Comparison	Waterborne Disease(s)
Colston 2020	Case-control	Peru	0.759 (high)	December 2011	Flood period vs non-flood period Flooded vs non-flooded area	Adenovirus 40/41 Astrovirus Enteroaggregative *E. coli* Sapovirus Rotavirus Shigella Campylobacter Cryptosporidium *Giardia*
López 2019	Prevalence	Argentina	0.83 (very high)	No	Flooded vs non-flooded area	Leptospirosis
Ding 2019	Case-control	China	0.758 (high)	No	Flood period vs non-flood period	Bacillary dysentery Amebic dysentery Other infectious diarrhea* Leptospirosis
Liu 2019	Case-control	China	0.758 (high)	No	Flood period vs non-flood period	Bacillary dysentery Typhoid Paratyphoid Other infectious diarrhea*
Liu 2018	Case-control	China	0.758 (high)	No	Flood period vs non-flood period	Typhoid
Togami 2018	Prevalence	Fiji	0.724 (high)	January and March 2012	Flood-associated vs not flood-associated	Leptospirosis
Matsushita 2018	Prevalence	Philippines	0.712 (high)	No	Flood period vs non-flood period	Leptospirosis
Mohd Radi 2018	Prevalence	Malaysia	0.804 (very high)	December 2014	Flood period vs non-flood period	Leptospirosis
Rieckmann 2018	Prevalence	Sub-Saharan Africa	0.541 (low)	No	Flood period vs. non-drought and non-flood periods	Cholera

Citation	Study Design	Country	Country HDI^	Specific Flood Reported	Comparison	Waterborne Disease(s)
de Alwis 2018	Cross-sectional	Fiji	0.724 (high)	No	Distance to modeled flood-risk areas, by quintiles	Typhoid
Ledien 2017	Prospective cohort	Cambodia	0.581 (medium)	No	Flooded vs non-flooded area	Leptospirosis
Gao 2016b	Case-control	China	0.758 (high)	No	Flood period vs non-flood period	Hepatitis A
Pal 2016	Prevalence	India	0.647 (medium)	May 2013	N/A	Hepatitis A
Gao 2016a	Case-control	China	0.758 (high)	June 2007	Flood period vs non-flood period	Bacillary dysentery Hepatitis A Hepatitis E Typhoid and paratyphoid Other infection diarrhea*
Lin 2015	Prospective cohort	Thailand	0.765 (high)	August 2009	Shelter vs community group	Leptospirosis Amoebiasis
Suwanpakdee 2015	Prevalence	Thailand	0.765 (high)	No	Flood period vs non-flood period	Leptospirosis
Koley 2014	Prevalence	India	0.647 (medium)	August 2008	N/A	Cholera
Agampodi 2014	Cross-sectional	Sri Lanka	0.78 (high)	January 2011	N/A	Leptospirosis
Akanda 2013	Prevalence	Bangladesh and India	0.641/0.647 (medium)	No	N/A	Cholera
Dechet 2012	Prevalence	Guyana	0.67 (medium)	January 2015	N/A	Leptospirosis
Wasiński 2012	Case-control	Poland	0.872 (very high)	Summer 2010	Flooded vs non-flooded area	Leptospirosis
Smith 2013	Prevalence	Australia	0.938 (very high)	December 2010	N/A	Leptospirosis

Citation	Study Design	Country	Country HDI^	Specific Flood Reported	Comparison	Waterborne Disease(s)
Amilasan 2012	Prevalence	Philippines	0.712 (high)	September 2009	N/A	Leptospirosis
Alam 2011	Prevalence	Bangladesh	0.641 (medium)	August 2007	N/A	Cholera
Zaki 2010	Prospective cohort	India	0.647 (medium)	July 2005	Disease positive vs negative	Leptospirosis Dengue
Carrel 2010	Cross-sectional	Bangladesh	0.641 (medium)	N/A	Flood protected vs non-flood protected area	Cholera
Bhardwaj 2008	Case-control	India	0.647 (medium)	August 2006	Disease positive vs negative	Leptospirosis
Hashizume 2008	Case-control	Bangladesh	0.641 (medium)	July 1998	Observed vs expected cases	Cholera Non-cholera diarrhea
Harris 2008	Prevalence	Bangladesh	0.641 (medium)	July 1998 July 2004 September 2004 July 2007	Flood period vs non-flood period	Rotavirus Cholera Enterotoxigenic *E. coli* Other infectious diarrhea*
Kawaguchi 2008	Cross-sectional	Lao PDR	0.604 (high)	No	Disease positive vs negative	Leptospirosis
Schwartz 2006	Prevalence	Bangladesh	0.641 (medium)	September 1988 July 1998 July 2004 September 2004	Flood period vs non-flood period	Cholera Shigella Salmonella *E. hystolytica* *G. lamblia* Rotavirus Other infectious diarrhea*
Tan 2004	Case-control	China	0.758 (high)	July 1998	Disease positive vs negative	*S. japonicum*
Karande 2003	Prevalence	India	0.647 (medium)	No	Disease positive vs negative	Leptospirosis
Kondo 2002	Prevalence	Mozambique	0.446	January 2000	N/A	Other infectious diarrhea*

Citation	Study Design	Country	Country HDI^	Specific Flood Reported	Comparison	Waterborne Disease(s)
			(low)			
Sur 2000	Prevalence	India	0.647 (medium)	July 1998	N/A	Cholera
Karande 2002	Prevalence	India	0.647 (medium)	July 2001	N/A	Leptospirosis
Barcellos 2001	Prevalence	Brazil	0.761 (high)	February 1996	Flooded vs non-flooded area	Leptospirosis
Barcellos 2000	Prevalence	Brazil	0.761 (high)	February 1996	N/A	Leptospirosis
Xu 2000	Prevalence	China	0.758 (high)	1974	Flood period vs non-flood period	Schistosoma
Xu 1999	Prevalence	China	0.758 (high)	1974	Flood period vs non-flood period	*S. japonicum*
Rahman 2019	Prevalence	India	0.647 (medium)	August 2018	N/A	Leptospirosis
Suryani 2016	Case-control	Indonesia	0.707 (high)	No	Disease positive vs negative	Leptospirosis
Ito 2015	Prevalence	Nigeria	0.534 (low)	2012	N/A	Schistosoma
Hagan 2013	Prospective cohort	Brazil	0.761 (high)	No	Disease positive vs negative	Leptospirosis
Henschel 2012	Prevalence	India	0.647 (medium)	No	Flood period vs non-flood period	Cholera
Wu 2008	Prevalence	China	0.758 (high)	1998	N/A	Schistosoma
Bich 2011	Prevalence	Vietnam	0.693 (medium)	October 2008	Flooded vs non-flooded area	Dengue Pink eye Dermatitis
Gertler 2015	Case-control	Germany	0.939	May 2013	Disease positive vs negative	Cryptosporidium

Citation	Study Design	Country	Country HDI^	Specific Flood Reported	Comparison	Waterborne Disease(s)
			(very high)			
Leal-Castellanos 2003	Cross-sectional	Mexico	0.767 (high)	No	Disease positive vs negative	Leptospirosis
Pradutkanchana 2003	Prevalence	Thailand	0.765 (high)	November 2000	N/A	Dengue Leptospirosis
CDC 2012	Prevalence	Pakistan	0.56 (medium)	July 2010	N/A	Cholera
Vanasco 2008	Prevalence	Argentina	0.83 (very high)	No	Disease positive vs negative	Leptospirosis

* OTHER INFECTIOUS DIARRHEA REFERRED TO CASES OF DIARRHEA DUE TO INFECTIONS OTHER THAN THE ONES IDENTIFIED BY NAME IN THE SPECIFIED STUDY. THESE CAUSES VARIED BY STUDY AND WERE NOT ALWAYS CLEAR.

^HUMAN DEVELOPMENT INDEX IS A MEASURE OF A COUNTRY'S DEVELOPMENT BASED ON LIFE EXPECTANCY, EDUCATION, AND GROSS NATIONAL INCOME PER CAPITA (AS A SURROGATE FOR STANDARD OF LIVING)

KEY: HDI – HUMAN DEVELOPMENT INDEX; N/A – NOT APPLICABLE; VS – VERSUS.
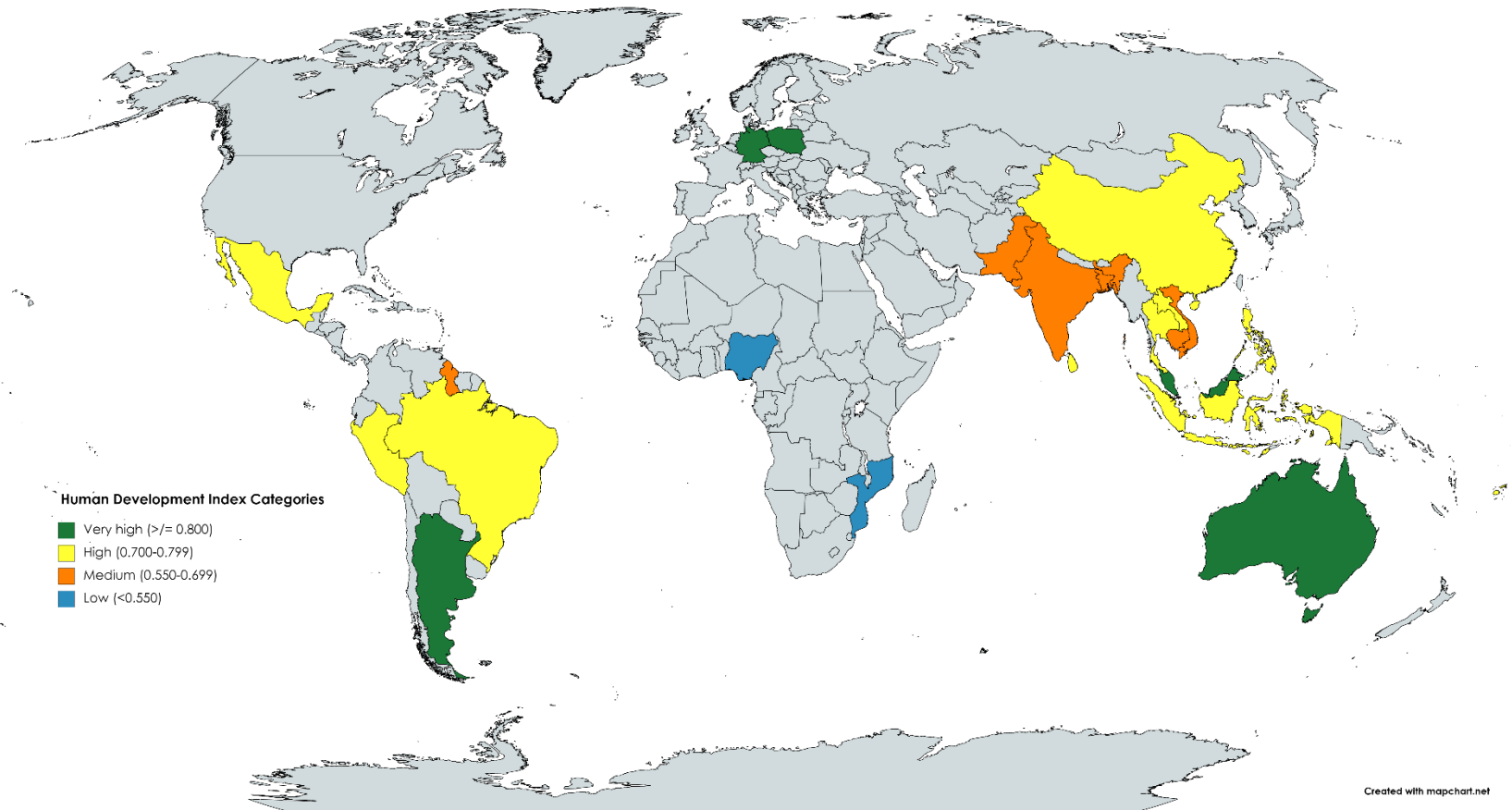
Figure 3. Countries Covered by Studies included in the Systematic Literature Review, by Human Development Index* Category

*HUMAN DEVELOPMENT INDEX IS A MEASURE OF A COUNTRY'S DEVELOPMENT BASED ON LIFE EXPECTANCY, EDUCATION, AND GROSS NATIONAL INCOME PER CAPITA (AS A SURROGATE FOR STANDARD OF LIVING)

Quality Assessment

The 12 case-control studies (Bhardwaj et al., 2008; Colston et al., 2020; Ding et al., 2019; Gao et al., 2016a; Gao et al., 2016b; Gertler et al., 2015; Hashizume et al., 2008; Liu et al., 2019; Liu et al., 2018; Suryani et al., 2016; Tan et al., 2004; Wasiński et al., 2012) were generally of high quality. Two studies (Colston et al., 2020; Gao et al., 2016b) were unclear on the identification and matching of cases and controls. Additionally, three studies (Gertler et al., 2015; Tan et al., 2004; Suryani et al., 2016) did not identify confounding factors. One study (Bhardwaj et al., 2008) used different criteria for cases and controls and one study (Wasinski et al., 2012) did not make clear the exposure period.

The 31 prevalence studies (Akanda et al., 2013; Alam et al., 2011; Amilasan et al., 2012; Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Bich et al., 2011; Centers for Disease Control and Prevention [CDC] 2012; Dechet et al., 2012; Harris et al., 2008; Henschel & Khalil, 2012; Ito & Egwunyenga, 2015; Karande et al., 2002; Karande et al., 2003; Koley et al., 2014; Kondo et al., 2002; López et al., 2019; Matsushita et al., 2018; Mohd Radi et al., 2018; Pal et al., 2016; Pradutkanchana et al., 2003; Rahman et al., 2019; Rieckmann et al., 2018; Schwartz et al., 2006; Smith et al., 2013; Sur et al., 2000; Sumanpakdee et al., 2015; Togami et al., 2018; Vanasco et al., 2008; Wu et al., 2008; Xu et al., 1999; Xu et al., 2000) were of moderate to high quality. While about half of the studies did not report detailed information about study subjects (Akanda 2013; Alam et al., 2011; Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Dechet et al., 2012; Koley et al., 2014; López et al., 2019; Pal et al., 2016; Rahman et al., 2019; Smith et al., 2013; Sumanpakdee et al., 2015; Xu et al., 1999; Xu et al., 2000), other quality issues were due to the study not providing enough information to evaluate the question. This included issues with the sample frame (Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Pal et al., 2016; Smith et al., 2013), study sampling (Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Smith et al., 2013; Sur et al., 2000); data analysis (Ito & Egwunyenga, 2015; Xu et al., 1999; Xu et al., 2000),

case definition and identification (Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Rahman et al., 2019), and response rate (Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Ito & Egwunyenga, 2015; Sur et al., 2000; Xu et al., 1999; Xu et al., 2000).

The 4 prospective cohort studies (Hagan et al., 2013; Ledien et al., 2017; Lin et al., 2015; Zaki & Shanbag, 2010) were of moderate quality. No study identified confounding factors and most (Hagan et al., 2013; Ledien et al., 2017; Lin et al., 2015) also had issues with follow-up reporting. The 5 cross-sectional studies (Agampodi et al., 2014; Carrel et al., 2010; de Alwis et al., 2018; Kawaguchi et al., 2008; Leal-Castellanos et al., 2003) were generally high quality, though two did not report details on study subjects (Carrel et al., 2010; de Alwis et al., 2018) and 1 did not identify confounding factors (Carrel et al., 2010). Full details of quality assessment can be found in Appendix B: Quality Assessment.

Summary of Findings

Conditions with significant increase linked to flooding

Studies of campylobacter, dermatitis, pink eye, and schistosomiasis reported an association between floods and an increase in infection. However, most conditions were only evaluated in 1 study. The risk of campylobacter was increased during flood time periods and flood areas based on a study in Peru (Colston et al., 2020). Both dermatitis and pink eye saw an increase in the proportion of patients diagnosed post-flood in flooded areas compared with non-flooded areas (Bich et al., 2011). The risk of schistosomiasis was evaluated in 4 studies reporting on 2 floods. Across several outcomes, including the odds of affected individuals having exposure to floodwater and the relative risk of schistosomiasis in years with flooding compared with normal or intermediate water levels, floods were significantly associated with infection (Tan et al., 2004; Wu et al., 2008; Xu et al., 1999; Xu et al., 2000). Full details of all study results can be found in Table 6.

Table 6. Conditions with Significant Increase Linked to Flooding

Citation	Time Period	Country	Comparison	Outcome Definition	Results
Campylobacter					
Colston 2020	2011	Peru	Flood time vs non-flood time; flood area vs non-flood area	Risk ratio	1.41 (95% CI: 1.01, 1.97)
Dermatitis					
Bich 2011	2008	Vietnam	Flooded areas vs non-flooded areas	Proportion of patients with condition who were diagnosed after flood	Rural: 96.5% vs 57.9% Urban: 88.2% vs 95.7% *P*<0.05
Pink Eye					
Bich 2011	2008	Vietnam	Flooded areas vs non-flooded areas	Proportion of patients with condition who were diagnosed after flood	Rural: 92.8% vs 64.3% Urban: 100% vs 45.5% *P*<0.05
Schistosomiasis					
Tan 2004	1998	China	Affected vs non-affected individuals	OR for duration of contagious water exposure due to swimming and paddling	10.034 (95% CI: 4.258, 23.646)
				OR for intensity of contagious water exposure due to occupational activities	5.584 (95% CI: 2.599, 11.996)
				OR for duration of contagious water exposure due to recreational activities	2.213 (95% CI: 1.517, 3.229)
Xu 2000/Xu 1999	1974 (controls: 1984, 1986)	China	High-level water years vs middle and low water level	Relative risk vs intermediate level	1.26 (95% CI: 1.22, 1.31)
				Relative risk vs low level	1.78 (95% CI: 1.71, 1.85)
Wu 2008	1998	China	Flood year vs non-flood years	N/A	The average number of acute schistosomiasis cases recorded in flood years was 2.8 times higher than in years when there was no, or very little, flooding.

KEY: CI – CONFIDENCE INTERVAL; N/A – NOT APPLICABLE; OR – ODDS RATIO; VS – VERSUS.

Conditions with mixed evidence

The majority of waterborne diseases identified by this review had mixed evidence regarding the link of flooding to outbreaks (Table 7). While many studies reported that flooding was related to disease, others showed no significant relationship, and some reported flooding was associated with a decrease in infection.

Cholera was reported on by 6 studies, of which 4 reported a significant increase in cases associated with flooding (Hashizume et al., 2008; Henschel & Khalil, 2012; Riechmann et al., 2018; Schwartz et al., 2006) and 2 reported either a significant increase or no significant association, depending on outcome (Akanda et al., 2013; Harris et al., 2008). The 2 studies reporting mixed evidence found that the association varied based on area or year assessed (Akanda et al., 2013; Harris et al., 2008).

Leptospirosis was reported on by 17 studies; there was more evidence for a positive association between leptospirosis and flooding than there was for a negative or no association. Ten studies reported a significant, positive association between leptospirosis and flooding (Barcellos & Sabroza 2001; Ding et al., 2019; Karande et al., 2003; Leal-Castellanos et al., 2003; López et al., 2019; Mohd Radi et al., 2008; Suryani et al., 2016; Togami et al., 2018; Vanasco et al., 2008; Zaki & Shanbag, 2010), four reported that the association varied by outcome (Bhardwaj et al., 2008; Hagan et al., 2013; Matsushita et al., 2018; Sumanpakdee et al., 2015), and 3 reported no significant association (Kawaguchi et al., 2018; Ledien et al., 2017; Wasinski et al., 2012). Studies that found a negative or no association reported these findings for outcomes assessing a specific area, specific year, or an amount of time post-flood. For example, one study from the Philippines reported that the risk of leptospirosis increased 1 and 2 weeks post-flood, decreased 4 and 5 weeks post-flood and had no association during the flood and 3, 6, and 7 weeks post-flood (Matshushita et al., 2018).

Typhoid fever, paratyphoid fever, and non-specified Salmonellosis were assessed in 4 studies (de Alwis et al., 2018; Gao et al., 2016a; Liu et al., 2018; Schwartz et al., 2006). One study from China found no difference in the odds of typhoid and paratyphoid fever when flood periods were compared with non-flood periods (Gao et al., 2016a). Additionally, a study from Bangladesh reported the same prevalence of salmonella in flood and non-flood periods (Schwartz et al., 2006). All other outcomes showed a positive association, including the number of cases per day reported in the study from Bangladesh.

Dysentery, including amebic dysentery, *E. histolytica*, and bacillary dysentery, was reported on in 3 studies (Ding et al., 2019; Gao et al., 2016a; Schwartz et al., 2006). In general, there was no significant association between dysentery and flooding except in the number of cases per day during flood vs non-flood periods in one study from Bangladesh (Schwartz et al., 2006).

Other conditions with mixed evidence in the literature include cryptosporidium (Colston et al., 2020; Gertler et al., 2015), giardia (Colston et al., 2020; Schwartz et al., 2006), *E. coli* (Colston et al., 2020; Harris et al., 2008), shigella (Colston et al., 2020; Schwartz et al., 2006), hepatitis A (Gao et al., 2016a; Gao et al., 2016b), rotavirus (Colston et al., 2020; Harris et al., 2008; Schwartz et al., 2006), sapovirus (Colston et al., 2020), diarrhea (Ding et al., 2019; Gao et al., 2016a; Harris et al., 2008; Hashizume et al., 2008; Liu et al., 2019; Schwartz et al., 2006). Possible explanations for the differing findings across studies are similar to those seen for the conditions discussed above: different outcome definitions and specific areas or years. Of note, a study conducted in Bangladesh contributed to mixed evidence across several conditions (cholera, *E. coli*, rotavirus, and diarrhea (Harris et al., 2008). This study reported the prevalence of each condition among patients with diarrhea; therefore, an increase in the prevalence in one study necessitates a decrease in others. Conditions showing a decline in response to flood may just be reflecting an increase in another infection.

Table 7. Conditions with Mixed Evidence

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
Cryptosporidium						
Gertler 2015	2013	Germany	N/A	Infected vs non-infected	Multivariable OR for "stays in flooded area"	5.50 (95% CI: 1.40, 21.56)
Colston 2020	2011	Peru	N/A	Early or late flood vs pre/post-flood or areas without flooding	Qualitative	No significant relationship was found with flooding
Giardia						
Schwartz 2006	1988, 1998, 2004	Bangladesh	N/A	Flood vs non-flood period	Cases/day	12 vs 5; *P*=0.002
					Prevalence	2% vs 2%; *P*=0.94
Colston 2020	2011	Peru	N/A	Early or late flood vs pre/post-flood or areas without flooding	Qualitative	No significant relationship was found with flooding
Cholera						
Rieckmann 2018	1990-2010	Sub-Saharan Africa	N/A	Flood period vs. non-drought and non-flood periods	IRR	144 (95% CI: 101, 208)
Akanda 2013	1998-2007	Bangladesh and India	N/A	Seasonal mean incidence and flood extent	Correlation: Dhaka	0.77; *P*<0.01
					Correlation: Matlab	0.81; 0.05 > *P*> 0.01
					Correlation: Bakerganj	0.37; *P*=NS
					Correlation: Kolkata	0.79; 0.05 > *P* > 0.01
Hashizume 2008	1998	Bangladesh	N/A	Observed vs expected cases	Observed/expected, flood period	5.9 (95% CI: 5.0, 7.0)
					Observed/expected, post-flood period	2.1 (95% CI: 1.9, 2.4)
Harris 2008	1998, 2004, 2007	Bangladesh	N/A	Flood year vs non-flood year	Prevalence comparison, 1998 flood	40% vs 13%; *P*<0.001
					Prevalence comparison, 2004 flood	33% vs 21%; *P*<0.001
					Prevalence comparison, 2007 flood	33% vs 35%; *P*=NS
Schwartz 2006	1988, 1998, 2004	Bangladesh	N/A	Flood vs non-flood period	Cases/day	200 vs 49; *P*<0.001
					Prevalence	37% vs 20%; *P*<0.001
Henschel 2012	1961-2008	India	N/A	Flood year vs non-flood year	Qualitative	Flood years demonstrate a

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
						higher average incident rate
E. coli						
Colston 2020	2011	Peru	Heat-stable enteroaggregative *E. coli*	Early or late flood vs pre/post-flood or areas without flooding	Risk ratio	1.73 (95% CI: 1.10, 2.71)
Harris 2008	1998, 2004, 2007	Bangladesh	Enterotoxigenic *E. coli*	Flood year vs non-flood year	Prevalence comparison, 1998 flood	9% vs 23%; *P*<0.001
Leptospirosis						
Lopez 2019	2009-2018	Argentina	N/A	Floodable vs non-floodable areas	Relative risk	2.97 (95% CI: 2.57, 3.42)
Ding 2019	2005-2012	China	N/A	Flood vs non-flood times	Relative risk	1.093; *P*=0.026
Togami 2018	2012	Fiji	N/A	Flood-associated vs not flood-associated	Risk ratio	3.37 (95% CI: 3.25, 3.51)
Matsushita 2018	2001-2012	Philippines	N/A	Association with flood	Relative risk lag 0	1.23 (95% CI: 1.00, 1.50)
					Relative risk lag 1 week	1.80 (95% CI: 1.59, 2.03)
					Relative risk lag 2 week	1.63 (95% CI: 1.41, 1.87)
					Relative risk lag 3 week	0.88 (95% CI: 0.76, 1.02)
					Relative risk lag 4 week	0.66 (95% CI: 0.56, 0.77)
					Relative risk lag 5 week	0.81 (95% CI: 0.69, 0.95)
					Relative risk lag 6 week	0.98 (95% CI: 0.86, 1.12)
					Relative risk lag 7 week	1.04 (95% CI: 0.83, 1.31)
Mohd Radi 2008	2014	Malaysia	N/A	During and post-flood vs preflood	OR for water level and incidence	1.102; *P*=0.002
Ledien 2017	2007-2009	Cambodia	N/A	Areas exposed to flooding vs areas not exposed to flooding	Risk ratio	1.61 (95% CI: 1,10, 1.52)
					Risk ratio during rainy season	2.03 (95% CI: 1.25, 3.28)
Suwanpakdee 2015	2010-2012	Thailand	N/A	Flood period vs period with no flooding	IRR overall 2010	4.03 (95% CI: 3.04, 5.35; *P*<0.01)
					IRR overall 2011	1.65 (95% CI: 1.31, 2.07; *P*<0.01)
					IRR overall 2012	0.66 (95% CI: 0.50, 0.88; *P*<0.01)

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
Wasinski 2012	2010	Poland	N/A	Flood affected area vs no flood	Relative risk	0
Zaki 2010	2005	India	N/A	Leptospirosis positive vs negative	OR for contact with flood water	24.01 (95% CI: 6.9, 82.5; *P*=0.000)
Bhardwaj 2008	2006	India	N/A	Leptospirosis positive vs negative	Adjusted OR, contact of injured part with flood water	6.69 (95% CI: 3.05, 14.64; *P*=0.00)
					Adjusted OR, highest flood level	0.46 (95% CI: 0.19, 1.14; *P*=0.09)
					Adjusted OR, use of flood water for cooking	1.79 (95% CI: 0.58, 5.46; *P*=0.30)
					Adjusted OR, Days of water logging	1.36 (95% CI: 0.59, 3.17; *P*=0.48)
					Adjusted OR, use of flood water for bathing	0.74 (95% CI: 0.21, 2.65; *P*=0.64)
					Adjusted OR, use of flood water for washing purpose	0.90 (95% CI: 0.31, 2.66; *P*=0.86)
Kawaguchi 2018	2006	Lao PDR	N/A	Leptospirosis positive vs negative	OR, recent flooding on one's own property	0.73 (95% CI: 0.39, 1.35; *P*=0.31)
Karande 2003	2000	India	N/A	Leptospirosis positive vs negative	Prevalence comparison for flood water contact	100% vs 45.7%; *P*<0.0001
Barcellos 2001	1996	Brazil	N/A	Inside flood risk area vs outside	Relative risk	2.13 (95% CI: 1.35, 3.37)
Suryani 2016	2011-2013	Indonesia	N/A	Leptospirosis positive vs negative	OR for flood history	2.688 (95% CI: 1.226, 8.895)
Hagan 2013	2004-2008	Brazil	N/A	Leptospirosis positive vs negative	OR for household elevation (per meter) - an inverse proxy for flood risk	0.98 (95% CI: 0.96, 0.99)
					OR for contact with flood water	0.49 (95% CI: 0.28, 0.84)
					OR for contact with floodwater and mud	2.27 (95% CI: 1.13, 4.71)
Leal-Castellanos 2003	2000	Mexico	N/A	Leptospirosis positive vs negative	OR for previous flooding once	1.49 (95% CI: 1.13, 1.96)
					OR for previous flooding twice	2.40 (95% CI:1.43, 4.02)
					OR for previous flooding more than twice	2.33 (95% CI:1.21, 4.52)
					OR for skin cuts or abrasion during flooding	4.76 (95% CI:3.59, 6.29)

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
Vanasco 2008	1999-2005	Argentina	N/A	confirmed diagnosis vs discarded diagnosis	Adjusted OR for exposure to flooding	4.49 (95% CI: 1.17, 17.25)
Salmonella/Typhoid Fever						
Liu 2018	2005-2012	China	Typhoid fever	flooded weeks vs non-flooded weeks	Relative risk at lag 1 week	1.46 (95% CI: 1.10, 1.92)
					Relative risk for cumulative effect of flood at lag 0-1 week	1.76 (95% CI: 1.21, 2.57)
de Alwis 2018	2013	Fiji	Typhoid fever	OR	Distance to modeled flood-risk areas, by quintiles	0.80 (95% CI: 0.69, 0.92; $P=0.002$)
Gao 2016a	2007	China	Typhoid and paratyphoid fever	flood period vs non-flood period	OR	0.40 (95% CI: 0.14, 1.14; $P>0.05$)
Schwartz 2006	1988, 1998, 2004	Bangladesh	Salmonella	Flood vs non-flood period	Case/day	11 vs 4; $P=0.001$
					Prevalence	2% vs 2%; $P=0.90$
Shigella						
Colston 2020	2011	Peru	N/A	Early or late flood vs pre/post-flood or areas without flooding	Risk ratio	2.86 (95% CI: 1.81, 4.52)
Schwartz 2006	1988, 1998, 2004	Bangladesh	N/A	Flood vs non-flood period	Case/day	29 vs 16; $P<0.001$
					Prevalence	5% vs 6%; $P=0.66$
Hepatitis A						
Gao 2016b	2005-2010	China	N/A	Flood period vs non-flood period	OR severe flood	1.28 (95% CI: 1.05, 1.55; $P=0.01$)
					OR moderate flood	1.16 (95% CI: 0.72, 1.87; $P=0.54$)
					OR mild flood	1.14 (95% CI: 0.87, 1.48; $P=0.34$)
Gao 2016a	2007	China	N/A	Flood period vs non-flood period	OR	1.40 (95% CI: 1.11, 1.77; $P<005$)
Rotavirus						
Colston 2020	2011	Peru	N/A	Early or late flood vs pre/post flood or areas without flooding	Risk ratio (late flood period)	5.30 (95% CI: 2.70, 10.40)
Harris 2008	1998, 2004, 2007	Bangladesh	N/A	Flood year vs non-flood year	Prevalence comparison, 1998 flood	16% vs 23%; $P<0.001$
					Prevalence comparison, 2004 flood	18% vs 25%; $P=0.01-0.001$

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
					Prevalence comparison, 2007 flood	12% vs 18%; *P*=0.01-0.001
Schwartz 2006	1988, 1998, 2004	Bangladesh	N/A	Flood vs non-flood period	Case/day	96 vs 68; *P*=0.004
					Prevalence	17% vs 26%; *P*=0.002
Sapovirus						
Colston 2020	2011	Peru	N/A	Early or late flood vs pre/post flood or areas without flooding	Risk ratio	0.52 (95% CI: 0.31, 0.89)
					Risk ratio (late flood period)	2,47 (95% CI: 1.79, 3.41)
Dysentery						
Ding 2019	2005-2012	China	Amebic dysentery	Flood vs non-flood times	OR	1.138 (95% CI: 1.075, 1.204; *P*=0.000)
Schwartz 2006	1988, 1998, 2004	Bangladesh	*E. histolytica*	Flood vs non-flood period	Case/day	10 vs 4; *P*=0.008
					Prevalence	2% vs 2%; *P*=NS
Ding 2019	2005-2012	China	Bacillary dysentery	Flood vs non-flood times	OR	1.017 (95% CI: 0.816; 1.267; *P*=0.880)
Gao 2016a	2007	China	Bacillary dysentery	Flood period vs non-flood period	OR	1.04 (95% CI: 0.97, 1.12; *P*>0.05)
Diarrhea						
Ding 2019	2005-2012	China	Other infectious diarrhea*	Flood vs non-flood times	Relative risk	1.986; *P*=0.005
					OR	1.667 (95% CI: 0.887, 3.133; *P*<0.112)
Liu 2019	2005-2012	China	All infectious diarrhea	Flood day + 14 days vs non flood period	Relative risk at lag 0-2 weeks	1.24 (95% CI: 1.11, 1.40)
Gao 2016a	2007	China	Other infectious diarrhea*	Flood period vs non-flood period	OR	1.10 (95% CI: 1.05, 1.15; *P*<0.05)
Hashizume 2008	1998	Bangladesh	Non-cholera diarrhea	Observed vs expected cases	Observed/expected, flood period	1.8 (95% CI: 1.6, 1.9)
					Observed/expected, post-flood period	1.2 (95% CI: 1.1, 1.3)
Harris 2008	1998, 2004, 2007	Bangladesh	Other infectious diarrhea*	Flood year vs non-flood year	Prevalence comparison, 1998 flood	24% vs 38%; *P*<0.001
					Prevalence comparison, 2004 flood	9% vs 8%; *P*=NS
					Prevalence comparison, 2007 flood	5% vs 8%; *P*=0.05-0.01

Citation	Time Period	Country	Specific Infection	Comparison	Outcome Definition	Results
Schwartz 2006	1988, 1998, 2004	Bangladesh	N/A	Flood vs non-flood period	Case/day	64 vs 52; *P*=0.13
					Prevalence	12% vs 21%; *P*=0.001

GREEN SHADED RESULTS INDICATE FLOODS WERE SIGNIFICANTLY RELATED TO AN INCREASE IN DISEASE; YELLOW SHADED RESULTS INDICATE FLOODS WERE SIGNIFICANTLY RELATED TO A DECREASE IN DISEASE.

* OTHER INFECTIOUS DIARRHEA REFERRED TO CASES OF DIARRHEA DUE TO INFECTIONS OTHER THAN THE ONES IDENTIFIED BY NAME IN THE SPECIFIED STUDY. THESE CAUSES VARIED BY STUDY AND WERE NOT ALWAYS CLEAR.

KEY: CI – CONFIDENCE INTERVAL; IRR – INCIDENCE RATE RATIO; N/A – NOT APPLICABLE; NS – NON-SIGNIFICANT; OR – ODDS RATIO; VS – VERSUS.

Conditions with significant decrease linked to flooding

Both adenovirus 40/41 and astrovirus showed a significant decrease in the risk of disease related to flooding (Colston et al., 2020). Specifics of study results can be found in Table 8.

Table 8. Conditions with Significant Decrease Linked to Flooding

Citation	Time Period	Country	Comparison	Outcome Definition	Results
Adenovirus 40/41					
Colston 2020	2011	Peru	Early or late flood vs pre/post flood or areas without flooding	Risk ratio	0.36 (95% CI: 0.23, 0.58)
Astrovirus					
Colston 2020	2011	Peru	Early or late flood vs pre/post flood or areas without flooding	Risk ratio	0.44 (95% CI: 0.29, 0.66)

KEY: CI – CONFIDENCE INTERVAL; VS – VERSUS.

Conditions with no significant link to flooding

Both dengue and hepatitis E showed no significant relationship with flooding (Bich et al., 2011; Gao et al., 2016a; Zaki & Shanbag, 2010). Specifics of study results can be found in Table 9.

Table 9. Conditions with No Significant Link to Flooding

Citation	Time Period	Country	Comparison	Outcome Definition	Results
Dengue					

Citation	Time Period	Country	Comparison	Outcome Definition	Results
Zaki 2010	2005	India	Dengue positive vs negative	OR for flood water contact	0.61 (95% CI: 0.31, 1.2; *P*=0.154)
Bich 2011	2008	Vietnam	Flooded areas vs non-flooded areas	Proportion of patients with condition who were diagnosed after flood	Rural: 86.7% vs 0 Urban: 85.7% vs 66.7%
Hepatitis E					
Gao 2016a	2007	China	Flood period vs non-flood period	OR	0.94 (95% CI: 0.67, 1.31; *P*>0.05)

KEY: CI – CONFIDENCE INTERVAL; OR – ODDS RATIO; VS – VERSUS.

Outbreaks linked to specific floods

Thirty-two publications reported on outbreaks linked to a specific flood (Agampodi et al., 2014; Alam et al., 2011; Amilasen et al., 2012; Barcellos & Sabroza, 2000; Barcellos & Sabroza, 2001; Bhardwaj et al., 2008; Bich et al., 2011; CDC 2012; Colston et al., 2020; Dechet et al., 2012; Gao et al., 2016a; Gertler et al., 2015; Harris et al., 2008; Hashizume et al., 2008; Ito & Egwunyenga 2015; Karande et al., 2002; Koley et al., 2014; Kondo et al., 2002; Lin et al., 2015; Mohd Radi et al., 2018; Pal et al., 2016; Pradutkanchana et al., 2003; Rahman et al., 2019; Schwartz et al., 2006; Smith et al., 2013; Sur et al., 2000; Tan et al., 2004; Togami et al., 2018; Wu et al., 2008; Xu et al., 1999; Xu et al., 2000; Zaki & Shanbag, 2010). A timeline showing years with outbreaks and the specific infections identified can be found in Figure 4. Timeline of Waterborne Disease Outbreaks Associated with Floods. Notably, there are only 2 years prior to the 1990s represented by the studies identified by this review. This lack of earlier studies precludes analysis of the frequency of outbreaks over time.

Figure 4. Timeline of Waterborne Disease Outbreaks Associated with Floods

Chapter 5 – Discussion

Summary

The literature on flood-related waterborne disease outbreaks covers several conditions across the globe. Despite this robust literature base, it is difficult to draw clear conclusions due to the varied comparisons and outcome definitions.

Campylobacter, dermatitis, pink eye, and schistosomiasis had positive associations with flooding. In contrast, adenovirus 40/41 and astrovirus had negative associations, and dengue and hepatitis E did not have significant associations with flooding. The evidence for most conditions is mixed, with cholera, leptospirosis, salmonella, dysentery, cryptosporidium, Giardia, *E. coli*, shigella, hepatitis A, rotavirus, sapovirus, and diarrhea falling into this category.

This review sought to answer two questions, yet the literature available does not allow for definitive answers:

- Has the epidemiology of waterborne disease related to floods changed over time?
  - While there are several studies covering floods over the past 20 years, the evidence on earlier time periods is limited. While this could be because there were not as many floods prior to 2000, it is also likely that as climate change and extreme weather events have become a higher priority, more researchers have conducted studies of these events. Without a long time period over which to compare rates of outbreaks, this question cannot be answered.
- Can this difference be related to climate change?
  - With no clear evidence for or against any change in the epidemiology of waterborne disease related to floods, the relation to climate change cannot be considered.

Public Health Implications

While this review did not find answers to the key questions set out *a priori*, the findings do identify several important implications for public health in a world likely to see more extreme weather events.

First, there is a need for prophylaxis against waterborne disease. Prophylaxis campaigns must differ by disease as pharmaceutical measures vary by infection. For example, several vaccines are available for cholera worldwide (CDC, 2018). However, their limited effectiveness and short duration of protection likely contribute to the reactive nature of distribution efforts, focusing on emergency response when epidemic surges were identified (WHO, 2017). In 2017, the WHO launched a global roadmap aimed at ending cholera that focuses on prevention efforts. In addition to vaccination campaigns, this effort calls for increasing sanitation infrastructure in cholera-endemic areas, as well as providing residents with education on preventing infection (WHO, 2017). Alternatively, a widely effective human leptospirosis vaccine has been difficult to develop, in part due to the multiple serovars circulating in the environment (Xu & Ye, 2018). With a vaccine still likely to be at least 10 years away, prevention efforts focus on education and avoiding contact with floodwaters (Felix et al., 2019; WHO, 2009) as well as chemoprophylaxis for travelers to endemic areas (Galloway, 2019).

Second, ongoing efforts to strengthen infrastructure against floods must be continued. As an example, in 2015, Bangladesh began a $2 million project to protect coastal areas. The infrastructure of shelters for floods and other disasters should also be considered (Cardno, 2015). One study identified by this review specifically considered the risks of shelters on waterborne disease (Lin et al., 2015) and found the congregation of displaced persons into crowded shelters results in additional risk of waterborne disease. This risk is seen in the aftermath of all types of disasters, including a Giardia outbreak after an earthquake in Colombia (Lora-Suarez et al.,

2002). Focusing on sanitation in shelters, such as the interventions used by UNHCR in refugee camps (United Nations High Commissioner for Refugees, 2015), mitigates disease concerns.

Finally, many of the countries assessed in the literature identified by this review have a medium-high to low score on the human development index, with few countries with a very high score included in the literature. These countries may have difficulty providing interventions for floods and waterborne disease due to limited resources and geographic access issues. Thus, the global public health community should work with at-risk countries to provide aid when needed.

Strengths and Limitations

The biggest strength of this review was the systematic approach taken. All studies reporting on a waterborne disease outbreak in conjunction with flooding were included; studies were not "cherry-picked" to include the best or most positive data. However, with a systematic review come inherent limitations. Publication bias, meaning studies are more likely to be published if they have positive or interesting results, may prevent a full understanding of the research question if negative results were not published. This review is also limited by the lack of evidence on earlier years. Finally, as this review limited the climate event to flooding, it may have missed studies of heavy rains, hurricanes, or other events that did not specifically mention floods. Importantly other climate-related disasters, such as drought, can impact water supply and lead to waterborne disease (Rieckmann et al., 2018).

Gaps in Evidence and Future Research

The major gap identified by this review is the lack of data prior to the 1990s. Future research using data from earlier years would help to clarify how the epidemiology of waterborne disease is or is not changing. Additionally, continuing research of the type identified by this review will also allow for a longitudinal comparison of waterborne disease epidemiology. Some included studies used the EM-DAT database to identify flooding in a specific region and time period. A larger study

encompassing multiple regions and a long time period using this database would also be a valuable addition to the literature base.

While not a gap, the varied evidence for most of the infections reported on did not allow for a clear picture of the contribution of floods to waterborne disease epidemiology. However, a recent meta-analysis of leptospirosis across 14 studies found flooding significantly increased the odds of disease (Naing et al., 2019). Similar studies that focus on outcomes able to be combined in quantitative ways could also clarify what impact flooding has on specific infections.

Conclusions

The lack of data on flood-related waterborne disease pre-1990 precludes clear conclusions about how the epidemiology of these conditions may be changing. However, there is ample evidence that flooding is related to waterborne disease outbreaks. Globally, the frequency of floods has increased since the 1970s and is expected to double over the next two decades (Lopez et al., 2020). Continued research on flood-associated waterborne disease will allow for future analysis of epidemiological changes in response to alterations in climate. In the meantime, public health officials in flood-prone areas should prepare for increases in waterborne disease by educating their constituents on flood safety and implementing interventions for prevention and treatment.

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Appendix A: Full Data Extraction

Data_Extraction_11OC
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Appendix B: Quality Assessment

Table 10. Johanna Briggs Institute Checklist for Case-Control Studies

Author Year	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	Were cases and controls matched appropriately?	Were the same criteria used for identification of cases and controls?	Was exposure measured in a standard, valid and reliable way?	Was exposure measured in the same way for cases and controls?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Was the exposure period of interest long enough to be meaningful?	Was appropriate statistical analysis used?
Colston 2020	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ding 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liu 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liu 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gao 2016b	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gao 2016a	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wasiński 2012	Yes	Yes	Yes	Yes	Yes	N/A	N/A	Yes	Unclear	Yes
Bhardwaj 2008	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hashizume2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tan 2004	Yes	Yes	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes
Suryani 2016	Yes	Yes	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes
Gertler 2015	Yes	Yes	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes

Table 11. Johanna Briggs Institute Checklist for Prevalence Studies

Author Year	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
López 2019	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Togami 2018	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Matsushita 2018	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Mohd Radi 2018	Yes	N/A	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Rieckmann 2018	Yes	N/A	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Pal 2016	Unclear	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Suwanpakdee 2015	Yes	N/A	Yes	No	N/A	Yes	Yes	Yes	N/A
Koley 2014	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Akanda 2013	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Dechet 2012	Yes	N/A	Yes	No	N/A	Yes	Yes	Yes	N/A
Smith 2013	Unclear	Unclear	Yes	No	N/A	Yes	Yes	Yes	N/A
Amilasan 2012	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Alam 2011	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Harris 2008	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Schwartz 2006	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Karande 2003	Yes	N/A	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Kondo 2002	Yes	N/A	Yes	Yes	N/A	Yes	Yes	Yes	N/A
Sur 2000	Yes	Unclear	Yes	Yes	N/A	Yes	Yes	Yes	Unclear
Karande 2002	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A

Author Year	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
Barcellos 2001	Unclear	Unclear	Yes	No	N/A	Unclear	Unclear	Yes	Unclear
Barcellos 2000	Unclear	Unclear	Yes	No	N/A	Unclear	Unclear	Yes	Unclear
Xu 2000	Yes	Yes	Yes	No	Unclear	Yes	Yes	Yes	Unclear
Xu 1999	Yes	Yes	Yes	No	Unclear	Yes	Yes	Yes	Unclear
Rahman 2019	Yes	Yes	Yes	No	N/A	Unclear	Unclear	Yes	N/A
Ito 2015	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear
Henschel 2012	Unclear	Unclear	Unclear	No	Unclear	Unclear	Unclear	Unclear	Unclear
Wu 2008	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	Yes	Unclear
Bich 2011	Yes	Yes	Yes	Yes	N/A	No	No	Yes	Unclear
Pradutkanchana 2003	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	N/A
CDC 2012	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	N/A
Vanasco 2008	Yes	N/A	Yes	No	N/A	Yes	Yes	Yes	N/A

Table 12. Johanna Briggs Institute Checklist for Cohort Studies

Author Year	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?
Ledien 2017	N/A	N/A	Yes	No	N/A	Yes	Yes	Yes	Unclear	Unclear	Yes
Lin 2015	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	Unclear	Unclear	Yes
Zaki 2010	N/A	N/A	Yes	No	N/A	Yes	Yes	Yes	Yes	N/A	Yes
Hagan 2013	N/A	N/A	Yes	No	N/A	Yes	Yes	Yes	No	Unclear	Yes

Table 13. Johanna Briggs Institute Checklist for Analytical Cross-sectional Studies

Author Year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
de Alwis 2018	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Agampodi 2014	Yes	Yes	Yes	Yes	N/A	N/A	Yes	Yes
Carrel 2010	Yes	No	Yes	Yes	No	N/A	Yes	Yes
Kawaguchi 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Leal-Castellanos 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix C: Biography & CV

Sarah Cadarette is a Master of Public Health student at the University of Nebraska Medical Center College of Public Health. Her studies have focused on epidemiology, biostatistics, and emergency preparedness. In the summer of 2020, she worked with the East-Central District Health Department in Columbus, NE and contributed to work on health equity and COVID-19 response. In addition to her studies, Ms. Cadarette has worked as a pharmaceutical consultant since 2011. In this role, she supports health economics and outcomes research by conducting systematic literature reviews and meta-analyses. Her work has provided her with experience in numerous oncological conditions, behavioral health, opioid use disorder, COPD, and asthma, among others. Ms. Cadarette has a bachelor's degree from Mount Holyoke College and a post-baccalaureate certificate in pre-medical studies from Brandeis University.

SARAH CADARETTE

PROFILE
- Public health student with interest in epidemiology and emergency preparedness
- Professional with nine years of experience in health economics and outcome research consultancy, focusing on systematic literature reviews and network meta-analyses
- Experience across a wide range of disease areas, including opioid misuse/abuse, antibiotic resistance, respiratory (COPD and asthma), multiple sclerosis, orphan diseases, type 2 diabetes, hepatitis C, and advanced oncology settings
- Skilled in MEDLINE (via PubMed), Embase, and Cochrane database searches, and EndNote, DistillerSR, and SAS software

EDUCATION

University of Nebraska Medical Center, Omaha, NE –Master of Public Health, Anticipated graduation December 2020

Brandeis University, Waltham, MA – Post-Baccalaureate Certificate in Premedical Studies, 2009

Mount Holyoke College, South Hadley, MA – Bachelor of Arts *cum laude*, 2007
Major: Religion **Minor:** Politics
2004-2004 Bernice MacLean Award for Excellence in Introductory Biology

RELEVANT EXPERIENCE

Xcenda	Nov. 2015 — Present
Assistant Director	Sept. 2017 – Present
Manager	Nov. 2015 — Sept. 2017

Palm Harbor, FL

- Serves as primary content developer on systematic and targeted literature reviews
- Contributes to new business development and innovation task forces
- Co-heads department training initiatives

Evidera (Formerly a division of United BioSource Corporation)	July 2011 — Nov. 2015
	April 2015—Nov.2015
Research Associate III	Oct. 2013—April 2015
Research Associate II	Oct.2012—Oct. 2013
Research Associate I	July 2011—Oct.2012
Research Assistant	

Lexington, MA

- Worked independently and collaboratively within a team to perform systematic literature reviews and meta-analyses
- Managed large databases for quantitative and qualitative projects
- Performed quality and logics checks to prepare data for analysis
- Drafted reports synthesizing evidence both quantitatively and qualitatively
- Operated as the internal project lead on both qualitative and quantitative projects

PUBLICATIONS

Manuscripts

Corren J, Kavati A, Ortiz B, Colby JA, Ruiz K, Maiese BA, **Cadarette SM**, Panettieri RA. Efficacy and safety of omalizumab in children and adolescents with moderate-to-severe asthma: a systematic literature review. *Allergy Asthma Proc.* 2017;38(4):250-263.

Martin AL, Marvel J, Fahrbach K, **Cadarette SM**, Wilcox TK, Donohue JF. The association of lung function and St. George's respiratory questionnaire with exacerbations in COPD: a systematic literature review and regression analysis. *Respir Res.* 2016;17:40.

Travers KU, Pokora TD, **Cadarette SM**, Mould JF. Major depressive disorder in Africa and the Middle East: a systematic literature review. *Expert Rev Pharmacoecon Outcomes Res.* 2013;13(5):613-30.

Posters

Tetzlaff J, **Cadarette SM,** O'Blenis P, Ruiz K. Pragmatic artificial intelligence-based reference screening in systematic reviews. Poster presented at: International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 2019; May 18-22, 2019; New Orleans, LA.

Cadarette SM, Douyon, L, Ranganathan P, Ballew N, Colby JA, Maiese BA, Slaff S, Wissinger E, Ruiz K. Systematic literature review (SLR) evaluating quality assessment tools (QAT). Poster presented at: International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 21st Annual European Congress; November 10-14, 2018; Barcelona, Spain.

Sarnes E, **Cadarette SM**, Sawchyn B, Gittings K, Kulp W, Siu E, Ruiz K, Wissinger E. A comparison of health technology assessment (HTA) requirements for systematic literature reviews (SLRs). Poster presented at: International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 20th Annual European Congress; November 4-8, 2017; Glasgow, Scotland.

Purayidathil FW, **Cadarette S**, Forys A, McLaughlin T, Shah M, Aigbogun MS. Utilizing administrative claims data to identify severity in patients with Alzheimer's disease: challenges and opportunities. Poster presented at: 9th Clinical Trials on Alzheimer's Disease; December 8-10, 2016; San Diego, CA.

Sanyal AJ, Martin AL, **Cadarette SM**, Henriksson K, Hartman B, Hansen MB. Global Trends in the management of nonalcoholic steatohepatitis (NASH): treatment patterns and outcomes. Poster presented at: The Liver Meeting; November 11-15, 2016; Boston, MA.

Gueron B, Nalpas C, Maiese BA, **Cadarette SM**, Campbell DJ, Arvin-Berod C, Duchesne I. Findings of a literature review in support of a patient count model (PCM) for hepatitis C virus (HCV) in the EU5. Poster presented at: International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 19th Annual European Congress; October 29-November 2, 2016; Vienna, Austria.

Sanyal AJ, Martin AL, **Cadarette SM**, Burns MD, Guranlioglu D, Kartman B, Henriksson KM, Hansen MB. A systematic literature review of the epidemiology and economic burden associated with non-alcoholic steatohepatitis. Poster presented at: The International Liver Conference; April 13-17, 2016; Barcelona, Spain.

Rael M, Benedict A, Ishak J, **Cadarette S**, Campioni M, Panjabi S. Indirect comparisons to assess the relative efficacy of carfilzomib + lenalidomide + dexamethasone versus panobinostat + bortezomib + dexamethasone and bortezomib + dexamethasone: a matching adjusted indirect comparison. Poster presented at: 57th Annual American Society of Hematology (ASH) Meeting and Exposition; December 5-8, 2015; Orlando, FL.

Rael M, Benedict A, Ishak J, **Cadarette S**, Campioni M, Panjabi S. Indirect comparison to assess the relative efficacy of carfilzomib + lenalidomide + dexamethasone versus bortezomib + thalidomide + dexamethasone: a matching adjusted indirect comparison. Poster presented at: 57th Annual American Society of Hematology (ASH) Meeting and Exposition; December 5-8, 2015; Orlando, FL.

Donohue JF, Marvel J, Martin AL, Travers KU, **Cadarette S**, Wilcox TK. Impact of change in lung function and COPD-related patient outcomes on exacerbations and hospitalizations: a systematic literature review. Poster presented at ISPOR 20th Annual International Meeting; May 16-20, 2015; Philadelphia, PA.

Ashaye AO, **Cadarette S**, Kinter ET. Economic burden of multiple sclerosis: a systematic review of the literature. Poster presented at: 2014 Joint ACRIMS and ECTRIMS Meeting; September 10-13, 2014; Boston, MA.

Ashaye AO, **Cadarette S**, Kinter ET. Multiple sclerosis and variation in health utilities: a systematic review of the literature. Poster presented at: 2014 Joint ACRIMS and ECTRIMS Meeting; September 10-13, 2014; Boston, MA.