LINKAGES BETWEEN EXTREME PRECIPITATION, WATER QUALITY, AND GASTROINTESTINAL ILLNESS

by

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Dedication

To my family and friends,

especially my parents. You raised me to ask difficult questions and to take chances in finding the answers, to build community, to seek adventure, to be thankful, and most of all to have a true sense of self and to maintain a positive outlook. These traits have shaped who I am and have helped on many occasions while completing this dissertation. Thank you! I love you.

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List of Abbreviations

AMS	American Meteorological Society
ASOS	Automated surface observing system
AT	Apparent temperature
BC	Beach closure
CDC	Center's for Disease Control and Prevention
CFU	Colony forming unit
CGH	Center for Global Health
CI	Confidence interval
CSS	Combined sewer system
CSO	Combined sewer overflow
DGHS	Director General of Health Services
DOW	Day of week
EPA	Environmental Protection Agency
ENSO	El Nino Southern Oscillation
FIPS	Federal information processing standard
GAM	Generalized additive model
GCV	Generalized cross validation
GI	Gastrointestinal illness
HHS	Health and Human Services
ICD-9	International Classification of Disease, 9th revision

ICD-10	International Classification of Disease, 10th revision
ICMR	Indian Council of Medical Research
ICLEI	Local Governments for Sustainability
IIPS	International Institute for Population Sciences and Macro International
IITM	Indian Institute of Tropical Meteorology
IMD	Indian Meteorological Department
IPCC	Intergovernmental Panel on Climate Change
IQR	Inter-quartile range
NCDC	National Climatic Data Center
NE	Northeast
NRDC	Natural Resources Defense Council
NSF	National Science Foundation
NWS	National Weather Service
PM	Particulate Matter
PRCP	Precipitation
PRECIS	Providing regional climates for impacts studies
RR	Risk ratio
SW	Southwest
TERI	The Energy and Research Institute
USGS	United States Geological Survey
WHO	World Health Organization

ABSTRACT

Background: The frequency, intensity, and duration of extreme weather events are expected to increase based on current climate model projections. Such changes, particularly those associated with extreme precipitation, will likely threaten water quality and exacerbate global health disparities. Vulnerable subpopulations include children, the elderly, and the poor.

Objectives: This dissertation evaluates the association between extreme precipitation and hospital admissions among: 1) a population in Chennai, India during 2004-2007, 2) the elderly in the Great Lakes Region in relation to beach closures during 2000-2006, and 3) the elderly in 132 U.S. cities during 1992-2006.

Methods: Daily hospital admissions were merged with daily meteorological data. Hospital admissions were examined for seasonal trends. Poisson regression and case-crossover models were fit to evaluate the association between extreme precipitation and daily hospital admissions. Season and age were explored as potential effect modifiers.

Results: In India, extreme precipitation ($\geq 90^{th}$ percentile) was positively associated with hospital admissions related to gastrointestinal illness (GI). The cumulative risk, estimated over a 15-day lag period, was 1.61 (95% confidence interval (CI): 1.29, 2.00) and was elevated among the young 2.65 (95% CI: 1.21, 5.80) and the old 1.68 (95% CI: 1.01, 2.80). Risk varied across seasons, peaking during pre-monsoon 1.58 (95% CI: 1.24, 1.90). In the Great Lakes Region, beaches were closed 10% of summer days. Precipitation above the 90^{th} percentile at lag 1 significantly predicted ($p < 0.05$) beach closures in 8 of the 12 cities. No consistent associations between beach closures and hospital admissions were seen when pooled across the 12 cities, 0.98 (95% CI: 0.94, 1.01). In 132 U.S. cities, nearly 1 million GI-related hospital admissions occurred. Overall, no positive associations between extreme precipitation and GI-related hospital admissions were observed. The overall national pooled estimate for risk of GI-related hospital admission at lag 15 was 1.01 (95% CI: 1.00, 1.02).

Conclusions: This work highlights the potential impacts of climate change on waterborne disease in the U.S. and India. The threat of more extreme weather events necessitates further study of how climate and weather are associated with hospital admissions and overall health.

Chapter 1

Introduction

1.1 CLIMATE CHANGE AND HUMAN HEALTH

Global climate change has emerged as one of the most urgent environmental health issues facing the world in the 21st century. Climate change is the most important puzzle humanity has had to contend with (NSF 2011). It is complex in its causes as well as its effects, and intricately linked to many facets of society such as agriculture, transportation, and especially health. Effective mitigation and adaptation strategies must be developed (NRDC 2011).

Climate change and associated changes in climate variability have the potential to affect human health in a variety of ways, by compromising food security, air quality, water quality and availability, and disease ecology. It has become evident that throughout the world many diseases are dependent on the local climate (EPA 2011). According to the Intergovernmental Panel on Climate Change (IPCC) report (IPCC 2007), the expected changes in climate will result in: (1) extended periods of exposure to allergens and some disease vectors, (2) shifts in the temporal and spatial distribution of diseases, (3) changes in temporal and spatial patterns of heat waves and flooding coupled with an overall increase in the occurrence and severity of extreme events, and (4) increases in extreme rainfall that will increase the risk of waterborne disease outbreaks. A comparative risk assessment conducted by the World Health Organization estimated that climate change is responsible for over 150,000 deaths per year, with the greatest disease burden due to increased diarrheal disease and malnutrition (WHO 2008; Campbell-Lendrum et al., 2003), and the most significant burden of disease falling on low- and middle-income countries.

Since climate change poses a significant threat to public health it necessitates that we reconceptualize how we define vulnerable populations and how we design strategies for protecting them (WHO 2011). As the world's climate continues to shift, exacerbating extremes in temperature and precipitation, it will endanger the health of people around the world (CDC 2011). Vulnerable communities in many parts of the world already face significant water-related challenges; the situation is expected to worsen as a result of climate change. Public health implications of these changes can already be seen in places where significant changes in human-environment interactions are occurring and in others where infectious diseases and vectors such as mosquitoes are emerging in places that were previously not at risk.

1.2 CLIMATE VARIABILITY AND WATERBORNE DISEASE

Around the world, many infectious diseases are transmitted through contaminated drinking water; in the U.S. alone drinking water is estimated to contribute to between 4.3 and 16.4 million cases of gastrointestinal illness (GI) per year (Messner et al. 2006; Tinker et al. 2010). The main route of exposure is ingestion of contaminated water often propagated via the fecal-oral route. The exposure pathway is complex, including multiple potential sources and a plethora of potential pathogens. Major causes of GI are: cholera, cryptosporidium, *Escherichia coli*, Giardia, Shigella, rotavirus, and Salmonella (Dennehy

2005).

Many waterborne pathogens are considered climate sensitive over seasonal and inter-seasonal time periods (Rose et al. 2001). Precipitation patterns influence the transport and survival of infectious microorganisms. Furthermore, excessive runoff and storm water overflow resulting from extreme precipitation can lead to peak concentrations of pathogens in surface water. It is likely that changes in climate variability and changing precipitation patterns will increase the risk of waterborne disease (Rose et al. 2000).

Several studies have investigated the linkages between drinking water quality indicators, such as turbidity and human health (Schwartz and Levin 1999; Aramini et al. 2000; Schwartz et al. 2000). Time series analysis has been used in many cases to evaluate the relationship between environmental parameters (e.g. precipitation and temperature) and waterborne disease. From 1948 to1994, 51% of waterborne disease outbreaks were preceded by extreme precipitation events (Curriero 2001). In Canada the combination of longer summers, increased drought, and more extreme precipitation were found to influence the risk of waterborne diseases (Charron et al. 2004). From 1975 to 2001, 92 waterborne outbreaks occurred in Canada, risk increased by a factor of 2.28 following above normal precipitation totals (<93rd percentile) (Thomas et al. 2006).

While increasing temperature can sometimes lead to inactivation of enteric pathogens, it can also have a positive effect on the growth and survival of pathogens increasing the risk of disease. Links have been made between weather patterns and the life cycle of pathogens, such as Cryptosporidium (King and Monis 2007; Rose et al. 2002), the transmission of waterborne zoonotic helminthes (Nithiuthai et al. 2004), and physiological changes in pathogen hosts, which may influence the shedding rate of pathogens such as *E.coli* O157 (Edrington 2006). Further evidence suggests that increasing water temperatures can increase the risk of infection from highly adaptive waterborne parasites that can survive in extreme environments (Gajadhar and Allen 2004). Ambient air temperature and extreme rainfall were positively associated with diarrheal disease in the Pacific Islands (Singh et al. 2001). Extreme rainfall has also been linked to GI-related hospital admissions (Checkley et al. 2000; Kovats et al. 2004) as well as documented waterborne disease outbreaks (Curriero et al. 2001, Rose et al. 2000, Rose et al. 2001). These associations are likely to vary both spatially and temporally, but that is not surprising given the complex causal pathway and number of potential causative agents.

Cholera is perhaps the most notable waterborne pathogen influenced by environmental parameters (Louis et al. 2003; Mendelsohn and Dawson 2008). Cholera dynamics display regular seasonal and inter-seaonal variability (Pascual et al. 2002). In the Lake Victoria Basin (Olago et al. 2007), Bangladesh (Pascual et al. 2000, Koelle et al. 2005, Harris et al. 2008; Rodo et al. 2002, Pascual et al. 2008), Peru (Checkley et al. 2000), and elsewhere, cholera outbreaks have been associated with the occurrence of El Nino Southern Oscillation (ENSO). Increasing temperatures and extreme precipitation have also been linked to increased incidence of infectious diseases in the Arctic (Parkinson and Butler 2005), in England and Wales (Nichols et al. 2009), *Salmonella* infections (Fleury et al. 2006; Kovats et al. 2004), cryptosporidiosis in Sub-Saharan Africa (Jagai et al. 2009), dysentery cases in Jinan, China (Zhang et al. 2008), and childhood illness related to fever and gastroenteritis (Lam 2007).

Seasonal variability can also influence relative pathogen abundance. In some cases, incidence is negatively correlated with environmental parameters; for example, rotavirus in the tropics thrives in colder and drier climates (Levy et al. 2008) and the concentration of enteric viruses in groundwater is negatively correlated with temperature (Yates et al. 1985). Cryptosporidium oocysts isolated from rivers in Hokkaido, Japan showed seasonal fluctuation increasing in numbers in late summer and decreasing to below detection in December (Tsushima et al. 2003). In Osaka City, Japan from April 1996 to March 1999, 64 outbreaks of acute nonbacterial gastroenteritis occurred and Norwalk-like viruses followed a seasonal pattern, peaking between January and March (Iritani et al. 2000). Studies related to waterborne disease and climate variability span a wide range of geographies and investigate a variety of disease causing agents.

1.3 VULNERABLE POPULATIONS

1.3.1 Low- and middle-income countries

In high-income countries the health sector is considered strong enough to withstand and adapt to threats associated with climate change, however, unequal access to health care, degrading water and sanitation infrastructure, land-use change, pollution, and an aging population will continue to undermine advances made in public health (Campbell-Lendrum et al. 2003, Patz et al. 2000, IPCC 2007, WHO 2004). In low- and middle-income countries, where communities are already experiencing a scarcity of resources, environmental degradation, high rates of infectious disease, weak infrastructure, and overpopulation, the health risks associated with climate change will be severe and the burden on existing health systems may be extreme (Patz et al. 2000).

While these low- and middle-income countries are only responsible for a small percentage of global greenhouse gas emissions, the adverse health effects associated with climate change will likely fall disproportionately on these populations. This inequity will further exacerbate global health disparities (McMichael et al. 2003; Patz and Olson 2006; Patz et al. 2007; Wiley and Gostin 2009).

Changes in temperature and precipitation will influence environmental transmission, geographic range, and the incubation period of many infectious diseases (Patz 1996). Tropical regions, where environmental and social factors are closely linked to the spread of disease, will witness significant changes in human-pathogen relationships (Sattenspiel 2000). Poverty is a primary, albeit distal determinant of disease; it is strongly associated with a lack of sanitation, poor neighborhood infrastructure, and poor living conditions, and is likely to increase both independently and as a result of climate change in the years ahead (Genser et al. 2008).

Diarrheal disease is the 5th leading cause of death in low- and middle-income countries. While poor sanitation, malnutrition, and a lack of access to potable water are more to blame than current climate conditions, as the climate shifts, the burden of diarrheal disease will continue to increase unless sanitation and public health services are improved.

1.3.2 Young and elderly populations

A disproportionate burden of disease often falls on the poor, the elderly, and those living in disadvantaged settings (Ebi and Paulson 2010; O'Neill and Ebi 2009). Children are often considered to be at much greater risk of infectious diseases (Glass et al.1991;

Jin et al. 1996). It is estimated that approximately 16.5 million children under five years of age experience between 21 and 37 million episodes of diarrhea annually; approximately 10.6% of hospitalizations in this age group are due to diarrhea (Glass et al. 1991).

In the context of weather-related morbidity, the elderly must also be considered a high-risk population, especially vulnerable to the combined effects of heat and infection. By 2030 the U.S. population over 60 is expected to double from approximately 0.5 million to nearly 1 million (Lutz et al. 2008). And by 2050, 22% of the world's population is expected to be 60 years old or older (UN 2009). A review of U.S. mortality data from 1979-1987 showed that death due to diarrhea was greatest in those 74 years and older compared to any other age group (Trinh and Prabhakar 2007). Diarrheal disease is a significant cause of morbidity and mortality among the elderly (Gangarosa et al. 1992) due to co-morbidities such as a weakened immune system, intestinal motility disorders, poor nutritional status and other chronic diseases.

1.4 RESEARCH OBJECTIVES

The purpose of this dissertation is to explore the linkages between extreme precipitation, water quality, and human health – adding to the body of work exploring this important field of research, introducing new methods, and making relevant recommendations. The underlying assumption is that extreme precipitation can contaminate both drinking and recreational water due to heavy runoff. Contamination can be measured using a variety of indicators such as turbidity and bacteria concentrations. The impact of contaminated water on health can be evaluated using several outcomes such as recorded waterborne outbreaks, self-reported gastrointestinal illness, or daily hospital admissions. The remainder of the dissertation is structured as follows:

Chapter 2, Recreational water quality and gastrointestinal illness in the Great Lakes region, evaluates the association between recreational water quality and GI-related hospital admissions among individuals 65 years and older in the Great Lakes region from 2000 to 2006, with a focus on 14 metropolitan areas. The primary objective of this study is to investigate the potential association between beach closures and GI-related hospital admissions, while controlling for meteorological conditions, over a 1-week lag. We also compare different methods used to control for long-term time trends in the hospital admissions data.

Chapter 3, Extreme precipitation and hospitalization admissions for gastrointestinal illness in Chennai, India, evaluates the association between precipitation and temperature on daily hospital admissions using data from two government hospitals in Chennai, India from 2004 to 2007. This study builds on one of the first time-series datasets available for this region and highlights the importance of building data monitoring and surveillance infrastructure.

Chapter 4, Precipitation and gastrointestinal illness among the elderly in 132 U.S. cities, evaluates the association between precipitation and GI-related hospital admissions among individuals 65 years and older in 132 U.S. cities from 1992 to 2006. The primary objective is to explore how the association varies across climate zones and whether environmental parameters such as drinking water source and location of combined sewer overflows influence risk of GI following extreme precipitation.

Chapter 5, Conclusions, knits the aforementioned chapters together, highlighting important research findings, making recommendations for decision-makers and public health practitioners, and ends with a section on future research directions building on this body of knowledge.

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Chapter 2

Recreational water quality and gastrointestinal illness in the Great Lakes region

2. ABSTRACT

Background: Heavy precipitation and subsequent stormwater runoff threaten water quality and human health. Vulnerable subpopulations, including children and the elderly, may be at an elevated risk of waterborne disease following heavy precipitation events and beach closures.

Methods: We estimated the association between beach closings and gastrointestinal illness (GI)-related hospital admissions over a one-week lag among people aged 65 and older in 12 Great Lakes cities from 2000 to 2006. Poisson regressions were fit in each city, controlling for meteorological conditions and long-term time trends in admissions. Multiple smoothing approaches were applied to evaluate the effect of different spline structures on risk estimates, including a method that avoids the potential bias of using a discontinuous time-series. City-specific estimates were combined to form an overall risk estimate for the Great Lakes region.

Results: Approximately 40,000 GI-related hospital admissions and over 2,500 beach closures were recorded from May through September in the 12 cities. On average, beaches were closed 10% of summer days. Precipitation above the 90^{th} percentile occurring one-day prior (lag 1) significantly predicted ($p < 0.05$) beach closures in 8 of the 12 cities. No consistent associations between beach closures and hospital admissions were seen: the combined risk ratio was 0.98 (95% confidence interval (CI): 0.94, 1.01) for lag 1; effect estimates at other lags were similar. Different control methods for long-term time trends did not alter the significance or magnitude of the association.

Conclusions: No association between GI-related hospital admissions and beach closures was seen, although heavy rain did predict beach closures. Given the importance of recreational and drinking water quality to health, studies with other, more specific, health outcomes across a wider age range are needed to evaluate risk. The exploration of time-trend control methods is relevant to a variety of environmental epidemiology studies and the methods presented here should be considered in future work.

2.1 INTRODUCTION

The concentration of bacterial indicators in recreational water, such as *Escherichia coli* (*E.coli*), has been linked to cases of waterborne disease in exposed individuals (Dufour and Wymer 2006; Marion et al. 2010; Wade et al. 2006, 2008). Health risks associated with exposure to contaminated recreational water include skin, eye, ear, and upper respiratory irritations and infections, as well as gastrointestinal illnesses (GI) (Cheung et al. 1990; Fleisher et al. 1996). Subpopulations at greater risk for contracting GI from contaminated water include children, the elderly, and individuals with compromised immune systems (CDC 2010; Santo Domingo and Hansel 2008; Wade et al. 2003).

The United States Environmental Protection Agency (EPA) standard for recreational water quality at freshwater beaches is daily *E.coli* concentrations less than 235 colony forming units (CFUs) per 100mL of water (Dufour and Wymer 2006; EPA 1986; Marion et al. 2010). Bacteria concentrations exceeding this standard trigger swimming advisories and/or beach closures to prevent exposure to waterborne pathogens. States with coastal waters designated for recreational use must adopt and implement monitoring programs according to the Beaches Environmental and Coastal Health (BEACH) Act of 2000.

Recreational water can be contaminated from both point and nonpoint sources including urban effluent, wildlife, domestic pets, agricultural runoff, beach sand, solid waste, stormwater runoff, and swimmers (Efstratiou 2001; Marsalek and Rochfort 2003; WHO 2003). Additionally, recreational water quality is influenced by precipitation and other hydrometeorological parameters (Ackerman and Weisberg 2003; Olyphant et al.

2003). Precipitation is positively correlated with *E. coli* concentrations in recreational water (Byappanahalli et al. 2010; Nevers and Whitman 2011; Whitman and Nevers 2008). Heavy precipitation and subsequent stormwater runoff can flush pathogens and other microorganisms directly into nearby surface water, resulting in increased concentrations of bacteria, and increased risk of waterborne disease (Curriero et al. 2001; Schuster et al. 2005; Patz et al. 2008). The number of beach closings and advisories in the United States in 2010 was among the highest in the last 20 years (Dorfman and Rosselot 2011). In the majority of instances, beach closings and advisories were due to bacteria levels exceeding health and safety standards. Under predicted climatic changes, more extreme rain events are expected to occur, particularly in the Great Lakes region, which may further exacerbate poor recreational water quality (Patz et al. 2008). Understanding the impact of extreme precipitation on GI is important to understanding the overall impact of changing climatic conditions on human health. Previous work has focused on the association between precipitation and bacteria concentrations in recreational water. Only simple statistical methods such as correlations (Haack et al. 2003), linear regression (Ackerman and Weisberg 2003; Sampson et al. 2006), and comparison of means (Scopel et al. 2006) have been used to previously address this question. Few epidemiological studies have looked at the association between precipitation and recreational water quality (or beach closures). Furthermore, our study is the first to investigate the association between beach closures and GI-related hospital admissions.

This work was predicated on the assumption that high concentrations of *E.coli* in recreational water in the Great Lakes are indicative of environmental conditions potentially associated with compromised water quality and increased risk of GI-related hospital admissions throughout the entire watershed. While swimmers may be directly impacted by poor recreational water quality, others may be exposed through less direct routes such as contaminated drinking water hydrologically linked to the contaminated recreational water. Our goal was to characterize potential associations between beach closures and GI-related hospital admissions among the elderly in the Great Lakes region, considering beach closures as a proxy for overall water quality, while controlling for meteorological conditions. Since recreational water quality data were only available during the summer months, we introduce an innovative method that controls for long-term time trends in the hospital admission data.

2.2 DATA AND METHODS

2.2.1 Study location

The Great Lakes region is home to more than 40 million people who utilize the water for drinking, fishing, recreation, and industry (Botts and Krushelnicki 1995; Patz et al. 2008; Wong et al. 2009). The region includes eight states in the U.S. and two provinces of Canada and encompasses over 1,000 beaches and 5,500 miles of shoreline (Dorfman 2006). The region currently experiences the highest percentage of beach closures due to adverse water quality compared with other freshwater and marine beaches in the U.S. (Dorfman and Rosselot 2010).

This study focused on 12 cities within the Great Lakes region for which sufficient beach closure data were available. To examine city-specific associations, beach closure data, available at the county level, were matched to their respective Metropolitan Statistical Areas (MSAs) for the counties for which beach closure and hospital admission data were available, thus forming the cities used in this analysis. The majority of cities correspond to only one county. Larger cities (Chicago, Cleveland, and Detroit) include several counties surrounding the city center.

2.2.2 Data sources and variables for analysis

Hospital admissions

Hospital admission records for individuals 65 years and older and enrolled in Medicare were obtained from the Centers for Medicare and Medicaid Services for the 12 cities from 2000 to 2006. Approximately 98 percent of all people in this age range are enrolled in Medicare (HHS 2010). The hospital admission records included date of admission, cause of admission (International Classification of Disease, 9th Revision (ICD-9)), and individual-level characteristics, including patient age, sex, race, and zipcode.

Cause of admission was defined as GI-related if the primary, secondary, or tertiary ICD-9 code was classified as (i) a pathogen specific intestinal infectious disease (ICD 001-007; 120-129), (ii) other and ill-defined intestinal infectious disease (008-009), or (iii) diarrheal disease-related symptoms (276, 558.9, 787) (Morris et al. 1996; Schwartz et al. 2000). Hospitalizations from these causes were collapsed into daily counts of GI-related illness for each of the 12 cities.

Recreational water quality and beach closures

Recreational water quality monitoring in the Great Lakes region most often occurs during the summer months. Daily recreational water quality data and/or beach closure data were obtained from the environmental and health organizations responsible for monitoring recreational water quality in the 12 cities included in this analysis. The water quality data provided a measurement of bacterial concentration at beaches within these cities during the summer swimming period (May 1-September 30) from 2000 to 2006. The data include either a daily concentration of *E. coli* or fecal coliforms in water samples, or a list of dates and locations for which recreational water advisories were issued due to high bacterial concentrations.

For water quality data recorded as measured bacterial concentrations, a beach was defined as closed if the concentration of *E.coli* or total coliforms was greater than or equal to the EPA standard of 235 or 200 CFUs per 100mL of water, respectively. Otherwise, a beach was defined as open. When duplicate water quality data were reported by the monitoring organization, a daily average concentration was recorded. The number of beaches monitored on a daily basis varied by county and year. Due to such inconsistencies in the data, a binary variable, *closed*, was created to describe whether a recreational water quality advisory was administered. This variable took the value of 1 if any beach within the city was closed on a particular day and 0 if all beaches within the city were open.

In Chicago and Rockford, water quality data were available as a list of dates when beach closures occurred, although the underlying decision to close a beach was based on the actual bacterial concentration measured in the water. Dates on which one or more beaches were closed within the city were coded as 1. On all other weekdays beaches were assumed to be open and coded as 0. Data were not imputed for weekend days and were left as missing when no date was listed.

Meteorological conditions

Hourly meteorological data including precipitation, temperature, dew point, and relative humidity, corresponding to the dates and cities for which beach closure data were available, were downloaded from the first order weather station of the National Weather Service (NWS) Cooperative Observer Program in each city (NWS 2010). Daily summaries were created from the hourly measurements for apparent temperature and total precipitation. Apparent temperature (AT), a measure of the combined effects of temperature and humidity, was calculated using the following formula: $AT = -2.653 + (0.994 * T_a) + (0.0153 * T_d^2)$, where T_a is equal to air temperature (˚C) and T_d is equal to dew point temperature (˚C) (Kalkstein and Valimont 1986; Steadman 1979).

Precipitation was categorized based on the measurable amount of precipitation that fell in each city using the limit of detection (0.01 inches, 0.25mm) (AMS 2011) and the city-specific summer time rainfall distribution. Categories were defined as precipitation equal to 0 (reference category), (1) greater than 0, but less than 0.01 inches (0.25mm), (2) greater than or equal to 0.01 inches, but less than the 90th percentile, and (3) greater than or equal to the 90th percentile. Thus, the effects of no, trace, moderate, and extreme precipitation were evaluated. The 90th percentile was chosen based on results from existing literature where Curriero et al. (2001) observed that 51 percent of waterborne outbreaks occurring in the U.S. from 1948 to 1994 were preceded by precipitation above the 90th percentile. Additionally, Rose et al. (2000) observed that between 20 and 40 percent of outbreaks occurring in the U.S. from 1971 to 2004 were associated with precipitation above the 90th percentile. Furthermore, during extreme precipitation events, combined sewer systems (CSSs) and runoff transport large amounts of both urban and agricultural runoff into nearby waterways, thus potentially contaminating recreational waters (Ackerman and Weisberg 2003; Byappanahalli et al. 2010; Dorfman and Mehta 2011; Haack et al. 2003; Sampson et al. 2006; Scopel et al. 2006; Whitman and Nevers 2008).

2.2.3 Statistical analysis

The primary goal of this study was to estimate the association between beach closures, a proxy for water quality throughout the watershed, and GI-related hospital admissions, while controlling for meteorological conditions. A secondary goal was to evaluate the use of various smoothing terms to determine the effect of using summer-only data in time-series data analysis, an important methodological question that has not previously been addressed.

Time-series analysis is commonly used in environmental epidemiology to evaluate short-term associations between environmental exposures such as air pollution or heat on health outcomes like morbidity or mortality (Schwartz et al. 1996; Dockery and Pope 1994). An essential feature of time-series analysis is the inclusion of a nonlinear term such as a spline to filter out long-term time trends in the health outcome or environmental predictor. Inclusion of a spline acts to isolate the short-term exposure of the health outcome while minimizing confounding by long-term time trends.

In some cases, where only certain seasons are of interest (e.g. summer), researchers conduct analyses using a discontinuous time-series, splicing together the seasons of interest over the study period. For example, some studies evaluating the association between ozone or extreme temperature and morbidity or mortality use summer-only data (Díaz et al. 2002; Metzger et al. 2010; Vaneckovaa et al. 2008). This method forces the estimate at the end of the season of interest in one year to match the estimate at the beginning of the season in the following year, without regard to effects of the "off season" on the estimate.

In our study, Poisson regression models were first fit without a spline term, then with a spline term estimated by the discontinuous summer-only time-series, and finally using a two-stage Poisson regression approach. In the two-stage approach, the spline term was initially estimated using the entire daily time-series of GI-related hospital admissions. The estimated spline fragments corresponding to the seven summers were then added to the Poisson regression model as offsets.

City-specific time-series plots of daily GI-related hospital admissions, daily beach closings, precipitation, and apparent temperature were created to examine long-term and seasonal trends, histograms were created to examine the consistency of the distribution of each variable across the 12 cities. City-specific descriptive statistics were summarized. Scatterplots were used as exploratory tools to visualize the bivariate associations between hospital admissions, beach closures, and meteorological variables.

To compare our data to existing literature in which precipitation during the previous 1-3 days predicts recreational water quality (Ackerman and Weisberg 2003; Haack et al. 2003; Scopel et al. 2006), a city-specific logistic regression was used to estimate the association between precipitation (PRCP) and beach closures (BC) over a 3-day lag period (Model 2.1).

Model 2.1:

$$\text{logit}[P(BC=1)] = ß_0 + ß_1 prcp_{lag1}$$

$$\text{logit}[P(BC=1)] = ß_0 + ß_1 prcp_{lag2}$$

$$\text{logit}[P(BC=1)] = ß_0 + ß_1 prcp_{lag3}$$

where BC is a binary variable representing the occurrence of a beach closure and precipitation is categorized based on the 90^{th} percentile.

Next, the crude association between BC and daily GI-related hospital admissions was evaluated using city-specific Poisson regression models. An overdispersion parameter was considered (McCullagh and Nelder 1989) and tested using Dean's test (Dean 1992) in each of these models. Standard errors of model parameters were adjusted accordingly.

Exploring lags

Observed health effects, such as GI-related hospital admissions, may lag behind environmental exposures due to delayed onset of clinical symptoms. Previous studies have reported a delayed onset of diarrheal disease following heavy rainfall events (Aramini et al. 2000; Curriero et al. 2001; Egorov et al. 2003; Schwartz et al. 2000). One explanation could be that incubation periods of waterborne pathogens range from one day, for pathogens such as *Shigella, Salmonella*, and *Rotavirus,* to up to two weeks for pathogens such as *Cryptosporidium* and *E.coli* (Haley et al. 2009; Jagai et al. 2009). Previous research has also described the peak rate of GI-related illness as occurring within 7 days of exposure (Eisenberg et al. 1998; Naumova et al. 2003). The 7-day lag period was chosen for this analysis to be consistent with the incubation period of most waterborne pathogens (Schwartz et al. 1997). Seven separate models were run using precipitation at single-day lags, 1 to 7 days prior to the hospitalization date, as the independent variable.

Exploring confounding by precipitation, apparent temperature, and day of week

As extreme precipitation can result in elevated turbidity measurements and increased concentrations of bacteria in surface waters (Ackerman and Weisberg 2003; Haack et al. 2003; Scopel et al. 2006), we hypothesized that extreme precipitation would be linked to beach closures and would also independently contribute to the burden of GI-related hospital admissions. The underlying assumption was that extreme precipitation leads to contamination throughout the watershed, potentially compromising both drinking and recreational water (Schijven and de Roda Husman 2005). To explore potential confounding by precipitation, daily precipitation was included in the model and was matched to the 7 single-day lags for beach closures.

Additionally, air temperature is an important environmental parameter influencing the replication, persistence, and transmission of pathogens in the environment (Checkley et al. 2000, Fleury et al. 2006; Naumova et al. 2006; Singh et al. 2001). Temperature can also affect the health of elderly populations (Trinh and Prabhakar 2007). Because temperature is associated with both the exposure and outcome of interest, it is a potential confounder. Continuous apparent temperature was included in the model to reflect the combined effects of temperature and humidity, matched to the lagged day of beach closure, 1 to 7 days prior to the date of hospital admission. An indicator variable for day of week (DOW) was also considered as a covariate because hospital admissions are known to vary by day of the week (Model 2.2).

Model 2.2: $\log[E(HA)] = ß_0 + ß_1 BC_{t-q} + ß_2 PRCP_{t-q} + ß_3 AT_{t-q} + ß_4 DOW_t$

where HA is daily hospital admissions, BC is a binary variable representing the occurrence of a beach closure, precipitation is categorized based on the 90^{th} percentile, t-q represents single-day lags 1-7 days prior to the day of hospital admission, AT represents apparent temperature, and DOW represents the day of week.

Exploring confounding by long-term time trends

To control for long-term time trends in hospital admissions, a nonlinear smoothing term for time was included in the Poisson regression model. Under the generalized additive model framework, this term was a penalized spline with smoothing parameters estimated to minimize the Generalized Cross Validation (GCV) score (Hastie and Tibshirani 1986, 1990). This model took the 7-year summer-only time-series and spliced the summer periods together and was fit with and without potential confounders (Model 2.3).

Model 2.3: $\log[E(HA)] = ß_0 + ß_1 BC_{t-q} + ß_2 PRCP_{t-q} + ß_3 AT_{t-q} + ß_4 DOW_t + s(time)$

where HA is daily hospital admissions, BC is a binary variable representing the occurrence of a beach closure, precipitation is categorized based on the 90^{th} percentile, t-q represents single-day lags 1-7 days prior to the day of hospital admission, AT represents apparent temperature, DOW represents the day of week, and s(time) represents a penalized spline on time.

The final stage of analysis was a two-stage Poisson regression, in which the entire time-series was modeled against GI-related hospital admissions to estimate a spline term for the entire 7-year study period (Model 2.4, Stage 1). The estimated spline fragments corresponding to the seven summers were then added to the full Poisson regression model as an offset. This model was also run with lags and potential confounders (Model 2.4, Stage 2). The purpose of including multiple spline structures was to evaluate the potential bias introduced when a discontinuous time-series is used to control for long-term time trends in the data.

Model 2.4, Stage 1: log[E(DailyGICount)] = s(time)

where s(time) represents a penalized spline on time.

Model 2.4, Stage 2: log[E(DailyGICount)] = $ß_0 + ß_1$BC_lagX + $ß_2$PRCP_lagX + $ß_3$AT_lagX + $ß_4$DOW + offset,

where BC is a binary variable representing the occurrence of a beach closure, precipitation is categorized as previously outlined, X represents single day lags 1-7 days prior to the event date, AT represents apparent temperature (°F), DOW represents the day of week, and offset represents the spline estimated from the full time-series.

Combining single city estimates

City-specific estimates were combined to obtain an overall summary estimate of the association between beach closures and GI-related hospital admissions across the Great Lakes region, controlling for precipitation, apparent temperature, day of week, and long-term time-varying confounders. To begin, we tested whether city-specific coefficients corresponding to the association between beach closures and GI-related hospital admissions were homogeneous across all 12 cities (Normand 1999). That is, we tested whether *k* city-specific summary statistics shared a common mean (θ):

H_0: $\theta_1 = \theta_2 = \ldots = \theta_k = \theta$

H_1: At least one θ_i is different from others

If the null hypothesis was upheld (p-value >0.05), a fixed-effect model was applied to pool the results using inverse-variance weighting. If the null hypothesis was rejected (p ≤0.05), a random-effects model, accounting for both within- and between-city variation, was applied (Berkey et al. 1995; Normand 1999). The fixed- and random-effects models were of the following form:

Fixed-effects model: $Y_i \sim N(\theta, s_i^2)$,

where θ is the central parameter of interest, and s_i^2 is the pooled variance.

Random-effects model: $Y_i \mid \theta_i, s_i^2 \sim N(\theta_i, s_i^2)$,

where θ is the central parameter and s^2 is the pooled variance.

All analyses were run using SAS Version 9.2 (SAS Institute, Cary NC) and R 12.0 (R Foundation for Statistical Computing, Vienna, Austria).

2.3 RESULTS

Twelve cities in the Great Lakes region were included in this analysis (Table 3.1); city locations and locations of monitored beaches are shown in Figure 2.1. Over the 7-year study period, approximately 40,000 GI-related hospital admissions were recorded in individuals over the age of 65 across the 12 cities (Table 2.2). The average number of daily GI-related hospital admissions ranged from 0.42 in Erie to 14.47 in Chicago, with an overall daily average of 2.66. According to the 2000 U.S. Census (U.S. Census Bureau 2000) the percent of the population over 65 ranged from 10% in Grand Rapids to above 14% in Erie, Cleveland, and Buffalo. Buffalo, in spite of having the highest percentage of elderly people (16%), had the third lowest percent of GI-related hospital admissions among the elderly (1.05%) suggesting that city-specific factors, other than population size, may be influencing the number of GI-related hospital admissions.

From 2000 to 2006, over 2,500 beach closures were issued during the swimming season, defined as 1 May to 30 September. On average, beaches were closed 10% of the time. However, in Chicago, Cleveland, and Milwaukee beaches were closed over 20% of the time. Daily precipitation during the swimming season in the Great Lakes region ranged from 0 to 4.45 inches (113 mm), with an overall mean daily total of 0.12 inches (3.05 mm). For all 12 cities, precipitation had a skewed distribution, with zero precipitation recorded on nearly 65% of days during the swimming season. Mean daily apparent temperature, for the region, was equal to 19ºC (67ºF). Apparent temperature and precipitation followed consistent seasonal trends throughout the study period across all cities. Table 3.3 lists the data sources for hospital admissions, recreational water quality, and meteorological data used in the regression analysis.

Extreme precipitation above the 90^{th} percentile, occurring on the previous day (lag 1), was a significant predictor ($p < 0.05$) of beach closures in 8 of the 12 cities (Buffalo, Cleveland, Detroit, Erie, Gary, Milwaukee, Rochester, and Toledo) (Table 2.4). However, results from the Poisson regression analysis did not reveal any consistent trends between beach closures and GI-related hospital admissions (Table 2.5). In Erie, Minneapolis, Rochester, and Toledo, beach closures were positively associated with GI-related hospital admissions among the elderly in at least one of the 7 different lag models. In Buffalo, Chicago, Cleveland, and Detroit, however, the association between beach closures and GI-related hospital admissions was negative in at least one of the 7 different lag models. In the four remaining cities Gary, Grand Rapids, Milwaukee, and Rockford no significant associations were found.

In the instances where beach closures were positively associated with GI-related hospital admissions, lags 1, 2, 3, and 7 were significant depending on the city; risk ratios ranged from 1.30 (95% confidence interval (CI): 1.00, 1.68) in Rochester at lag 3 to 1.76 (95% CI: 1.13, 2.75) in Minneapolis at lag 1. Controlling for precipitation, apparent temperature, day of week, and long-term time trends did not significantly alter the risk estimates corresponding to beach closures; the crude and adjusted models provided similar results. Results did not change dramatically when precipitation the preceding week categorized as extreme was used to capture the cumulative effect --- when the period 1-week prior was defined as having extreme precipitation. When the results were pooled across the 12 cities, the overall effect estimate, for all 7 lags, was insignificant and hovered near 1.00 (Table 2.5, Figure 2.2).

When the results from the different spline structures were compared, no significant differences were observed. In cities where a significant association was observed in at least one of the 7 different lag models, that association was consistent across spline structures. In cities where no association was observed for any lag, that also remained consistent across spline structures.

While the different spline structures used to control long-term time trends did not alter the significance or magnitude of the associations reported, there was an observable difference between the two different spline estimates (Figure 2.3). Using Detroit as an example, the spline estimated from the discontinuous time-series (Model 2.3) did not overlap with the spline estimated from the entire time-series in the two-stage analysis (Model 2.4). In all instances the spline estimated from the entire time-series was numerically different from that estimated from the discontinuous time-series.

2.4 DISCUSSION

In general, no significant or consistent association between beach closures and GI-related hospital admissions among the elderly was found in Great Lakes cities. The pooled regional estimate showed no overall association between beach closures and GI-related hospital admissions in the Great Lakes region. However, extreme precipitation, above the 90^{th} percentile, occurring 1-day prior was a significant predictor of beach closures in 8 of the 12 cities. In this study, novel methodology to control for long-term time trends using season-specific data was proposed and results using three different spline structures were compared. While no significant differences in the effect estimates were observed in this analysis, the two-stage Poisson model, which utilizes the full time-series to control for long-term time trends in the outcome variable, is recommended for future work focused on season-specific analyses.

The two-stage spline structure (Model 2.4) can be applied to a variety of studies where only one season is of interest. By comparing results from the two-stage spline model to results from a model with no spline as well as a spline estimated from the discontinuous summer-only time-series, we addressed an important methodological question: What is the most appropriate way to conduct time-series analysis when exposure data is only available for a portion of the year? Results, in this case, did not differ markedly across the three different modeling approaches. However, GI-related hospital admissions did not display significant variability between summer, the season of interest, and the rest of the year. If hospital admissions had varied significantly across seasons, this two-stage spline structure would control for such variability. In cases with high variability across seasons in the response variable, the two-stage spline model is a more appropriate way to minimize confounding by long-term time trends. Furthermore, differences in effect estimates are more likely to be observed between a discontinuous time-series model and a two-stage time-series model, which utilizes the full time-series, when the health outcome data has greater inter-seasonal variability.

Although the results presented here do not reveal a consistent or significant association between beach closures and GI-related hospital admissions, from existing literature it is clear that recreational water quality has the potential to adversely impact health outcomes. Although recreational water quality was considered a proxy for overall water quality in this analysis, this proxy metric has limitations. The number of elderly people directly exposed to poor water quality at beaches in the Great Lakes is likely very low, and the contributors to recreational water quality differ from the contributors to drinking water quality, which is likely the predominant exposure. Using recreational water quality as a proxy for overall water quality may be too far removed from the exposure pathway to establish an observable association with hospital admissions among the elderly.

Previous research confirms that precipitation is linked to water quality indicators such as *E.coli* concentrations and turbidity (Ackerman and Weisberg 2003; Haack et al. 2003); however, the lag at which this association is strongest has not yet been adequately identified. *E. coli* concentrations in recreational waters are estimated to peak approximately 24 to 72 hours following precipitation events in the Great Lakes region (Byappanahalli et al. 2010; Whitman and Nevers 2008). Previous research has also reported a delayed onset of diarrheal disease following extreme precipitation and related increases in water quality indicators, indicating degraded water quality following heavy rainfall events (Curriero et al. 2001; Drayna et al. 2010; Egorov et al. 2003; Morris et al. 1996; Rose et al. 2000; Schwartz et al. 2000). However, the timeframe where risk is highest has yet to be determined. Recreational water quality at Great Lakes beaches is likely too distal of an indicator to cause an observable spike in GI-related hospital admissions among the elderly. More work is planned by our group to investigate the direct effects of precipitation on GI-related hospital admissions among the elderly using Medicare admissions data.

Considering the impact of precipitation on recreational water quality, Sampson et al. (2006) found no association between rainfall and bacteria at any of their 15 sites along the Wisconsin shores of Lake Superior, their water samples were taken following any rain event of at least 0.25 inches (6 mm). In contrast, our study evaluated extreme precipitation events, above the 90th percentile 0.40 inches (10.16 mm), which were a significant predictor of recreational water quality in a majority of cities. Results from a specific location should not necessarily be used to make decisions regarding beach closures at other locations (Sampson 2006). For example, Haack et al. (2003) concluded that rainfall 48 to 72 hours prior was significantly associated with *E.coli* concentrations at three Southern beaches in Grand Traverse Bay in Lake Michigan, but only 24 hours prior at Western and Eastern beach locations.

Precipitation is frequently modeled as a continuous variable, although its distribution is highly skewed, with many 0 values recorded. Results from our analysis suggest that precipitation should be modeled in a way that accommodates the skewed distribution and the nonlinear associations often observed between precipitation and the outcome of interest. Modeling precipitation as a categorical variable, as we did, is a suitable approach. Future work should use a consistent definition of extreme precipitation so that decision-makers in different regions can have a shared understanding when considering policy and interventions.

One of the primary limitations of this analysis is related to data specificity; GI-related hospital admissions are dramatically underreported and the etiology is rarely identified (Charron et al. 2004; Ford 1999). The symptoms associated with exposure to contaminated recreational water are relatively broad-spectrum symptoms; therefore, it is challenging to observe direct associations between exposure and outcome. Additionally, the period of interest is quite limited: on average only 35% of summer days had measurable amounts of precipitation. Further, recreational water quality monitoring was not consistent over the study period. Because the association between recreational water quality and hospital admissions is only being investigated in select cities in the Great Lakes region, conclusions may not be applicable to marine or estuarine recreational waters or other regions of the country where socio-demographic, meteorological, and hydrodynamic conditions may vary.

The primary focus of this study was to estimate the association between beach closures and GI-related hospital admissions among the elderly across a wide geographic region over a 7-year time period, using uniform, standard statistical methodology. The results linking recreational water quality to extreme precipitation at lag 1 provide support for a rain-based public health warning system where beach managers and public health professionals could issue a beach closure based on weather forecasts to minimize exposure to contaminated recreational water and reduce the risk of disease (Frick and Ge 2007; Nevers and Whitman 2005). Early detection of recreational water contamination and rapid response can reduce human exposure and will help minimize the risk of waterborne disease.

2.5 CONCLUSIONS AND FUTURE WORK

In a majority of the 12 Great Lakes cities, extreme precipitation ($\geq 90^{th}$ percentile) at lag 1 was significantly associated with beach closures, however, no consistent trend was observed between beach closures and GI-related hospital admissions among the elderly. In the few instances where there was an association, controlling for confounders and the use of various spline structures to control for long-term time trends did not alter the significance or magnitude of the results. Nonetheless, the potential for recreational water quality to adversely impact human health must be considered in the context of a changing climate. Climate models for the Great Lakes region predict a rise in extreme precipitation events (Patz et al. 2008). In order to predict future health outcomes, it is critical to understand how current meteorological factors drive seasonal patterns of water quality and disease (Jagai et al. 2009).

During heavy precipitation events, the capacity of combined sewer systems (CSSs) can be exceeded resulting in direct discharge of sewage and stormwater into receiving waters, which has the potential to introduce high levels of bacterial contaminants into the environment (EPA 2008). Currently, the EPA estimates that 850 billion gallons of raw sewage and stormwater are released annually into U.S. waterways and that combined sewer overflows (CSOs) occur 43,000 times per year (EPA 2004). Because CSSs carry both stormwater and untreated wastewater, they have a high potential to contaminate waterways and lead to beach closures. CSOs can cause or contribute to water quality impairments, beach closures, contamination of drinking water supplies, and other environmental and human health problems (EPA 2007). Future research on recreational water quality should focus on the role of CSOs and other factors such as land cover, soil type, bedrock, and drinking water source that may influence the abundance and transport of pathogens in the environment. Specifically, future work should look at whether there is an increased likelihood of beach closures due to microbial contamination at beaches in close proximity to CSOs, downstream of heavily urbanized areas, and nearby agricultural land. The impact of interventions such as rain barrels, rain gardens, riparian zones, and agricultural best management practices that help reduce runoff and minimize the concentration of contaminants found in runoff should also be explored. Finally, enhanced monitoring and surveillance of recreational water quality in the Great Lakes region will help to inform future models and improve our ability to link environmental variables to health outcomes.

Table 2.1 Great Lakes cities included in this analysis, defined as the county or counties surrounding the Metropolitan Statistical Area.

City	State	County
Buffalo	NY	Erie
Chicago	IL	Cook
		Lake
		McHenry
		Will
Cleveland	OH	Cuyahoga
		Lake
		Lorain
Detroit	MI	Macomb
		Oakland
		Wayne
Erie	PA	Erie
Gary	IN	Lake
Grand Rapids	MI	Kent
Milwaukee	WI	Milwaukee
Minneapolis	MN	Ramsey
Rochester	NY	Monroe
Rockford	IL	Winnebago
Toledo	OH	Lucas

Table 2.2 Summary statistics for 12 Great Lakes cities, including population over 65, GI-related hospital admissions, beach closures, and average meteorological conditions during the swimming season from 2000 to 2006.

City	Population over 65 years (percent of total population)	Mean daily GI-related hospital admissions (total; percent of population over 65)	Mean daily beach closures (total)	Mean daily total precipitation mm (inches)	Mean daily apparent temperature °C (°F)
Buffalo, NY	151,258 (16)	1.48 (1,589; 1.05)	0.93 (292)	2.79 (0.11)	18.99 (66.19)
Chicago, IL	747,777 (11)	14.47 (15,498; 2.07)	0.61 (506)	3.05 (0.12)	20.39 (68.71)
Cleveland, OH	284,788 (15)	4.89 (5,236; 1.84)	1.47 (535)	3.05 (0.12)	20.22 (68.39)
Detroit, MI	491,592 (12)	7.35 (7,871; 1.60)	0.71 (342)	2.79 (0.11)	20.44 (68.80)
Erie, PA	40,256 (14)	0.42 (453; 1.13)	0.40 (103)	3.05 (0.12)	19.38 (66.89)
Gary, IN	63,234 (13)	0.95 (1,022; 1.62)	0.90 (293)	3.3 (0.13)	20.27 (68.49)
Grand Rapids, MI	59,625 (10)	0.69 (740; 1.24)	0.43 (15)	3.3 (0.13)	19.14 (66.46)
Milwaukee, WI	121,685 (13)	2.38 (2,545; 2.10)	0.90 (376)	3.05 (0.12)	19.06 (66.31)
Minneapolis, MN	59,502 (12)	1.95 (2,092; 3.52)	0.23 (17)	3.3 (0.13)	19.33 (67.79)
Rochester, NY	95,779 (13)	0.80 (860; 0.90)	0.40 (145)	3.05 (0.12)	19.29 (66.22)
Rockford, IL	35,450 (13)	0.51 (612; 1.73)	0.10 (75)	3.30 (0.13)	20.14 (68.26)
Toledo, OH	59,441 (13)	0.57 (609; 1.02)	0.44 (115)	3.05 (0.12)	20.44 (68.8)

[1]The swimming season was defined as 1 May through 30 September

Table 2.3 Data sources for hospital admissions, meteorological, and recreational water quality data.

Data type	Data source
Hospital Admission Data	Centers for Medicare and Medicaid Services
Meteorological Data	National Weather Service Cooperative Observer Program
Recreational Water Quality Data (county, state)	
Cook, Lake, McHenry, Will, and Winnebago, IL	Illinois Department of Public Health: Environmental Health
Lake, IN	Indiana Department of Environmental Management
Kent, Macomb, Oakland, and Wayne, MI	MI Department of Natural Resources and the Environment
Ramsey, MN	Ramsey County Public Works
Erie and Monroe, NY	NY State Health Department
Cuyahoga, Lake, Lorain, and Lucas, OH	Ohio Department of Health
Erie, PA	Erie County Department of Health
Milwaukee, and Waukesha, WI	Wisconsin Department of Natural Resources

Table 2.4 City-specific odds ratios[1] (p-value) evaluating the association between daily categorical precipitation[2] 1-day previous (lag 1) and beach closures in 12 Great Lakes cities from 2000-2006.

Precipitation Category	OR (p-value)			
	Buffalo, NY	**Chicago, IL**	**Cleveland, OH**	**Detroit, MI**
0 < prcp < 0.01	2.42 (0.14)	1.69 (0.23)	1.77 (0.30)	1.28 (0.68)
0.01 ≤ prcp < 90th percentile	2.94 (< 0.001)	1.34 (0.14)	1.65 (0.07)	1.42 (0.13)
prcp ≥ 90th percentile	16.93 (< 0.001)	1.20 (0.41)	7.39 (0.00)	4.02 (< 0.001)
	Erie, PA	**Gary, IN**	**Grand Rapids, MI**	**Milwaukee, WI**
0 < prcp < 0.01	0.00 (0.98)	1.48 (0.70)	-----	0.93 (0.89)
0.01 ≤ prcp < 90th percentile	2.31 (0.09)	1.53 (0.15)	1.71 (0.54)	1.41 (0.22)
prcp ≥ 90th percentile	10.21 (< 0.001)	2.01 (0.05)	0.57 (0.64)	2.01 (0.04)
	Minneapolis, MN	**Rochester, NY**	**Rockford, IL**	**Toledo, OH**
0 < prcp < 0.01	2.00 (0.59)	2.67 (0.03)	0.00 (0.09)	2.02 (0.29)
0.01 ≤ prcp < 90th percentile	1.33 (0.75)	1.91 (0.03)	0.51 (0.17)	1.24 (0.55)
prcp ≥ 90th percentile	1.60 (0.50)	5.67 (< 0.001)	0.66 (0.40)	9.07 (< 0.001)

[1]Logistic regression, Model 1: logit[(BC)] = ß0 + ß1prcp_cat2_lag1 + ß2prcp_cat3_lag1 + ß3prcp_cat4_lag1, where BC is a binary variable representing the occurrence of a beach closure

[2]Reference category where precipitation is equal to 0 inches

Table 2.5 City-specific risk ratios[1] (95% confidence interval) evaluating the association between daily beach closures and GI-related hospital admissions among people 65 years and older over a 1-week lag using a two-stage spline structure in 12 Great Lakes cities, including a pooled estimate, from 2000-2006.

	Buffalo, NY	**Chicago, IL**	**Cleveland, OH**	**Detroit, MI**	**Erie, PA**
lag 1	0.96 (0.79, 1.16)	0.96 (0.91, 1.00)	0.99 (0.90, 1.09)	1.01 (0.94, 1.08)	1.49 (0.90, 2.46)
lag 2	0.97 (0.79, 1.19)	1.02 (0.97, 1.07)	1.05 (0.95, 1.17)	1.00 (0.93, 1.08)	1.67 (1.02, 2.76)
lag 3	1.04 (0.85, 1.28)	1.00 (0.95, 1.05)	0.88 (0.80, 0.98)	0.97 (0.90, 1.05)	1.15 (0.69, 1.93)
lag 4	0.98 (0.81, 1.20)	1.01 (0.96, 1.06)	0.96 (0.86, 1.06)	0.99 (0.92, 1.07)	1.23 (0.70, 2.18)
lag 5	0.78 (0.63, 0.96)	1.02 (0.97, 1.07)	1.02 (0.92, 1.14)	0.92 (0.86, 0.99)	0.49 (0.22, 1.06)
lag 6	0.92 (0.75, 1.12)	1.02 (0.98, 1.08)	1.03 (0.93, 1.15)	0.95 (0.88, 1.02)	1.54 (0.89, 2.65)
lag 7	0.92 (0.75, 1.12)	1.00 (0.96, 1.05)	0.96 (0.87, 1.06)	0.97 (0.90, 1.04)	0.94 (0.52, 1.68)
	Gary, IN	**Grand Rapids, MI**	**Milwaukee, WI**	**Minneapolis, MN**	**Rochester, NY**
lag 1	0.90 (0.71, 1.15)	0.70 (0.22, 2.13)	1.05 (0.89, 1.24)	1.76 (1.13, 2.75)	0.84 (0.64, 1.10)
lag 2	1.08 (0.85, 1.38)	1.74 (0.74, 4.09)	1.02 (0.87, 1.20)	1.13 (0.72, 1.75)	0.86 (0.65, 1.12)
lag 3	1.01 (0.80, 1.28)	1.13 (0.51, 2.51)	0.99 (0.84, 1.17)	1.08 (0.68, 1.69)	1.30 (1.00, 1.68)
lag 4	1.03 (0.81, 1.31)	1.26 (0.50, 3.17)	1.03 (0.88, 1.21)	0.70 (0.40, 1.22)	0.96 (0.73, 1.26)
lag 5	0.99 (0.78, 1.25)	0.66 (0.17, 2.57)	1.08 (0.92, 1.27)	1.14 (0.69, 1.86)	0.97 (0.74, 1.28)
lag 6	1.11 (0.87, 1.41)	1.49 (0.49, 4.50)	0.99 (0.84, 1.16)	1.10 (0.73, 1.67)	1.03 (0.79, 1.35)
lag 7	0.87 (0.69, 1.11)	2.41 (0.75, 7.77)	1.07 (0.91, 1.26)	0.75 (0.51, 1.10)	1.19 (0.92, 1.53)
	Rockford, IL	**Toledo, OH**	**Pooled - Estimate**		
lag 1	1.11 (0.67, 1.82)	0.97 (0.68, 1.38)	0.98 (0.95, 1.01)		
lag 2	0.78 (0.42, 1.43)	0.70 (0.47, 1.02)	1.01 (0.98, 1.05)		
lag 3	0.83 (0.46, 1.50)	1.13 (0.77, 1.65)	0.98 (0.95, 1.02)		
lag 4	1.04 (0.62, 1.74)	0.64 (0.43, 0.97)	1.00 (0.96, 1.03)		
lag 5	1.35 (0.85, 2.13)	1.03 (0.71, 1.48)	0.99 (0.95, 1.02)		
lag 6	0.77 (0.42, 1.43)	1.01 (0.71, 1.45)	1.01 (0.97, 1.04)		
lag 7	1.30 (0.81, 2.10)	1.67 (1.22, 2.30)	0.99 (0.96, 1.03)		

[1]Two-stage Poisson regression adjusted for meteorological conditions, day of week, and long-term time trends

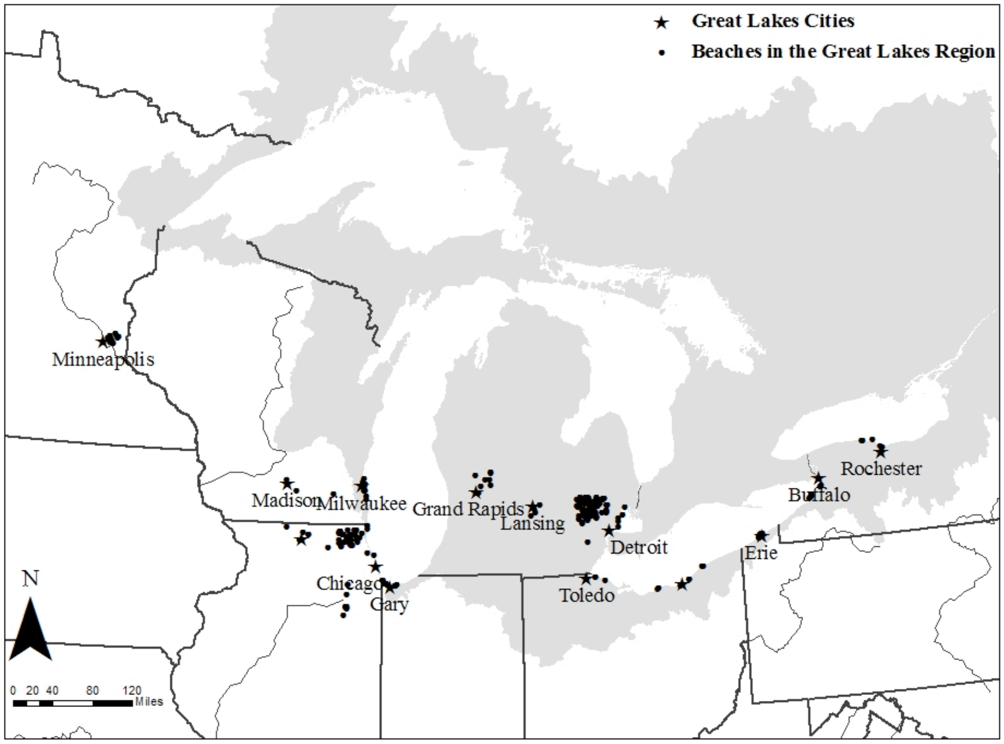

Figure 2.1 Twelve cities and neighboring beaches in the Great Lakes region. Cities, defined as the county or counties surrounding the city center, and beaches shown here were included in the analysis.

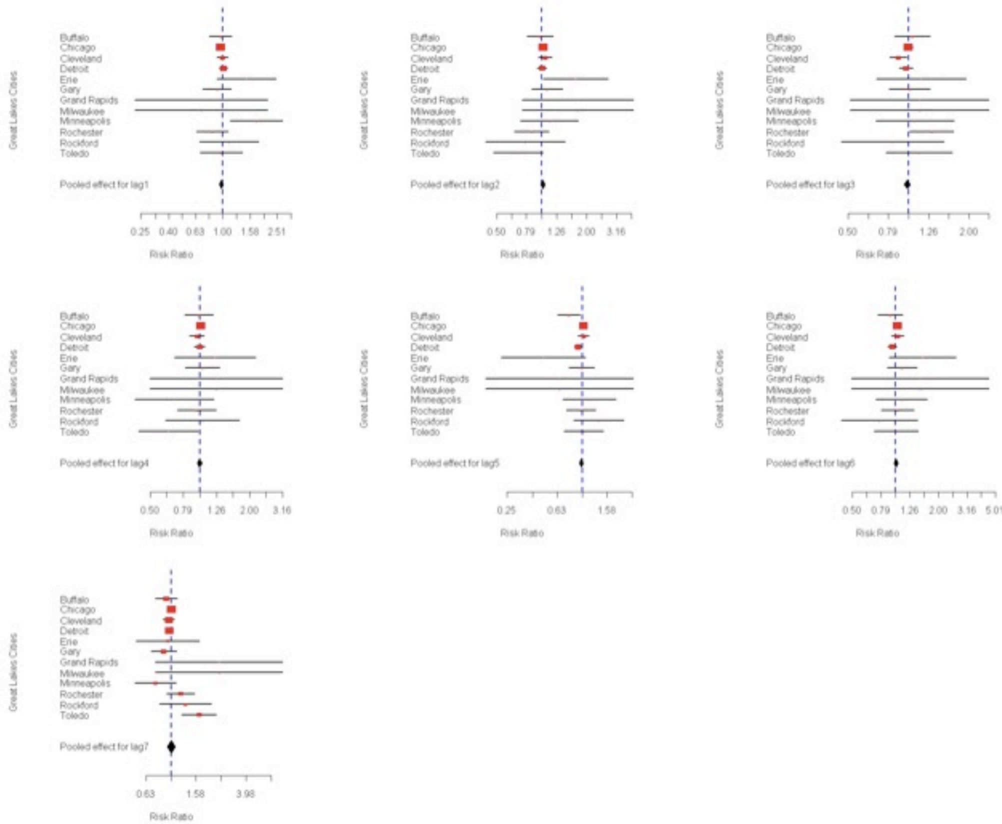

Figure 2.2 Individual and pooled estimates across the 12 Great Lakes cities using the two-stage spline structure for all 7 single-day lags, controlling for meteorological conditions, day of week, and long-term time trends.

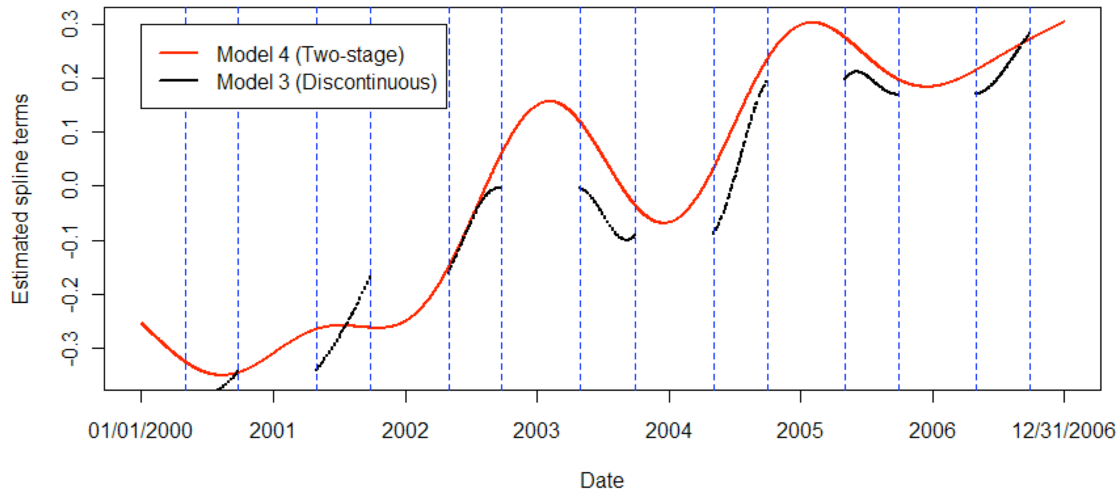

Figure 2.3 The discontinous summer-only spline compared to the spline estimated using the entire 7-year time-series in the two-stage spline model, using Detroit, MI as an example.

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Chapter 3

Extreme precipitation and hospital admissions for gastrointestinal illness in Chennai, India

3. ABSTRACT

Background: The increased frequency, intensity, and duration of extreme weather events from climate change is expected to exaggerate global health disparities. This study evaluated the association between extreme precipitation and hospital admissions in Chennai, India.

Methods: Daily hospital admission data from two government hospitals in Chennai were merged with daily meteorological data from Chennai International Airport for 2004-2007. Poisson regression models were fit to evaluate the association between extreme precipitation ($\geq 90^{th}$ percentile) and hospital admissions over a 15-day lag period, controlling for apparent temperature, day of week, and long-term time-trends. Season and age were explored as potential effect modifiers.

Results: Extreme precipitation was consistently associated with hospital admissions due to gastrointestinal illness (GI). The risk among people of all ages for being hospitalized for GI associated with extreme precipitation occurring in the previous 15 days was 1.61 (95% confidence interval (CI): 1.29, 2.00). Among the young the estimate was 2.65 (95%

CI: 1.21, 5.80), and the old 1.68 (95% CI: 1.01, 2.80). Risk also varied across seasons, with a 1.58 times increase in hospitalizations among all ages during the pre-monsoon (95% CI: 1.24, 1.90) compared to a 1.31 times increase during northeast monsoon (95% CI: 1.19,1.37) and no significant trends during winter and southwest monsoon.

Conclusions: Extreme precipitation was associated with GI-related hospital admissions in Chennai, India, with elevated risks among the young and old. Given the predicted increase in extreme weather events and increased weather variability, populations in India may be at an increased risk of waterborne disease.

3.1 INTRODUCTION

Global climate change is expected to influence the frequency, intensity, and duration of extreme weather events, which will affect water quality and quantity, and thus has the potential to adversely impact human health. High-risk areas include those already experiencing a scarcity of resources, environmental degradation, high rates of infectious disease, weak infrastructure, and overpopulation (Patz et al. 2005). Vulnerable populations include the elderly, children, urban populations, and the poor (Ebi and Paulson 2010; Gangarosa et al. 1992; O'Neill and Ebi 2009; Trinh and Prabhakar 2007). India, with its ever-increasing population and rate of urbanization, will be particularly vulnerable to the effects of global climate change. Understanding the current relationship between climate variability and human health will be important as India works to integrate existing public health programs with climate change adaptation strategies and early warning systems (Bush et al. 2011).

Diarrheal disease remains among the top five causes of death in low- and middle-income countries, particularly among children under five (Boschi-Pinto et al. 2008). However, research linking weather variability to diarrheal disease in these countries is sparse. Diarrheal disease is often transmitted via the fecal-oral route and contaminated water is a key conduit of exposure (Ford 1999). While evidence from elsewhere in the world shows that waterborne disease outbreaks are preceded by extreme precipitation events (Curriero et al. 2001) and that seasonal variability influences relative waterborne pathogen abundance (Naumova et al. 2007), the association between meteorological conditions and hospital admissions has not been well documented in India. Cholera is perhaps the most well studied waterborne pathogen; outbreaks have been linked to extreme precipitation and temperature in the Lake Victoria Basin (Olago et al. 2007), Bangladesh (Pascual et al. 2000, 2008), Peru (Checkley et al. 2000), and elsewhere in the world. Extreme meteorological conditions have also been linked to cryptosporidiosis in Sub-Saharan Africa (Jagai et al. 2009) and dysentery cases in Jinan, China (Zhang et al. 2008).

However, in most countries exposure data is not easily linked to health data. The majority of environmental epidemiologic studies in low- and middle-income countries have focused on the cross-sectional prevalence of disease (Balakrishnan 2011). This study is unique in that it utilizes a 4-year time-series dataset of hospital admissions. The goals of this study were (1) to describe seasonal fluctuations in daily hospital admissions in Chennai, India from 2004 to 2007 and (2) to evaluate the association between extreme precipitation and gastrointestinal (GI)-related hospital admissions.

3.2 DATA AND METHODS

3.2.1 Study location

Chennai is the fifth largest city in India with an estimated population of 4.34 million people and a population density of 24,682 per km^2 (63,926 per mi^2); Chennai is one of the most densely populated cities in the world (Census of India 2001). The Chennai Water Board and Chennai Metro Water are responsible for "contributing positively towards health and quality of life of the citizens of Chennai city by providing good quality safe drinking water at a reasonable price" (chennaimetrowater.com). Drinking water in Chennai comes from a variety of sources including surface water and a desalinization plant built in 2010 that filters approximately 250 million liters of sea water per day. Approximately 70% of Chennai's population has sufficient access to safe drinking water. However, nearly a tenth of Chennai's population live in disadvantaged slum-like settings where access to safe drinking water is severely limited (Chandramouli 2003; McKenzie 2009).

3.2.2 Hospital admission data

Hospital admission data from two government hospitals in Chennai were collected from 2004 to 2007 as part of the Indian Council of Medical Research funded project *Human Health Risk Evolution of Air Pollutants in Chennai, India* conducted at Sri Ramachandra University (Balakrishnan 2011). The hospital admission data were collected from Madras Medical College (MMC) and Kilpauk Medical College (KMC).

Hospital admissions were classified based on the International Classification of Disease, 10th revision (ICD-10). Admissions were defined as GI-related if the primary, secondary, or tertiary ICD-10 code was listed as intestinal infectious disease (A00-A09), helminthiases (B65-B83), or GI-related symptoms (R11-nausea and vomiting, R50-fever, R51-headache) (Morris et al. 1996; Schwartz et al. 2000). Data from the two hospitals were combined and collapsed into daily counts. Hospital admissions lacking an ICD-10 code were categorized as unclassified.

3.2.3 Meteorological data

Hospital admission data were merged with daily meteorological data, monitored at the Chennai International Airport and available from the National Climatic Data Center (NCDC) Global Surface Summary of the Day (NCDC 2011). Meteorological parameters extracted included precipitation, temperature, dewpoint, and relative humidity. Apparent temperature (AT) was calculated to represent the combined effects of temperature and humidity using the following formula: $AT = -2.653 + (0.994 * T_a) +(0.0153 * T_d^2)$, where T_a is air temperature (˚C) and T_d is dew point temperature (˚C) (Kalkstein and Valimont 1986; Steadman 1979).

For this analysis, precipitation was categorized using the overall distribution during the study period (2004-2007) to assign cut-points. Categories were defined as precipitation equal to 0 millimeters (mm) (reference category); greater than 0, but less than the 90th percentile; and greater than or equal to the 90th percentile (12.7 mm or 0.5 inches).

3.2.4 Statistical analysis

Time-series plots of hospital admission (all-cause, GI-related, and unclassified) and meteorological data were created to check for consistency and to observe seasonal trends. Histograms were created to examine the distribution of each variable. Descriptive statistics were calculated to summarize the variables of interest.

We hypothesized that extreme precipitation (≥90th percentile) would be associated with an increased risk of GI-related hospital admissions, but not all-cause hospital admissions. With daily counts of hospital admissions as the dependent variable, Poisson regression models were fit with the precipitation categories as the independent variables. An overdispersion parameter was included to account for instances where the sample variance was not equal to the sample mean (McCullaugh and Nelder 1989). Dean's test was used to formally test for overdispersion (Dean 1992).

Lags

GI-related hospital admissions were expected to peak several days after the occurrence of an extreme precipitation event due to delayed environmental transport of pathogens and delayed onset of clinical symptoms. Previous studies have reported a delayed onset of GI up to several days following heavy rainfall events (Aramini et al. 2000; Curriero et al. 2001; Egorov et al. 2003; Schwartz et al. 2000). Incubation periods of waterborne pathogens can range from one day, for pathogens such as *Shigella, Salmonella*, and *Rotavirus,* to up to two weeks for pathogens and bacteria such as *Cryptosporidium* and *E.coli* (Haley et al. 2009; Jagai et al. 2009). To account for this variability, different lag structures were examined. Poisson regression models were fit with 15 separate single-day lags, 1-15 days prior to the day of hospital admission (Model 3.1). A distributed lag model was also used to evaluate the cumulative effect over the entire 15-day period (Gasparrini et al. 2010) (Model 3.2).

Distributed lag models are common in air pollution studies (Braga et al. 2002; Pope and Schwartz 1996; Schwartz 2000); they provide a systematic way to investigate the distribution of effect over time. The underlying assumption of the distributed lag model is that hospital admissions today are dependent on precipitation occurring yesterday (1-day effect) as well as precipitation occurring two days previous (2-day lag effect), three days previous (3-day lag effect), etc. Because precipitation levels on days close together are likely to be correlated, a high degree of collinearity is likely, which can produce unstable estimates of the individual ß's. To gain more stable estimates in the distributed lag model, coefficients were constrained using the lag number to fit a fourth degree polynomial function (Schwartz 2000). Using the generalized additive model framework the constrained distributed lag has the following form: $\text{Log}(E(Y)) = n_0W_0 + \ldots + n_dW_d$, where the coefficients of the *W's* correspond to the parameters of a polynomial distributed lag. This approach allows the cumulative effect of precipitation to be modeled over the 15-day period, simultaneously estimating the non-linear and delayed effects of extreme precipitation.

Model 3.1: $\log\left[E\left(HA_t\right)\right] = \beta_0 + \beta_1 PRCP_{t-q} + \beta_2 AT_{t-q} + \beta_3 DOW_t + s(time)_t$

where *HA* refers to daily hospital admissions, *PRCP* is categorical daily precipitation, *q* denotes the lag 1-15 days prior to the hospital admission, *AT* is apparent temperature, *DOW* is day of week, and *s(time)* is a smooth function of time.

Model 3.2:

$$\log\left[E\left(HA_t\right)\right] = \beta_0 + \beta_1 PRCP_t + \ldots + B_j PRCP_{t-q} + \beta_2 AT_{t-q} + \beta_3 DOW_t + s(time)_t$$

where *HA* refers to daily hospital admissions, *PRCP* is categorical daily precipitation, *q* denotes the lag 1-15 days prior to the hospital admission, *AT* is apparent temperature, *DOW* is day of week, and *s(time)* is a smooth function of time.

Confounding and effect modification

Air temperature was considered a potential confounder because it can influence the replication, persistence, and transmission of pathogens in the environment (Fleury et al. 2006; Naumova et al. 2006; Checkley et al. 2000; Singh et al. 2001) as well as the health of vulnerable populations (Kovats and Akhtar 2008; Trinh and Prabhakar 2007).

Continuous apparent temperature was used to reflect the combined effects of temperature and humidity and was matched to the lagged day of categorical precipitation in the models. An indicator variable representing the day of week (DOW) on which the hospitalization occurred was also included as a potential confounder.

To control for long-term time trends in hospital admissions, a nonlinear smoothing term for time (i.e., a penalized spline) was included. The smoothing parameters were chosen to minimize the Generalized Cross Validation score in the generalized additive model (Hastie and Tibshirani 1986, 1990).

Vulnerable populations include the very young and the very old that may be at a greater risk of GI-related hospital admissions; therefore, effect modification by age was explored using a stratified analysis. Consistent with definitions from the World Health Organization (WHO 2011a) and the U.S. Department of Health and Human Services (HHS 2010), young was defined as less than 6 years of age, while old was defined as 65 years and older. Individuals between 6 and 65 were categorized as intermediate. Separate models were fit using daily counts of hospital admissions for each age category as the outcome.

The Indian monsoon season is characterized by extreme precipitation that contributes to >85% of India's annual rainfall (Vialard et al. 2011). The extreme precipitation is the result of a large-scale temperature differential that exists between the Indian continent and the Indian Ocean. To explore the effect of season a stratified analysis was run with season defined according to the Indian Meteorological Department (IMD) (IMD 2011) and Vialard et al. (2011) as: winter (January-February), pre-monsoon

(March-May), southwest monsoon (SW) (June-September), and northeast (NE) monsoon (October-December).

Stratifying by season creates a discontinuous time-series. Previous work has addressed this methodological constraint by using a two-stage Poisson regression technique (Bush et al. 2011, unpublished data). In the two-stage model, the entire time-series was used to estimate a spline term (Model 3.3, Stage 1). The estimated spline fragments corresponding to the season of interest were then added to the full Poisson regression model as an offset. This model was also run with lags and potential confounders, but only for the single day lag models (Model 3.3, Stage 2).

Model 3.3, Stage 1: $\log\left[E\left(HA\right)\right] = s\left(time\right)$

where *s(time)* is a smooth function of *time*.

Model 3.3, Stage 2: $\log\left[E\left(HA\right)\right] = \beta_0 + \beta_1 PRCP_{t-q} + \beta_2 AT_{t-q} + \beta 3 DOW_t + offset$,

where *HA* refers to the daily hospital admissions, *PRCP* is categorical daily precipitation represented as 2 dummy variables, *q* denotes the lag 1-15 days prior to the hospital admission, *AT* represents daily apparent temperature matched to the lagged day of precipitation, *DOW* represents day of week, and *offset* represents the spline estimated from the full time-series.

In the final stage of analysis, data were stratified by age as well as by season and results were compared across all strata. Model results using single day lags were compared to results from the distributed lag model. All analyses were run using SAS

Version 9.2 (SAS Institute, Cary NC) and R 12.0 (R Foundation for Statistical Computing, Vienna, Austria).

Effect estimates were calculated using the ß coefficient corresponding to extreme precipitation (≥90th percentile) where zero precipitation was the reference category. The model parameter associated with extreme precipitation was exponentiated to determine the risk ratio. The 95% confidence intervals for the risk estimates were calculated based on the standard error (s.e.) (+/− 1.96*s.e.). The risk ratios can be interpreted as the multiplicative increase in risk of GI-related hospital admissions following days with extreme precipitation (≥90th percentile) compared to days with no precipitation at certain single-day lags (1-15 days previous) or as the cumulative risk of GI-related hospital admissions following a 15-day period of extreme precipitation compared to a non-extreme 15-day period. In the stratified analysis, results can be interpreted as the increase in risk for certain age or season categories.

3.3 RESULTS

The two government hospitals and Chennai International Airport are located in Chennai, the capital city of India's southernmost state, Tamil Nadu (Figure 3.1). Daily precipitation in Chennai during the study period ranged from 0 to 283 mm (11.14 inches) (Table 3.1, Figure 3.2). Daily average apparent temperature during the study period was consistently 33°C (91°F) (Figure 3.3). Precipitation showed a skewed distribution over the 4-year study period; out of a total 1,461 days, 991 days (68%) had 0 mm precipitation and 424 days (29%) with greater than 0 mm. Precipitation data were missing on 46 days (3%).

GI-related hospital admissions accounted for approximately 4% of all hospital admissions (Table 3.2, Figure 3.4). Unclassified hospital admissions made up about 1% of all hospital admissions for the years 2004 to 2006, but increased to 11% in 2007. In most cases, there were more old than young admissions across all three categories of hospital admissions (all-cause, GI-related, and unclassified).

The number of all-cause hospital admissions varied from 57,237 in winter to 107,809 in SW monsoon (Table 3.2). Cause-specific admissions varied from 2,344 in winter to 4,893 in SW monsoon. Unclassified hospital admissions varied from 1,090 in winter to 5,265 in NE monsoon.

3.3.1 Single day lags

In the single day lag models, no significant association between extreme precipitation and all-cause hospital admissions was observed. However, extreme precipitation was significantly associated with GI-related hospital admissions at all lags, excluding 1 and 3. At lag 15, risk of GI-related hospital admissions was 1.25 times higher following extreme precipitation compared to days without precipitation (95% confidence interval (CI): 1.16, 1.34). When controlling for AT, DOW, and long-term time trends, the positive association between extreme precipitation and GI-related hospital admissions was attenuated; risk, at lag 15, as only 1.13 times higher (95% CI: 1.06, 1.21) (Table 3.3, Figure 3.5b). All-cause and unclassified hospital admissions were not associated with extreme precipitation at lag 15 in the adjusted model (Figure 3.5a and c).

Among the young, GI-related hospital admissions were positively associated with extreme precipitation at several lags, risk at lag 15 was 1.34 times higher following extreme precipitation compared to days without precipitation (95% CI: 1.09, 1.60) (Figure 3.5e). No consistent trend was seen among the young for all-cause or unclassified admissions. Among the old, all-cause and unclassified hospital admissions were not associated with extreme precipitation (Figure 3.5g), while GI-related hospital admissions were again positively associated with extreme precipitation at several lags, risk at lag 15 was 1.34 times higher following extreme precipitation compared to days without precipitation (95% CI: 1.16, 1.52) (Figure 3.5h). Among the intermediate age group, which excluded the young and old, trends were consistent with those seen for the overall population, revealing a positive association with GI-related hospital admissions with a risk at lag 15 1.12 times higher following extreme precipitation (95% CI: 1.04, 1.20).

3.3.2 Distributed lag

The overall patterns of association observed in the distributed lag models were fairly consistent with the results from the single-day lag models. The positive association between extreme precipitation and GI-related hospital admissions was similarly attenuated when controlling for AT, DOW, and long-term time trends with a cumulative RR of 1.61 (95% CI: 1.29, 2.00) (Table 3.3, Figure 3.6b) compared to a cumulative RR of 2.38 (95% CI: 1.88, 3.01) for the unadjusted model.

Among the young, no association with extreme precipitation was seen for all-cause or unclassified admissions, but the cumulative risk of GI-related hospital admissions was 2.65 times higher following 15-days of extreme precipitation compared to a normal 15-day period (95% CI: 1.21, 5.80) (Figure 3.6e). Among the old, GI-related admissions were positively associated with extreme precipitation at several lags, with

1.68 times higher risk following extreme precipitation (95% CI: 1.01, 2.80) (Figure 3.6h). As expected, the intermediate age group showed results consistent with the overall population: no association for all-cause or unclassified admissions, but a positive association for GI-related admissions at several lags with a cumulative risk 1.61 times higher following 15-days of extreme precipitation (95% CI: 1.27, 2.04) (Figure 3.6h).

3.3.3 Analysis of season

Stratifying by season, using the two-stage Poisson regression technique, extreme precipitation was most often associated with GI-related hospital admissions during pre-monsoon and NE monsoon. In some cases, predominantly during winter, the model could not converge as a result of low daily hospital admission counts and too few extreme precipitation events. At lag 15 during pre-monsoon, there was a 1.58 times higher risk of GI-related hospital admissions following extreme precipitation (95% CI: 1.24, 1.90) and a 1.31 times higher risk during NE monsoon (95% CI: 1.19, 1.37). No changes in risk were observed for all-cause or unclassified admissions.

Among the young, risk of GI-related admissions during NE monsoon was elevated 1.85 (95% CI: 1.45, 2.24) and risk among unclassified admissions during SW monsoon was elevated 1.79 (95% CI: 1.14, 2.45). Among the old, risk of GI-related admissions during pre-monsoon was elevated 2.84 (95% CI: 2.26, 3.42) as well as during NE monsoon 1.34 (95% CI: 1.07, 1.61). Results for the intermediate age group were largely consistent with results for the overall population, risk of GI-related hospital admissions during pre-monsoon was 1.46 (95% CI: 1.10, 1.81) and during NE monsoon 1.29 (95% CI: 1.16, 1.42). However, the risk of all-cause admissions also increased among the intermediate age group during winter, 1.35 (95% CI: 1.05, 1.64) and during pre-monsoon, 1.18 (95% CI: 1.03, 1.33).

3.4 DISCUSSION

While in most cases all-cause admissions were not significantly associated with extreme precipitation, GI-related hospital admissions were consistently associated with extreme precipitation in both the single-day and distributed lag models. Observed risk ratios for GI-related admissions were elevated among the young and old when compared to the general population. Looking across seasons, risk of GI-related hospital admissions was elevated during pre-monsoon and NE monsoon.

The clear association between extreme precipitation and GI-related hospital admissions presented herein could have profound implications for public health in low- and middle-income countries with a high burden of GI. If early-warning systems were developed in tandem with weather prediction models it is feasible that a large number of GI-related hospital admissions could be avoided. Examples include water boiling advisories or alternative water supplies when extreme rain events are expected or have occurred. Such a clear link should certainly be considered as new interventions and adaptation strategies are developed.

Several studies have tried to characterize the Indian monsoon season and to define current trends in precipitation on both a national and regional scale within India. While some research discusses the impact of changing precipitation patterns on drought and flooding, few studies have looked at the impact of heavy precipitation and flooding on the burden of waterborne disease in this region. Little if any evidence of how risk varies across age and season exists. Recent findings report an increased frequency of heavy rain events, but a decreasing number of rainy days and total precipitation (Kumar and Jain 2011). In addition, the number of severe cyclonic storms off the Indian Coast and associated rainfall has increased, with an observed decrease in precipitation during the summer monsoon (or the SW monsoon as defined herein) and increasing trend in precipitation during both the pre- and post-monsoon (or NE monsoon as defined herein) (Dash 2007).

The elevated risk of GI-related hospitalization during pre-monsoon that was observed is inconsistent with the original hypothesis that risk would be highest during the NE monsoon season, which is traditionally the wettest season. However, the changing trend in precipitation observed by Dash (2007), if true in Chennai, could explain the elevated risk estimates during pre-monsoon. Nonetheless, other factors must also be influencing water quality and waterborne disease. The risk of GI, like other climate-related risks, is highly dependent on local factors. It could be that higher temperatures during pre-monsoon favor pathogen survival and transmission, thus increasing the risk of GI-related hospital admissions. Another potential explanation could be compromised water quality during drier seasons, such as pre-monsoon, because of insufficient water availability. Additionally, personal behaviors regarding washing and hygiene could potentially be affected by reduced availability of water. A study investigating hospital admissions in Dhaka found that rates of disease increased during both high and low rainfall extremes (Hashizume 2007). A study evaluating the effect of precipitation on waterborne outbreaks in England and Wales (Nichols et al. 2009) similarly concluded that both high and low rainfall precedes drinking water related outbreaks.

Much of the work focusing on waterborne disease in India summarizes the overall burden waterborne disease, especially among children under five (WHO 2008). Previous research has also looked at the association between poor water quality due to flooding and shortages of clean water that can lead to the spread of diarrheal disease (WHO 2011b). In some cases, severe outbreaks of waterborne disease have been directly associated with flooding, such as in the district of West Bengal (Sur 2000). But the majority of these studies do not compare the risk of disease across seasons. It is also important to realize that until recently, morbidity data in low- and middle-income countries such as India was essentially unavailable, particularly in electronic form.

This study exemplifies the importance of high-quality data to the field of environmental epidemiology. When high quality data is available, a variety of statistical methods can be used to analyze long-term and season-specific trends. Stratification is one method for evaluating the effect of season. In other instances, researchers may choose to look at extreme conditions, such as El Niño during which atypical precipitation and temperature conditions prevail. In either case the goal is to evaluate how extreme weather patterns affect disease. Studying what happens to disease during extreme weather events gives us a window into the future where such extremes are expected to become more common (Cooney 2011).

The primary limitation of this study is that waterborne disease remains highly underreported and the exact etiology is rarely identified. This is especially true in low- and middle-income countries like India (Charron et al. 2004; Ford 1999). The symptoms associated with exposure to contaminated water are relatively broad-spectrum symptoms. Additionally, GI-related hospital admissions may be caused by foodborne pathogens and other factors unrelated to water quality or precipitation. Therefore, the signal linking exposure and outcome can be obscured. Nevertheless, this study makes use of a unique 4-year time-series dataset that combines cause-specific hospital admission data with city-specific meteorological data for one of the largest cities in India. It provides a glimpse of the important work remaining to be done on climate-sensitive health issues in low- and middle-income countries.

Overall water usage is expected to increase as a result of population growth and urbanization. As the population continues to increase, per capita water consumption will also increase further limiting access to safe drinking water. The continued growth of cities will also result in increased amounts of wastewater that must be properly treated and removed. The demand for water-intense crops is also projected to rise. Changing water consumption patterns and increased pressure on water systems from growing urban populations and expanding agriculture will add additional pressure to an already overburdened water system. The interaction of these different factors related to water quality and quantity create high-risk scenarios for water contamination during heavy rain events, suggesting that future work should evaluate how changing land use patterns and population density influence the risk of waterborne disease. In light of the multiple threats that India may face in the years ahead (Rao 2010), the impacts of climate change must be evaluated in the context of other global environmental factors such as urbanization, deforestation, and the growing population. Environmental parameters measured by remote satellite imaging and subsequent indicators have the potential to provide global coverage of changing environmental conditions, but also to predict future risks and inform adaptation strategies (Ford et al. 2009).

3.5 CONCLUSIONS

This study characterized the seasonal variability in hospital admissions in Chennai, India using a unique four-year time-series dataset. GI-related hospital admissions were positively associated with extreme precipitation (≥90th percentile). Risk was elevated during pre-monsoon and NE monsoon. The young and the old were often at higher risk of GI-related hospital admissions. These results in combination with projected changes in precipitation patterns suggest that climate change will have important implications for human health in India where global health disparities and challenges in managing water resources already exist.

Figure 3.1 Location of Kilpauk Medical College, Madras Medical College, and Chennai International Airport in Chennai, India.

Table 3.1 Daily average meteorological conditions by year and by season in Chennai, India 2004-2007.

	Precipitation (mm) (mean, range)	Apparent Temperature (°C) (mean, range)
By year		
2004	4 (0-162)	33 (25-39)
2005	7 (0-283)	33 (25-39)
2006	4 (0-143)	33 (25-41)
2007	4 (0-139)	32 (25-39)
By season		
Winter (Jan - Feb)	0 (0-23)	28 (25-33)
Pre-Monsoon (March - May)	1 (0-122)	35 (29-41)
Southwest Monsoon (June - Sept)	4 (0-162)	35 (29-39)
Northeast Monsoon (Oct - Dec)	11 (0-283)	31 (25-36)
Entire Period (2004-2007)	5 (0-283)	33 (25-41)

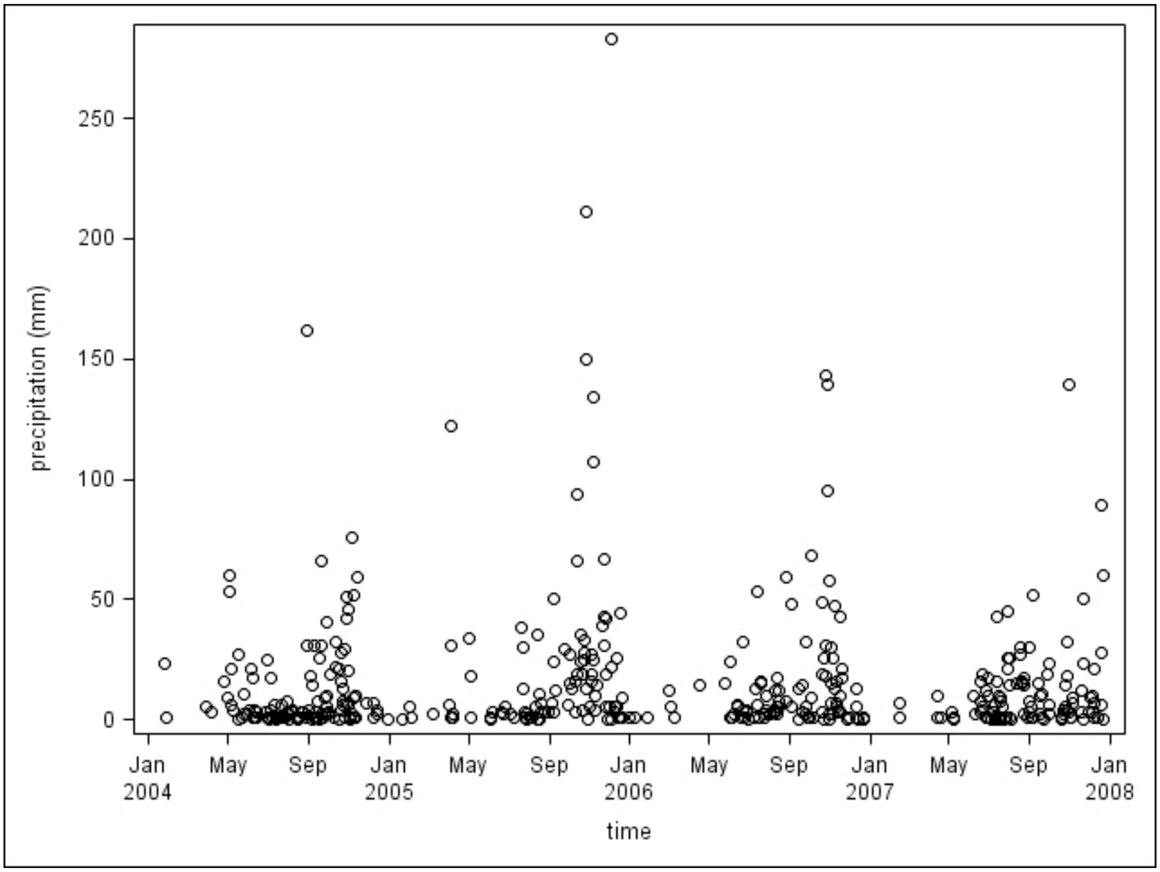

Figure 3.2 Daily precipitation in Chennai, India from 2004 to 2007.

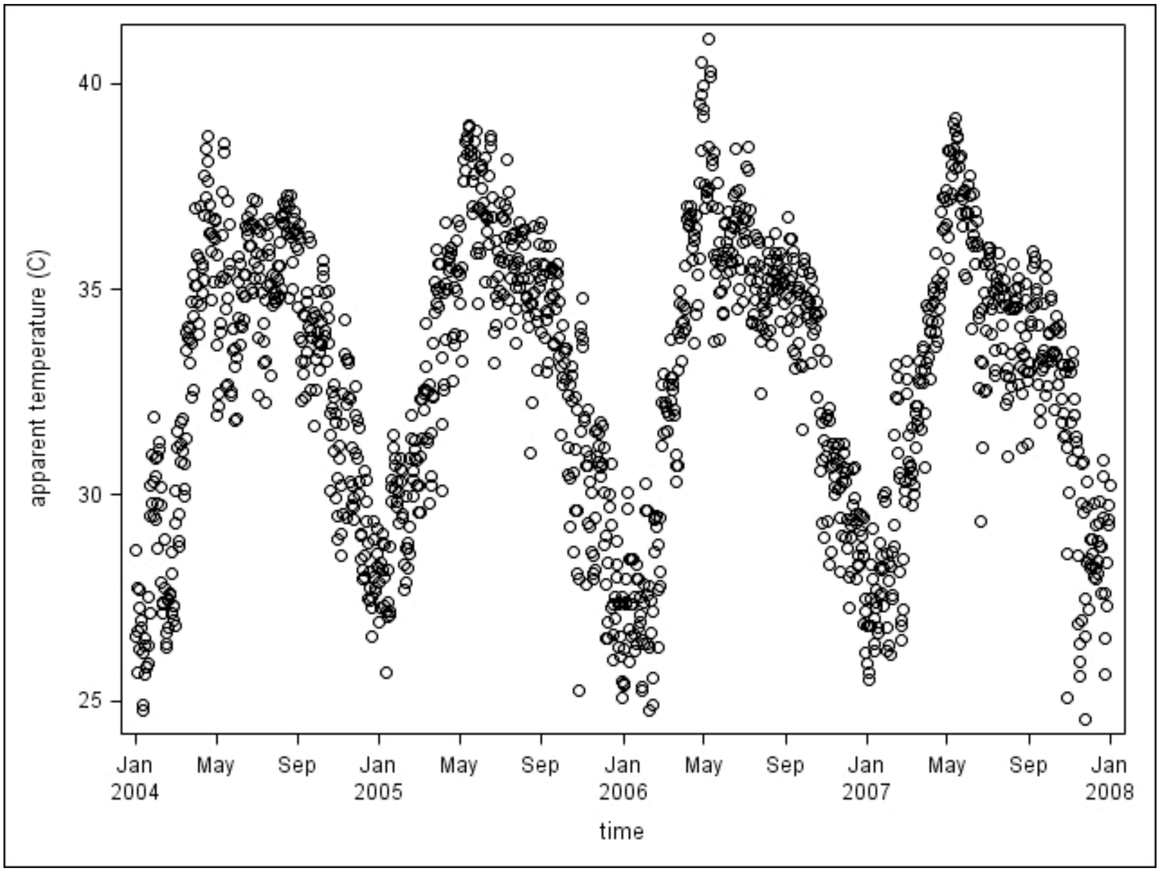

Figure 3.3 Daily average apparent temperature in Chennai, India from 2004 to 2007.

Table 3.2 Daily hospital admissions summed by year, season, age (young < 6 years of age; old ≥ 65 years of age), and cause from two government hospitals in Chennai, India 2004-2007.

	All-cause total (young; old)	GI-related[1] total (young; old)	Unclassified total (young; old)
By year			
2004	46,981 (1,788 4,295)	2,639 (153; 248)	440 (11; 38)
2005	76,170 (3,570; 7,156)	4,321 (195; 403)	1,094 (30; 38)
2006	117,508 (10,131; 9,541)	4,692 (130; 482)	1,282 (41; 53)
2007	95,065 (9,537; 7,731)	3,071 (73; 345)	10,923 (102; 1,143)
By season			
Winter (Jan - Feb)	57, 237 (3,699; 5,105)	2,344 (69; 241)	1,090 (25; 63)
Pre-Monsoon (March - May)	84,444 (5,440; 7,153)	3,550 (117; 353)	3,519 (45; 324)
Southwest Monsoon (June - Sept)	107,809 (8,616; 8,979)	4,893 (180; 491)	3,865 (81; 273)
Northeast Monsoon (Oct - Dec)	86,234 (7,301; 7,486)	3,936 (185; 393)	5,265 (33; 612)
Entire Period (2004-2007)	335,724 (25,026; 28,723)	14,723 (551; 1,478)	13,739 (184; 1,272)

[1]Cases were defined as GI-related if the primary, secondary, or tertiary ICD-10 code was listed as intestinal infectious disease (A00-A09), helminthiases (B65-B83), or GI-related symptoms (R11-nausea and vomiting, R50-fever, R51-headache).

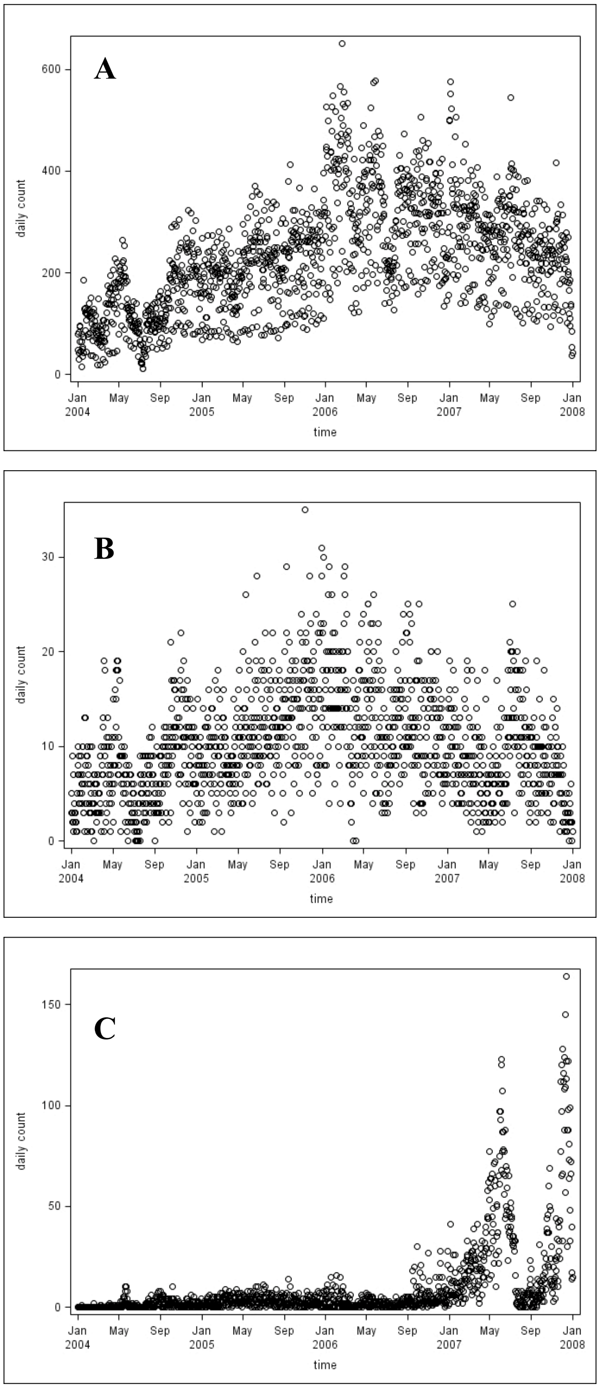

Figure 3.4 Daily hospital admissions from two government hospitals in Chennai, India from 2004 to 2007 classified by cause: a) all-cause, b) GI-related, and c) unclassified.

Table 3.3 Risk (95% confidence interval) for hospitalization associated with precipitation (≥90th percentile) classified by cause of admission and stratified by age. Risk ratios corresponding to the single day lag model (lag 15) and the distributed lag model (cumulative 15-day) are reported, season-specific results are reported for the single day lag model (lag 15).

	Cause of admission	Single day lag Lag 15 RR (95% CI)	Distributed lag Cumulative RR (95% CI)
Adjusted model	All-cause	1.01 (0.97, 1.05)	1.01 (0.89, 1.15)
	GI-related	1.13 (1.06, 1.21)	1.61 (1.29, 2.00)
	Unclassified	0.88 (0.72, 1.05)	0.32 (0.18, 0.56)
Young (<6)	All-cause	1.00 (0.92, 1.06)	1.06 (0.84, 1.34)
	GI-related	1.34 (1.09, 1.60)	2.65 (1.21, 5.80)
	Unclassified	0.67 (0.22, 1.12)	1.04 (0.29, 3.74)
Old (≥65)	All-cause	1.03 (0.97, 1.09)	0.98 (0.81, 1.19)
	GI-related	1.34 (1.16, 1.52)	1.68 (1.01, 2.80)
	Unclassified	0.91 (0.68, 1.13)	0.09 (0.03, 0.32)
Intermediate (6-64)	All-cause	1.03 (0.99, 1.07)	1.05 (0.92, 1.20)
	GI-related	1.12 (1.04, 1.20)	1.61 (1.27, 2.04)
	Unclassified	0.89 (0.72, 1.05)	0.16 (0.09, 0.30)

		Winter (Jan-Feb)	Pre-monsoon (March-May)	Southwest monsoon (June-Sept)	Northeast monsoon (Oct-Dec)
Adjusted model	All-cause	1.22 (0.94, 1.50)	1.14 (0.99, 1.29)	0.99 (0.92, 1.06)	1.04 (0.99, 1.10)
	GI-related	1.15 (0.58, 1.72)	1.58 (1.24, 1.90)	0.97 (0.82, 1.12)	1.31 (1.19, 1.37)
	Unclassified	0.94 (-0.62, 2.50)	0.51 (-0.71, 1.73)	0.93 (0.38, 1.47)	0.43 (-0.02, 0.87)
Young (<6)	All-cause	0.78 (-0.26, 1.82)	0.75 (0.24, 1.26)	1.09 (0.95, 1.22)	0.96 (0.83, 1.09)
	GI-related	--	1.21 (0.11, 2.32)	0.77 (0.15, 1.40)	1.85 (1.45, 2.24)
	Unclassified	--	--	1.79 (1.14 (2.45)	0.33 (-0.46, 1.13)
Old (≥65)	All-cause	1.09 (0.65, 1.53)	1.12 (0.87, 1.36)	1.02 (0.90, 1.13)	1.04 (0.96, 1.13)
	GI-related	--	2.84 (2.26, 3.42)	1.06 (0.72, 1.39)	1.34 (1.07, 1.61)
	Unclassified	2.47 (1.11, 3.84)	0.43 (-1.24, 2.10)	1.02 (0.30, 1.73)	-0.36 (-0.22, 0.93)
Intermediate (6-64)	All-cause	1.35 (1.05, 1.64)	1.18 (1.03, 1.33)	0.98 (0.90, 1.06)	1.07 (1.00, 1.13)
	GI-related	1.37 (0.77, 1.97)	1.46 (1.10, 1.81)	0.97 (0.80, 1.13)	1.29 (1.16, 1.42)
	Unclassified	0.98 (-0.52, 2.48)	0.53 (-0.67, 1.73)	0.85 (0.28, 1.43)	-0.42 (-0.05, 0.89)

[1]Cases were defined as GI-related if the primary, secondary, or tertiary ICD-10 code was listed as intestinal infectious disease (A00-A09), helminthiases (B65-B83), or GI-related symptoms (R11-nausea and vomiting, R50-fever, R51-headache).
[2]All models, excluding the unadjusted model, control for apparent temperature, day of week and time.
[3]In some cases (--) model did not converge because of low hospital admission counts and too few extreme precipitation events.

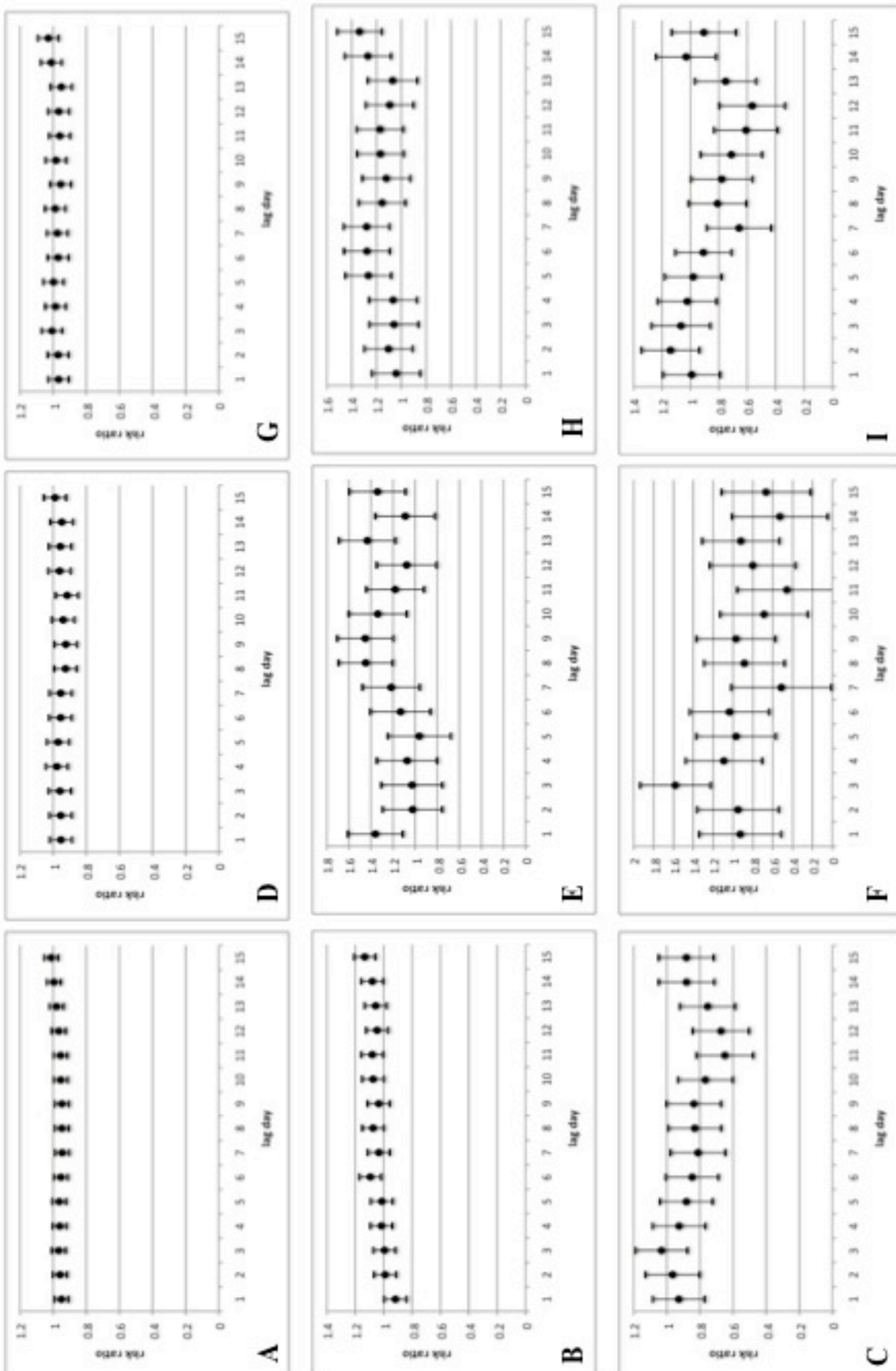

Figure 3.5 The estimated effects of extreme precipitation on hospital admissions over 15 single-day lags among the general population for a) all-cause, b) GI-related, and c) unclassified; among the young for d) all-cause, e) GI-related, and f) unclassified; among the old for g) all-cause, h) GI-related, and i) unclassified, with 95% confidence intervals plotted.

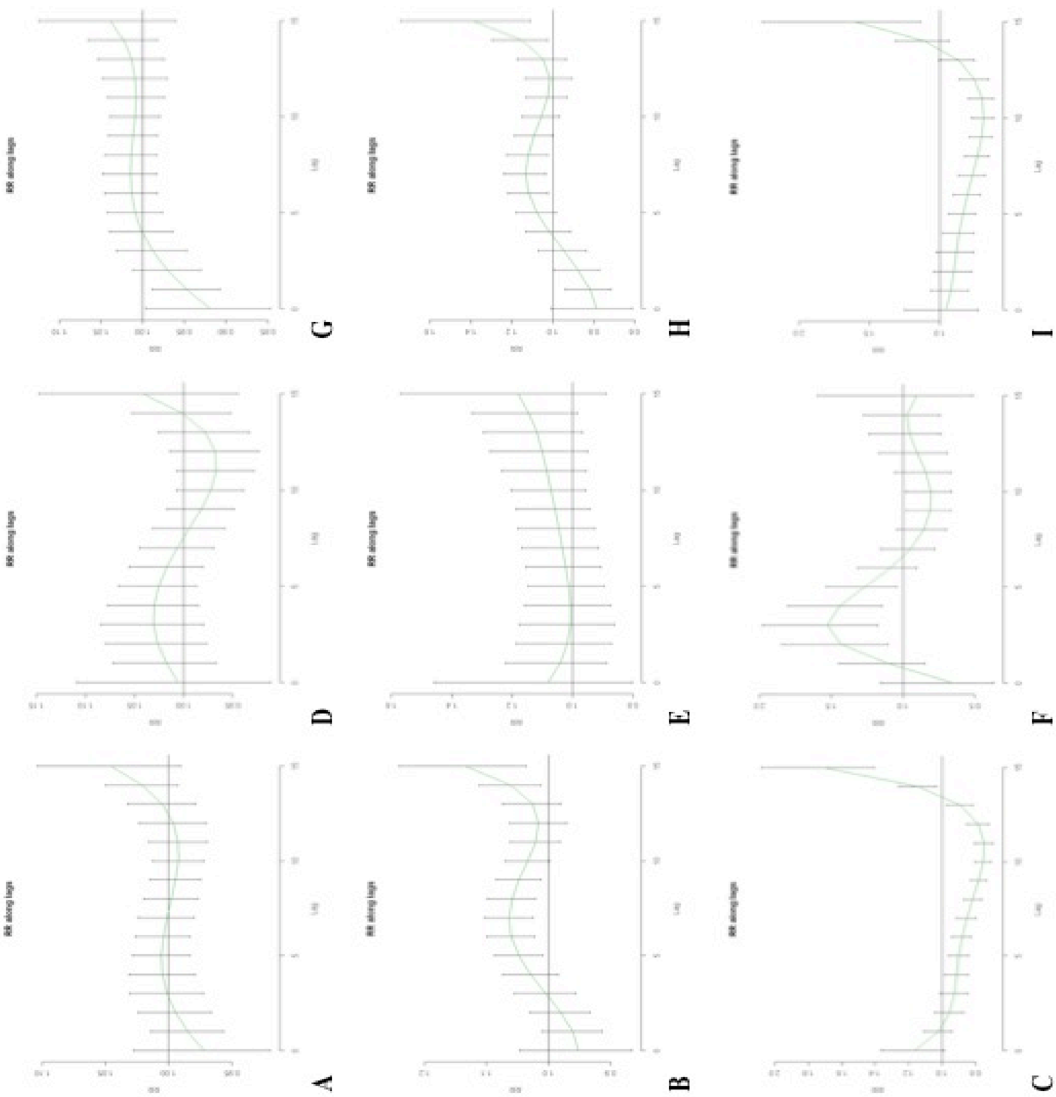

Figure 3.6 The estimated effects of extreme precipitation on hospital admissions from a 15 day constrained distributed lag model among the general population for a) all-cause, b) GI-related, and c) unclassified; among the young for d) all-cause, e) GI-related, and f) unclassified; among the old for g) all-cause, h) GI-related, and i) unclassified, with 95% confidence intervals plotted.

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Chapter 4

Precipitation and gastrointestinal illness among the elderly in 132 U.S. cities

4. ABSTRACT

Background: Under projected climate scenarios, the occurrence of extreme precipitation events will increase, potentially influencing drinking water quality and the risk of waterborne disease.

Objectives: We evaluated the association between extreme precipitation and gastrointestinal illness (GI) among the elderly in 132 U.S. cities between 1992 and 2006.

Methods: We merged city-specific daily GI-related Medicare hospital admissions with mean apparent temperature and precipitation, and applied time-stratified case-crossover analysis. We calculated city-specific associations between extreme precipitation ($\geq 90^{th}$ percentile) and GI-related hospital admissions, controlling for apparent temperature, at multiple lags. We evaluated season, drinking water source, and the number of combined sewer outfalls as potential effect modifiers. Estimates were combined across the 132 cities and by climate zone to provide regional risk estimates.

Results: Overall, no positive associations between extreme precipitation and GI-related hospital admissions were observed, except at a few lags. Season, drinking water source,

and presence of CSOs did not modify the results. The overall risk estimate at lag 15 was 1.01 (95% confidence interval (CI): 1.00, 1.02) and the overall national pooled estimate for risk of GI-related hospital admission following a 15-day period of extreme precipitation was 0.98 (95% confidence interval: 0.97, 0.99).

Conclusions: This multi-city study of extreme precipitation and GI-related hospital admissions did not reveal significant associations. However, the risk of GI-related hospital admissions under changing climatic conditions remains an important issue. Future research using different data sources and looking at health outcomes in other age categories may have different results.

4.1 INTRODUCTION

In the next 100 years global average surface temperature will increase at least 2°C (Pachauri and Reisinger 2007). Such drastic changes in temperature will shift the global climate, affecting the occurrence of extreme events, and threatening human health both directly and indirectly. Such changes can also be expected to affect the burden of various infectious diseases (Bates et al. 2008). Warmer temperatures also mean a more dynamic hydrologic cycle (Patz et al. 2000), which can be expected to influence the burden and distribution of water-related diseases.

Several epidemiologic studies have shown that rainfall and flooding contribute to waterborne disease outbreaks. Extreme precipitation events influence the mechanisms by which waterborne pathogens enter the water system as well as the concentration of pathogens present (Unc and Goss 2003). Enteric pathogens responsible for causing water-related diseases classified as gastrointestinal illness (GI) include: *Escherichia coli*, *Salmonella*, *Shigella*, *Cryptosporidium*, *Giardia, Campylobacter jejuni*, *Clostridium difficile*, *Rotavirus*, and *Calicivirus* (Dennehy 2005). Increased prevalence of gastrointestinal illness (GI) following a flood has been observed in India (Mondal et al. 2001), Brazil (Heller et al. 2003) and Bangladesh (Schwartz et al. 2006). An association between extreme rainfall events and monthly reports of waterborne disease outbreaks was reported for the entire U.S. where more than half of waterborne outbreaks were preceded by precipitation events at or above the 90th percentile (Curriero et al. 2001)

Turbidity, a measurement of the amount of light scattered by suspended particles in water, is commonly used as an indicator for the risk of microbial contamination and as a measure of the effectiveness of the public drinking water treatment process. Turbidity often increases sharply following a rainfall event because runoff washes sediments, nutrients, and potentially pathogens into surface waters. An inter-quartile range (IQR) increase in turbidity at the wastewater treatment plant in Philadelphia, PA was associated with a 9% increase in hospitalization due to GI among the elderly (Schwartz et al. 2000). Similarly, in Milwaukee, WI, GI-related hospital admissions were positively associated with drinking water turbidity (Morris 1996). Additional studies have shown that transmission of waterborne pathogens is higher during the rainy season (Kang et al. 2001; Nchito et al. 1998).

The association between precipitation and waterborne disease is further complicated by temperature. Rising temperatures can be expected to increase pathogen replication, persistence, survival, and transmission, influencing the overall distribution of waterborne disease. Positive associations between monthly temperature and waterborne disease have been reported in the Pacific Islands (Singh et al. 2001), Australia (McMichael et al. 2003), and Israel (Vasilev 2003). In Alberta, Canada, the incidence of enteric infections by *Salmonella*, pathogenic *E. coli*, and *Campylobacter* was strongly associated with ambient temperature between 1992 and 2000 (Fleury et al. 2006). However, in other cases high temperatures may inactivate pathogens. In the tropics, rotavirus prefers colder and dryer seasons (Levy et al. 2008). Awareness of such seasonal variability in pathogen survival is important in the modeling as well as the prevention of disease and is the first step towards understanding the relationship between climate and disease (Pascual et al. 2002).

Independent of season, a disproportionate burden of disease often falls on the poor, the elderly, and those living in disadvantaged settings (Ebi and Paulson 2010;

O'Neill and Ebi 2009). In the context of weather-related morbidity, the elderly must be considered a high-risk population, vulnerable to the combined effects of heat and infection. By 2030 the U.S. population over 60 is expected to double to nearly 1 million (Lutz et al. 2008). Waterborne disease, also commonly referred to as diarrheal disease, is a significant cause of morbidity and mortality among the elderly due to co-morbidities such as a weakened immune system, intestinal motility disorders, poor nutritional status and other chronic diseases (Trinh and Prabhakar 2007). A review of U.S. mortality data from 1979-1987 showed that death due to diarrhea was greatest in those 74 years and older compared to any other age group (Trinh and Prabhakar 2007). Understanding how increasing climate variability may impact extreme weather conditions and subsequently contribute to the burden of waterborne disease is important for inferring the effects of climate change on human health. This paper evaluates the association between precipitation and GI-related hospital admissions among the elderly in 132 U.S. cities from 1992 to 2006.

4.2 DATA AND METHODS

4.2.1 Study population

Hospital admission (HA) records for individuals 65 years and older and enrolled in Medicare were obtained from the Centers for Medicare and Medicaid Services. Approximately ninety-eight percent of all people in this age range are enrolled in Medicare (HHS 2010). The hospital admission records include date of admission, cause of admission, and individual-level characteristics including patient age, sex, race, and zipcode. Data for 132 cities were used. Medicare records link cases to their county of residence, so the 132 cities were defined as the metropolitan statistical area (MSA), which can be one or more counties.

4.2.2 Hospital admissions

Hospital admissions were classified according to the International Classification of Disease, 9th revision (ICD-9) and were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious diseases (001-009) or helminthes (120-129). Previous analyses have defined relevant cases as hospitalizations classified as intestinal infectious diseases (001-009), unspecified noninfectious gastroenteritis and colitis (558.9) (Morris et al. 1996; Schwartz et al. 2000; Tinker at al. 2010) as well as electrolyte disorders (276) and nausea and vomiting (787) (Schwartz 2000). To provide a basis for comparison, pathogen specific (001-007; 120-129), other and ill-defined intestinal infections (008-009), and (iii) GI-related symptoms (276, 558.9, 787) were combined into one category, defined as GI-related hospital admissions. Cases of interest were extracted from the Medicare dataset for the years 1992 through 2006.

4.2.3 Meteorological conditions

Meteorological parameters including precipitation, temperature, dew point, and relative humidity were extracted from the National Weather Service Cooperative Observer Program. These hourly measurements were taken at the first order weather station located at the international airport in each city as part of the automated surface observing system (ASOS). Daily summaries were created from the hourly measurements for each city for apparent temperature (˚C) and daily total precipitation (inches).

Apparent temperature (AT) was calculated using the following formula: $AT = -2.653 + (0.994 * T_a) + (0.0153 * T_d^2)$, where T_a is equal to air temperature (˚C) and T_d is equal to dew point temperature (˚C) (Kalkstein and Valimont 1986; Steadman 1979). Cities were then assigned to climate regions based on the U.S. Department of Energy's Energy Information Administration's climate zones (DOE 2011), which is based on the annual number of cooling-degree days (sum of daily mean temperatures above 65°F) and heating-degree days (sum of daily mean temperatures below 65°F).

For this analysis, precipitation was categorized based on the city-specific rainfall distribution. Categories were defined as precipitation less than the 90^{th} percentile (reference category) and greater than or equal to the 90^{th} percentile. The 90^{th} percentile was chosen based on previous literature that found 51 percent of waterborne disease outbreaks occurring in the U.S. between 1948-1994 were preceded by precipitation above the 90^{th} percentile (Curriero et al. 2001). Additionally, Rose (2000) observed that between 20 to 40 percent of outbreaks occurring in the U.S. from 1971-2004 were associated with precipitation above the 90^{th} percentile.

4.2.4 Community-level variables

Drinking water source is an obvious risk factor for waterborne disease because pathogens can be introduced at the source (especially when drinking water is supplied by surface water open to the influx of pathogens from multiple sources), in the distribution system, or at the point of use. In the U.S. between 4.3 and 11.7 million cases of GI are attributable to public drinking water systems (Colford et al. 2006). Both point (e.g. wastewater treatment plant) and nonpoint sources (e.g. agricultural runoff) contribute to contamination of drinking water sources. As runoff moves over the ground it picks up and carries contaminants, which can be deposited in surface waters or seep into groundwater. To evaluate the impact of drinking water source on the association between precipitation and GI-related hospital admissions, we obtained United States Geological Survey (USGS) data on public drinking water supply (USGS 2011). These data present water-use estimates by county and support the state-level water-use estimates published in the USGS Circular 1344, *Estimated Use of Water in the United States in 2005*. All States have estimates of the total population and the total population served by public water supply. Most, but not all States have estimates of the public supply population served by specific sources, either surface water or groundwater. These water supply data were merged with the original meteorological and hospital admission data by county Federal Information Processing Standard (FIPS) code.

Combined sewer systems (CSSs), which carry both stormwater and municipal wastewater, can release directly into waterways at combined sewer outfalls. During heavy precipitation events, the capacity of CSSs can be exceeded resulting in direct discharge of sewage and stormwater into receiving waters. This occurrence is termed a combined sewer overflow (CSO). When combined sewers overflow, high levels of bacterial contaminants are released into the environment (EPA 2007, 2008). Currently, EPA estimates that 850 billion gallons of raw sewage and stormwater are released annually into U.S. waterways and that CSOs occur 43,000 times per year (EPA 2004). In order to evaluate whether the presence of CSSs in a community influence the risk of GI-related hospital admissions, the location and number of combined sewer outfalls in each city was determined using the U.S. EPA Envirofacts database (Table 5.S1). The

Envirofacts database integrates information about facilities required to report activity to a state or federal system from a variety of databases and includes latitude and longitude information. Available data includes information about hazardous waste, toxic and air releases, Superfund sites, and water discharge permits. Data on drinking water source was available for 2005 and was downloaded in August 2011. For this analysis, the variable included was the presence of absence of an outfall, which was assumed constant over the study period. The actual occurrence of a CSO, a time-varying factor, was not modeled.

4.2.5 Statistical analysis

To evaluate the association between city-specific precipitation and GI-related hospital admissions city-specific time-stratified case-crossover analysis using conditional logistic regression, was applied (Maclure 1991; Levy et al. 2001). The case-crossover approach, similar to a matched case-control study, is used to study the association between transient exposures (in this case, daily precipitation) and acute outcomes (in this case, daily GI-related hospital admissions). Exposure status during the case period is compared to that during the control period, when the event did not occur (Lumley and Levy 2000). Time-stratified referent selection minimizes bias and is the standard approach (Janes et al. 2005, Mittleman 2005).

Case periods were defined as the day of hospitalization for the selected causes. Pathogen specific (001-007; 120-129), other and ill-defined intestinal infections (008-009), and GI-related symptoms (276, 558.9, 787) were combined to create a *GI-related* case category. Controls were selected using the time-stratified approach proposed by

Levy et al. (2001), by dividing the study period into monthly strata. Controls were then selected from within each stratum to match the day of week on which the case occurred. Selecting referent periods in this way controls for fixed confounders such as age, race, and sex; it also controls for long-term time-varying, or seasonal, trends. All duplicate cases, defined as cases occurring for the same person more than once in the same month were removed entirely from the dataset and were not included in the analysis to maintain proper exposure classification for cases and controls.

City-specific time-series plots of daily GI-related hospital admissions, precipitation, and apparent temperature were created. Histograms were made to examine the consistency and distribution of each variable and city-specific descriptive statistics were calculated.

Lags

Observed health effects may lag behind exposure due to delayed onset of clinical symptoms or delayed environmental transport of pathogens. Incubation periods can range from one to two days for pathogens like *Shigella, Salmonella*, and *Rotavirus* to up to two weeks for pathogens such as *Cryptosporidium* and *E.coli* (Haley et al. 2009; Jagai et al. 2009). Previous studies have reported a delayed onset of diarrheal disease following heavy rainfall events and subsequent increased turbidity measurements at water treatment plants (Aramini et al. 2000; Curriero et al. 2001; Egorov et al. 2003; Schwartz et al. 2000). In the first stage of analysis, city-specific odds ratios evaluating the association between GI-related hospital admissions and extreme precipitation were calculated (Model 4.1).

Model 4.1: $\text{Log}\ \frac{P(Y_{ij} = 1 / x_{ij})}{P(Y_{ij} = 0 / x_{ij})} = \alpha_i + \beta_1 PRCP_{t-q}$,

where *PRCP* is categorical precipitation, and *q* denotes the lag 1-15 days prior to the hospital admission.

To account for the potential time lag, precipitation was evaluated using various lag structures:

1. 15 separate single-day lag models, including category of precipitation 1-15 days prior to the day of hospital admission
2. 2 additional models representing category of precipitation during 7 and 15-day periods prior to the day of hospital admission, to capture the cumulative effect.

Confounding and effect modification by apparent temperature

In the second stage of analysis, confounding by daily mean apparent temperature (AT) was explored (Model 4.2). Temperature has been shown to influence the survival and transport of pathogens in the environment and increase an individual's susceptibility to infection (Fleury et al. 2006; Singh et al. 2001; Vasilev 2003). High humidity might prevent desiccation, thus promoting pathogen survival and transport in the environment. AT was included as a potential confounder based on *a priori* evidence suggesting its relation to both the predictor and the outcome. Other potential confounders (age, sex, race, day of week, season) were controlled for by study design.

Model 4.2: $\text{Log}\ \frac{P(Y_{ij} = 1 / x_{ij})}{P(Y_{ij} = 0 / x_{ij})} = \alpha_i + \beta_1 PRCP_{t-q} + \beta_2 AT_{t-q}$, where *PRCP* is categorical precipitation, *AT* represents apparent temperature, and *q* denotes the lag 1-15 days prior to the hospital admission.

To further explore the role of AT, effect modification was evaluated. Daily apparent temperature (˚C) was categorized as: (1) $AT \leq 0$, (2) $0 < AT \leq 13$, (3) $13 < AT \leq 27$, and (4) $AT > 27$. City-specific models were run separately for days within each category. Models were run over the same 1-15 day lag period. Results were then pooled across all cities for each category of AT. This allowed differentiation between freezing and excessively high temperatures that might threaten the survival and persistence of waterborne pathogens in the environment.

Effect modification by season

In the third stage of analysis, season was evaluated as a potential effect modifier of the association between extreme precipitation and hospital admissions. Season is expected to modify the association because the hypothesis that extreme precipitation may carry pathogens to nearby waterways, thus contaminating possible drinking water sources. This pathway may only be relevant when temperatures are above freezing and precipitation falls as rain on thawed ground during certain seasons. Seasonal differences in vegetation cover may also affect this pathway. To evaluate effect modification by season, a stratified analysis was done where seasons were defined as: winter (December-February), spring (March-May), summer (June-August), and fall (September-November).

Combining single-city estimates

City-specific estimates were pooled to obtain an overall summary estimate of the association between extreme precipitation and GI-related hospital admissions. Summary estimates were also calculated for each climate zone. First, city-specific coefficients corresponding to the effect of extreme precipitation were tested for homogeneity across all of the 132 cities and across climate zones (Normand 1999), testing whether the cities shared a common mean at specific lags:

H_0: $\theta_1 = \theta_2 = \ldots = \theta_k = \theta$

H_1: At least one θ_i is different from others.

If the null hypothesis was upheld ($p > 0.05$), a fixed-effect model was applied to pool the results using inverse-variance weighting. If the null hypothesis was rejected ($p < 0.05$), a random-effects model, accounting for both within- and between-city variation, was applied (Berkey et al. 1995; Normand 1999).

Effect modification by community-level variables

To evaluate whether risk estimates are dependent on drinking water source and number of combined sewer outfalls, we fit a meta-regression model with the following form: $\beta_i = \beta_0 + Z_i$, where β_i was the city-specific coefficient corresponding to the effect of extreme precipitation in city *i* and Z_i was the community variable of interest in city *i,* as has been done in previous work (O'Neill et al. 2005). For each city, a value for Z was assigned corresponding to the percent of public drinking water sourced from surface water, percent of public drinking water sourced from groundwater, and the number of CSOs.

Effect estimates were calculated using the ß coefficient corresponding to extreme precipitation (≥90th percentile) where precipitation categorized as less than the 90th percentile was the reference category. The model parameter associated with extreme precipitation was exponentiated to determine the odds ratio. The 95% confidence intervals for the risk estimates were calculated based on the standard error (s.e.) (+/− 1.96*s.e.). The odds ratios can be interpreted as the increase in risk of GI-related hospital admissions following days with extreme precipitation (≥90th percentile) compared to days with zero to moderate precipitation at certain single-day lags (1-15 days previous). Regarding the 7 and 15-day periods, precipitation over the 7- and 15-day periods was categorized based on the moving average distribution of rainfall. The odds ratios corresponding to those coefficients can be interpreted as the increase in risk of GI-related hospital admissions when precipitation during the preceding 7- or 15-day periods was extreme (≥90thpercentile) compared to when it was not. For the stratified analysis, results are season-specific. All analyses were run using PROC PHREG in SAS Version 9.2 (SAS Institute, Cary NC) and R 12.0 (R Foundation for Statistical Computing, Vienna, Austria).

4.3 RESULTS

The 132 cities included in this analysis (Table 4.S2) represent diverse climate zones that exist across the U.S. (Figure 4.1). The number of cities in each climate zone varied from 18 in climate zone 1 to 36 in climate zone 2 (Table 4.1). Climate zone number increases from 1 to 5 in a southward direction, as daily mean temperatures increase. Average daily precipitation did not vary dramatically between climate zones, ranging from 0.0008 inches in climate zone 4 to 0.0012 inches in climate zone 5 (Table 4.2). Daily average apparent temperature showed greater variation, ranging from 8˚C in climate zone 1 to 23˚C in climate zone 5 (Table 4.2).

Over the study period (1992-2006), GI-related hospital admissions varied from 72,216 cases in climate zone 1 to 374,216 cases in climate zone 2 (Table 4.2). The time-stratified referent selection used in this analysis resulted in approximately a 1:3 ratio of cases periods to control periods. Duplicate cases, defined as admissions occurring more than once within the same month for the same person, occurred on average 21% of the time across all 132 cities and ranged from 13% to 33% depending on the city.

There was heterogeneity in the observed association between extreme precipitation and GI-related hospital admissions. Different lags showed a positive association depending on the city, but no clear pattern emerged. While individual cities showed a positive association at some lags, pooling across all cities and climate zones resulted in a null association. In the adjusted model, controlling for apparent temperature, no positive association was seen at any lag. The overall risk estimate was 1.01 (95% confidence interval (CI): 1.00, 1.02) at lag 15 and the cumulative estimate was 0.98 (95% CI: 0.97, 0.99) corresponding to the 15-day period. Figure 4.2 (top) shows city-specific associations for lag 15 in the single-day lag model, controlling for apparent temperature. When pooled by climate zone, modest associations were observed at later lags; climate zone 3 had the highest estimate of 1.03 (95% CI: 1.01, 1.05) at lag 15 (Table 4.3). Significance of the association did not vary in the model evaluating the 15-day cumulative effect (Figure 4.2, bottom).

In the analysis stratified by season, results did not vary significantly. Lags 12 to 15 most commonly revealed a modest association. For example, the risk estimate pooled across all cities revealed a very modest association at lag 15 during winter and spring, 1.02 (95% CI: 1.01, 1.04) (Table 4.4 and Table 4.5). Pooling by climate zone, in spring, climate zone 1 and 3 were at an elevated risk at lag 15, 1.08 (95% CI: 1.02, 1.14) and 1.05 (95% CI: 1.01, 1.08) (Table 4.5). During fall, only climate zone 3 was at an elevated risk, 1.05 (95% CI: 1.01, 1.09) (Table 4.7).

When pooled across all 132 cities, AT was not a significant effect modifier, risk was not drastically altered based on AT category. However, freezing temperatures did show a slight association, with a four percent increase in risk of being hospitalized at lag 15: 1.04 (95% CI: 1.02, 1.07).

Community-level variables used in the meta-regression included the percent of the public water supply sourced by surface water, ranging from 0-100% with an average of 61%; the percent of the public water supply sourced by groundwater, ranging from 0-100% with an average of 39%; and the number of combined sewer outfalls in each city (Table 4.S3, Figure 4.3). Only 20 of the cities had outfalls inside the boundary of the metropolitan area as defined in this analysis. In those 20 cities the number of outfalls ranged from 1 in Dayton and Kansas City to 137 in New York City (with an average of 24 and a median of 7 across all 20 cities). The meta-regression analysis was run using city-specific coefficients corresponding to the effect of extreme precipitation for each of the 15 single-day lags. The analysis did not reveal any consistent trends (Table 4.8). However, on a few occasions in the season-stratified analysis, drinking water source explained between 24-30% of the variability in observed odds ratios and on one occasion the number of outfalls explained 47% of the variability.

5.4 DISCUSSION

No association between extreme precipitation and GI-related hospital admissions was observed. Positive associations were only observed at later lags, in climate zones 1 and 3. Extensive heterogeneity exists in the association across individual cities. Several single cities showed a positive association in at least one of the single-day lag models. However, in the adjusted model, pooling across all cities resulted in a null estimate.

Research investigating the linkages between climate change and waterborne disease is still in its early stages compared to the work being done on heat, air pollution, and vectorborne diseases. In those more traditional areas of research a range of methods have been developed to study the potential associations (Basu 2009; Gosling et al. 2009), whereas most work linking climate change and waterborne disease has used time-series analysis utilizing Poisson regression (Hashizume 2007; Schwartz et al. 2000; Heaney 2011). A handful of water-related studies, however, have utilized the case-crossover design (Nichols 2009; Thomas 2006). This study utilized case-crossover design, pooling effect estimates across a large number of cities and using meta-regression to evaluate the role of community-level variables. Integrating individual and community-level data is an important step in the evaluation of the factors influencing waterborne disease and potential routes of exposure.

The overall lack of association presented herein is likely a result of exposure misclassification resulting from use of precipitation as a proxy for exposure to waterborne pathogens. Recognizing the limitations of using city-specific precipitation as the exposure variable, the goal was to use readily available meteorological data in this analysis. A study investigating the association between turbidity, a common proxy for water quality, and emergency room visits for GI in Atlanta, GA (Tinker at al. 2010) found no association between filtered water turbidity and hospital admissions. However, raw water turbidity revealed modest risk ratios. For example a 10-unit increase in daily minimum turbidity of the raw influent resulted in a risk estimate of 1.06 (95% CI: 1.04, 1.08) and a 10-unit increase in maximum turbidity of the raw influent resulted in a risk estimate of 1.02 (95% CI: 1.01, 1.03), which are comparable to some of the risk estimates we present.

An additional limitation of this study is underreporting of GI in traditional disease surveillance systems. Around the world, GI-related hospital admissions are dramatically underreported and the etiology is rarely identified (Charron et al. 2004; Ford 1999; Payment and Hunter 2001). In addition to being underreported, the exposure pathway leading to GI-related hospital admissions is very complex. GI-related hospital admissions may occur independent of contaminated water, such as through contaminated food or person-to-person contact, which are pathways unrelated to water quality or precipitation. Therefore, the signal linking precipitation and GI-related hospital admissions has a high potential to be obscured. A lack of data regarding drinking water source, treatment, and age of the drinking water system is a further limitation of this analysis. Where available, this data should be integrated with future analysis.

The overall goal of this analysis was to characterize the potential association between extreme precipitation and GI-related hospital admissions in order to capture the spatial and temporal trends in risk. Multiple lags and moving averages were defined *a priori,* in order to minimize concern about multiple comparisons. Even without adjustment for multiple comparisons, the results were null, so no further analysis was done. Since the results were null, we did not adjust for multiple testing. Because little is known about the impact of extreme precipitation on GI-related hospital admissions, our goal was to characterize the associations in a large number of cities over a 15-day lag period, which is consistent with the incubation period of most waterborne pathogens. A major strength of this analysis is its comprehensive nature and the fact that uniform methods were applied to a large number of communities over a fifteen year time period. It is the first multi-city study to evaluate the association between extreme precipitation and GI-related hospital admissions using case-crossover analysis.

One of the disadvantages of using case-crossover analysis is its limited ability to evaluate the temporal trend in effect. Distributed-lag nonlinear models (DLNM) introduced by Gasparrini et al. (2010) using R (package: DLNM) allow for the simultaneous evaluation of the non-linear and delayed effects of a certain predictor on the health outcome of interest. DLNM has only previously been used in tandem with traditional Poisson regression models. Few studies have attempted to evaluate potential non-linear and delayed effects within a case-crossover design. Guo et al. (2011) recently utilized DLNM within the case-crossover design based on the premise that the case-crossover design using conditional logistic regression is a unique case of time series analysis (Guo et al. 2011; Lu and Zeger 2007). While we used 7 and 15-day periods to estimate cumulative exposure and provide a rough estimate of the overall effect, inclusion of the DLNM in future analyses will allow for a more robust analysis of the cumulative effect of extreme precipitation on GI-related hospital admissions.

While this study evaluated community-level variables linking drinking water and wastewater infrastructure as a potential modifier of the association of precipitation with GI-related hospital admissions, other variables likely influence the characteristics of runoff following extreme precipitation and subsequently water quality. One example is karst topography, defined as a region with high levels of carbonate rock such as limestone or dolomite; this type of bedrock is highly permeable, often associated with sinkholes and caves. This unique characteristic makes it possible for surface water and groundwater to mix in these regions, which means contaminants often confined to surface water can mix with groundwater and that there is a reduced capacity for contaminants to be filtered out by soil (Dura 2010). Data characterizing bedrock as karst (or not) is available across the U.S. By overlaying this data with the county boundaries of the metropolitan areas used to define the cities in this analysis, we could create an indicator variable for the presence of karst topography. Future analyses should focus on cities with karst topography to evaluate whether the risk of GI-related hospital admissions following extreme precipitation is higher in these regions.

Percent green space in a city (or the inverse, impervious surface) is a second factor that may influence water quality, impacting the way water moves over the surface potentially depositing pathogens and contaminants in nearby waterways. Data on development and land cover are widely available from the U.S. Census and the National Land Cover Dataset. The percent green space could be determined for each city, and the values could be used in a meta-regression as was done with drinking water source percentages. One limitation is that the city boundaries do not necessarily correspond to watershed boundaries. A more robust analysis would first define the watersheds for each county and then characterize risk within the watersheds based on the relevant community-level variables.

This study focused solely on the health of the elderly above the age of 65. However, children can also be especially susceptibile to GI-related diseases. It is estimated that approximately 16.5 million children under five years of age experience between 21 and 37 million episodes of diarrhea annually; approximately 10.6% of hospitalizations in this age group are attributable to diarrhea (Glass et al. 1991). Future work should evaluate risk across age categories with particular attention to children under 5 years of age.

4.5 CONCLUSIONS

Overall, our work provides little evidence of the association between extreme precipitation and GI-related hospital admissions in the U.S. among the elderly. While individual cities showed a positive association at some lags, pooling across all cities and climate zones resulted in a null association in most cases. No seasonal trends were apparent. Modest associations were seen at later lags in climate zones 1 and 3. The meta-regression did not reveal any consistent trends, but on a few occasions drinking water source and the number of CSOs were linked to risk of GI-related hospital admissions. Future work will help develop the evidence base for understanding how we can protect human health as precipitation and other weather patterns shift, creating conditions that could potentially threaten water quality in many communities.

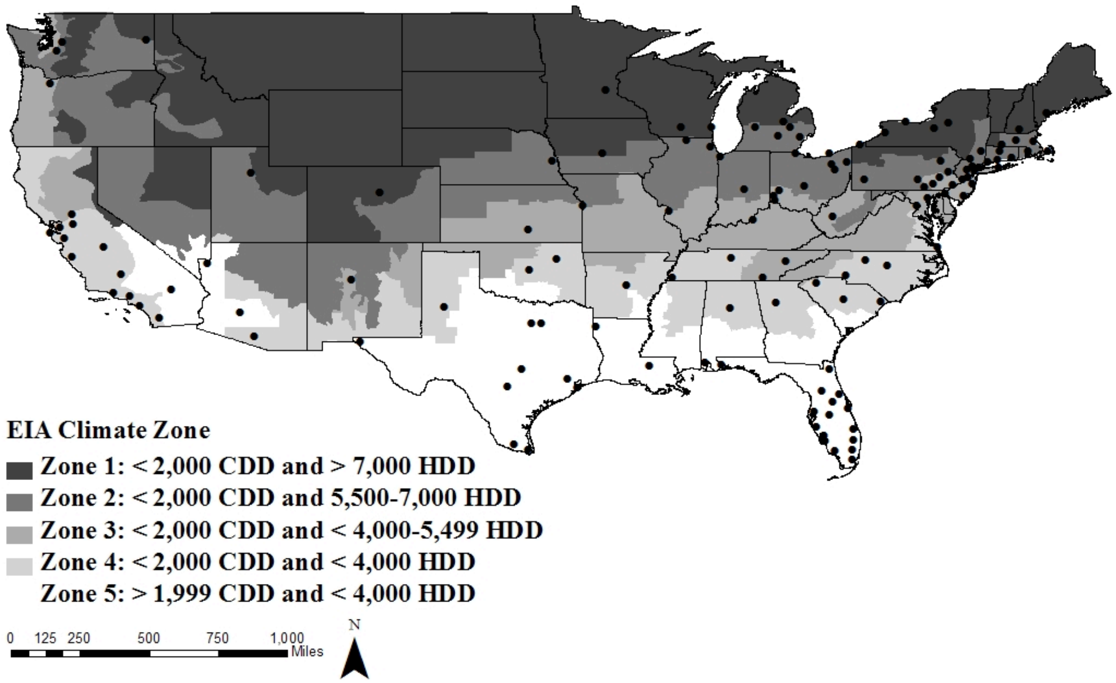


Figure 4.1 The 132 U.S. cities included in this analysis and their corresponding climate zones, on the 30-year average (1971-2000) of heating degree days (HDD) (sum of daily mean temperatures below 65°F) and cooling degree days (CDD) (sum of daily mean temperatures above 65°F).

Table 4.1 Climate zone classifications and the number of cities corresponding to each climate zone.

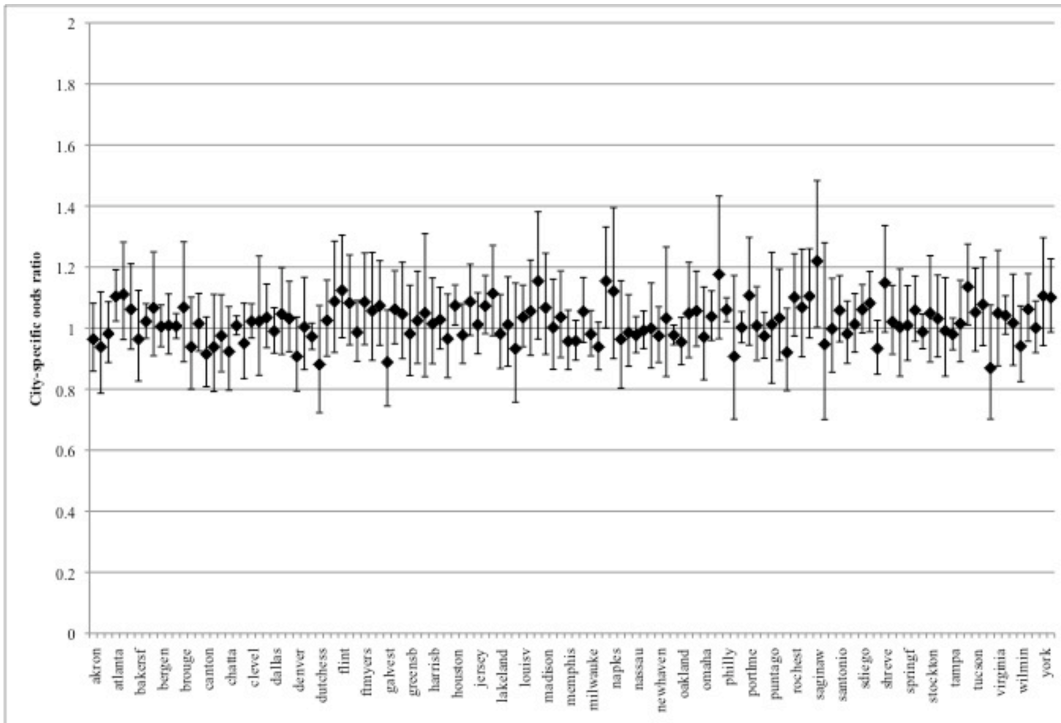
Climate zone	CDD[1]	HDD[2]	Number of cities
1	< 2,000	> 7,000	18
2	< 2,000	5,500 - 7,000	36
3	< 2,000	4,000-5,499	22
4	< 2,000	< 4,000	25
5	≥ 2,000	< 4,000	31

[1]Cooling-degree day (CDD), daily mean temperatures above 65°F
[2]Heating-degree day (HDD), daily mean temperature below 65°F

Table 4.2 Precipitation, apparent temperature and GI-related hospital admissions among the elderly in 132 U.S. cities categorized by climate zone for the period 1992 to 2006.

Climate zone	N	Daily precipitation mm (range)	Daily apparent temperature ˚C (range)	GI-related[1] hospital admissions total
1	18	0.023 (0.009-0.033)	8.13 (-13.17-33.52)	72,216
2	36	0.027 (0.006-0.033)	9.59 (-13.57-36.45)	374,216
3	22	0.029 (0.014-0.036)	12.56 (-11.08-36.64)	171,729
4	25	0.021 (0.005-0.040)	15.71 (-4.44-35.20)	107,250
5	31	0.031 (0.003-0.045)	23.28 (-0.15-37.53)	197,876

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.



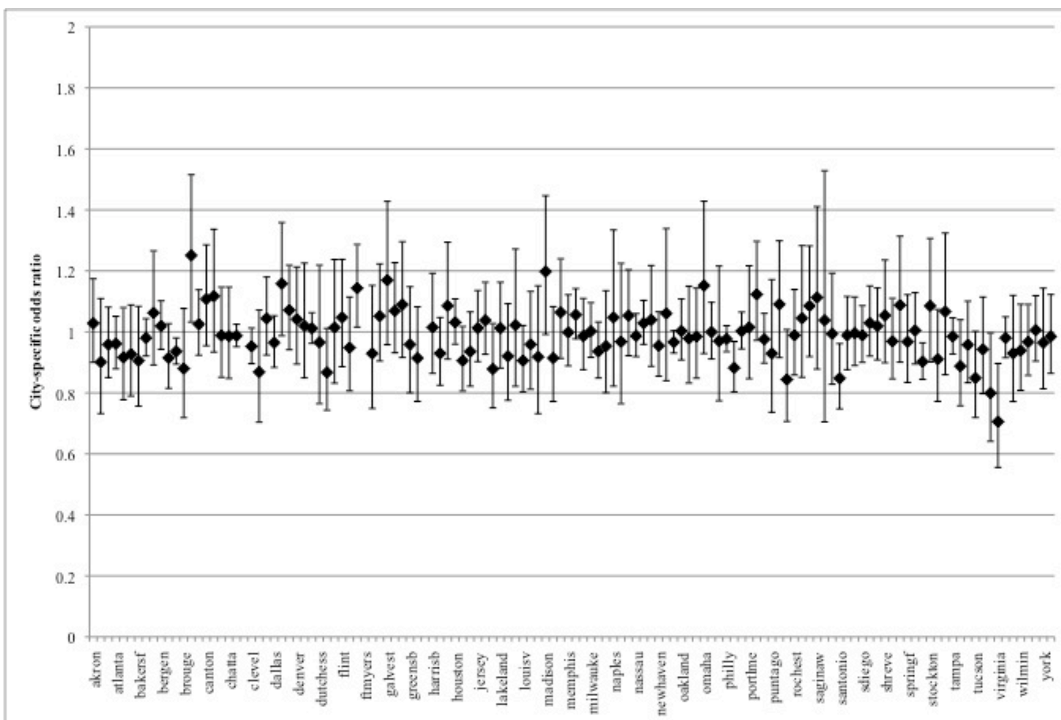


Figure 4.2 City-specific associations between GI-related hospital admissions and extreme precipitation (≥90th percentile) at lag 15 (top); and when the preceding 15-day period was extreme (≥90th percentile) (bottom), controlling for apparent temperature.

Table 4.3 Pooled risk estimates of GI-related hospital admissions among Medicare beneficiaries at the 90th percentile of precipitation (95% CI), across lags, for all cities and each climate zone, controlling for apparent temperature.

Lag	All	Climate zone 1	Climate zone 2	Climate zone 3	Climate zone 4	Climate zone 5
Lag1	0.99 (0.98, 0.99)	0.99 (0.96, 1.02)	0.98 (0.97, 1.00)	0.99 (0.97, 1.01)	0.98 (0.96, 1.00)	0.99 (0.97, 1.01)
Lag2	0.99 (0.98, 0.99)	0.99 (0.97, 1.02)	0.99 (0.97, 1.00)	0.98 (0.97, 1.00)	0.98 (0.96, 1.01)	0.99 (0.97, 1.01)
Lag3	1.00 (0.99, 1.00)	1.01 (0.98, 1.03)	0.99 (0.98, 1.01)	0.99 (0.97, 1.01)	1.00 (0.98, 1.03)	1.00 (0.98, 1.02)
Lag4	0.99 (0.99, 1.00)	1.01 (0.98, 1.04)	0.99 (0.98, 1.01)	0.98 (0.96, 1.00)	1.00 (0.98, 1.03)	1.00 (0.98, 1.02)
Lag5	0.99 (0.98, 1.00)	1.00 (0.97, 1.03)	0.99 (0.98, 1.00)	0.98 (0.96, 1.00)	1.00 (0.98, 1.03)	0.99 (0.97, 1.01)
Lag6	0.99 (0.98, 1.00)	0.98 (0.95, 1.01)	0.99 (0.97, 1.00)	1.01 (0.99, 1.03)	1.00 (0.97, 1.02)	0.99 (0.97, 1.01)
Lag7	1.00 (0.99, 1.01)	0.97 (0.94, 1.00)	1.00 (0.97, 1.01)	1.01 (0.99, 1.03)	1.00 (0.98, 1.02)	1.01 (0.99, 1.03)
Lag8	0.99 (0.98, 1.00)	1.03 (1.00, 1.07)	0.98 (0.97, 1.00)	1.00 (0.98, 1.02)	1.01 (0.98, 1.03)	0.98 (0.96, 1.00)
Lag9	0.99 (0.98, 1.00)	0.99 (0.97, 1.02)	0.99 (0.98, 1.00)	1.00 (0.98, 1.02)	0.99 (0.96, 1.01)	0.99 (0.97, 1.01)
Lag10	1.00 (0.99, 1.00)	1.00 (0.98, 1.03)	1.00 (0.99, 1.01)	1.00 (0.98, 1.02)	0.98 (0.96, 1.01)	0.99 (0.97, 1.01)
Lag11	1.00 (0.99, 1.01)	1.01 (0.98, 1.04)	1.00 (0.99, 1.02)	0.99 (0.98, 1.01)	0.99 (0.96, 1.01)	0.98 (0.96, 1.00)
Lag12	1.00 (1.00, 1.01)	1.01 (0.98, 1.04)	1.01 (0.99, 1.02)	1.03 (1.01, 1.05)	0.98 (0.96, 1.00)	0.99 (0.97, 1.01)
Lag13	1.00 (0.99, 1.01)	1.01 (0.98, 1.04)	1.01 (1.00, 1.02)	1.00 (0.98, 1.02)	1.00 (0.97, 1.02)	0.99 (0.97, 1.01)
Lag14	1.00 (1.00, 1.01)	1.02 (0.99, 1.05)	1.00 (0.99, 1.01)	1.00 (0.98, 1.02)	1.00 (0.98, 1.03)	1.00 (0.98, 1.02)
Lag15	1.01 (1.00, 1.02)	1.01 (0.98, 1.04)	1.00 (0.99, 1.01)	1.03 (1.01, 1.05)	1.02 (0.99, 1.04)	1.02 (1.00, 1.04)
7-day moving average	0.98 (0.97, 0.99)	0.99 (0.96, 1.02)	0.98 (0.97, 0.99)	0.98 (0.96, 1.00)	0.99 (0.96, 1.01)	0.96 (0.94, 0.98)
15-day moving average	0.98 (0.98, 0.99)	0.99 (0.96, 1.03)	0.98 (0.97, 0.99)	0.98 (0.96, 1.00)	0.98 (0.95, 1.00)	1.00 (0.98, 1.02)

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.

Table 4.4 Pooled risk estimates of GI-related hospital admissions among Medicare beneficiaries at the 90th percentile of precipitation (95% confidence interval), across lags, for all cities and each climate zone, controlling for apparent temperature, during *winter*.

Lag	**All**	**Climate zone 1**	**Climate zone 2**	**Climate zone 3**	**Climate zone 4**	**Climate zone 5**
Lag1	0.98 (0.96, 1.00)	0.98 (0.92, 1.04)	0.98 (0.96, 1.01)	0.97 (0.94, 1.01)	0.95 (0.91, 0.99)	1.01 (0.97, 1.06)
Lag2	0.98 (0.96, 1.00)	1.04 (0.98, 1.10)	0.98 (0.95, 1.00)	0.96 (0.93, 0.99)	0.97 (0.93, 1.01)	0.99 (0.95, 1.04)
Lag3	0.99 (0.98, 1.01)	1.04 (0.98, 1.11)	0.99 (0.96, 1.01)	0.99 (0.96, 1.03)	1.01 (0.97, 1.05)	0.96 (0.92, 1.01)
Lag4	1.00 (0.98, 1.01)	1.01 (0.95, 1.07)	0.99 (0.97, 1.02)	0.98 (0.95, 1.02)	1.01 (0.97, 1.05)	1.01 (0.97, 1.06)
Lag5	1.00 (0.98, 1.01)	1.00 (0.95, 1.06)	0.99 (0.97, 1.02)	0.98 (0.94, 1.01)	1.02 (0.98, 1.06)	1.01 (0.97, 1.06)
Lag6	0.98 (0.96, 0.99)	1.01 (0.95, 1.07)	0.97 (0.94, 0.99)	0.97 (0.93, 1.00)	1.02 (0.98, 1.07)	0.95 (0.91, 1.00)
Lag7	1.02 (1.00, 1.03)	0.99 (0.93, 1.05)	1.02 (0.99, 1.04)	1.01 (0.98, 1.05)	1.03 (0.99, 1.07)	1.03 (0.98, 1.08)
Lag8	0.99 (0.98, 1.01)	1.08 (1.02, 1.15)	0.97 (0.95, 1.00)	0.97 (0.94, 1.01)	1.01 (0.97, 1.06)	1.01 (0.96, 1.06)
Lag9	1.00 (0.98, 1.01)	0.98 (0.93, 1.04)	0.98 (0.96, 1.01)	1.02 (0.98, 1.05)	1.02 (0.97, 1.06)	1.01 (0.96, 1.06)
Lag10	1.01 (0.99, 1.02)	1.03 (0.97, 1.09)	1.02 (1.00, 1.05)	0.99 (0.96, 1.03)	0.99 (0.95, 1.03)	1.01 (0.96, 1.06)
Lag11	1.00 (0.99, 1.02)	1.01 (0.95, 1.07)	1.00 (0.97, 1.02)	1.01 (0.98, 1.05)	1.01 (0.97, 1.05)	0.99 (0.94, 1.04)
Lag12	1.01 (1.00, 1.03)	1.02 (0.96, 1.08)	1.01 (0.99, 1.04)	1.05 (1.02, 1.09)	0.99 (0.95, 1.03)	0.98 (0.94, 1.03)
Lag13	1.00 (0.99, 1.02)	1.00 (0.95, 1.06)	1.00 (0.98, 1.03)	1.01 (0.97, 1.05)	0.99 (0.95, 1.03)	1.01 (0.96, 1.06)
Lag14	1.00 (0.99, 1.02)	1.01 (0.95, 1.07)	1.01 (0.99, 1.04)	0.99 (0.95, 1.02)	0.98 (0.94, 1.02)	1.04 (0.99, 1.09)
Lag15	1.02 (1.01, 1.04)	1.04 (0.98, 1.11)	1.02 (0.99, 1.04)	1.04 (1.00, 1.08)	1.00 (0.96, 1.05)	1.03 (0.98, 1.08)
7-day moving average	0.97 (0.95, 0.99)	1.03 (0.95, 1.10)	0.96 (0.93, 0.99)	0.92 (0.8, 0.96)	0.98 (0.94, 1.02)	1.00 (0.96, 1.03)
15-day moving average	1.01 (0.98, 1.03)	1.06 (0.98, 1.15)	1.03 (0.99, 1.07)	0.96 (0.91, 1.02)	1.00 (0.96, 1.05)	0.99 (0.95, 1.04)

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.

Table 4.5 Pooled risk estimates of GI-related hospital admissions among Medicare beneficiaries at the 90th percentile of precipitation (95% confidence interval), across lags, for all cities and each climate zone, controlling for apparent temperature, during *spring*.

Lag	All	Climate zone 1	Climate zone 2	Climate zone 3	Climate zone 4	Climate zone 5
Lag1	0.99 (0.97, 1.00)	0.98 (0.93, 1.04)	0.98 (0.96, 1.00)	0.99 (0.96, 1.03)	0.99 (0.94, 1.03)	1.01 (0.97, 1.06)
Lag2	0.99 (0.98, 1.01)	1.02 (0.97, 1.08)	1.00 (0.97, 1.02)	0.97 (0.93, 1.00)	0.99 (0.94, 1.03)	1.01 (0.97, 1.06)
Lag3	1.00 (0.99, 1.02)	0.98 (0.93, 1.03)	1.02 (0.99, 1.04)	0.98 (0.95, 1.02)	1.01 (0.96, 1.05)	0.99 (0.95, 1.04)
Lag4	1.00 (0.99, 1.02)	1.00 (0.94, 1.05)	1.01 (0.99, 1.04)	0.99 (0.95, 1.02)	1.01 (0.96, 1.06)	1.00 (0.96, 1.05)
Lag5	0.99 (0.98, 1.01)	1.00 (0.94, 1.05)	0.99 (0.97, 1.01)	0.98 (0.95, 1.02)	1.02 (0.97, 1.07)	1.00 (0.96, 1.05)
Lag6	1.01 (0.99, 1.02)	0.99 (0.93, 1.04)	1.01 (0.99, 1.03)	1.03 (0.99, 1.07)	0.99 (0.95, 1.04)	0.98 (0.94, 1.03)
Lag7	1.00 (0.98, 1.01)	0.98 (0.93, 1.04)	0.99 (0.97, 1.02)	1.01 (0.98, 1.05)	0.99 (0.94, 1.04)	1.00 (0.96, 1.05)
Lag8	0.99 (0.98, 1.01)	1.01 (0.95, 1.06)	0.99 (0.96, 1.01)	0.99 (0.96, 1.03)	1.02 (0.97, 1.07)	0.99 (0.95, 1.04)
Lag9	0.99 (0.97, 1.00)	1.00 (0.94, 1.05)	0.98 (0.96, 1.00)	1.00 (0.96, 1.03)	0.98 (0.94, 1.03)	0.98 (0.94, 1.03)
Lag10	0.99 (0.97, 1.00)	1.02 (0.97, 1.08)	0.97 (0.95, 1.00)	1.01 (0.97, 1.04)	0.98 (0.94, 1.03)	0.99 (0.95, 1.04)
Lag11	1.01 (0.99, 1.02)	1.05 (0.99, 1.11)	1.00 (0.98, 1.03)	1.00 (0.97, 1.04)	1.00 (0.96, 1.05)	0.98 (0.93, 1.02)
Lag12	1.01 (0.99, 1.03)	1.03 (0.97, 1.09)	1.00 (0.98, 1.02)	1.01 (0.98, 1.05)	1.00 (0.95, 1.04)	1.03 (0.99, 1.08)
Lag13	0.99 (0.98, 1.01)	0.96 (0.91, 1.02)	0.99 (0.97, 1.02)	1.00 (0.96, 1.03)	1.03 (0.98, 1.07)	0.97 (0.92, 1.01)
Lag14	1.00 (0.99, 1.02)	1.01 (0.95, 1.07)	0.99 (0.97, 1.02)	1.02 (0.98, 1.05)	1.03 (0.98, 1.07)	1.00 (0.95, 1.04)
Lag15	1.02 (1.01, 1.04)	1.08 (1.02, 1.14)	1.00 (0.98, 1.03)	1.05 (1.01, 1.08)	1.02 (0.97, 1.06)	1.02 (0.98, 1.07)
7-day moving average	0.99 (0.97, 1.01)	0.97 (0.92, 1.03)	0.99 (0.96, 1.01)	0.99 (0.95, 1.03)	1.00 (0.95, 1.05)	099 (0.95, 1.03)
15-day moving average	0.96 (0.95 (0.98)	0.95 (0.88, 1.02)	0.96 (0.93, 0.99)	0.96 (0.92, 1.01)	0.97 (0.92, 1.01)	1.00 (0.95, 1.05)

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.

Table 4.6 Pooled risk estimates of GI-related hospital admissions among Medicare beneficiaries at the 90th percentile of precipitation (95% confidence interval), across lags, for all cities and each climate zone, controlling for apparent temperature, during *summer* .

Lag	All	Climate zone 1	Climate zone 2	Climate zone 3	Climate zone 4	Climate zone 5
Lag1	0.98 (0.97, 1.00)	1.00 (0.94, 1.06)	0.98 (0.95, 1.0)	0.99 (0.95, 1.03)	1.00 (0.94, 1.06)	0.97 (0.94, 1.01)
Lag2	0.99 (0.98, 1.01)	0.96 (0.90, 1.02)	0.99 (0.96, 1.01)	1.01 (0.97, 1.05)	1.02 (0.96, 1.09)	0.99 (0.95, 1.02)
Lag3	1.00 (0.98, 1.01)	1.00 (0.94, 1.06)	0.98 (0.96, 1.01)	0.99 (0.95, 1.03)	0.99 (0.92, 1.05)	1.04 (1.00, 1.07)
Lag4	1.00 (0.98, 1.01)	1.04 (0.98, 1.11)	0.99 (0.97, 1.02)	0.98 (0.94, 1.02)	1.03 (0.97, 1.09)	0.99 (0.96, 1.03)
Lag5	0.98 (0.97, 1.00)	1.01 (0.95, 1.07)	0.97 (0.95, 1.00)	0.99 (0.95, 1.03)	0.99 (0.93, 1.06)	0.98 (0.94, 1.01)
Lag6	1.01 (0.99, 1.03)	0.98 (0.92, 1.04)	1.00 (0.97, 1.02)	1.04 (1.00, 1.08)	1.03 (0.97, 1.10)	1.02 (0.98, 1.06)
Lag7	1.01 (0.99, 1.02)	0.95 (0.89, 1.01)	1.00 (0.98, 1.03)	1.02 (0.98, 1.06)	1.00 (0.94, 1.06)	1.02 (0.98, 1.05)
Lag8	1.00 (0.98, 1.02)	1.03 (0.97, 1.09)	0.98 (0.96, 1.01)	1.05 (1.01, 1.09)	0.99 (0.93, 1.06)	1.00 (0.96, 1.03)
Lag9	1.00 (0.98, 1.01)	1.02 (0.96, 1.09)	1.01 (0.99, 1.04)	0.98 (0.94, 1.02)	0.95 (0.89, 1.01)	0.99 (0.96, 1.03)
Lag10	1.00 (0.98, 1.01)	1.00 (0.94, 1.06)	1.02 (0.99, 1.04)	0.99 (0.95, 1.02)	0.97 (0.91, 1.04)	0.97 (0.93, 1.00)
Lag11	0.98 (0.97, 1.00)	1.00 (0.94, 1.07)	1.00 (0.97, 1.02)	0.97 (0.93, 1.01)	0.91 (0.86, 0.97)	0.98 (0.95, 1.02)
Lag12	1.00 (0.98, 1.01)	1.00 (0.96, 1.06)	0.98 (0.96, 1.01)	0.99 (0.95, 1.04)	1.01 (0.95, 1.06)	1.01 (0.97, 1.04)
Lag13	1.00 (0.98, 1.02)	1.02 (0.96, 1.08)	1.02 (0.99, 1.04)	0.98 (0.94, 1.02)	0.98 (0.92, 1.04)	0.98 (0.94, 1.01)
Lag14	1.02 (1.00, 1.03)	1.04 (0.98, 1.11)	1.01 (0.99, 1.04)	1.01 (0.98, 1.06)	1.05 (0.99, 1.11)	1.00 (0.96, 1.03)
Lag15	1.00 (0.99, 1.02)	0.96 (0.90, 1.02)	1.00 (0.97, 1.02)	1.01 (0.98, 1.05)	1.06 (1.00, 1.13)	1.01 (0.98, 1.05)
7-day moving average	0.99 (0.97, 1.00)	0.99 (0.94, 1.05)	0.98 (0.96, 1.01)	1.00 (0.97, 1.04)	1.02 (0.97, 1.08)	0.99 (0.95, 1.02)
15-day moving average	0.99 (0.97, 1.01)	1.03 (0.98, 1.09)	0.98 (0.95, 1.00)	0.99 (0.95, 1.03)	1.03 (0.98, 1.08)	0.99 (0.95, 1.04)

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.

Table 4.7 Pooled risk estimates of GI-related hospital admissions among Medicare beneficiaries at the 90th percentile of precipitation (95% confidence interval), across lags, for all cities and each climate zone, controlling for apparent temperature, during *fall*.

Lag	All	Climate zone 1	Climate zone 2	Climate zone 3	Climate zone 4	Climate zone 5
Lag1	1.00 (0.98, 1.02)	1.02 (0.95, 1.08)	1.00 (0.98, 1.03)	1.01 (0.97, 1.05)	1.03 (0.97, 1.09)	0.97 (0.93, 1.01)
Lag2	0.99 (0.97, 1.01)	0.96 (0.90, 1.02)	0.99 (0.96, 1.02)	1.02 (0.98, 1.06)	0.99 (0.94, 1.05)	0.98 (0.94, 1.02)
Lag3	1.00 (0.98, 1.02)	1.01 (0.95, 1.07)	0.99 (0.97, 1.02)	1.00 (0.96, 1.05)	1.00 (0.95, 1.06)	1.01 (0.97, 1.06)
Lag4	0.99 (0.97, 1.01)	1.00 (0.94, 1.07)	0.98 (0.96, 1.01)	0.98 (0.94, 1.03)	0.98 (0.93, 1.04)	1.01 (0.97, 1.06)
Lag5	1.00 (0.98, 1.02)	0.99 (0.93, 1.06)	1.01 (0.98, 1.04)	0.99 (0.95, 1.03)	0.98 (0.92, 1.04)	1.00 (0.96, 1.04)
Lag6	0.98 (0.96, 1.00)	0.98 (0.92, 1.04)	0.97 (0.95, 1.00)	1.01 (0.97, 1.05)	0.95 (0.89, 1.00)	1.00 (0.96, 1.04)
Lag7	0.99 (0.97, 1.01)	0.98 (0.92, 1.05)	0.99 (0.96, 1.01)	0.99 (0.95, 1.03)	0.96 (0.91, 1.02)	1.02 (0.98, 1.07)
Lag8	0.99 (0.98, 1.01)	1.05 (0.98, 1.11)	1.00 (0.98, 1.03)	1.00 (0.96, 1.04)	1.01 (0.95, 1.07)	0.95 (0.91, 0.99)
Lag9	1.00 (0.98, 1.01)	0.99 (0.93, 1.06)	0.99 (0.96, 1.02)	1.01 (0.97, 1.05)	0.99 (0.93, 1.05)	1.00 (0.96, 1.05)
Lag10	1.00 (0.99, 1.02)	0.98 (0.92, 1.04)	1.00 (0.98, 1.03)	1.02 (0.98, 1.06)	0.99 (0.93, 1.05)	1.01 (0.97, 1.05)
Lag11	1.00 (0.99, 1.02)	0.98 (0.92, 1.04)	1.02 (1.00, 1.05)	1.00 (0.96, 1.04)	0.98 (0.92, 1.04)	0.98 (0.94, 1.02)
Lag12	1.01 (0.99, 1.03)	1.00 (0.94, 1.07)	1.01 (0.99, 1.04)	1.02 (0.98, 1.07)	0.99 (0.93, 1.05)	0.99 (0.95, 1.03)
Lag13	1.02 (1.01, 1.04)	1.08 (1.01, 1.14)	1.03 (1.00, 1.05)	1.01 (0.97, 1.05)	0.99 (0.94, 1.06)	1.02 (0.98, 1.06)
Lag14	1.00 (0.99, 1.02)	1.04 (0.98, 1.10)	1.00 (0.98, 1.03)	1.01 (0.97, 1.05)	0.97 (0.92, 1.03)	0.99 (0.96, 1.04)
Lag15	1.01 (0.99, 1.02)	0.97 (0.91, 1.03)	0.99 (0.96, 1.01)	1.05 (1.01, 1.09)	1.00 (0.94, 1.06)	1.04 (1.00, 1.08)
7-day moving average	0.99 (0.97, 1.00)	0.98 (0.92, 1.04)	0.98 (0.96, 1.01)	1.00 (0.96, 1.04)	0.96 (0.90, 1.01)	1.00 (0.96, 1.04)
15-day moving average	0.98 (0.97, 1.00)	0.99 (0.92, 1.06)	0.98 (0.95, 1.01)	1.00 (0.96, 1.04)	0.92 (0.86, 0.97)	1.01 (0.97, 1.06)

[1]Hospital admissions were defined as GI-related if the primary, secondary, or tertiary ICD-9 code was listed as intestinal infectious disease or GI-related symptoms.

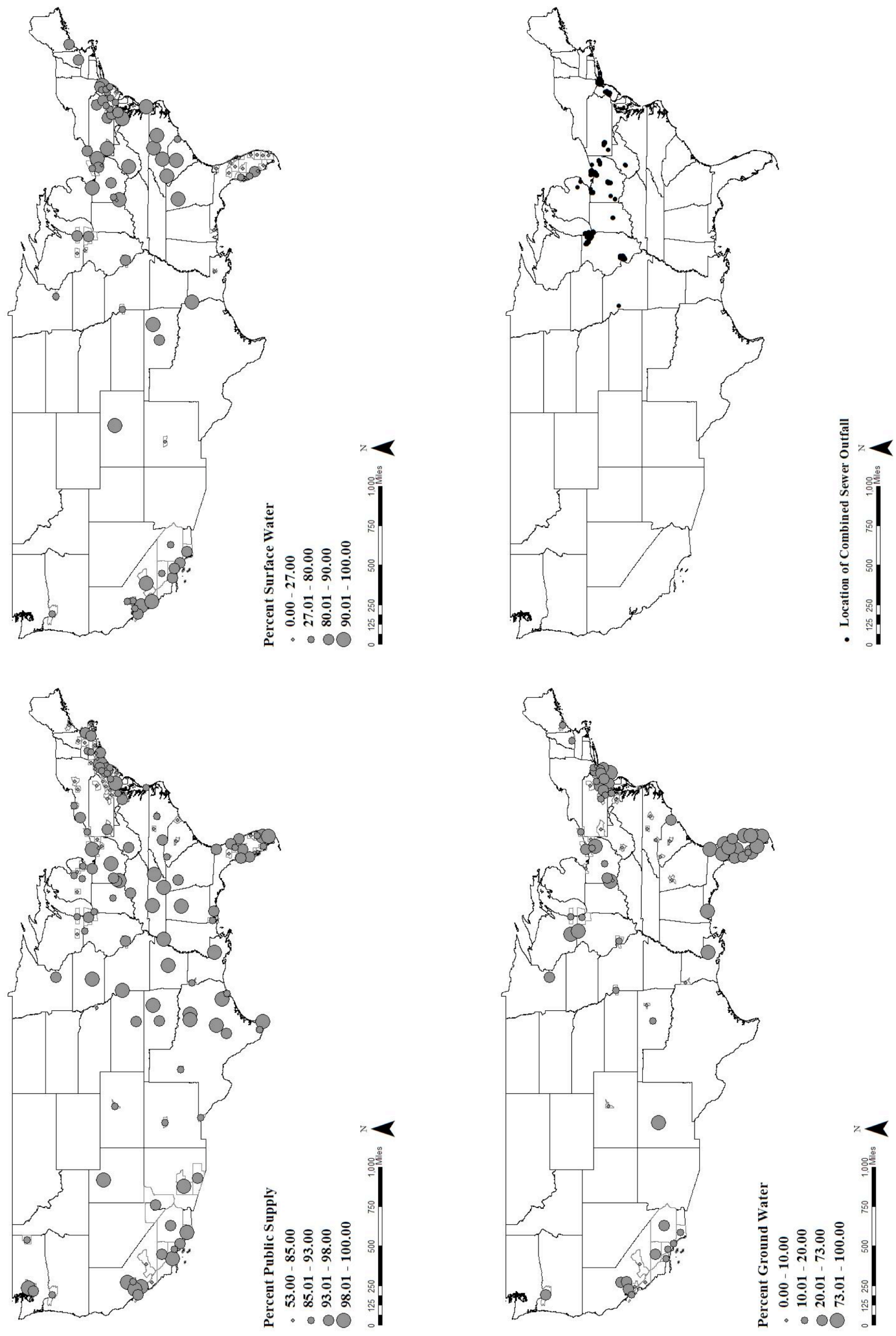


Figure 4.3 Variables used in the meta-regression presented by city including percent public water supply, percent sourced from surface water, percent sourced from groundwater, and the number of combined sewer overflows located inside the boundary of the metropolitan area.

Table 4.8 Pearson correlation coefficients evaluating the association between city-specific odds ratios and community-level variables[1] used in the meta-regression, stratified by season.

	Adjusted[2]			**Winter**			**Spring**			**Summer**			**Fall**		
	GW	**SW**	**CSO**	**GW**	**SW**	**CSO**	**GW**	**SW**	**CSO**	**GW**	**SW**	**CSO**	**GW**	**SW**	**CSO**
Lag1	-0.09	0.09	0.01	-0.09	0.09	-0.03	0.15	-0.16	-0.20	0.24	-0.25	-0.13	0.05	-0.03	0.47
Lag2	-0.09	0.10	0.04	0.06	-0.05	-0.05	-0.03	0.02	0.18	0.16	-0.15	-0.22	-0.12	0.13	0.15
Lag3	-0.04	0.04	-0.09	-0.17	0.17	0.05	-0.05	0.06	0.13	-0.04	0.05	-0.22	-0.01	0.00	-0.13
Lag4	0.11	-0.12	0.19	0.01	-0.01	0.26	-0.16	0.16	0.17	0.23	-0.23	-0.11	0.21	-0.22	-0.02
Lag5	0.07	-0.07	-0.02	0.13	-0.13	0.06	0.03	-0.03	-0.22	0.05	-0.05	0.24	0.12	-0.11	-0.13
Lag6	-0.16	0.15	0.06	0.02	-0.02	0.01	-0.07	0.07	0.01	0.00	0.00	0.20	0.02	-0.04	-0.06
Lag7	-0.12	0.12	-0.13	-0.01	0.02	-0.03	-0.01	0.00	0.04	-0.04	0.04	-0.30	0.02	-0.01	0.12
Lag8	-0.21	0.21	-0.09	-0.12	0.12	0.00	-0.12	0.11	-0.03	-0.30	0.31	-0.13	-0.03	0.03	-0.01
Lag9	-0.19	0.19	0.06	-0.15	0.14	0.00	-0.30	0.30	0.07	-0.10	0.10	-0.03	-0.02	0.02	0.04
Lag10	-0.10	0.10	0.12	-0.07	0.08	0.21	0.03	-0.02	0.04	-0.05	0.05	-0.05	-0.05	0.04	-0.20
Lag11	-0.20	0.20	0.08	-0.24	0.26	0.06	-0.04	0.05	-0.02	-0.17	0.17	-0.03	-0.21	0.22	0.14
Lag12	-0.16	0.15	-0.11	-0.21	0.20	0.08	0.12	-0.11	-0.26	-0.08	0.08	-0.13	-0.08	0.07	0.17
Lag13	0.02	-0.02	-0.07	-0.03	0.02	0.06	-0.15	0.16	-0.23	0.13	-0.13	-0.04	0.19	-0.19	-0.07
Lag14	-0.09	0.10	-0.01	-0.01	0.01	0.05	-0.21	0.21	-0.13	0.04	-0.04	0.25	0.08	-0.07	-0.11
Lag15	-0.05	0.04	-0.19	0.15	-0.16	-0.07	0.08	-0.07	-0.10	-0.05	0.04	0.05	0.00	0.00	-0.29
7-day period	0.11	-0.11	-0.08	0.16	-0.14	-0.10	-0.09	0.09	0.01	-0.06	0.07	-0.06	0.17	-0.18	-0.12
15-day period	0.03	-0.04	0.07	0.17	-0.17	0.23	-0.02	0.02	0.03	-0.05	0.05	-0.20	0.06	-0.08	-0.17

[1]GW refers to groundwater, SW refers to surface water, CSO refers to the number of combined sewer overflows located within the metropolitan area.
[2]Adjusted model controls for apparent temperature.

Table 4.S1 Steps used to access and download data from U.S. EPA Envirofacts regarding combined sewer overflows (CSOs) across the U.S.

Go to the Envirofacts homepage (http://www.epa.gov/enviro/)
Select *PCS Customized Search*
Select *Pipe Schedule-Outfalls* from the list of subjects
Select *Effluent Limits & Allowable Discharges* and then *Facility Information*
Click *Step 2: Retrieve Tables for Selected Subjects*
Select the tables to be included in the output by clicking in the box next to the tables (select all)
Click *Step 3: Select Columns*
Select one or more items to be included in the output (be sure to select *Outfall Type Code* and *Pipe Latitude and Pipe Longitude*)
Click *Step 4: Enter Search Criteria*
Enter search criteria and organize the output page, under *Output Options for Selected Columns*, in column name *outfall type code* select *In* from the operator definition dropdown menu and enter "C" in the search value field (this is the code for CSO)
Click *Search Database*
Click *Output as CSV file*

Table 4.S2 List of 132 Cities included in analysis.

Akron, OH
Albuquerque, NM
Allentown, PA
Atlanta, GA
Atlantic City, NJ
Austin, TX
Bakersfield, CA
Baltimore, MD
Barnstable, MA
Baton Rouge, LA
Bergen-Passaic, NJ
Birmingham, AL
Boston, MA
Brownsville, TX
Buffalo, NY
Canton, OH
Charleston, WV
Charlotte, NC
Chattanooga, TN
Chicago, IL
Cincinnati, OH
Cleveland, OH
Columbia, SC
Columbus, OH
Dallas, TX
Dayton, OH
Daytona Beach, FL
Denver, CO
Des Moines, IA
Detroit, MI
Dutchess County, NY
El Paso, TX
Erie, PA
Flint, MI
Fort Myers, FL
Fort Pierce, FL
Fort Worth, TX
Fresno, CA
Ft. Lauderdale, FL
Galveston, TX
Gary, IN
Grand Rapids, MI
Greensboro, NC
Greenville, SC
Hamilton, OH
Harrisburg, PA
Hartford, CT
Honolulu, HI
Houston, TX
Indianapolis, IN
Jacksonville, FL
Jersey City, NJ
Kansas City, MO-KS
Knoxville, TN
Lakeland, FL
Lancaster, PA
Lansing, MI
Las Vegas, NV-AZ
Little Rock, AR
Los Angeles, CA
Louisville, KY
Lubbock, TX
Madison, WI
McAllen, TX
Melbourne, FL
Memphis, TN
Miami, FL
Middlesex, NJ
Milwaukee, WI
Minneapolis-St. Paul, MN
Mobile, AL
Naples, FL
Nashua, NH
Nashville, TN
Nassau, NY
New Haven, CT
New London, CT
New York, NY
Newark, NJ
Newburgh, NY
Oakland, CA
Ocala, FL
Oklahoma City, OK
Omaha, NE
Orange County, CA
Orlando, FL
Pensacola, FL
Philadelphia, PA
Phoenix, AZ
Pittsburgh, PA
Portland, ME
Portland, OR
Providence, RI
Punta Gorda, FL
Raleigh, NC
Reading, PA
Rochester, NY
Rockford, IL
Sacramento, CA
Saginaw, MI
Salinas, CA
Salt Lake City, UT
San Antonio, TX
San Diego, CA
San Francisco, CA
San Jose, CA
Sarasota, FL
Scranton, PA
Seattle, WA
Shreveport, LA
Spokane, WA
Springfield, MA
St. Louis, MO
Stamford-Norwalk, CT
Stockton-Lodi, CA
Syracuse, NY
Tacoma, WA
Tampa, FL
Toledo, OH
Trenton, NJ
Tucson, AZ
Tulsa, OK
Utica, NY
Ventura County, CA
Virginia Beach, VA
Washington, DC-MD-VA
West Palm Beach, FL
Wichita, KS
Wilmington, DE
Worcester, MA
York, PA
Youngstown, OH

Table 4.S3 City-specific community-level variables used in the meta-regression analysis.

City	Climate zone	Public supply percent	Ground water percent	Surface water percent	CSOs[1] count
akron	2	78.15	16.05	83.95	
albuq	2	91.12	99.85	0.15	
allent	2	85.06	19.14	80.86	
atlanta	3	96.88	0.59	99.41	
atlantic	4	75.28	97.26	2.74	
austin	5	99.50			
bakersf	4	92.77	21.55	78.45	
baltim	3	89.30	19.38	80.62	
barnst	2	82.00			
bergen	2	95.52	16.27	83.73	4
birming	4	99.08			
boston	2	95.83			
brouge	5	99.20	100.00	0.00	
browns	5	100.00			
buffalo	1	93.62			
canton	2	75.99	92.05	7.95	8
charlest	3	92.79	0.06	99.94	2
charlot	4	97.32	1.43	98.57	
chatta	3	99.15			
chicago	2	96.30	13.40	86.60	108
cincin	3	98.84	5.37	94.63	
clevel	2	98.86	72.46	27.54	42
columbia	4	79.02	2.11	97.89	
columbus	2	99.32	13.95	86.05	28
dallas	4	100.00			
daybeach	5	93.14	100.00	0.00	
dayton	3	96.29	21.84	78.16	1
denver	1	92.50	0.56	99.44	
desmoi	1	99.76			
detroit	2	92.38			2
dutchess	2	65.53			
elpaso	5	91.67			
erie	1	85.11	13.89	86.11	
flint	2	70.28			
fresno	4	84.41	9.00	91.00	
ftlaud	5	99.74	100.00	0.00	

ftmyers	5	84.20	93.73	6.27	
ftpierce	5	81.27	100.00	0.00	
ftworth	5	100.00			
galvest	5	91.36			
gary	2	90.60			5
grapids	2	68.48			
greensb	4	78.62	3.42	96.58	
greenvi	3	92.37	0.47	99.53	
hamilton	3	98.01	100.00	0.00	3
harrisb	2	82.88	12.74	87.26	
hartford	2	90.22			
honolulu	5	99.87	100.00	0.00	
houston	5	100.00			
indian	2	91.40			2
jacksonv	5	94.35	100.00	0.00	
jersey	2	100.00	0.00	100.00	
kansas	3	100.00	14.75	41.94	1
knoxv	3	99.19			
lakeland	5	97.64	100.00	0.00	
lancast	3	58.90	31.28	68.72	
lansing	2	85.55			
lasvegas	5	94.09			
losang	5	91.35	17.78	82.22	
louisv	3	94.31			
lrock	4	100.00			
lubbock	4	90.00			
madison	1	83.59	100.00	0.00	
mcallen	5	88.96			
melbourn	5	96.34	73.00	27.00	
memphis	4	99.70			
miami	5	98.80	100.00	0.00	
middles	3	98.50	41.12	58.88	
milwauke	1	91.29	19.95	80.05	
minneap	1	97.56	49.56	50.44	
mobile	5	90.72			
naples	5	85.79	91.50	8.50	
nashua	1	64.61	15.34	84.66	
nashv	4	99.70			
nassau	3	92.82			43
newark	2	92.74	38.69	61.31	
newburgh	2	79.43			
newhaven	2	83.29			
newlond	2	84.76			

nyc	2	99.67			137
oakland	4	98.12	24.63	75.37	
ocala	5	53.09	100.00	0.00	
oklahoma	4	97.95	18.24	81.76	
omaha	2	82.74			
orange	4	97.75	12.75	87.25	
orlando	5	89.22	100.00	0.00	
pensac	5	95.28	100.00	0.00	
philly	3	85.80	26.60	73.40	32
phoenix	5	98.83			
pittsb	2	96.01	3.89	96.11	20
portlme	1	84.34	18.07	81.93	
portlor	3	88.34	49.12	50.88	
provid	2	94.31			
puntago	5	78.50	20.00	80.00	
raleigh	4	85.27	9.68	90.32	
reading	3	67.56	42.80	57.20	
rochest	1	92.29			
rockf	2	85.35	100.00	0.00	
sacram	3	98.92	38.62	61.38	
saginaw	1	87.50			
salinas	4	84.55	7.00	93.00	
saltlake	1	98.86			
santonio	5	93.15			
sarasota	5	98.08	58.93	41.07	
scranton	2	84.52	9.72	90.28	
sdiego	4	99.66	17.33	82.67	
seattle	1	98.24			
sfranc	4	96.36	16.58	83.42	
shreve	5	91.90	2.35	97.65	
sjose	4	99.19	6.66	93.34	
spokane	1	85.18			
springf	1	92.00			
stamford	2	76.22			
stlouis	2	95.62	10.57	89.43	29
stockton	4	86.08	25.67	74.33	
syracuse	1	79.00			
tacoma	1	93.30			
tampa	5	96.59	67.12	32.88	
toledo	2	94.45	0.00	100.00	7
trenton	3	89.13	29.54	70.46	3
tucson	4	97.76			
tulsa	4	98.43	0.00	100.00	

utica	1	83.63			
ventura	4	99.75	10.17	89.83	
virginia	4	91.56	0.00	100.00	
wdc	3	97.31	1.05	98.95	
wichita	3	96.72			
wilmin	3	98.33	45.28	54.72	
worcest	2	83.00			
wpalmb	5	90.49	85.16	14.84	
york	2	73.34	13.96	86.04	
youngst	2	80.75	2.67	97.33	7

[1]Location of combined sewer overflow (CSO) based on U.S. Environmental Protection Agency Envirofacts database.

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Chapter 5

Conclusions

5.1 CHAPTER SUMMARIES

Chapter 1 served as a literature review highlighting current research on climate change and human health with a specific focus on water-related resources and waterborne disease. The purpose of Chapter 1 was to provide sufficient background information for subsequent evaluation and discussion of the linkages between extreme precipitation, water quality, and gastrointestinal illness.

Chapter 2 was an analysis of the association between extreme precipitation, recreational water quality, and risk of GI-related hospital admissions in the Great Lakes region. Poisson regression models were fit in each city. City-specific estimates were then combined to form an overall risk estimate for the region. Precipitation above the 90th percentile at lag 1 predicted beach closures, however, beach closures were not significantly associated with GI-related hospital admissions, 0.98 (95% confidence interval (CI): 0.94, 1.01).

Chapter 3 evaluated the association between extreme precipitation and hospital admissions in Chennai, India. Poisson regression models were fit to evaluate the association between extreme precipitation ($\geq$90th percentile) and hospital admissions over a 15-day lag period, controlling for apparent temperature, day of week, and long-term time-trends. Season and age were explored as potential effect modifiers. Extreme precipitation was not associated with all-cause hospital admissions, however, extreme precipitation was associated with GI-related hospital admissions, 1.61 (95% CI: 1.29, 2.00), with elevated risks among the young 2.65 (95% CI: 1.21, 5.80) and old 1.68 (95% CI: 1.01, 2.80). With the predicted increase in extreme weather events and increased weather variability, certain populations in India may be at an increased risk of waterborne disease.

Chapter 4 evaluated the association between extreme precipitation and gastrointestinal illness among the elderly in 132 U.S. cities from 1992 to 2006. Time-stratified case-crossover analysis was used to evaluate the association between extreme precipitation and GI-related hospital admissions. Unlike traditional Poisson regression, this study design implicitly controls for long-term time-trends and individual confounders such as age and gender. City-specific associations between extreme precipitation ($\geq 90^{th}$ percentile) and GI-related hospital admissions, controlling for apparent temperature, at multiple lags, and evaluated season, drinking water source, and the presence of combined sewer outfalls as potential effect modifiers. Estimates were combined across the 132 cities and by climate zone. Overall, no positive associations between extreme precipitation and GI-related hospital admissions were observed. Season, drinking water source, and the number of combined sewer outfalls did not modify the results. The overall national pooled estimate for risk of GI-related hospital admission at lag 15 was 1.01 (95% CI: 1.00, 1.02). This study was the first multi-city study to evaluate the association between extreme precipitation and GI-related hospital admissions using case-crossover analysis.

5.2 GLOBAL BURDEN OF WATERBORNE DISEASE

Globally, waterborne disease is among the top 10 causes of disease and death among the general population and is the second leading cause of death among children under five. It is estimated that more than five million people die each year because of unsafe drinking water and inadequate sanitation (Anon 1996). According to the WHO, there are approximately two billion cases of diarrheal disease per year resulting in 1.5 million deaths among children (Payment and Hunter 2001). Even more staggering is the fact that these diseases are largely preventable. The provision of safe drinking water and sanitation services would result in 200 million fewer cases of waterborne disease and 2.1 million fewer deaths (Payment and Hunter 2001).

The burden of waterborne disease can differ markedly between regions due to socio-environmental factors such as local water quality, access to alternative drinking water sources, and individual behaviors. Previous research concludes that in areas with poor environmental sanitation, improvements in drinking water have little or no effect, however, in areas with good community sanitation, incidence of diarrhea can be significantly reduced (VanDerslice and Briscoe 1995).

While our knowledge of water-related risks and risk factors has grown immensely over the years, it remains difficult to estimate the global burden of waterborne disease because risk depends on such a myriad of factors. In high-income countries, deficiencies in treatment and distribution systems, contamination of source water, and the emergence of resistant pathogens pose new and serious threats to human health. Deteriorating infrastructure, particularly in inner cities, presents a huge risk. Currently, it is estimated that between 4.3 and 11.7 million cases of GI per year are attributable to public drinking water systems in the United States (Colford et al. 2006). Approximately 35% of GI cases are attributable to the consumption of drinking water that meets current water quality standards (Payment et al. 2001). While the U.S. has a system to monitor foodborne illnesses, there is no national surveillance system for the incidence of GI attributable to drinking water. Improved monitoring and surveillance of GI would improve our understanding of current and future risks. With high quality data we would be better able to observe and predict seasonal patterns and be better prepared to predict the effects of future climate scenarios.

There remains insufficient data to estimate the long-term effects of climate change on health, as it relates to water quality and quantity. Precipitation models in particular lack precision, which make long-term regional projections difficult. Therefore, it is challenging to assess the long-term impacts of climate change on water resources and the burden of waterborne disease. Future work must address limitations in current climate modeling as well as waterborne disease surveillance on a regional basis. The development of new monitoring systems should be linked to already existing disease surveillance programs. Interactions between disease and climate variability must be studied in the context of local socio-environmental factors.

5.3 DRAWING COMPARISONS BETWEEN THE U.S. AND INDIA

Significant differences in risk were observed between U.S. cities and Chennai, India. This may be, in part, because the quality and consistency of drinking water treatment differs substantially between the two countries. The Safe Drinking Water Act (SDWA) authorizes the U.S. EPA to set health-based drinking water standards. The

SDWA focuses on filtration and disinfection, but also recognizes source water protection, operator training, funding for water system improvements, and public information as important components of safe drinking water. According to the 2000 Census of India, only 50% of the Chennai population has access to drinking water via a household tap. Regardless of the source, drinking water treatment is not well documented. Therefore, it is reasonable to expect a greater percentage of the population in Chennai to be exposed to contaminated drinking water. In particular, individuals in Chennai may be exposed to higher concentrations of bacterial pathogens such as *Campylobacter, E.coli, Salmonella,* and *Shigella*, as those are the most likely to be removed by effective filtration and disinfection in the U.S. Higher exposure to waterborne pathogens via drinking water in Chennai is one potential explanation for the increased risk of GI-related hospital admissions observed in Chennai compared to the null findings reported in a majority of U.S. cities.

Another possible explanation for the difference in observed risk is bias in reporting. Hospital admission data from the U.S. and India are likely to differ. One obvious difference is that only Medicare data were used in the U.S. analysis, limiting the analysis to individuals 65 years and older. While this limits the scope of the analysis to the elderly, it also means that nearly 100% of the population under investigation have health insurance and are perhaps more likely to seek medical attention. GI is highly underreported in both the U.S. and India, but information on who is more likely to seek medical attention in one country compared to another and factors affecting this decision is lacking. Chennai has a variety of hospital services varying from public to private. However, this analysis was limited to two government hospitals, which likely cater to individuals in lower socio-economic strata. Given the potential for more limited resources in Chennai, hospital admissions in Chennai may reflect only the most extreme cases of GI. Capturing only the most extreme cases could explain the increased risk of GI-related hospital admissions following extreme precipitation in Chennai. These explanations are only speculative at this point. Future analyses should attempt to quantify the differences in risk attributable to differences in data sources and societal context

The results presented herein must be interpreted in the context of these broader social and environmental factors. The results in one city may not extrapolate to another because of different implications for exposure to pathogens linked to extreme precipitation due to variability in infrastructure, water systems, and behaviors which all influence susceptibility of the population under investigation. These socio-environmental factors should also inform the development of future interventions and adaptation strategies, as the needs and resources of one community are likely to be distinct from any other.

5.4 ADAPTATION IN RESPONSE TO CLIMATE CHANGE

A valid assessment of the health risks associated with climate change requires an equally critical examination of the vulnerability of populations and their ability to respond to climate-related risks (Ebi et al. 2006). According to the Intergovernmental Panel on Climate Change: *Adaptation* is the adjustment of natural or human systems in response to actual or expected climatic stimuli or their effects, which moderates harm or exploits beneficial opportunities, whereas *adaptive capacity* is the ability of a system to adjust to climate change, to moderate potential damages, to take advantage of opportunities, or to cope with the consequences.

Adaptive capacity, therefore, is a function of many social and environmental factors, which interact in complex ways. In many cases the risk of waterborne disease and the ability of a community to minimize associated health risks is related to access: Access to clean-potable water; access to sanitation; access to information. The WHO has concluded that high-income countries will have a minimal increase in risk of diarrhea incidence per degree (°C) increase in temperature and will not experience a greater burden of disease as a result of climate change. Low- and middle- income countries, however, will remain at high risk (McMichael et al. 2003). It will take the combined effort of scientists, policy-makers, and community organizers to take appropriate measures to both identify and minimize risk of waterborne disease in the face of climate change. In order to reach this goal, local governments will need to provide adequate access to safe drinking water and sanitation, effective water-resource management, protection of drinking water sources, and effective monitoring and response to waterborne outbreaks. Basic improvements in access to potable water and sanitation can increase adaptive capacity in many parts of the world, while simultaneously improving public health (McMichael et al. 2003).

Severe health costs associated with climate change, climate variability, and climate-related disasters are expected. There will be indirect costs associated with children missing school, or women spending more time gathering water. In the U.S. assuming a population of 300 million individuals, the estimated cost of waterborne illness ranges from 269-806 million U.S. dollars for medical costs and 40-107 million for absences from work (Payment and Hunter 2001). Such figures can only underscore the enormous economic cost of endemic gastrointestinal illnesses, even in societies where they are not perceived to be a problem (Payment and Hunter 200; Roberts and Foegeding 1991). While local governments and officials should take steps to improve infrastructure in an attempt to reduce exposure and reduce associated health care costs, it is also vitally important that the health care sector, primarily in high-income countries where resources allow, take steps to reduce their carbon footprint.

5.5 RECOMMENDATIONS

The level of carbon dioxide in the atmosphere has already reached a tipping point, as the concentration has reached an estimated 460ppm of carbon dioxide equivalents. Changes to the climate system are now considered inevitable and perhaps even irreversible. Risk assessments must focus on the health-related impacts. A threat this large should unite us across political and ideological boundaries. As the intricate web linking climate change to environmental quality and human health becomes more widely understood and accepted, scientists must engage with policy makers and the public in order to design effective programs addressing the health risks posed by climate change.

Taking steps to prepare for these changes is crucial. According to the International Council for Local Environmental Initiatives (ICLEI), “Resilience is the capacity of a community to respond creatively, preventatively, and proactively to change or extreme events, thus mitigating crisis or disaster.” Cities should prioritize a vulnerability assessment in order to identify the most significant vulnerabilities. Risks must be evaluated at a regional scale and intervention programs should be designed to address these regional, city-specific challenges. As stated on the ICLEI website, “Action at the local level is the most effective method of reducing, mitigating, and preventing disasters. Local governments can reduce the impact of disasters on their communities by increasing their community's resilience."

According to the Natural Resources Defense Council, assessing vulnerabilities is a key step in developing effective adaptation and intervention programs. In the context of the research presented herein, it will be important to assess future water availability as well as the occurrence of extreme precipitation, drought, and risk of flooding. In addition to measuring and predicting meteorological variables, the assessment of socio-environmental factors is also critical. One example is the vulnerability of drinking water sources and distribution systems. Community leaders must also start to think about climate change vulnerability in terms of emergency preparedness and risk management planning. Local planning is key. But, in the end, only effective implementation of measures to both mitigate and adapt to climate change can ensure that our communities are best prepared to face the coming challenges related to their water resources.

5.6 COMBINED SEWER SYSTEMS – A SERIOUS THREAT

Combined sewer systems (CSSs), which carry both stormwater and municipal wastewater in combination with decaying public water supply infrastructure continue to threaten water quality in cities across the U.S.. During heavy precipitation events, the capacity of these CSSs can be exceeded resulting in direct discharge of sewage and stormwater into receiving waters, which can introduce high levels of bacterial contaminants into the environment (EPA 2008). Currently, EPA estimates that 850 billion gallons of raw sewage and stormwater are released annually into U.S. waterways and that CSOs occur 43,000 times per year (EPA 2004).

The occurrence of CSOs has been linked to climatic factors (EPA 2007). Under predicted climatic changes, more extreme rain events are expected to occur, particularly in the Great Lakes region, which may overwhelm combined sewer systems and further exacerbate poor recreational water quality in the region (Patz 2008). An increased awareness of the relationship between precipitation and water quality has the potential to inform future regulations for beach closing advisories and the development of web-based tools (using real-time data) to predict when contamination levels are high and communicate the increased risk to the public.

Reducing stormwater runoff may be an effective way to protect water quality. The use of rain barrels, rain gardens, green roofs, and riparian zones can help reduce runoff. Furthermore, early detection of recreational water contamination and rapid response can reduce human exposure and will help minimize the risk of waterborne disease. Improved monitoring and reporting of recreational water quality is important to building a strong database for future analysis. As weather prediction technology continues to improve, water resource managers and public health officials should utilize forecasting technology to anticipate threats and communicate risks to the public. The association between heavy precipitation and recreational water quality varies spatially and temporally, but the link is evident. Improved water quality monitoring in real-time is necessary in order to make decisions that will protect water quality today, and in the future. Taking steps to reduce stormwater runoff and contamination of surface waters has the potential to reduce the risk of waterborne disease.

Still, far more information and resources are needed if we are to develop effective early warning systems through environmental surveillance and modeling (Ford et al. 2009). Critical needs to predict the effect of environmental change on waterborne disease include the following points adapted from Ford et al. (2009):

- increased knowledge of disease incidence and pathogen loading
- characterization of pathogen sources and reservoirs
- monitoring of indicators to gather source, transport, and exposure information
- more quantitative data for risk assessment, and
- better health surveillance data.

5.7 FUTURE WORK

Over the last several decades, various global environmental changes have threatened the progress of public health. There have been extensive changes in land use, migration, freshwater quality and availability, and population composition, all of which have the potential to influence disease patterns. However, the adverse effects of climate change have the potential to outweigh all the others. Under current climate models, mean temperatures are predicted to increase by at least 4°C and mean precipitation patterns will become more variable, with extreme events occurring more frequently in much of the world. For centuries, climate has been linked to disease and human migration. As a result, migration is increasingly being placed in the context of human vulnerability to climate change (McLeman and Hunter 2010).

Predicted changes in climate, coupled with shifts in land use and population, will significantly decrease the availability and access of freshwater (Lankao 2010). These changes are likely to increase the risk of waterborne disease. The overall impact, however, will depend on the socio-environmental characteristics, or vulnerability factors, that determine an individual's susceptibility to disease and a community's ability to respond.

A better understanding of how climate-related risks vary by location and how population characteristics similarly vary is critical to identifying high-risk areas and populations. Such information can inform the design of effective adaptation strategies and public health programs with the goal of reducing both exposure to potential climate-related risks and the associated health outcomes.

Environmental parameters measured by remote satellite imaging show the greatest promise for providing global coverage of changing environmental conditions, satellite imaging may be critical for effective disease prediction and thus future mitigation of epidemic and pandemic diseases (Ford et al. 2009). The best opportunities to adapt to climate change are linked with actions that address the underlying causes of vulnerability (Hardoy and Romero Lankao 2011). Environmental health research has an obligation to better define the risks posed by climate-related hazards around the world. There is a unique opportunity for environmental health scientists, as we straddle the line between basic and applied research, to improve the capacity for multidisciplinary research while developing more integrated public health programs in response to climate change.

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Appendix

Impacts of Climate Change on Public Health in India: Future Research Directions

2. ABSTRACT

Background: Climate change and associated increases in climate variability will likely exacerbate global health disparities. More research is needed, particularly in developing countries, to accurately predict the anticipated impacts and inform effective public health interventions.

Objectives: Building on information presented at the 2009 Joint Indo-US Workshop on Climate Change and Health in Goa, India. We reviewed relevant literature and data, addressed gaps in knowledge, and identified priorities and strategies for future research in India.

Discussion: The scope of the problem in India is enormous, based on the potential for climate change and associated climate variability to exaggerate endemic malaria, dengue, yellow fever, cholera and Chikungunya, as well as chronic disease, particularly amongst the millions of people who already experience poor sanitation, malnutrition and a shortage of drinking water. On-going efforts to study these risks were discussed but remain scant. A universal theme of the recommendations developed was the importance of improving the surveillance, monitoring and integration of meteorological,

environmental, geospatial, and health data while working in parallel to implement adaptation strategies.

Conclusions: It will be critical for India to invest in improvements in information infrastructure that promote interdisciplinary collaborations while developing adaptation strategies in response to climate change. This will require unprecedented levels of collaboration across diverse institutions in India and abroad. The data can be used in research on the anticipated impacts of climate change on health that reflect India's diverse climates and populations. Local human and technical capacity for risk communication must also be enhanced.

2.1 INTRODUCTION

2.1.1 Climate change and human health

Although low-and middle-income countries are responsible for only a small percentage of global greenhouse gas emissions, the adverse health effects associated with climate change will likely fall disproportionately on their populations. This inequity will further exacerbate global health disparities (McMichael et al. 2003; Patz et al. 2007; Patz and Olson 2006; Wiley and Gostin 2009). High-risk areas include those already experiencing a scarcity of resources, environmental degradation, high rates of infectious disease, weak infrastructure, and overpopulation (Patz et al. 2005). In particular, tropical regions will experience significant changes in human-pathogen relationships because of climate change (Sattenspiel 2000). Changing temperatures and precipitation patterns linked to climate change will further affect health by changing the ecology of various vectorborne diseases such as malaria, dengue, chikungunya, Japanese encephalitis, Kala Azar and filariasis (Bhattacharya et al. 2006; Dhiman et al. 2008). Vulnerable populations include the elderly, children, urban populations, and the poor (Ebi and Paulson 2010; O'Neill and Ebi 2009).

The goals of this report are to briefly summarize relevant literature and highlight the enormous challenges and opportunities for innovative research, with a particular focus on India. Such research is needed to pave the way for unique and pioneering solutions that can improve public health in the face of increasing climate variability. Therefore, we will review the current state of the science relevant to the 2009 Joint Indo-U.S. Workshop on Climate Change and Health that was held in Goa, India and then discuss the observed relationships between climate variability and human health, specifically in relation to the Indian subcontinent, concluding with ideas for future research.

Potential health impacts discussed at the Goa Workshop fell into three categories: heat stress and air pollution, waterborne disease, and vectorborne disease focusing on malaria. Additional crosscutting sessions covered climate modeling for India, adaptation and vulnerability, surveillance and early warning systems, integration of spatial analysis, and bridging policy and science. We acknowledge that the potential physical and social impacts of climate change in India will likely be diverse and that many additional important factors were not considered in our Workshop, such as food yields, malnutrition, child growth, river flow, monsoon rain patterns, and freshwater availability. Nevertheless, we believe the Goa Workshop served to target many of the major public health concerns associated with climate change and began the process of conceptualizing research needs and approaches that are integrative and achievable in low- and middle-income countries.

2.2 IMPACTS IN INDIA

2.2.1 The 2009 joint Indo-U.S. workshop on climate change and health

The workshop was held in Goa, India on August 30 – September 2, 2009; it was cosponsored by the University of Michigan's Center for Global Health (CGH), the U.S. Centers for Disease Control and Prevention (CDC)'s National Center for Environmental Health, and the Indian Council of Medical Research (ICMR). Scientists from the co-sponsoring institutions, along with other partners from academia, government, and non-governmental organizations, met under the auspices of the existing Indo-U.S.

Collaboration in Environmental and Occupational Health to discuss the current state of the science, identify gaps in understanding, and outline future research directions related to the human health effects of climate change in India. The focus was prediction and prevention in India and discussions touched on the tremendous opportunities and significant challenges associated with designing, initiating, and conducting research as well as pursuing related public health programming to improve public health infrastructure in the face of climate change.

2.2.2 The scope of the problem and current research

Poverty and baseline vulnerability

Many of the predicted effects of climate change are likely to become a reality in India. India is very diverse - geographically, climatically, and culturally (Figure 2.1, A). It represents 1/6 of the world's population, supported on 1/50 of the world's land and 1/25 of the world's water (Singh et al. 2010). With its huge and increasing population (~1.2 billion) and rate of urbanization, India is undergoing enormous change; climate change poses an overwhelming stressor that will magnify existing health threats. A greater understanding of the relationship between climate variability and human health in a country such as India could aid in the development of new prevention strategies and early warning systems, with implications throughout the developing world. Future studies must work to more explicitly define the relationship between climate variability and emerging/re-emerging infectious diseases such as dengue, yellow fever, cholera, and chikungunya (Shope 1991), as well as chronic diseases related to cardiovascular and respiratory illness, asthma, and diabetes. Millions of people below the poverty line and those in rural areas represent high-risk populations who are exposed to myriad health risks including poor sanitation, pollution, malnutrition, and a constant shortage of clean drinking water. However, as awareness and public health infrastructure increase, the burden of climate-related diseases may be negated (Dhiman et al. 2010).

Waterborne infectious disease

The burden of waterborne disease in India is enormous (Figure 2.1, Panel B). However, estimates vary widely because of a lack of reporting, poor surveillance, and minimal data infrastructure. A report from the Ministry of Health and Family Welfare estimates that nearly 40 million people are affected by waterborne disease every year, which places a large burden on both the health sector and the economic sector. As a consequence, there are approximately 73 million lost work days or $600 million lost dollars each year (Mandal 2008). Although the WHO estimates that 900,000 Indians die each year from drinking contaminated water and breathing polluted air (WHO and UNICEF 2000), the Indian Ministry of Health estimates 1.5 million deaths annually among 0- to 5-year-old children. Cholera provides a specific example with approximately 600,000 cases reported by the WHO, but 3 to 5 million cases estimated by Zuckerman et al. (2007). Approximately 73% of the rural population in India does not have proper water treatment and 74% do not have sanitary toilets (International Institute for Population Sciences and Macro International (IIPS) 2007). Freshwater availability in India is also a concern; available water is expected to decrease from 1,820 m^3 per capita to less than 1,000 m^3 by 2025 because of the combined effects of population growth and climate change (Intergovernmental Panel on Climate Change 2007).

Research in this area must be both temporally and spatially specific. Furthermore, it requires local monitoring of the appropriate climate and disease variables (Patz et al. 2002) because underreporting impedes the development of effective prevention strategies. It is critical to build a data infrastructure and conduct such research in India so that regional-specific models based on climate and health can be developed. A systems approach focusing on health outcomes is critical to the success of future research in this area (Batterman et al. 2009). As predictive models improve, region-specific action plans and adaptation strategies can be developed.

Heat stress and air pollution

The summer of 2010 was the hottest summer on record in India with temperatures approaching 50˚C (122˚F); the effects were far-reaching including hospitalization because of heatstroke, the suffering of livestock, and severe drought in some regions that affected health as well as agriculture (Burke 2010). Research linking temperature and health effects in India is sparse. However, in a study of 12 international urban areas that included Delhi, McMichael et al. (2008) found a 3.94% (95% CI: 2.80-5.08%) increase in mortality for each 1˚C increase above 29˚C. Hajat et al. (2005) reported that individuals 0-14 years old had greater vulnerability to temperature increases in Delhi than did those 15-64 years old or in the ≥65 year-old age group. These findings are in direct contrast with results from cities in Europe and the United States, that consistently identify the elderly as the most vulnerable age group. Hajat et al. (2005) also found that harvesting (whereby increases in mortality on one day are followed by substantial decreases in mortality in subsequent days) accounted for almost all temperature-related mortality in

London, whereas in Delhi, the increase in mortality due to high temperatures was not followed by an immediate drop in mortality. This suggests that in Delhi, individuals who died on days with higher temperatures were not already near death.

Limited work has been conducted on the combined effects of weather, climate variability, and increased air pollution in India (Agarwal et al. 2006; Karar et al. 2006). One study that investigated the effects of air pollution on respiratory disease found that emergency department visits increased by approximately 20% because of high levels of pollutants in Delhi (Pande et al. 2002). In a second study based in Chennai, India, Ghosh et al. (2010) concluded that short-term exposure to particulate matter (PM_{10}) resulted in an estimated risk ratio of 1.0044 (95% confidence interval: 1.002, 1.007) per a 10 $\mu g\ m^{-3}$ increase in daily average PM concentrations; this risk estimate is comparable to similar estimates from other countries. An important contribution of this study, relevant to other low- and middle-income countries, was the development of new methods to address specific limitations of routinely collected data such as missing measurements and small footprints of air pollution monitors, but the link to temperature remains to be explored. Some work has been done on seasonal air quality monitoring (Pulikesi et al. 2006), however, the relationship of temperature, ozone, and health requires further investigation (Doherty et al. 2009). Indoor air pollution presents yet another major health threat, with 32% of deaths in South Asia attributable to the burning of solid fuels in poor, small, unventilated houses (Smith 2000, WHO 2004). Whether these health risks will be exacerbated as a result of climate change is yet to be determined, but co-benefit interventions aimed at reducing the health impacts associated with indoor air pollution, decreasing the release of green house gases from the burning of solid fuel, and preventing deforestation by introducing alternative, more efficient stoves and fuels will have positive implications for health and society.

Vectorborne disease

India has approximately 2 million confirmed cases of malaria per year (Kumar et al. 2007). Like most infectious diseases, prevalence varies by region (Figure 2.1, Panel C and D). Although WHO concludes that approximately 15,000 individuals die from malaria each year in India (WHO 2008), a recent study by Dhingra et al. (2010) estimates approximately 200,000 malaria deaths per year in India before 70 years of age and 55,000 in early childhood. As Dhingra et al. (2010) suggest, accurate estimation of malaria mortality in India is difficult because correctly diagnosed episodes are successfully treated and do not result in death; in fatal cases without medical intervention malaria is easily mistaken for some other life-threatening fever; and in most rural areas where death from malaria is common, proper medical attention at the time of death is rare. These challenges, which hold true in many low- and middle-income countries, make it difficult to use hospital-based data to assess the association between climate variability and malaria, as disease burden may be vastly underestimated.

In India, 65% of malaria cases are reported from six regions (Orissa, Jharkhand, Madya Pradesh, Chattsgarh, West Bengal and the North East). In Orissa, the disease has much more serious proportions than even in sub-Saharan Africa (Narain 2008). A 2001 WHO report estimated the disability adjusted life years lost because of all vectorborne diseases in the country to be 4.2 million, and malaria is believed to account for nearly half of this (Dash et al. 2008). The emergence and rapid spread of drug resistant strains of malaria further compound the problem. Chloroquine used to be the drug of choice for all kinds of malaria and was highly prescribed in India until 1973 when resistance was detected in *Plasmodium falciparum*. Chloroquine is no longer as effective, with increasing reports of *Plasmodium vivax* developing resistance (Dash et al. 2008). In addition, the use of chloroquine, which selects against *P.vivax*, has allowed *P. falciparum* to become the dominant parasite (Singh et al. 2004), a pattern with important epidemiological consequences, as it is the most virulent form of malaria in the region.

In arid and semi-arid regions of India, where malaria is epidemic, rainfall variability has been shown to drive the inter-annual variability of the disease (Akhtar and McMichael 1996; Bouma and van der Kaav 1994; Laneri et al. 2010) and was the basis of one of the first early-warning systems for the disease in this region. Evidence suggests rainfall variability plays an important role and that a long-term trend in increasing temperature during the 20th century is sufficient to significantly increase the abundance of vectors (Pascual et al. 2009). Monthly parasite incidence was positively correlated with temperature, precipitation, and humidity (Devi and Jauhari 2006). The implications of this association as it relates to long-term climate change remain an important open question. For other regions of India, monsoonal rains have been linked to an increase in the frequency and magnitude of extreme rain events, whereas the frequency of moderate events has been decreasing with no significant change in the mean in the last fifty years (Goswami et al. 2006). Temperature plays a major limiting role at high altitudes preventing epidemic malaria from reaching the highest altitudes. The consequence of climate change in highland regions in northern India is another important open question, especially given the predictions of increasing temperatures in these regions (Beig 2009).

Little is known about the influence of climate variability or climate change on the prevalence of malaria in Indian urban areas (Kumar et al. 2007). The issue of urban malaria becomes even more important when considering the rapid expansion of the urban and periurban environments, water storage techniques, and rising poverty levels.

2.2.3 The need for adaptation

Although adaptation to climate impacts has attracted substantial attention recently, the effectiveness of specific strategies in relation to greater resilience of public health systems remains under-investigated. Adaptating to climate change will be necessary and will occur at physiological, behavioral, social, institutional, and organizational scales. To take advantage of already ongoing adaptations for creating more effective public health responses to climate change impacts, – especially for poor rural communities whose access to healthcare is extremely limited even in the current policy environment – developing a baseline understanding of the region-specific demographic, social and ecological determinants of health will be necessary. In designing public health responses, factors that must be considered include the population's age structure, socio-economic profile, baseline prevalence of climate-sensitive diseases, public awareness of risk, the built environment, existing infrastructure, available public health services, and autonomous responses to climate impacts on health that households and communities might undertake by themselves (McMichael 2004). Furthermore, adaptation strategies in response to climate variability and change must be designed on specific temporal and spatial scales relevant to India. Taking steps now to adjust to current climate variability and modifying existing programs to address the anticipated impacts of climate change will make future adaptation strategies more effective (Ebi et al. 2006). The same changes may also aid in reaching additional environmental and social objectives, such as more equitable education, empowerment of women, and improved sanitation. These community-based initiatives should be complemented by government interventions. A variety of stakeholders, including those who will be affected most by climate change impacts, must be involved in the problem solving process to enhance human and technical capacity across sectors at both local and national levels (Agrawal 2009; Ebi and Semenza 2008). Failure to invest now will likely increase the severity of consequences in the future (Haines et al. 2006).

Potential adaptation strategies in India could focus on controlling infectious diseases by removing vector breeding sites, reducing vector-human contact via improved housing, coordinating monitoring of mosquitoes, pathogens and disease burden. Another potential focus area for adaptation could be improving sanitation and drinking water by supporting inexpensive and effective water treatment, and increasing rainwater harvesting, safe storage, and grey-water reuse. In some areas, the focus may shift to flood, heatwave, and emergency preparedness including strategies to address the additional risks placed on displaced populations from these and other climate-related hazards. One possible outcome could be the development of an integrated early warning system, emergency response plan and refugee management plan, along with increased capacity to provide shelter, drinking water, sanitation, and sustainable agricultural products to the most vulnerable populations.

2.2.4 Current surveillance and data sources

Successful work in this area requires that the health sector partner closely with climate scientists and development professionals to move beyond the assessment of climate variability and disease-outcomes to predictive models accounting for climate change to facilitate targeted adaptation. Partnerships with both the government and non-government sector will also be necessary. An integrated disease surveillance system already exists under the Director General of Health Services (DGHS); any new work on climate change and health should be linked to the already existing system. The Energy and Resources Institute (TERI) in Delhi, India is one example of such a group linking research and action by increasing awareness within India and sharing the ‘developing country’ perspective on climate change with the rest of the world. Activities at TERI range from operating as a think tank at the local level to forging global alliances for collaborative research. Collaborative work is also being conducted at the National Institute of Malaria Research in partnership with Mercedes Pascual at The University of Michigan to assess the impacts of climate change on malaria and dengue at a national scale as well as short-, medium-, and long-term adaptation strategies. In addition, this same partnership is developing an evidence-based assessment of biophysical determinants of malaria in the northeastern states of India and a framework for adaptating measures for malaria control under climate change scenarios. Several other non-governmental organizations are working on climate change in India such as the Local Governments for Sustainability (ICLEI) with a regional office in New Delhi, Resources for the Future, which is partnering closely with the Public Health Foundation of India, and Toxics Link, which is working on traditional environmental health with a new focus on climate change.

Retrospective studies investigating climate variability and health dominate the literature, leaving predictive and prospective studies related to climate change open to be explored. However, both prospective and retrospective studies rely on high-quality data. Working groups at the Goa Workshop were able to identify existing and relevant long-term data sets that can be used for environmental epidemiological analysis. For example both the Indian Institute of Tropical Meteorology (IITM) and the India Meteorological Department (IMD 2010) have useful meteorological data with varying degrees of access. Additional government surveys such as the Census of India and the National Family Health Survey, India provide important information on social and economic variables. In some cases, individual investigators have accessed government hospital datasets and have daily all-cause mortality, albeit over a limited geography. The same goes for air pollution data, such as data on particulate matter (PM), which have been accessed at certain locations of interest such as Chennai (Ghosh et al. 2010). The use of exposure and emission models can help to fill in where air pollution data are missing, however, consistent monitoring of PM, ozone, and nitrogen oxides over a greater geographic area is needed. In cases where the data already exists, more work is needed to identify and access this type of long-term data, creating uniform repositories. In cases where it does not exist, surveillance and monitoring of relevant variables will be critical to the success of future-prospective climate and health research endeavors. Furthermore, regional climate models for India such as PRECIS (Providing Regional Climates for Impacts Studies) developed at the IITM must be integrated with health data if we are going to transition away from surveying the health effects associated with climate variability to predicting the effects of climate change.

Changes to the current information infrastructure needed for this effort will depend on new or enhanced collaborations across multiple disciplines and among diverse institutions. Given the region-specific nature of the relationship between climate variability and health, further research is required throughout India. Satellite and geospatial technology may provide new insights regarding the geographic distribution of risk and disease. Integration of social, demographic, and land cover data with health data will aid in describing a holistic health scenario, which will help identify sustainable health solutions. These research needs and methodological limitations are relevant to many low- and middle-income countries. India, with its current health infrastructure and large population, can serve as an important natural laboratory for developing relevant strategies for promoting and managing climate-health research in many parts of the world.

2.3 RECOMMENDATIONS

2.3.1 Environmental monitoring and surveillance

There is a great need to improve environmental monitoring and surveillance systems in low- and middle-income countries such as India. New research initiatives should focus on collecting high-quality, long-term data on climate-related health outcomes with the dual purpose of understanding current climate-health associations and predicting future scenarios. Health outcomes of interest, for which such data should be collected, include total morbidity and mortality, non-communicable diseases such as cardiovascular-, respiratory-, and circulatory-diseases, and asthma, as well as infectious diseases such as cholera, malaria, TB, typhoid, hepatitis, dysentery, tick borne encephalitis, and other vectorborne and waterborne diseases. Such monitoring also requires the collection of appropriate climatic (e.g. temperature and precipitation) and non-climatic data (e.g. ozone). Surveillance of extreme weather conditions and risk indicators such as mosquito abundance or pathogen load is also necessary. Such data gathering should occur in conjunction with already existing public health programs and health centers. Where the necessary public health infrastructure does not exist, the anticipated risks associated with climate change, should motivate international action to build such infrastructure. The collection of such diverse data necessitates the creation of linkable and documented repositories for meteorological, air pollution, and health data. Such a virtual network, or clearinghouse, will help researchers as well as practitioners as they work towards defining climate-health associations and designing effective interventions. Such monitoring provides the information and feedback necessary to take action in response to the anticipated changes in climate and expected burden on the public health infrastructure.

2.3.2 Geospatial technology

Geographic information systems and spatial analysis must be further developed; they are very useful tools when conducting vulnerability assessments, assessing environmental exposures, prioritizing research, and disseminating findings to decision-makers and the public alike (Jerrett et al. 2010). Remote sensing and environmental monitoring are particularly useful to catalog variables such as air pollution and heat exposure. Social data from census and surveys, which can be layered with the exposure data using geographic information systems provide information on sensitivity and adaptive capacity, at both the individual and community levels. Data on land use and land cover can provide additional information on relevant environmental factors that influence risk and vulnerability.

Such a spatial information infrastructure provides the necessary data-integration framework to combine information on human-environment interactions from a variety of sources. Vulnerability assessments can be conducted spatially and temporally through integration of such social and environmental data. Risk maps can incorporate social and ecological risk factors in an attempt to characterize the existing spatial heterogeneity. This is a very effective tool when predicting prevalence, targeting resource distribution, and designing control programs for different infectious diseases such as malaria (Ageep et al. 2009; Haque et al. 2010; Reid et al. 2010; Tonnang et al. 2010). An example of such work, which grew out of the Goa Workshop, will focus on the effect of socio-economic status on the association between climate and malaria.

2.3.3 Human and technical capacity

For these new surveillance methods and analytical techniques to be effective, countries like India will need to enhance their human and technical capacity for risk communication. This could take the form of public education on climate change and associated health impacts to enhance awareness, and to influence lifestyle, behavior, and individual choices to protect and improve health. Such health promotion materials could manifest as low-tech flyers and advertisements as well as more high-tech materials including web- and mobile-phone based alerts. On the other end of the spectrum, developing capacity could take on a more holistic approach, such as region and city-specific climate action plans and early warning system for heat stress events, droughts, hurricanes, and floods.

2.4 CONCLUSIONS

Studies of climate variability and human health indicate a great deal of heterogeneity in the reported associations. This heterogeneity is partially due to differences in study design, but climatic and socioeconomic differences that vary by location also influence the burden of disease. It is not clear if results from one region can be extrapolated to others. Therefore, it is important to develop a comprehensive catalog of climate-related changes and associated health outcomes across the range of environments and populations likely to be affected. A better understanding of the effects of climate change on health in India will be best achieved through studies specific to climates and populations in India.

In 2008 India developed the National Action Plan on Climate Change promising further enhancement of ecological sustainability as part of India's development path, signaling their involvement in the international discussion on climate change. Countries like India have a tremendous opportunity to guide our future trajectory regarding sustainable development and adaptation to climate change, but it will take the combined effort of policy makers and scientists from around the world to address the complex challenges associated with climate change and human health.

In conclusion, innovative, multi-disciplinary investigations using environmental epidemiologic methods to elucidate health risks posed by climate change and associated climate variability in regions such as India are possible. However, such work will require expanded partnerships among researchers, governments and communities to develop a co-benefit strategy that addresses public health challenges and risks associated with climate change. Adoption and implementation of these research initiatives will provide the necessary tools and infrastructure to pose interesting scientific questions and design effective solutions to the complex issues imposed by climate change.

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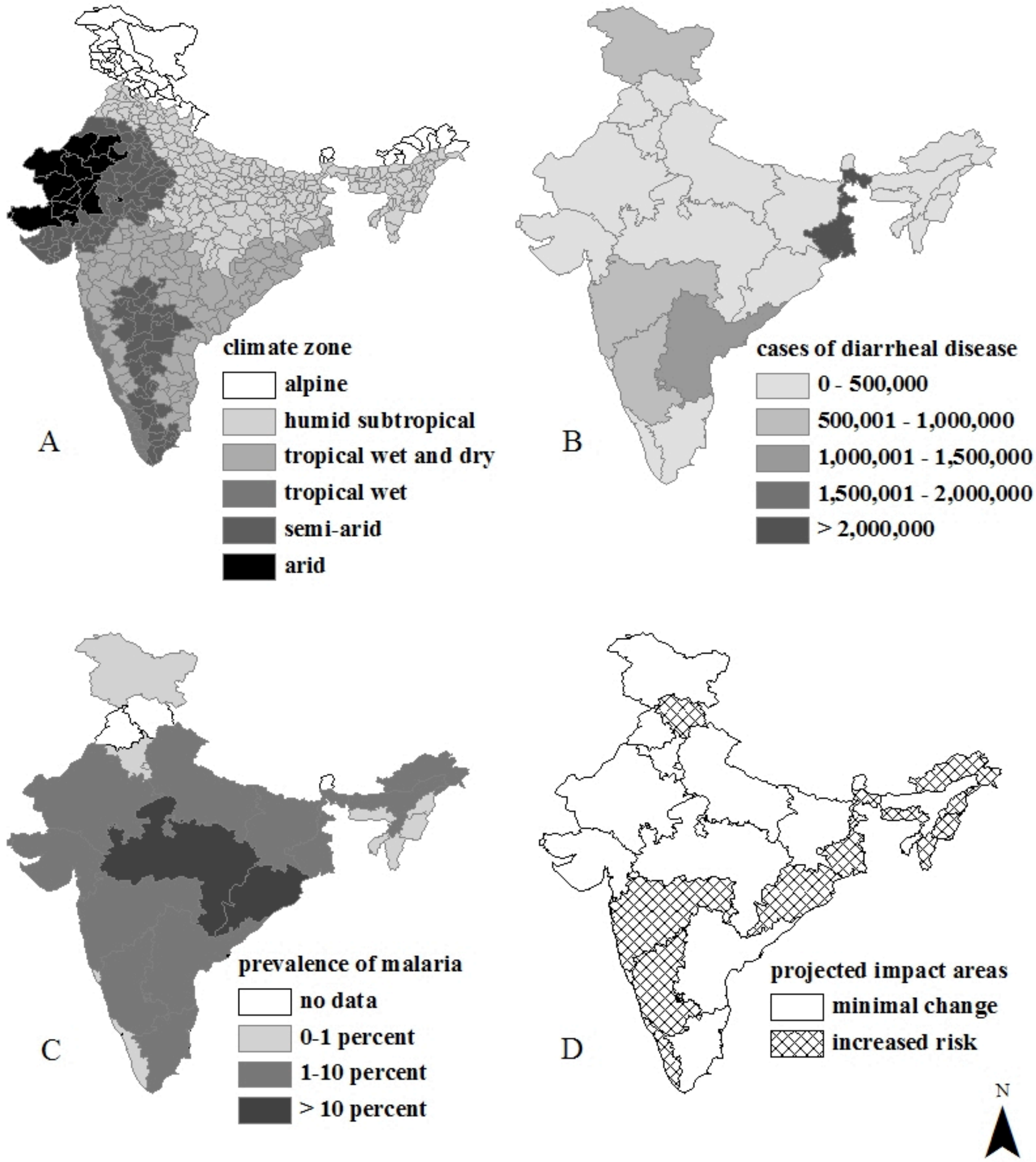

Figure 2.1 Interactions between climate and health in India: A) Climate zones in India based on the Köppen classification demonstrating the diversity of climates that exist in India, B) State-specific estimates of diarrheal disease cases across India in 2006, C) Regional estimates of malaria prevalence across India in 2002, D) Regions in India where the prevalence of malaria is predicted to increase because of changes in climate. Panel A is adapted from WikiProject India Maps and is licensed under a Creative Commons Attribution-Share Alike 3.0 license (http://creativecommons.org/licenses/by-sa/3.0/). Panel B is adapted from Mandal 2008. Panels C and D are adapted from Bhattacharya et al. 2006.

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