



Published in final edited form as:

Sci Total Environ. 2022 February 25; 809: 151108. doi:10.1016/j.scitotenv.2021.151108.

Hurricane Flooding and Acute Gastrointestinal Illness in North Carolina

Arbor J.L. Quist¹, Mike Dolan Fliss², Timothy J. Wade³, Paul L. Delamater⁴, David B. Richardson⁵, Lawrence S. Engel⁵

¹Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA 90032, USA

²Injury Prevention Research Center, University of North Carolina, Chapel Hill, NC 27514, USA

³Public Health and Environmental Systems Division, United States Environmental Protection Agency, Chapel Hill, NC 27514, USA

⁴Department of Geography, University of North Carolina, Chapel Hill, NC 27514, USA

⁵Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC 27599, USA

Abstract

Hurricanes often flood homes and industries, spreading pathogens. Contact with pathogen-contaminated water can result in diarrhea, vomiting, and/or nausea, known collectively as acute gastrointestinal illness (AGI). Hurricanes Matthew and Florence caused record-breaking flooding in North Carolina (NC) in October 2016 and September 2018, respectively. To examine the relationship between hurricane flooding and AGI in NC, we first calculated the percent of each ZIP code flooded after Hurricanes Matthew and Florence. Rates of all-cause AGI emergency department (ED) visits were calculated from NC's ED surveillance system data. Using controlled interrupted time series, we compared AGI ED visit rates during the three weeks after each hurricane in ZIP codes with a third or more of their area flooded to the predicted rates had these hurricanes not occurred, based on AGI 2016–2019 ED trends, and controlling for AGI ED visit rates in unflooded areas. We examined alternative case definitions (bacterial AGI) and

CORRESPONDING AUTHOR: Arbor J.L. Quist, arborqui@usc.edu, 2001 N Soto St, Los Angeles, CA 90032.

CRedit Author Statement

Arbor J.L. Quist: Conceptualization, methodology, software, formal analysis,

Mike Dolan Fliss: Methodology, software, writing – review and editing

Timothy J. Wade: Supervision, writing – review and editing

Paul L. Delamater: Supervision, writing – review and editing

David B. Richardson: Methodology, writing – review and editing, supervision

Lawrence S. Engel: Methodology, supervision, writing – review and editing

The authors declare they have no actual or potential competing financial interests.

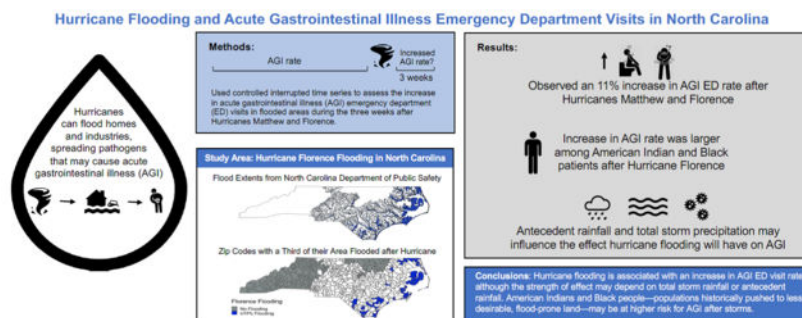
Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

effect measure modification by race and age. We observed an 11% increase (rate ratio (RR): 1.11, 95% CI: 1.00, 1.23) in AGI ED visit rates after Hurricanes Matthew and Florence. This effect was particularly strong among American Indian patients and patients aged 65 years and older after Florence and elevated among Black patients for both hurricanes. Florence's effect was more consistent than Matthew's effect, possibly because little rain preceded Florence and heavy rain preceded Matthew. When restricted to bacterial AGI, we found an 85% (RR: 1.85, 95% CI: 1.37, 2.34) increase in AGI ED visit rate after Florence, but no increase after Matthew. Hurricane flooding is associated with an increase in AGI ED visit rate, although the strength of effect may depend on total storm rainfall or antecedent rainfall. American Indians and Black people—historically pushed to less desirable, flood-prone land—may be at higher risk for AGI after storms.

Graphical Abstract



Keywords

floods; hurricanes; interrupted time series analysis; gastrointestinal illness; environmental epidemiology; disaster epidemiology

INTRODUCTION:

Hurricanes can be deadly, traumatizing, and can impair human health (An et al. 2019; Curran et al. 2018; Waddell et al. 2021). In addition to immediate injuries, heavy rain and flooding increase pathogen transport and can cause illness when contaminated water is ingested or comes in contact with the skin or eyes (de Man et al. 2016; Levy et al. 2016; Yu et al. 2018). Flooding of wastewater treatment facilities, sewage systems, animal waste management systems, and hazardous waste sites can release chemicals and pathogens, thus contaminating floodwater, soil, groundwater, and surface waters that are sources for domestic and municipal drinking water (Humphrey et al. 2019; Laner et al. 2009). Contact with waterborne pathogens can cause acute gastrointestinal illness (AGI), defined as diarrhea, vomiting, or nausea that often occur with abdominal pain or fever (Roy et al. 2006). Diarrheal diseases are a leading cause of death worldwide, causing 1.3 million deaths annually, including half a million deaths among children under five years of age (Global Burden of Diarrhoeal Diseases Collaborators 2017). While rates of AGI-related deaths are much lower in the United States (US), where there are approximately 0.65 AGI episodes/person-year, children and older adults remain disproportionately affected, and

environmental exposures can increase risk of AGI (Colford et al. 2006; Messner et al. 2006; Roy et al. 2006). AGI can encompass a range of enteric illnesses caused by various viruses, bacteria, and protozoa, as well as non-infectious agents (Roy et al. 2006). Surface waters have been found to have higher concentrations of *Escherichia coli*, enterococci, *Salmonella*, *Campylobacter*, *Giardia*, and *Cryptosporidium* after extreme rainfall and flood events, and may cause AGI 1–14 days after exposure (Atherholt et al. 1998; Bergholz et al. 2016; Jiang et al. 2015; Nguyen et al. 2017; Soneja et al. 2016; Yard et al. 2014). Prior studies suggest that severe flooding—which often occurs during and after hurricanes—may be associated with AGI, especially in people who come in contact with floodwater (de Man et al. 2016; Ding et al. 2013; Levy et al. 2016; Lin et al. 2015; Reacher et al. 2004; Schnitzler et al. 2007; Wade et al. 2004, 2014). However, very few studies have examined the effect of hurricane flooding on AGI in North Carolina (NC), the third most hurricane-prone US state, and few studies have assessed racial disparities of AGI (Layock and Choi 2020; Setzer and Domino 2004).

In the eastern US, heavy precipitation events have risen over the past 30 years, with autumns becoming wetter (Carter and Jones 2014). Sixteen hurricanes have made landfall in NC in the last 30 years, and heavy precipitation events are expected to increase in the future due to the warming climate (Carter and Jones 2014; North Carolina Climate Office). NC is an especially important place to examine the effects of flooding as a third of its residents (approximately 3.3 million, far more than most states) obtain their drinking water from household wells or other small residential water systems, which stand at higher risk of contamination than community water supplies (DeFelice et al. 2016; Johnson and Belitz 2017; Maupin et al. 2014). The estimated cost of AGI-related emergency department (ED) visits in NC due to microbial contamination in drinking water exceeds 40 million US dollars annually (DeFelice et al. 2016).

There are a number of reasons to expect that hurricane-related flooding may increase pathogen transport and AGI rate in eastern NC. Many residents in eastern NC use private well water. As the second leading hog producer in the US, NC houses 9 million hogs, which are mainly concentrated in its hurricane-prone eastern region (North Carolina Agricultural Statistics 2017; Hogs Inventory in North Carolina 2020). These hogs, nearly as many as total statewide human residents, generate more fecal waste than the entire statewide human population, and this waste is concentrated into less than 4,000 feces lagoons (Environmental Working Group & Waterkeeper Alliance 2016). Hurricanes that hit NC may flood these lagoons, transporting fecal bacteria that may cause AGI into nearby waterways (Wing et al. 2002). The intersection of hog farms and flooding creates layered environmental and climate justice issues, as these industrial hog operations are disproportionately located near racial minorities and low-income populations and in flood-prone areas (Wing and Johnston 2014; Wing et al. 2002).

Hurricane Matthew (October 2016) and Hurricane Florence (September 2018) were the two largest, deadliest, and costliest hurricanes to strike NC in the past 15 years. Both Category 1 storms upon reaching NC, Hurricanes Matthew and Florence led to the loss of 25 and 40 lives in NC, respectively, and cost \$1.5 billion and \$22 billion, respectively, in NC alone (Stewart and Berg 2019; Stewart 2017). Hurricane Florence was the wettest cyclone

recorded in NC, dropping 8 trillion gallons of water statewide in one week and drenching parts of the state with up to 36 inches of rain (Guterl et al. 2018). The maximum rainfall in NC from Hurricane Matthew was 19 inches. However, Hurricane Matthew occurred only five weeks after heavy rain (up to 13 inches) from Hurricane Hermine and nine days after episodes of severe heavy rain (up to 10 inches) and flooding across central and eastern NC, which compounded the damage due to waterlogged soil (PRISM Climate Group). Hurricanes Matthew and Florence broke high water records on numerous NC rivers and flooded many of the same areas in eastern NC (Stewart and Berg 2019; Stewart 2017).

While many studies have examined the association of precipitation, heavy precipitation, and flooding on AGI, very few (4 of the 40 flooding articles reviewed by Levy *et al.*, 2016) have examined the extreme flooding caused by hurricanes (Centers for Disease Control and Prevention (CDC) 2000; Chhotray et al. 2002; Levy et al. 2016; Setzer and Domino 2004). This is the first study, to our knowledge, to examine the increase in all-cause AGI ED visit rate in flooded areas during the weeks after hurricane flooding in NC. This paper investigates how the relationship between hurricane flooding and AGI ED visit rate varies in areas with different amounts of flooding, during different flood exposure periods, and among different age and racial groups. As two major hurricanes—Matthew and Florence—struck NC within two years, this study examines and compares the effects of different hurricanes on AGI ED visits.

METHODS:

Study Population

This study examines the AGI ED rate among NC residents in 2016–2019 and the change in AGI ED rate after Hurricanes Matthew and Florence. Cases include NC residents who visited a NC ED during the study period and had an AGI-related diagnosis code. As the finest resolution of statewide AGI data available was at the ZIP code level, all analyses were conducted at this level.

Exposure

We used Hurricane Matthew and Hurricane Florence flood extent data from the NC Department of Public Safety (DPS). These flood extents were based on effective and preliminary flood maps, observed rainfall, storm surge, Flood Inundation Mapping and Alert Network (FIMAN) flood gauges, and photographs. We calculated the percent of area that each ZIP code was flooded during Hurricanes Matthew or Florence using their respective flood extents and the 2017 ZIP code boundaries. For analysis purposes, a ZIP code was categorized as flooded if one third or more of its area was flooded. We chose this cut point because it enabled us to focus on heavily flooded ZIP codes and provided enough AGI cases for sub-analyses.

Outcome

Acute gastrointestinal illness (AGI) was measured using data from the North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), a public health surveillance system containing records of all civilian ED visits to hospitals in NC. We

tabulated the daily number of AGI cases at the ZIP code-level of patients' billing address, the ZIP code being the finest geographic level of information available for cases. Diagnostic codes (International Classification of Diseases, Tenth Revision; ICD-10) were used to identify intestinal infectious illness (A00-A09), unspecified noninfectious gastroenteritis and colitis (K52.3, K52.89, K52.9), diarrhea (R19.7), and nausea and vomiting (R11.10-R11.12) as AGI ED visits. Similar diagnosis codes have been used in other studies of flooding and AGI (DeFelice et al. 2016; Drayna et al. 2010; Wade et al. 2014). Although many *Clostridium difficile* infections (A04.7) are acquired in hospitals rather than through exposure to contaminated water, we included *C. difficile* infections in our AGI definition because some *C. difficile* infections in humans have been linked to pigs and because a recent study found an association between flooding and an increase in *C. difficile* hospital visits (Keessen et al. 2013; Lin et al. 2015). Our main analyses focused on the occurrence of ED visits for AGI during a three-week period after the hurricanes because there may be a lag between water contamination and exposure to the contaminated water, because flooding from Hurricanes Matthew and Florence lasted about a week in some areas, and because most of the pathogens in floodwater that can cause AGI have at most a two-week incubation period.

Covariates

To examine effect measure modification (EMM), we used individual-level covariates on patients' race, ethnicity, age, and health insurance status, and we used area-level covariates for rurality and well water usage. The 2015 U.S. Geological Survey estimated the number of people in each county who use private well water, and we used this data to create ZIP code-level well water usage estimates (Dieter et al. 2018). Patients were categorized as "White non-Hispanic" if their reported race in the ED data was White and they were not reported to be Hispanic. We were able to separately analyze White non-Hispanic, Black, and American Indian patients, but due to insufficient case counts during the three weeks after the hurricanes, we combined Asian, Pacific Islander, Hispanic, and Other Race patients into an Other Race category. Rurality was measured using a continuous geographic isolation scale that classifies ZIP codes according to their access to resources; this measure was split into quartiles when examining effect measure modification by rurality (Doogan et al. 2018). Precipitation data was provided from the PRISM Climate Group as 4km-by-4km raster data (PRISM Climate Group), which we transformed into 1km-by-1km point data then aggregated to 2017 ZIP code polygons, assigning the ZIP code the maximum precipitation recorded in the ZIP code for the day. Before conducting models of the effect of hurricane flooding on AGI ED visit rate, we first examined how the weekly precipitation and weekly AGI rate changed over time before and after the hurricanes.

Population at risk

We estimated the full population and stratum-specific population (by age category, race/ethnicity, health insurance status) using the American Community Survey (ACS) five-year estimates for each year during our four-year study period (e.g., the 2012–2016 ACS estimates released in 2017 were used for the 2016 outcome data and the 2014–2018 ACS estimates were used for the 2018 outcome data). These yearly ACS data on age, race, ethnicity, health insurance status, and overall population were available at the block

group-level. Estimates were assigned to the centroids of each 2010 census block within a block group based on the proportion of the block group population within that block. We aggregated these block centroid data to create ZIP code-level population estimates. We did not use census data at the ZIP code tabulation area (ZCTA) level due to the spatiotemporal mismatch between ZCTAs and ZIP codes (Grubestic and Matisziw 2006; Krieger et al. 2002). We examined all changes in ZIP codes from 2016–2019 and assigned all ZIP codes to the 2017 ZIP code polygon they contained.

Statistical methods

We used controlled interrupted time series (CITS) to examine how daily AGI ED visit rates during the three weeks after each hurricane compared to the predicted rates had these hurricanes not occurred, based on AGI ED visits trends in 2016–2019 and controlling for the AGI ED visit rate change in control areas after the hurricanes. We opted not to include earlier outcome data because of changes in hospital reporting over time, with several large changes in 2015 and 2016, and because of the change from ICD-9 to ICD-10 diagnostic codes in October 2015. Between 2016 and 2019, the change in total number of AGI ED visits from year to year was always below 10%; however, the number of AGI ED visits in 2015 was over 20% lower than that of 2016 because of systematic changes in the NC DETECT system, reporting issues, and the addition of some hospitals to NC DETECT in 2016 (NC DETECT Participating Hospitals 2020). These changes created a discontinuity in the quality and comparability of the data over a longer period.

A three-week exposure period—the expected window for any increase in AGI rate—was defined for each hurricane from the day of hurricane landfall in NC (day 1). Each ZIP code was compared to itself over time, which allowed for control of ZIP code-level characteristics that did not change over the four-year period, such as overall sociodemographic factors, healthcare access, rurality, hog density, and nearby pollution sources. We added a control group of unflooded ZIP codes to control for any change in AGI ED visit rate in unflooded areas after each hurricane, thus accounting for potential time-varying confounders.

Separate CITS models were run for each hurricane. To isolate the effect of the large hurricane of interest (Matthew or Florence), we removed from analyses the eight-week periods after other large hurricanes that produced over one foot of maximum precipitation (namely, Hurricanes Hermine, Matthew, and Florence). We excluded a shorter period from analyses if the hurricane of interest occurred less than eight weeks after another large hurricane, as was the case with Hurricanes Hermine and Matthew (see Figure 1). We also excluded the five weeks after the three-week hurricane exposure period as a washout period, as our preliminary results suggested large hurricanes may affect the AGI ED visit rate for up to eight weeks. Nevertheless, the effect diminished over time and we expected that the majority of storm-related AGI cases occurred within three weeks after each hurricane. For example, in the analysis of Hurricane Florence, which struck NC on September 14, 2018, we removed all data from September 3–December 3, 2016 to remove the effects of Hurricanes Hermine and Matthew, as well as October 5–November 9, 2018 as the washout period for Hurricane Florence. Thus, we were able to focus on how the AGI ED visit rate in the three

weeks following Florence (September 14-October 5, 2018) compared to the AGI ED visit rate predicted at this time, without other large hurricanes confounding the effect.

To account for overdispersion in the ED visit data, we used quasi-Poisson models that included indicator variables for the three-week post-hurricane flood period and the flooded ZIP codes, as well as time-control variables for the day of week, month, year, and an interaction between month and year. To estimate the difference in rate during the hurricane flood period between the 33% flooded ZIP codes and the unflooded ZIP codes, we included interaction terms between the flooded ZIP code indicator variable and every other covariate. The model included an offset of the yearly population within each ZIP code (derived from yearly ACS data) to build population-based AGI ED visit rates. We derived estimates using the following equation:

$$\log(\lambda_t) = \beta_0 + \beta_1\text{period} + \beta_2\text{group} + \beta_3\text{year} + \beta_4\text{month} + \beta_5\text{dow} + \beta_6\text{month} * \text{year} + \beta_7\text{group} * \text{month} + \beta_8\text{group} * \text{year} + \beta_9\text{group} * \text{dow} + \beta_{10}\text{group} * \text{period}$$

where $\log(\lambda_t)$ = AGI ED visit rate at time t, period = flood period (pre-flood=0, three-week post-flood=1), group = exposure group (control group/0% flooded=0, flood group/ 33% flooded=1), and dow = day of week. Our effect estimate of interest, β_{10} , represents the difference between the change in the AGI ED visit rate in the control (group=0) and the flooded group (group=1) that is associated with hurricane flooding, based on previous trends. If the rate ratio is above 1, then it can be translated into the percent increase ($[\text{RR}-1]*100$ =percent increase) in AGI ED rate, based on 2016–2019 (i.e., pre-flood) trends and controlling for AGI ED rate changes after the hurricane in unflooded areas (LaMorte 2018). To examine the combined effect of Hurricanes Matthew and Florence, we conducted a random-effects meta-analysis of the rate ratios from the CITS analyses of Hurricanes Matthew and Florence using the DerSimonian-Laird method (DerSimonian and Laird 1986; Jackson et al. 2010).

We also assessed effect measure modification (EMM) on the multiplicative scale using separate product-term interactions between covariates of interest (i.e., age category, race/ethnicity, well water use, health insurance status, and rurality) with the flooded ZIP code indicator variable (group) and the three-week post-hurricane period indicator variable (e.g., group*period*race/ethnicity category). Population offsets were created by taking the logarithm of the full population or stratum-specific population (by age category, race/ethnicity, health insurance status) from the previously described ACS five-year population estimates.

Sensitivity analyses

We conducted sensitivity analyses examining various flood exposure periods (i.e., AGI ED visit rate in the 1, 2, 3, 4, and 5 weeks after each hurricane) and various cut points to classify a ZIP code as flooded (i.e., 20%, 25%, 33%, 40%, 45%, 50% of the ZIP code flooded). We also conducted separate analyses restricted to bacterial intestinal infections and viral intestinal infections, as well as an overall pathogen-specific analysis where the ICD-10 diagnostic codes indicated a specific bacteria, virus, or protozoa (e.g., *Salmonella*,

E. coli, *Clostridium difficile*, Giardia, Cryptosporidiosis, Norwalk agent, Rotavirus; see Supplementary Table 1). To understand the effect of our control on our CITS results, we conducted interrupted time series analyses (ITS, without a control) of the association between various amounts of Matthew and Florence flooding and the change in three-week post-hurricane AGI ED visit rate. We also conducted supplementary ITS analyses of cumulative six-day hurricane-related precipitation and three-week AGI ED rate.

Because Hurricanes Matthew and Hermine occurred five weeks apart and Hermine may have influenced the effect of Matthew, we conducted a sub-analysis where we included AGI data during and after Hermine. As communities are often evacuated before large hurricanes, especially before Hurricane Florence, we also conducted an analysis where we excluded ZIP codes from counties under mandatory evacuation, because many of these people evacuated their homes and were likely not exposed to the flood exposure to which we had assigned them. Lastly, we examined model robustness by comparing the results between quasi-Poisson, Poisson, and negative binomial models for the main analyses (negative binomial models did not converge for most sub-analyses due to the small number of cases). Robust standard errors were used to calculate 95% confidence intervals using the *sandwich* package in R. All analyses were performed in R (Version 3.6.2) (R: A language and environment for statistical computing 2019).

RESULTS:

In 2016–2019, there were 868,691 AGI ED visits in NC by residents with a NC billing ZIP code. Overall, AGI ED visits were driven by seasonal patterns, with the highest number of AGI-related visits during the winter months and lowest number during the fall months (Supplementary Figure 1). During the three weeks after Hurricane Matthew, there were 330 AGI ED visits of patients from NC ZIP codes with a third or more of their area flooded and 368 AGI ED visits of patients from similarly flooded NC ZIP codes after Hurricane Florence. After Hurricane Matthew, 81 ZIP codes experienced 33% flooding and 579 ZIP codes experienced no flooding, while after Hurricane Florence 95 ZIP codes experienced 33% flooding and 367 ZIP codes experienced no flooding, based on the flood extent data from NC DPS (Figure 2). Among all 473 ZIP codes that received any flooding during Hurricane Matthew, the mean percentage of the ZIP code that flooded was 21.1% and the median was 13.3%, compared to Hurricane Florence, in which the mean of the 685 flooded ZIP codes was 16.5% and the median was 8.6%. However, for our main analyses, we excluded flooded ZIP codes with <33% flooding. Areas that flooded 33% during Hurricanes Matthew and Florence were slightly more rural, had a higher hog density and a larger proportion of White non-Hispanics, American Indians, and uninsured residents compared to NC's general population (Table 1). When examining the weekly precipitation and weekly AGI rate over time, we observed higher levels of precipitation and higher AGI ED visit rates in the weeks before Hurricane Matthew in areas that were heavily flooded from Matthew (Figure 3). In comparison, we observed relatively lower levels of precipitation and lower AGI visit rates in the weeks before Hurricane Florence.

We observed a 15% increase in AGI ED visit rate (rate ratio (RR)=1.15, 95% CI: 0.97, 1.32, Table 2) after Hurricane Matthew and a 9% increase in AGI ED rate (RR=1.09, 95% CI:

0.93, 1.24) after Hurricane Florence compared to the expected AGI ED rate based on 2016–2019 trends, controlling for any AGI ED rate changes after the hurricanes in the unflooded areas (Table 2). The CITS pooled rate ratio for Hurricanes Matthew and Florence together, during the three weeks after each hurricane, was 1.11 (95% CI: 1.00, 1.23). When assessing EMM by race, we consistently saw a small increase in AGI ED visit rate among Black patients after both hurricanes compared to the expected rate had there not been a hurricane (Matthew RR=1.09, 95% CI: 0.82, 1.36; Florence RR=1.17, 95% CI: 0.92, 1.41). Among American Indians, we did not observe any increase in AGI ED visit rate after Hurricane Matthew (RR=0.73, 95% CI: 0.21, 1.25), but we observed an 168% increase in AGI ED rate (RR=2.68, 95% CI: 1.96, 3.41) after Hurricane Florence. However, this large increase in AGI ED rate is based on only 34 AGI ED visits in flooded areas during the three weeks after Florence among American Indian patients. The AGI ED visit rate among adults 65 and older increased 9% (RR=1.09, 95% CI: 0.81, 1.38) after Hurricane Matthew and 31% (RR=1.31, 95% CI: 1.06, 1.56) after Hurricane Florence. While the AGI ED rate among children under age 5 increased slightly after Hurricane Matthew, we observed no effect after Hurricane Florence among this group (although the number of cases in these groups was small, n=41 and 35, respectively, and the confidence intervals of the rate ratios were wide). We did not observe strong EMM by rurality and health insurance, although we found a consistent 20% increase in AGI ED visit rate after both hurricanes among those on public health insurance. While we observed a 10–15% increase in AGI ED rate after the hurricanes in areas where the majority of residents are on private well water, these results were not consistently larger than the increase of AGI ED rate in areas with a small proportion of residents on private well water (Table 2).

When the CITS analyses were restricted to bacterial intestinal infection ED visits, we saw an 85% increase in AGI ED visit rate after Hurricane Florence (RR=1.85, 95% CI: 1.37, 2.34), but a slight, albeit highly imprecise, decrease after Hurricane Matthew (RR=0.75, 95% CI: 0.06, 1.45). We did not observe any changes in viral intestinal infection ED visit rate after either hurricanes (Matthew: RR=1.15, 95% CI=0.54,1.76; Florence: RR=1.05, 95% CI=0.47, 1.63). There were not enough cases during the three weeks after the hurricanes to examine protozoal enteric infections or any specific pathogens.

We also examined different flood exposure periods and different cut points for the percent of ZIP code flooded. The increase in AGI ED visit rate after Hurricane Matthew increased steadily as the percent of ZIP code flooded increased (Figure 4a). For Hurricane Florence, the effect was largest in magnitude among residents in 33% and 40% flooded ZIP codes but did not show a monotonic trend. As the cut point for percent of ZIP code flooded increased, the number of ZIP codes and of AGI ED visits in ZIP codes designated as flooded decreased and the confidence intervals increased. For Hurricane Florence, the increase in AGI ED visit rate in ZIP codes 33% flooded was strongest during the first week following the hurricane (RR=1.20, 95% CI: 0.93, 1.46) and decreased monotonically as the flood exposure period increased. In contrast, the increase in AGI ED rate after Hurricane Matthew was lowest during the first week (RR=1.01, 95% CI: 0.72, 1.30) and showed no clear relationship with flood exposure period (Figure 4b). We also observed a very strong increase in bacterial AGI during the first week after Hurricane Florence in ZIP codes with a third

or more of the area flooded, but this was based on only 15 bacterial AGI ED visits in the flooded areas during the week (RR=3.41, 95% CI: 2.75, 4.06; data not shown).

The ITS results by flood category illustrate that during the three weeks after Hurricane Matthew, the AGI ED visit rate was significantly higher than predicted in areas with 0% of the ZIP code flooded (control areas for CITS), areas with less than 10% of the ZIP code flooded, and areas with 33–59% of the ZIP code flooded (Figure 5). However, after Hurricane Florence, the AGI ED rate increased as percent flooding increased after 33% flooding, with no substantial increase in areas with 0–32% flooding.

Our main results were much stronger when we examined the association between 33% hurricane flooding and AGI without a control group (ITS), with a rate ratio of 1.95 (95% CI: 1.69, 2.20) after Hurricane Matthew (compared to CITS RR= 1.15, 95% CI: 0.97, 1.32) and a rate ratio of 1.25 (95% CI: 1.02, 1.48) after Hurricane Florence (compared to CITS RR=1.09, 95% CI: 0.93, 1.24). In our supplementary ITS analyses of cumulative six-day hurricane-related precipitation and three-week AGI ED visit rate, we found the strongest effect in areas that received rain in the lowest quartile (0–6.5 inches) of total Hurricane Matthew precipitation (although effects were seen in every quartile of rainfall during Matthew) (Supplementary Table 3). However, the effects of the total rain received during Hurricane Florence on AGI were mostly null. When we included the five-week extremely wet period before Hurricane Matthew (which may itself have caused increased AGI) in the main CITS analysis, the association during the three weeks after Hurricane Matthew attenuated to a weak 4% increase in AGI ED rate in areas 33% flooded (RR=1.04, 95% CI: 0.87, 1.21).

The results from the sensitivity analysis excluding mandatorily evacuated counties were slightly stronger than our main results (RR=1.23, 95% CI: 1.09, 1.36 for Hurricane Florence, data not shown). Results were very similar overall when we conducted the main analysis using Poisson, quasi-Poisson, and negative binomial models (Supplementary Table 2). However, the negative binomial models were unstable when examining EMM and we opted against the Poisson models because of the overdispersion of the count data (Ver Hoef and Boveng 2007).

DISCUSSION:

We observed an 11% increase in all-cause AGI ED visit rate during the three weeks after Hurricanes Matthew and Florence struck NC in ZIP codes with at least a third of their area flooded compared to the predicted rates in these areas had these hurricanes not occurred, controlling for any AGI ED visit rate change in unflooded control areas after the hurricanes. We consistently observed an increase in AGI ED rate after Hurricane Florence in our sensitivity analyses, while the effect of Hurricane Matthew on increased AGI was less consistent in these sensitivity analyses. During the first week after the hurricanes, we observed a 20% increase in AGI ED visit rate after Hurricane Florence, but no increase after Hurricane Matthew. After Hurricane Florence, the increase in AGI ED rate was strongest among American Indian and Black patients and among adults aged 65 and older. When restricted to bacterial enteric infection ED visits, we found an 85% increase in bacterial

AGI ED visit rate after Hurricane Florence, but we observed no increase after Hurricane Matthew (although these estimates were based on only 27 and 17 cases of bacterial AGI visits in areas 33% flooded during the three weeks after Hurricanes Florence and Matthew, respectively). While the increase in all-cause AGI ED rate during the three weeks after Hurricanes Matthew (15% increase) and Florence (9% increase) were similar, our sensitivity analyses highlight some of the differences between the storms' effects.

Differences between the storms' antecedent rainfall and overall storm rainfall may be responsible for the discrepancy in findings between Hurricanes Matthew and Florence, particularly in the bacterial AGI analysis and the analysis with a one-week exposure period where we observed strong associations in each after Hurricane Florence and no association after Hurricane Matthew. Hurricane Matthew struck NC shortly after other heavy rain events while a relatively dry period preceded Hurricane Florence. These differences in antecedent rainfall and AGI ED visit rate increase may be explained by the concentration-dilution hypothesis, which is supported by most studies on extreme rain in relation to diarrhea, according to a 2020 meta-analysis (Kraay et al. 2020). The concentration-dilution hypothesis proposes that heavy rainfall following a dry period can flush fecal material and other pathogens from soil and surfaces into surface water, increasing AGI incidence (Kraay et al. 2020; Levy et al. 2016). However, heavy precipitation after a wet period often dilutes pathogen concentration in surface water, decreasing AGI incidence (Kraay et al. 2020). This may explain the null association between Hurricane Matthew flooding and bacterial AGI ED visits, as two very heavy rain events affected similar areas of NC five weeks and nine days prior to Hurricane Matthew, while little rain fell during the two months before Hurricane Florence (Figure 3). Hurricane Florence was also substantially wetter than Hurricane Matthew, with Florence's maximum rainfall almost double Matthew's maximum rainfall (Stewart and Berg 2019; Stewart 2017). The consistency of the Hurricane Florence effect across different models and the strong effect for bacterial AGI suggest that the association we observed is not due to chance or bias and is likely caused by an increase in waterborne bacteria after Florence. Our confidence in the observed effects during the three weeks after Hurricane Matthew is tempered by the null results for the one-week analysis and bacterial AGI analysis, although these null results may be caused by a dilution effect.

Hurricanes Matthew and Florence drenched most of NC, and many ZIP codes that did not flood (our control areas) still received heavy precipitation above the ZIP codes' 99th percentile of daily precipitation (see Figure 3). Heavy rain above the 99th percentile of an area's precipitation has been associated with AGI, regardless of flooding (Bush et al. 2014; Drayna et al. 2010; Guzman Herrador et al. 2015; Kraay et al. 2020; Levy et al. 2016; Tornevi et al. 2015). Thus, our CITS analyses could only examine the effect of heavy flooding after hurricanes compared to areas that received heavy rain but no flooding. In our supplementary ITS analyses of cumulative six-day hurricane-related precipitation and AGI ED visit rate, we observed strong effects in ZIP codes that received rain in the lowest quartile. This association may also have been related to rain during the weeks before Hurricane Matthew, which occurred in areas that were both flooded and not flooded by the hurricane (Figure 3). The effects from total rain received during Hurricane Florence on AGI were mostly null, possibly indicating that heavy rain in the control areas were not reducing the association between hurricane flooding and AGI during Hurricane Florence as

they were for Hurricane Matthew in the CITS analyses. Because the heavy rain received in the unflooded areas may also be associated with increased AGI, our CITS results for the effect of hurricane flooding on AGI are likely a conservative underestimation of the causal effect of hurricane flooding on AGI, especially for Hurricane Matthew. The stronger ITS results of hurricane flooding and AGI ED visit rate may be a more accurate representation of the effect of the hurricane on AGI rates.

Our main analyses used CITS, as it controls for both time-varying and time-invariant confounders when the pre-event characteristics between the control area and exposed area are comparable (Bernal et al. 2017; Linden 2017). Despite some demographic differences between groups, the control group was able to adjust for temporal factors to examine the effect of flooding specifically compared to areas with no flooding, but possibly with heavy rain (see Supplementary Tables 4 and 5). In addition to the robust CITS methods, this study also benefits from inclusion of two different severe hurricanes, with varying amounts of rainfall and different pre-hurricane conditions, that affected similar areas. Most studies on this topic either examine many heavy rain/flooding events or a single hurricane (Drayna et al. 2010; Gleason and Fagliano 2017; Jagai et al. 2015; Lee et al. 2019; Lin et al. 2015; Setzer and Domino 2004; Soneja et al. 2016). However, to focus on the hurricanes individually, we removed data around other large hurricanes from the analyses. As Hurricane Hermine hit NC five weeks before Hurricane Matthew, we excluded AGI data from the five weeks before Matthew in attempt to isolate the independent effect of Matthew. We chose to examine Hurricanes Matthew and Florence and not Hermine because Matthew and Florence were by far the largest and deadliest hurricanes to strike NC in recent years. While restricting data from time series analysis is not ideal, storms occasionally occur shortly after another.

Our results are generally consistent with other U.S.-based studies that reported a small increase in AGI rate after flooding, although many of these studies examined less severe flooding (Centers for Disease Control and Prevention (CDC) 2000; Levy et al. 2016; Lin et al. 2019; Wade et al. 2004, 2014). A recent review found that 76% of 25 published statistical analyses on flooding and diarrhea reported a significant positive association, especially when the flooding followed a dry period (Levy et al. 2016). A case-crossover study in China found an increase in reported infectious cases of diarrhea in the few days after flooding, with the strongest association two days after the flood in Fuyang (about 17 inches of precipitation) and five days after the flood in Bozhou (about 11 inches of precipitation)(Ding et al. 2013). A case-crossover study in Massachusetts, 2003–2007, found flooding to be associated with increased gastrointestinal illness-related emergency room visits 0–4 days after flooding (Wade et al. 2014). The researchers attributed about 7% of these visits to the flooding and hypothesized that these flood-related AGI visits were due to contact with water contaminated with enteric viruses, given the short incubation period. In a second study, this research group also found an increase in *Clostridium difficile* infections in the 7–13 days after flooding (Lin et al. 2015). In our sub-analysis of bacterial AGI ED visits, 80% of the bacterial AGI ED visits after Hurricane Florence were related to *C. difficile*. While often nosocomial infections, *C. difficile* infections may be linked to flooding and exposure to hogs and hog manure (Keessen et al. 2013; Lin et al. 2015). As we saw the largest increase in bacterial AGI ED visits during the first week after Hurricane Florence in ZIP codes flooded

33% (although based on 15 cases during this week), we hypothesize that this immediate effect is likely due to direct contact with bacteria-contaminated water.

To the best of our knowledge, no other studies have examined the effect of hurricane flooding and AGI in NC aside from Setzer and Domino, who were limited by county-month-level data and who assessed exposure to Hurricane Floyd (1999) via the Federal Emergency Management Agency's (FEMA) assessment of socioeconomic impact of Floyd instead of flooding (Setzer and Domino 2004). They observed a small increase in *T. gondii*- and adenovirus-related outpatient visits after Hurricane Floyd, although these pathogens are primarily spread by meat and person-to-person contact, respectively. They also found an increase in visits for ill-defined intestinal infections in counties severely and moderately affected by the hurricane. Our study builds on the study by Setzer and Domino by using finer resolution data and more robust analytic methods.

Our finding of increased AGI ED visit rates after hurricane flooding is further supported by studies of post-hurricane water contamination data. One study found elevated concentrations of *E. coli*, dissolved organic nitrogen, dissolved organic carbon, and phosphate in rivers after Hurricane Matthew during the 2–3 weeks when rivers were above flood stage compared to below flood stage (Humphrey et al. 2019). Another study found concentrations of *E. coli* and *Salmonella Typhimurium* in surface waters to be a hundred times greater after Hurricane Florence than after Hurricane Michael (a hurricane with significantly less rain that struck NC four weeks after Florence) (Kisling et al. 2019). These bacteria may directly cause bacterial enteric infection or are associated with the presence of other bacteria that may cause AGI.

This study uses all-cause AGI ED visits as the main outcome, which is one of the broadest indicators of health effects that arise from waterborne pathogens (Messner et al. 2006). This broad AGI case definition enabled us to have a sufficient sample size for our sub-analyses while also capturing the large proportion of AGI cases that lacked pathogen-specific details on the discharge record. However, AGI has many possible etiologies and comorbidities, including causes unrelated to waterborne pathogens. Our sensitivity analyses restricted to bacterial and viral AGI ED visits attempt to address this limitation. These analyses were limited by the small number of bacterial and viral AGI ED visits in flooded areas during the three weeks after the storm, which additionally precluded other agent-specific sub-analyses. We were unable to consider individual pathogens because many AGI-related diagnoses are made without laboratory testing and, therefore, do not specify pathogens. Even when testing is performed, it is frequently not reflected or incorrectly reflected in the diagnosis code on the discharge record (Scallan et al. 2018). Additionally, most AGI is self-limiting and does not require treatment at a health facility. Our outcome data consist only of AGI episodes that resulted in ED visits, which are expected to represent a fairly small proportion of total AGI in the population, suggesting that the true effects may be underestimated if AGI ED visits are an unbiased estimate of true AGI in the community (Mead et al. 1999). One U.S. population-based study projected that only about 20% of people with acute diarrheal illness sought medical care and 6.4% visited an emergency department (Jones et al. 2007).

We did not see consistent patterns between hurricanes in our sub-analyses of various racial and ethnic groups (aside from a constant increase in AGI among Black patients), but the differences may be related to total storm rainfall, antecedent rainfall, small sample size, and the large amount of missing race data in NC DETECT in 2016. Additionally, it is unknown how frequently the NC DETECT race and ethnicity data are self-reported or are assumed by receptionists or clinicians. Moreover, NC DETECT improved their race variable collection practices in 2016, so race analyses of Hurricane Matthew may be less accurate. While 14.3% of all ED visits were missing a race classification in 2016, this decreased to about 1.5% in 2017–2019. Most of the missing race data were concentrated in central and western NC, control areas that were unaffected by the hurricanes. In supplementary analyses, we used multiple imputation to impute missing race, and we obtained similar results (Supplementary Table 6). Although the race data in this study are imperfect, we include them in our analyses as a proxy for various unidentified economic, historical, behavioral, and environmental factors (Lin and Kelsey 2000; VanderWeele and Robinson 2014).

While several studies find AGI incidence to be higher among White non-Hispanics than Hispanic or Black people (Jones et al. 2007; Lee et al. 2019; Roy et al. 2006; Soneja et al. 2016; White et al. 2009), other studies have found no difference by race (Gleason and Fagliano 2017) or higher rates of diarrhea-related hospitalization among Black and Hispanic children compared to non-Hispanic Whites (Malek et al. 2006). The racial differences we observed in the relationship between hurricane flooding and AGI ED visit rate are likely due to racial disparities in income, wealth, and healthcare access, which are caused by structural racism, white supremacy culture, discriminatory policies, and historical differences (Gravlee 2009; Lin and Kelsey 2000). People of color and low-income residents have been—and are—regularly left to settle on the least desirable land, whether flood-prone, toxin-filled, or nonarable. For example, the first U.S. town incorporated by Black residents, Princeville, NC, was floodplain land unwanted by Whites that has since been destroyed multiple times from hurricane flooding (Kendall 2007). For centuries, Native Americans continued to lose their land and were killed or forced (or pressured) to relocate to less desirable land. Industrial hog operations in NC expanded during the 1990s and early 2000s in flood-prone areas heavily populated by Black and Native American residents (Wing and Johnston 2014)—the same areas where many enslaved Blacks resided in the 18th and 19th centuries (MacNell 2015). As we observed that hurricane flooded areas had a higher hog density than unflooded areas, and as bacterial AGI ED visits like those related to *C. difficile* may be linked to hog manure (Keessen et al. 2013), the increase in AGI rate in flooded areas after Hurricanes Matthew and Florence may be related to hurricane-related runoff from hog CAFOs. Black communities have also historically been systematically excluded from regulated public water supplies (MacDonald Gibson and Pieper 2017). Additionally, rural communities in eastern NC frequently have poor healthcare access and have a high percent of uninsured residents, which means reduced access to preventative care and increased risk for health problems (Hardy; North Carolina Institute of Medicine 2018). We observed such differences in our data as the ED rate (total ED visits/population of subgroup) was higher for people on public insurance than people on private insurance and higher among American Indian and Black patients compared to White non-Hispanic patients (see Supplementary Table 7). Other studies have found Black Americans to be less likely to use primary care and more likely

to use EDs than White Americans, but these care disparities are greatly reduced when accounting for medical mistrust (Arnett et al. 2016; LaCalle and Rabin 2010). Several studies have also found Hispanic individuals to be less likely than non-Hispanic White individuals to use EDs, due to lack of trust and fear of deportation, which may account for the low ED rate we observed among Hispanics (Allen and Cummings 2016; Beniflah et al. 2013; Maldonado et al. 2013).

This study's strengths include its robust CITS methods to control for time-invariant and time varying confounders, its use of four years of recent data, and its sensitivity analyses. However, we were limited by our data's geographic specificity, which indicate the ZIP code of the patient's billing address but do not identify the ED's location or whether the patient was displaced prior to or during the hurricane. The data does not reveal whether patients with AGI ED diagnostic codes and ZIP codes that were flooded had evacuated the area before the hurricane and had no exposure to floodwater or had stayed in the area and were directly or indirectly exposed to floodwaters. Our sensitivity analysis that excluded counties with mandatory evacuation orders during hurricanes were slightly stronger than our main results, suggesting that displacement may only slightly attenuate the observed association between hurricane flooding and AGI ED rate.

Conclusions

While some studies have examined the association between rainfall or flooding and AGI, very few have focused on hurricanes, which often produce particularly extreme rainfall that can contaminate surface water. Hurricanes Matthew and Florence were both powerful storms with record-breaking flooding. Overall, we found an 11% increase in AGI ED visit rate in ZIP codes that were a third or more flooded compared to the expected AGI ED rates in the ZIP codes had the hurricanes no occurred, controlling for any change in AGI ED visit rate in unflood areas that may have received heavy rain. This effect was larger among Black and American Indian patients following Hurricane Florence. Flooded areas also had a higher density of hogs than did unflooded areas, and the flooding of large hog manure lagoons and hurricane-related runoff from hog CAFOs may spread pathogens that can cause AGI. We also observed a stronger effect between hurricane flooding and bacterial intestinal infection ED visits after Hurricane Florence, but no apparent effect after Hurricane Matthew, which may be due to the wet period that preceded Matthew and the dry period that preceded Florence.

ZIP codes with a third or more of their areas flooded are areas where hurricane recovery lasted months or years. Many hurricane survivors in these areas who visited EDs because of AGI during the three weeks after these large hurricanes may be the same people who were also dealing with damage to their homes, relocation, loss of belongings, family harms, community damage, and/or shock from the ongoing disaster. Climate change will continue to bring more frequent and intense disasters; the disaster context and related mental health impacts are co-morbidities to the environmental health effects—such as AGI—resulting from disasters. As flood-prone regions are often disproportionately lower income, more rural, and with higher percent people of color, flooding events and subsequent health consequences (including but not limited to AGI) are manifestations of historical and present-

day environmental racism. State, local, and community interventions should consider these equity issues when acting to prevent and respond to such disasters.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS:

Sources of funding: University of North Carolina Dissertation Completion Fellowship, National Institute of Environmental Health Sciences T32 training grant.

The views expressed in this article do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.

The North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT) is an advanced, statewide public health surveillance system. NC DETECT is funded with federal funds by North Carolina Division of Public Health (NC DPH), Public Health Emergency Preparedness Grant (PHEP), and managed through a collaboration between NC DPH and the University of North Carolina at Chapel Hill Department of Emergency Medicine's Carolina Center for Health Informatics (UNC CCHI). The NC DETECT Data Oversight Committee does not take responsibility for the scientific validity or accuracy of methodology, results, statistical analyses, or conclusions presented.

REFERENCES:

- Allen L, Cummings J. 2016. Emergency Department Use Among Hispanic Adults: The Role of Acculturation. *Med Care* 54:449–456; doi:10.1097/MLR.0000000000000511. [PubMed: 26908087]
- An R, Qiu Y, Xiang X, Ji M, Guan C. 2019. Impact of Hurricane Katrina on Mental Health among US Adults. *Am J Health Behav* 43:1186–1199; doi:10.5993/AJHB.43.6.15. [PubMed: 31662176]
- Arnett MJ, Thorpe RJJ, Gaskin DJ, Bowie J V, LaVeist TA. 2016. Race, Medical Mistrust, and Segregation in Primary Care as Usual Source of Care: Findings from the Exploring Health Disparities in Integrated Communities Study. *J Urban Health* 93:456–467; doi:10.1007/s11524-016-0054-9. [PubMed: 27193595]
- Atherholt TB, LeChevallier MW, Norton WD, Rosen JS. 1998. Effect of rainfall on Giardia and crypto. *J Am Water Works Assoc* 90:66–80; doi:10.1002/j.1551-8833.1998.tb08499.x.
- Beniflah JD, Little WK, Simon HK, Sturm J. 2013. Effects of immigration enforcement legislation on Hispanic pediatric patient visits to the pediatric emergency department. *Clin Pediatr (Phila)* 52:1122–1126; doi:10.1177/0009922813493496. [PubMed: 23836808]
- Bergholz PW, Strawn LK, Ryan GT, Warchocki S, Wiedmann M. 2016. Spatiotemporal Analysis of Microbiological Contamination in New York State Produce Fields following Extensive Flooding from Hurricane Irene, August 2011. *J Food Prot* 79:384–391; doi:10.4315/0362-028X.JFP-15-334. [PubMed: 26939648]
- Bernal JL, Cummins S, Gasparrini A. 2017. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol* 46:348–355; doi:10.1093/ije/dyw098. [PubMed: 27283160]
- Bush KF, O'Neill MS, Li S, Mukherjee B, Hu H, Ghosh S, et al. 2014. Associations between extreme precipitation and gastrointestinal-related hospital admissions in Chennai, India. *Environ Health Perspect* 122:249–254; doi:10.1289/ehp.1306807. [PubMed: 24345350]
- Carter L, Jones J. 2014. Climate Change Impacts in the United States: The Third National Climate Assessment. *US Glob Chang Res Progr*; doi:10.7930/J0Z31WJ2.
- Centers for Disease Control and Prevention (CDC). 2000. Morbidity and mortality associated with Hurricane Floyd--North Carolina, September-October 1999. *MMWR Morb Mortal Wkly Rep* 49:369–372. [PubMed: 10821481]
- Chhotray GP, Pal BB, Khuntia HK, Chowdhury NR, Chakraborty S, Yamasaki S, et al. 2002. Incidence and molecular analysis of *Vibrio cholerae* associated with cholera outbreak subsequent to the

- super cyclone in Orissa, India. *Epidemiol Infect* 128:131–138; doi:10.1017/s0950268801006720. [PubMed: 12002529]
- Colford JMJ, Roy S, Beach MJ, Hightower A, Shaw SE, Wade TJ. 2006. A review of household drinking water intervention trials and an approach to the estimation of endemic waterborne gastroenteritis in the United States. *J Water Health* 4 Suppl 2: 71–88. [PubMed: 16895086]
- Curran T, Bogdanovski DA, Hicks AS, Bilaniuk JW, Adams JM, Siegel BK, et al. 2018. The effects of Hurricane Sandy on trauma center admissions. *Eur J trauma Emerg Surg Off Publ Eur Trauma Soc* 44:137–141; doi:10.1007/s00068-017-0791-9.
- de Man H, Mughini Gras L, Schimmer B, Friesema IHM, DE Roda Husman AM, VAN Pelt W. 2016. Gastrointestinal, influenza-like illness and dermatological complaints following exposure to floodwater: a cross-sectional survey in The Netherlands. *Epidemiol Infect* 144:1445–1454; doi:10.1017/S0950268815002654. [PubMed: 26554647]
- DeFelice NB, Johnston JE, Gibson JM. 2016. Reducing Emergency Department Visits for Acute Gastrointestinal Illnesses in North Carolina (USA) by Extending Community Water Service. *Environ Health Perspect* 124:1583–1591; doi:10.1289/EHP160. [PubMed: 27203131]
- DerSimonian R, Laird N. 1986. Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188; doi:10.1016/0197-2456(86)90046-2. [PubMed: 3802833]
- Dieter C, Maupin M, Caldwell R, Harris M, Ivahnenko T, Lovelace J, et al. 2018. Estimated use of water in the United States in 2015: U.S. Geological Survey Circular 1441.
- Ding G, Zhang Y, Gao L, Ma W, Li X, Liu J, et al. 2013. Quantitative analysis of burden of infectious diarrhea associated with floods in northwest of Anhui Province, China: a mixed method evaluation. *PLoS One* 8:e65112; doi:10.1371/journal.pone.0065112. [PubMed: 23762291]
- Doogan NJ, Roberts ME, Wewers ME, Tanenbaum ER, Mumford EA, Stillman FA. 2018. Validation of a new continuous geographic isolation scale: A tool for rural health disparities research. *Soc Sci Med* 215:123–132; doi:10.1016/j.socscimed.2018.09.005. [PubMed: 30227352]
- Drayna P, McLellan SL, Simpson P, Li S-H, Gorelick MH. 2010. Association between rainfall and pediatric emergency department visits for acute gastrointestinal illness. *Environ Health Perspect* 118:1439–1443; doi:10.1289/ehp.0901671. [PubMed: 20515725]
- Environmental Working Group & Waterkeeper Alliance. 2016. Exposing Fields of Filth. Available: <https://www.ewg.org/research/exposing-fields-filth> [accessed 9 October 2019].
- Gleason JA, Fagliano JA. 2017. Effect of drinking water source on associations between gastrointestinal illness and heavy rainfall in New Jersey. *PLoS One* 12:e0173794–e0173794; doi:10.1371/journal.pone.0173794. [PubMed: 28282467]
- Global Burden of Diarrhoeal Diseases Collaborators. 2017. Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Infect Dis* 17:909–948; doi:10.1016/S1473-3099(17)30276-1. [PubMed: 28579426]
- Gravlee CC. 2009. How race becomes biology: embodiment of social inequality. *Am J Phys Anthropol* 139:47–57; doi:10.1002/ajpa.20983. [PubMed: 19226645]
- Grubestic TH, Matisziw TC. 2006. On the use of ZIP codes and ZIP code tabulation areas (ZCTAs) for the spatial analysis of epidemiological data. *Int J Health Geogr* 5:58; doi:10.1186/1476-072X-5-58. [PubMed: 17166283]
- Guterl F, Godlewski N, Nestel M. 2018. How Global Warming Is Turbocharging Monster Storms Like Hurricane Florence. *Newsweek*.
- Guzman Herrador BR, de Blasio BF, MacDonald E, Nichols G, Sudre B, Vold L, et al. 2015. Analytical studies assessing the association between extreme precipitation or temperature and drinking water-related waterborne infections: a review. *Environ Heal* 14:1–12; doi:10.1186/s12940-015-0014-y.
- Hardy S The Price of Pork. *Endeavors*.
- Hogs Inventory in North Carolina. 2020. United States Dep Agric Natl Agric Stat Serv. Available: <https://quickstats.nass.usda.gov/> [accessed 15 February 2021].
- Humphrey C, Iverson G, Skibieli C, Sanderford C, Blackmon J. 2019. Geochemistry of Flood Waters from the Tar River, North Carolina Associated with Hurricane Matthew. *Resour* 8; doi:10.3390/resources8010048.

- Jackson D, White IR, Thompson SG. 2010. Extending DerSimonian and Laird's methodology to perform multivariate random effects meta-analyses. *Stat Med* 29:1282–1297; doi:10.1002/sim.3602. [PubMed: 19408255]
- Jagai JS, Li Q, Wang S, Messier KP, Wade TJ, Hilborn ED. 2015. Extreme Precipitation and Emergency Room Visits for Gastrointestinal Illness in Areas with and without Combined Sewer Systems: An Analysis of Massachusetts Data, 2003–2007. *Environ Health Perspect* 123:873–879; doi:10.1289/ehp.1408971. [PubMed: 25855939]
- Jiang C, Shaw KS, Upperman CR, Blythe D, Mitchell C, Murtugudde R, et al. 2015. Climate change, extreme events and increased risk of salmonellosis in Maryland, USA: Evidence for coastal vulnerability. *Environ Int* 83:58–62; doi:10.1016/j.envint.2015.06.006. [PubMed: 26093493]
- Johnson T, Belitz K. 2017. Domestic well locations and populations served in the contiguous U.S.: 1990. *Sci Total Environ* 607–608C: 658–668.
- Jones TF, McMillian MB, Scallan E, Frenzen PD, Cronquist AB, Thomas S, et al. 2007. A population-based estimate of the substantial burden of diarrhoeal disease in the United States; FoodNet, 1996–2003. *Epidemiol Infect* 135:293–301; doi:10.1017/S0950268806006765. [PubMed: 17291364]
- Keessen EC, Harmanus C, Dohmen W, Kuijper EJ, Lipman LJA. 2013. Clostridium difficile infection associated with pig farms. *Emerg Infect Dis* 19:1032–1034; doi:10.3201/eid1906.121645. [PubMed: 23735347]
- Kendall T 2007. “The people what makes the town”: The semiotics of home and town spaces in Princeville, NC. *North Carolina Folk J* 54.1: 33–53.
- Kisling T, Bonham N, Nguyen T, Shisler J, Jutla A. 2019. Impacts of Extreme Events on Composition of Pathogens in the Environment. *Am Geophys Union Fall Meeti*.
- Kraay ANM, Man O, Levy MC, Levy K, Ionides E, Eisenberg JNS. 2020. Understanding the Impact of Rainfall on Diarrhea: Testing the Concentration-Dilution Hypothesis Using a Systematic Review and Meta-Analysis. *Environ Health Perspect* 128:126001; doi:10.1289/EHP6181. [PubMed: 33284047]
- Krieger N, Waterman P, Chen JT, Soobader M-J, Subramanian S V, Carson R. 2002. Zip code caveat: bias due to spatiotemporal mismatches between zip codes and US census-defined geographic areas--the Public Health Disparities Geocoding Project. *Am J Public Health* 92:1100–1102; doi:10.2105/ajph.92.7.1100. [PubMed: 12084688]
- LaCalle E, Rabin E. 2010. Frequent users of emergency departments: the myths, the data, and the policy implications. *Ann Emerg Med* 56:42–48; doi:10.1016/j.annemergmed.2010.01.032. [PubMed: 20346540]
- LaMorte WW. 2018. Measures of Associations: Risk Ratios and Rate Ratios (Relative Risk). *Bost Univ Sch Public Heal*. Available: https://sphweb.bumc.bu.edu/otlt/mph-modules/ep/ep713_association/ep713_association3.html.
- Laner D, Fellner J, Brunner PH. 2009. Flooding of municipal solid waste landfills--an environmental hazard? *Sci Total Environ* 407:3674–3680; doi:10.1016/j.scitotenv.2009.03.006. [PubMed: 19345983]
- Layock R, Choi C. 2020. Which US states are hit most often by hurricanes? Finder. Available: <https://www.finder.com/states-with-the-most-hurricanes> [accessed 10 January 2021].
- Lee D, Chang HH, Sarnat SE, Levy K. 2019. Precipitation and Salmonellosis Incidence in Georgia, USA: Interactions between Extreme Rainfall Events and Antecedent Rainfall Conditions. *Environ Health Perspect* 127:97005; doi:10.1289/EHP4621. [PubMed: 31536392]
- Levy K, Woster AP, Goldstein RS, Carlton EJ. 2016. Untangling the Impacts of Climate Change on Waterborne Diseases: a Systematic Review of Relationships between Diarrheal Diseases and Temperature, Rainfall, Flooding, and Drought. *Environ Sci Technol* 50:4905–4922; doi:10.1021/acs.est.5b06186. [PubMed: 27058059]
- Lin CJ, Richardson DB, Hilborn ED, Weinberg H, Engel LS, Wade TJ. 2019. Emergency Department Visits for Acute Gastrointestinal Illness After a Major Water Pipe Break in 2010. *Epidemiology* 30:893–900; doi:10.1097/EDE.0000000000001083. [PubMed: 31430266]
- Lin CJ, Wade TJ, Hilborn ED. 2015. Flooding and Clostridium difficile Infection: A Case-Crossover Analysis. *Int J Environ Res Public Health* 12:6948–6964; doi:10.3390/ijerph120606948. [PubMed: 26090609]

- Lin SS, Kelsey JL. 2000. Use of race and ethnicity in epidemiologic research: concepts, methodological issues, and suggestions for research. *Epidemiol Rev* 22:187–202; doi:10.1093/oxfordjournals.epirev.a018032. [PubMed: 11218371]
- Linden A 2017. Persistent threats to validity in single-group interrupted time series analysis with a cross over design. *J Eval Clin Pract* 23:419–425; doi:10.1111/jep.12668. [PubMed: 27804216]
- MacDonald Gibson J, Pieper KJ. 2017. Strategies to Improve Private-Well Water Quality: A North Carolina Perspective. *Environ Health Perspect* 125:76001; doi:10.1289/EHP890.
- MacNeil N 2015. The influence of slavery on the locations of North Carolina's industrial hog operations. 17th Annu North Carolina Environ Justice Netw Summit Role Int Solidar Achiev Environ Justice.
- Maldonado CZ, Rodriguez RM, Torres JR, Flores YS, Lovato LM. 2013. Fear of discovery among Latino immigrants presenting to the emergency department. *Acad Emerg Med Off J Soc Acad Emerg Med* 20:155–161; doi:10.1111/acem.12079.
- Malek MA, Curns AT, Holman RC, Fischer TK, Bresee JS, Glass RI, et al. 2006. Diarrhea- and rotavirus-associated hospitalizations among children less than 5 years of age: United States, 1997 and 2000. *Pediatrics* 117:1887–1892; doi:10.1542/peds.2005-2351. [PubMed: 16740827]
- Maupin M, Kenny J, Hutson S, Lovelace J, Barber N, Linsey K. 2014. Estimated Use of Water in the United States in 2010. Circular 1405.; doi:10.3133/cir1405.
- Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C, et al. 1999. Food-related illness and death in the United States. *Emerg Infect Dis* 5:607–625; doi:10.3201/eid0505.990502. [PubMed: 10511517]
- Messner M, Shaw S, Regli S, Rotert K, Blank V, Soller J. 2006. An approach for developing a national estimate of waterborne disease due to drinking water and a national estimate model application. *J Water Health* 4 Suppl 2: 201–240. [PubMed: 16895092]
- NC DETECT Participating Hospitals. 2020. Available: <https://ncdetect.org/participating-hospitals/> [accessed 2 April 2021].
- Nguyen HQ, Huynh TTN, Pathirana A, Van der Steen P. 2017. Microbial Risk Assessment of Tidal-Induced Urban Flooding in Can Tho City (Mekong Delta, Vietnam). *Int J Environ Res Public Health* 14; doi:10.3390/ijerph14121485.
- North Carolina Agricultural Statistics. 2017.
- North Carolina Climate Office. Landfalling Tropical Cyclones in the Southeastern US: North Carolina. Available: <https://climate.ncsu.edu/climate/hurricanes/landfalling> [accessed 28 March 2021].
- North Carolina Institute of Medicine. 2018. North Carolina Cty Heal Profiles, North Carolina Inst Med. Available: <http://nciom.org/map/> [accessed 10 December 2018].
- PRISM Climate Group. Oregon State Univ. Available: <http://prism.oregonstate.edu> [accessed 5 June 2020].
- R: A language and environment for statistical computing. 2019.
- Reacher M, McKenzie K, Lane C, Nichols T, Kedge I, Iversen A, et al. 2004. Health impacts of flooding in Lewes: a comparison of reported gastrointestinal and other illness and mental health in flooded and non-flooded households. *Commun Dis public Heal* 7: 39–46.
- Roy SL, Scallan E, Beach MJ. 2006. The rate of acute gastrointestinal illness in developed countries. *J Water Health* 4 Suppl 2: 31–69. [PubMed: 16895085]
- Scallan E, Griffin PM, McLean HQ, Mahon BE. 2018. Hospitalisations due to bacterial gastroenteritis: A comparison of surveillance and hospital discharge data. *Epidemiol Infect* 146:954–960; doi:10.1017/S0950268818000882. [PubMed: 29655383]
- Schnitzler J, Benzler J, Altmann D, Mucke I, Krause G. 2007. Survey on the population's needs and the public health response during floods in Germany 2002. *J Public Health Manag Pract* 13:461–464; doi:10.1097/01.PHH.0000285197.23932.3e. [PubMed: 17762689]
- Setzer C, Domino ME. 2004. Medicaid outpatient utilization for waterborne pathogenic illness following Hurricane Floyd. *Public Health Rep* 119:472–478; doi:10.1016/j.phr.2004.07.004. [PubMed: 15313110]
- Soneja S, Jiang C, Romeo Upperman C, Murtugudde R, S Mitchell C, Blythe D, et al. 2016. Extreme precipitation events and increased risk of campylobacteriosis in Maryland, U.S.A. *Environ Res* 149:216–221; doi:10.1016/j.envres.2016.05.021. [PubMed: 27214137]

- Stewart S, Berg R. 2019. National Hurricane Center Tropical Cyclone Report: Hurricane Florence (AL062018).
- Stewart SR. 2017. National Hurricane Center Tropical Cyclone Report: Hurricane Matthew (AL142016).
- Tornevi A, Barregard L, Forsberg B. 2015. Precipitation and primary health care visits for gastrointestinal illness in Gothenburg, Sweden. *PLoS One* 10:e0128487; doi:10.1371/journal.pone.0128487. [PubMed: 26020929]
- VanderWeele TJ, Robinson WR. 2014. On the Causal Interpretation of Race in Regressions Adjusting for Confounding and Mediating Variables. *Epidemiology* 25.
- Ver Hoef JM, Boveng PL. 2007. Quasi-Poisson vs. negative binomial regression: how should we model overdispersed count data? *Ecology* 88:2766–2772; doi:10.1890/07-0043.1. [PubMed: 18051645]
- Waddell SL, Jayaweera DT, Mirsaeidi M, Beier JC, Kumar N. 2021. Perspectives on the Health Effects of Hurricanes: A Review and Challenges. *Int J Environ Res Public Health* 18; doi:10.3390/ijerph18052756.
- Wade TJ, Lin CJ, Jagai JS, Hilborn ED. 2014. Flooding and emergency room visits for gastrointestinal illness in Massachusetts: a case-crossover study. *PLoS One* 9:e110474; doi:10.1371/journal.pone.0110474. [PubMed: 25329916]
- Wade TJ, Sandhu SK, Levy D, Lee S, LeChevallier MW, Katz L, et al. 2004. Did a severe flood in the Midwest cause an increase in the incidence of gastrointestinal symptoms? *Am J Epidemiol* 159: 398–405. [PubMed: 14769644]
- White A, Kinlin L, Johnson C, Spain C, Ng V, Fisman D. 2009. Environmental Determinants of Campylobacteriosis Risk in Philadelphia from 1994 to 2007. *Ecohealth* 6:200–208; doi:10.1007/s10393-009-0246-9. [PubMed: 19953295]
- Wing S, Freedman S, Band L. 2002. The potential impact of flooding on confined animal feeding operations in eastern North Carolina. *Environ Health Perspect* 110:387–391; doi:10.1289/ehp.02110387.
- Wing S, Johnston J. 2014. Industrial Hog Operations in North Carolina Disproportionately Impact African-Americans, Hispanics and American Indians. Title VI Complain.
- Yard EE, Murphy MW, Schneeberger C, Narayanan J, Hoo E, Freiman A, et al. 2014. Microbial and chemical contamination during and after flooding in the Ohio River-Kentucky, 2011. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 49:1236–1243; doi:10.1080/10934529.2014.910036. [PubMed: 24967556]
- Yu P, Zaleski A, Li Q, He Y, Mapili K, Pruden A, et al. 2018. Elevated Levels of Pathogenic Indicator Bacteria and Antibiotic Resistance Genes after Hurricane Harvey's Flooding in Houston. *Environ Sci Technol Lett* 5:481–486; doi:10.1021/acs.estlett.8b00329.

Highlights

- Gastrointestinal-related emergency department visits may increase after hurricanes
- Prior rain may influence effect of hurricane flooding on gastrointestinal illness
- American Indian and Black residents are disproportionately affected by hurricanes

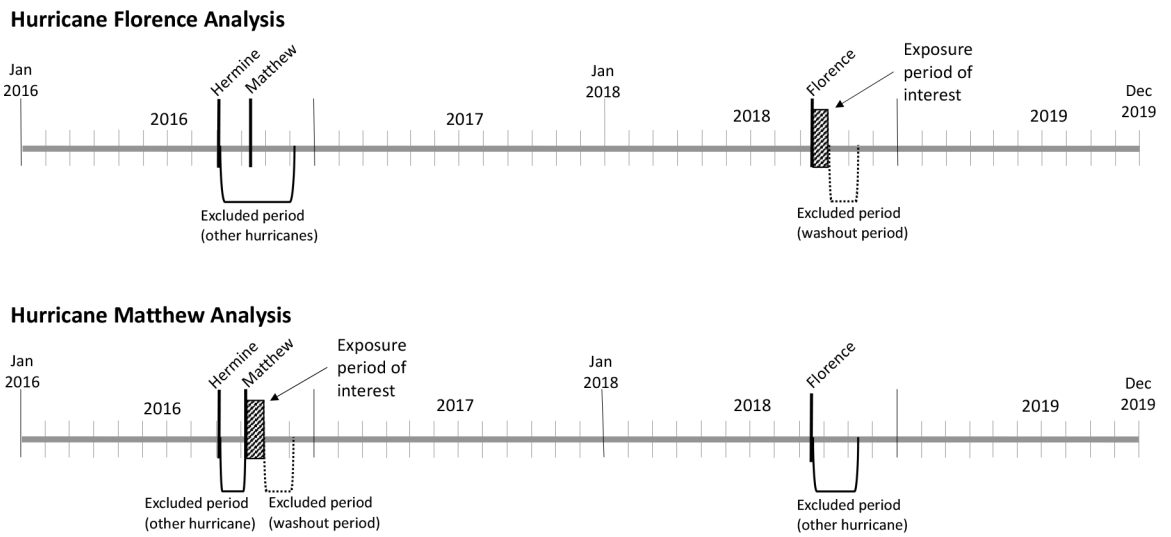


Figure 1. Summary of controlled interrupted time series analysis, including three-week exposure periods of interest (hashed rectangle), 5-week washout periods after the exposure periods (brackets with dotted lines), and excluded periods for other large hurricanes (brackets with solid lines).

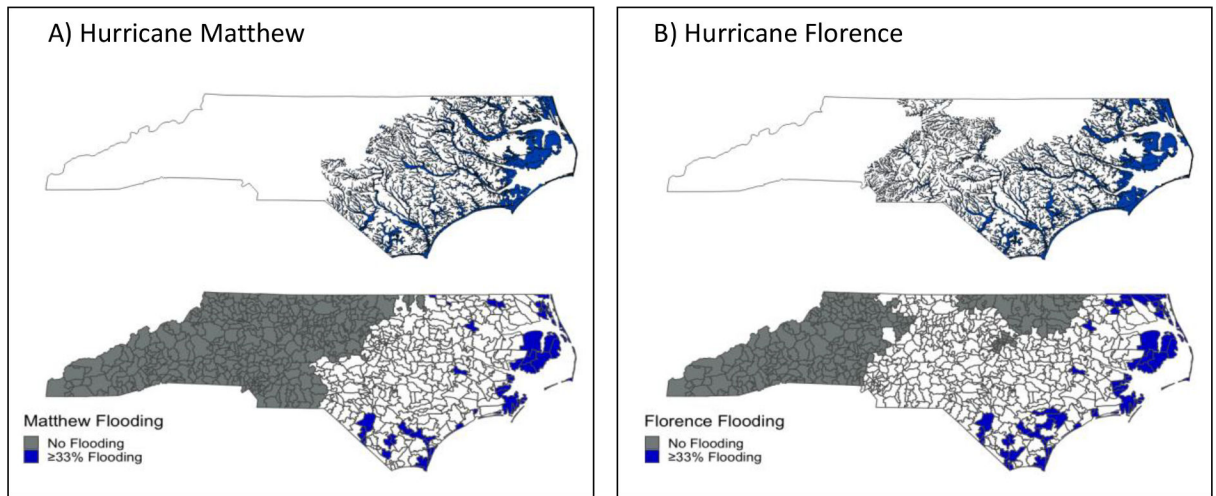


Figure 2. Maps of A) Hurricane Matthew flood extent and Hurricane Matthew flooded ZIP codes (at least one third of the ZIP code area flooded after the hurricane, N=81) and unflooded ZIP codes; B) Hurricane Florence flood extent and flooded (N=97) and unflooded ZIP codes. Flood extents created and provided by the North Carolina Department of Public Safety.

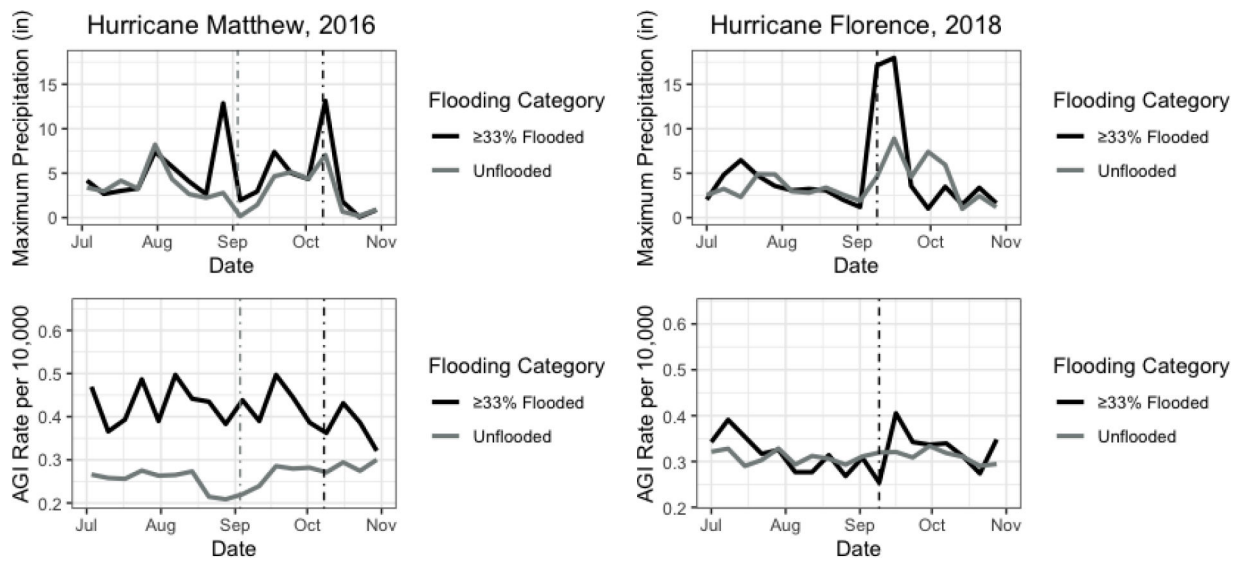


Figure 3. Maximum precipitation and AGI ED visit rate per 10,000 people by week by flooding category before and after Hurricanes Matthew and Florence. AGI ED visit rate per 10,000 from AGI ED visit data from NC DETECT, with ZIP code population data (from American Community Survey) as the denominator. The week that Hurricanes Matthew (October 14, 2016) and Florence (September 14, 2018) arrived in NC are indicated with vertical black dashed lines, with Hurricane Hermine (September 3, 2016) indicated in a vertical grey dashed line.

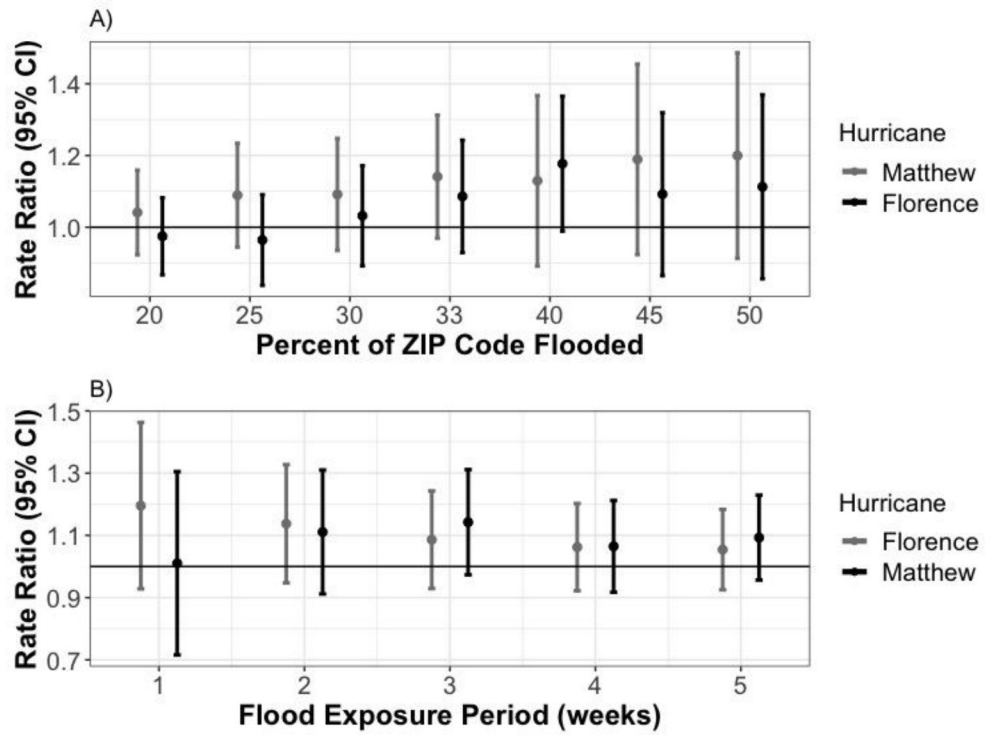


Figure 4. Rate ratios and 95% confidence intervals for controlled interrupted time series models for Hurricanes Matthew and Florence, with A) various flooding cut points and B) various exposure periods. Flooding cut points (above which ZIP code is categorized as flooded) range from 20% of the ZIP code flooded from the hurricane to 50% of the ZIP code flooded (using a three-week exposure window). Flooding exposure periods range from the one week after the hurricane to five weeks after the hurricane (using 33% as the cut point for flooded ZIP code). Main analyses used a flood exposure period of three weeks and a percent ZIP code flooding of 33%. Number of AGI ED visits during the three weeks after hurricane in ZIP codes designated as flooded: Matthew: 20%: 903, 25%: 427, 30%: 375, 33%: 321, 40%: 158, 45%: 122, 50%: 106. Florence: 20%: 1039, 25%: 680, 30%: 449, 33%: 368, 40%: 265, 45%: 149, 50%: 123. Number of AGI ED visits in ZIP codes flooded 33% during the various flood exposure periods: Matthew: 1 week: 86, 2 weeks: 211, 3 weeks: 330, 4 weeks: 421, 5 weeks: 539. Florence: 1 week: 152, 2 weeks: 255, 3 weeks: 368, 4 weeks: 485, 5 weeks: 598.

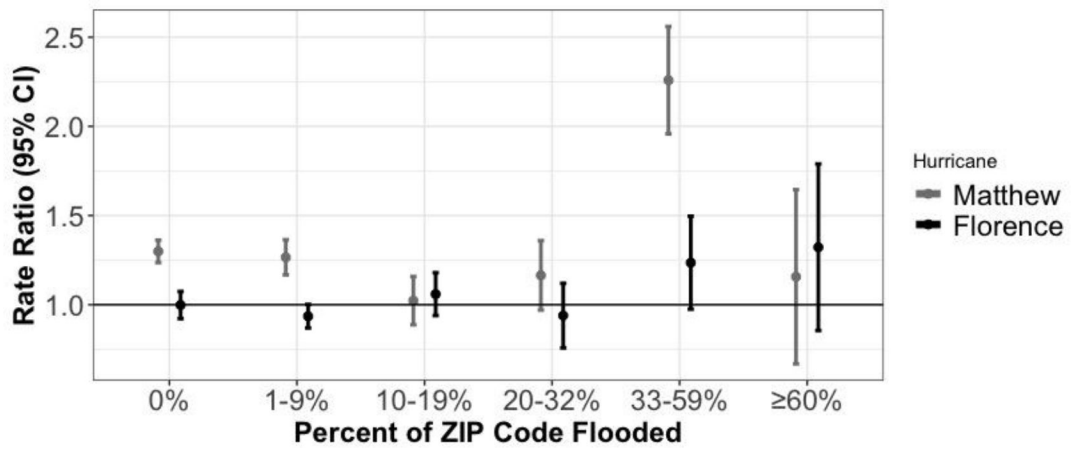


Figure 5.

The association between various amounts of flooding and three-week AGI ED rate from interrupted time series (ITS, no control group) analyses for Hurricanes Matthew and Florence. Number of AGI ED visits during the three weeks after hurricane in ZIP codes designated as flooded: Matthew: 0%: 6173, 1-9%: 1850, 10-19%: 1068, 20-32%: 704, 33-59%: 281, 60%: 49. Florence: 0%: 3721, 1-9%: 5142, 10-19%: 1645, 20-32%: 671, 33-59%: 300, 60%: 68.

Comparison of demographics and characteristics of the hurricane-exposed ZIP codes and unflooded ZIP codes, by hurricane flooding. The hurricane-exposed areas are ZIP codes with at least one third of their area flooding and the unflooded ZIP codes acted as the control in the controlled interrupted time series analysis.

Table 1.

	Hurricane Matthew			Hurricane Florence		
	North Carolina Overall	ZIP codes Flooded	33% Unflooded ZIP codes (control)	ZIP codes Flooded	33% Unflooded ZIP codes (control)	ZIP codes Flooded
Total Population (N)	10,051,041	313,505	5,686,637	392,560	3,019,011	3,019,011
White non-Hispanic, N (%)	6,396,100 (63.6)	233,462 (74.5)	3,879,033 (68.2)	292,639 (74.6)	2,227,087 (73.8)	2,227,087 (73.8)
Black, N (%)	2,127,232 (21.2)	44,726 (14.3)	1,018,923 (17.9)	57,483 (14.6)	434,559 (14.4)	434,559 (14.4)
American Indian, N (%)	109,073 (1.1)	8,594 (2.7)	25,266 (0.4)	8,851 (2.3)	19,535 (0.7)	19,535 (0.7)
Hispanic, N (%)	914,745 (9.1)	16,981 (5.4)	496,185 (8.7)	21,995 (5.6)	219,312 (7.3)	219,312 (7.3)
Uninsured, N (%)	1,186,236 (12.1)	44,768 (14.6)	746,281 (13.3)	54,316 (14.3)	392,169 (13.2)	392,169 (13.2)
Number of hogs	8,769,433	91,213	150,721	378,865	165,671	165,671
Hog density (hogs/sqmi)	176.5	27.2	6.4	85.4	9.8	9.8
Rurality score*	7.19	7.69	6.85	7.68	7.11	7.11
Median annual income (\$)	48,194	48,306	46,150	47,819	42,861	42,861
Area (sqmi)	49,712	3,358	23,491	4,432	16,903	16,903
Number of ZIP codes	1082	81	599	97	382	382

* Higher score indicates more rural area (based on geographic isolation scale)(Doogan et al. 2018)

Table 2.

The association between Hurricanes Matthew and Florence flooding and AGI, main effect and effect measure modification stratum-specific rate ratios, calculated with controlled interrupted time series. Flood exposed areas were ZIP codes with a third or more of their area flooded and control areas were ZIP codes with no hurricane flooding. A three-week exposure period was used for these analyses, starting the day that the hurricane struck NC. The sample size (n) reported is the number of AGI ED visits during the three weeks after the hurricane in ZIP codes flooded 33%. The outcome of all-cause AGI ED visits was used for all analyses except the pathogen-specific AGI sub-analyses, where we restricted to bacterial AGI, viral AGI, or all bacterial and viral and protozoal AGI.

	Hurricane Matthew	n cases	Hurricane Florence	n cases
Main result	1.15 (0.97, 1.32)	330	1.09 (0.93, 1.24)	368
Effect measure modification:				
Race				
American Indian	0.73 (0.21, 1.25)	20	2.68 (1.96, 3.41)	34
Black	1.09 (0.82, 1.36)	84	1.17 (0.92, 1.41)	102
Non-Hispanic White	1.10 (0.93, 1.28)	201	0.95 (0.78, 1.13)	207
Other	1.01 (0.50, 1.51)	12	1.21 (0.74, 1.67)	25
Age				
Under 5	1.12 (0.77, 1.47)	41	0.98 (0.62, 1.33)	35
Age 5–17	1.39 (1.00, 1.77)	32	0.78 (0.35, 1.22)	23
Age 18–64	1.10 (0.91, 1.29)	187	1.07 (0.89, 1.25)	211
Age 65+	1.09 (0.81, 1.38)	64	1.31 (1.06, 1.56)	92
Insurance				
Private	1.03 (0.76, 1.30)	66	1.21 (0.97, 1.45)	94
Public	1.19 (1.00, 1.38)	197	1.21 (1.03, 1.40)	206
Self-pay/uninsured	1.08 (0.80, 1.36)	62	0.96 (0.68, 1.23)	63
Rurality				
Metropolitan	1.19 (0.95, 1.43)	131	1.10 (0.84, 1.36)	114
Micropolitan	1.16 (0.91, 1.40)	140	1.09 (0.83, 1.35)	138
Small Town	0.94 (0.50, 1.39)	22	0.86 (0.45, 1.26)	35
Rural	1.04 (0.67, 1.42)	37	1.13 (0.86, 1.40)	81
Well Water				
<25% on well water	1.12 (0.93, 1.32)	163	1.16 (0.97, 1.35)	174
25–50% on well water	1.43 (1.20, 1.66)	67	0.91 (0.64, 1.18)	88
>50% on well water	1.10 (0.86, 1.33)	86	1.15 (0.91, 1.39)	83
Pathogen-specific AGI				
Bacterial	0.75 (0.06, 1.45)	17	1.85 (1.37, 2.34)	27
Viral	1.15 (0.54, 1.76)	19	1.05 (0.47, 1.63)	17
Bacterial, Viral, & Protozoal	0.97 (0.51, 1.43)	36	1.39 (1.02, 1.75)	44
Combined Result	1.11 (1.00, 1.23)			