HURRICANE FLOODING, INDUSTRIAL HOG OPERATIONS, AND ACUTE GASTROINTESTINAL ILLNESS IN NORTH CAROLINA

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ABSTRACT

Arbor J.L. Quist: Hurricane Flooding, Industrial Hog Operations, and Acute Gastrointestinal Illness in North Carolina
(Under the direction of Lawrence S. Engel)

North Carolina (NC) is the third most hurricane-prone US state and second leading hog producer. Most NC hogs are housed in concentrated animal feeding operations (CAFOs). Hurricane flooding can inundate hog manure lagoons, transporting potentially pathogenic microorganisms into surface water. Drinking contaminated water can result in diarrhea, vomiting, and/or nausea, known as acute gastrointestinal illness (AGI).

To investigate the effects of NC's costliest recent storms, Hurricanes Matthew (2016) and Florence (2018), we calculated AGI emergency department (ED) visit rates from ZIP code-level surveillance data during 2016-2019. Using controlled interrupted time series, we compared AGI ED 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 the hurricanes not occurred. We estimated ZIP code-level hog CAFO exposure using swine permit data and inverse distance weighting. Using inverse probability of treatment weighting, we created a control with similar demographics to the high hog exposed population and calculated rate ratios using quasi-Poisson models. We assessed the increase in AGI ED rates during the three weeks after the hurricanes in ZIP codes with flooded CAFOs, with flooding but no CAFOs, and with CAFOs but no flooding.

We found hurricane flooding to be associated an 11% increase in AGI ED rate (95% CI: 1.00, 1.23) after the hurricanes. We found high hog exposure to be associated with a higher AGI ED rate than no hog exposure (RR=1.17, 95% CI: 1.08, 1.26) and observed increased AGI ED rates among American

Indian and Black patients when restricted to rural areas. ZIP codes with hog CAFOs within the flood extents experienced an increase in AGI ED rates during the weeks after the hurricanes compared to the rates in these areas during comparable non-hurricane periods. Areas with hog CAFOs and hurricane flooding had a higher proportion of people of color and lower median incomes than NC overall.

Hurricane flooding and hog CAFO exposure highlight environmental and climate justice issues. Black and American Indian residents may disproportionally suffer from AGI in NC, especially residents who live near hog CAFOs and during periods following hurricane flooding.

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LIST OF ABBREVIATIONS

ACS	American Community Survey
AGI	Acute gastrointestinal illness
ATT	Average treatment effect in the treated
CAFO	Concentrated animal feeding operation
CITS	Controlled interrupted time series
DEQ	Department of Environmental Quality
DPS	Department of Public Safety
ED	Emergency department
EMM	Effect measure modification
EPA	Environmental Protection Agency
FEMA	Federal Emergency Management Agency
FIMAN	Flood Inundation Mapping and Alert Network
GI	Gastrointestinal illness
ICD-10	International Classification of Diseases, Tenth Revision
IDW	Inverse distance weighting
IPTW	Inverse probability of treatment weighting
IPTW-ATT	Inverse probability of treatment weighting [estimating the] average treatment effect in the treated
ITS	Interrupted time series
MRSA	Methicillin-resistant *Staphylococcus aureus*
NC	North Carolina
NC DETECT	North Carolina Disease Event Tracking and Epidemiologic Collection Tool
POC	People of color

SSLW	Steady state live weight
SQMI	Square miles
US	United States
ZCTA	ZIP code tabulation area
ZIP	Zone improvement plan
95% CI	95% confidence interval

CHAPTER I: INTRODUCTION AND SPECIFIC AIMS

Introduction

Hurricanes can be deadly, traumatizing, and cause various health problems. In addition to immediate harms inflicted by drowning and being struck from trees and debris, hurricanes can damage hospitals, flood hazardous waste sites and animal manure pits, and damage septic systems and water treatment and distribution systems.[1–3] Damage to drinking water infrastructure can result in contaminated drinking water.[4,5] Heavy wind and flooding can spread contaminants from many different industries, and environmental contamination caused by hurricanes varies by region. As North Carolina (NC) is the second leading producer of hogs in the United States with 9 million hogs,[6] hurricanes that hit NC may result in exposure to pathogenic microorganisms when hog waste pits flood and these microorganisms contaminate the waterways.[7]

Heavy rain and flooding have been linked to an increase in gastrointestinal illness rates because sewer overflows, overwhelmed municipal water systems, and damaged septic systems increase the spread of pathogens.[8–11] Flooded industrial hog farms may contribute to increased gastrointestinal illness in NC after hurricanes because of the density of hogs in the eastern, hurricane-prone region of NC. Although pathogens from human waste carry greater risk for human infection than pathogens from hog waste,[12] hogs in NC produce a greater volume of waste than the entire statewide human population, with the hog waste concentrated in uncovered waste pits in eastern NC.[13]

Most of the state’s hogs are housed, by the thousands, at large concentrated animal feeding operations (CAFOs).[14] The massive amount of manure produced by these hogs is collected in uncovered pits, or lagoons, and sprayed on land as a fertilizer. However, as the land cannot absorb all of the waste, these practices often spread pathogens and chemicals that invariably pollute the air and water.[7] Communities that live near hog CAFOs have reported numerous health problems, including throat, eye, and nose irritation, headaches, diarrhea, methicillin-resistant *Staphylococcus aureus* (MRSA) infections, and reduced quality of life.[15] Hog CAFOs are densely concentrated in several counties in eastern NC that are mostly rural, have a higher percentage of people of color than the rest of the state, and are also home to many other harmful exposures like poultry CAFOs and landfills.[16–18] Because of the area's rurality, many residents near CAFOs use private wells, which, because they are usually not treated, may be at higher risk of contamination than community water supplies.[19,20] Hog waste contains pathogens, including *Escherichia coli* O157:H7, Salmonella, Campylobacter, and Giardia, that have the potential to cause diarrhea, vomiting, nausea, or other gastrointestinal tract distress.[21–23] These conditions are often collectively referred to as acute gastrointestinal illness (AGI).[19,24] AGI causes pain, disrupts work and school, and can be harmful for health, especially in young children and older adults.[25] Furthermore, AGI-related emergency department (ED) visits in NC due to microbial contamination in drinking water exceed $40 million annually.[20]

These environmental and health issues could worsen after hurricanes because the lagoons that hold hog manure are susceptible to flooding or breaching during hurricanes and heavy rain events, further spreading harmful pathogens.[7,26] Hurricane Matthew in 2016 and Hurricane Florence in 2018 flooded many of the same areas in NC, spreading potentially dangerous contaminants and harming health. Climate change models project that NC will continue to see an increase of heavy precipitation events, making it important to understand the connection between flooding, CAFOs, and health to develop appropriate interventions.[27]

The objectives of this study were to understand the relationships between hurricane flooding and AGI, hog CAFO exposure and AGI, and the combined effect of hurricane flooding and hog CAFO exposure on AGI in NC. We used surveillance data from the North Carolina Disease Event Tracking and

Epidemiologic Collection Tool (NC DETECT) to obtain ZIP code-level information on AGI-related ED visits during 2016-2019. We used geocoded flood inundation data from the NC Department of Public Safety and geocoded CAFO data from the NC Department of Environmental Quality. This was the first study examine how hog CAFO exposure in hurricane flooded areas affects the all-cause AGI ED visit rate and the first to assess the association between CAFO exposure and AGI ED visit rate in NC.

Specific Aims

Aim 1. Determine the association between hurricane flooding and rates of AGI.

1.1 Examine the relationship between hurricane flooding from Matthew and Florence and AGI ED visit rates in NC on the ZIP code level using controlled interrupted time series analysis, 2016-2019.

Aim 2. Examine the relationship between hog CAFO exposure and rates of AGI.

2.1 Analyze the relationship between hog CAFO exposure and AGI ED visit rates, cross-sectionally 2016-2019, by NC ZIP code.

2.2 Examine race/ethnicity, rurality, and age category as effect measure modifiers of the relationship between hog CAFO exposure and AGI ED visit rate within ZIP codes.

Aim 3. Examine how hog CAFO exposure modifies the relationship between hurricane flooding and rates of AGI.

3.1 Examine how hog CAFO exposure modifies the relationship between Hurricane Matthew and Florence flooding and AGI ED visits by ZIP code, 2016-2019.

3.2 Describe and compare the demographics of ZIP codes with flooded hog CAFOs, unflooded hog CAFOs, and no CAFO exposure.

CHAPTER II: BACKGROUND AND SIGNIFICANCE

NC is the second leading producer of hogs in the United States. The majority of its 9 million hogs are densely located in the eastern, flood-prone part of the state.[6] Each year, NC hogs produce almost 10 billion gallons of fecal waste, which is stored in uncovered pits, or lagoons, and regularly sprayed onto nearby fields.[13,28] The manure contains various pathogens, antibiotics, and nutrients that can harm the environment and human health.[21–23] Hurricanes that hit NC expose humans to these contaminants, potentially resulting in illness when hog lagoons are flooded and pathogens contaminate the waterways.[7] The combined effect of living near industrial hog operations and in an area prone to flooding during heavy storms may further increase one's risk for gastrointestinal illness after hurricanes.

Background of Hog Operations

NC has been a main producer of hogs since the 18th century, when hogs roamed free on open land. Historically, NC was home to thousands of small family-owned farms with crop and livestock diversity. These farms used animal waste for fertilizer or safely disposed of the trivial amount of waste on their own land.[14,29] However, from 1982 to 2017, NC's hog population increased from approximately 2 million to 9 million, and hogs transitioned from living on small family farms to being densely housed in large concentrated animal feeding operations (CAFOs).[6] Because one CAFO usually houses 2,000-10,000 hogs in a small area, CAFOs often produce more waste than can be properly managed on their land.[19,30] Hogs in CAFOs typically live on slatted flooring that allows their urine and feces to be flushed from confinement buildings into large waste ponds called lagoons. Hog waste is liquefied and sprayed from lagoons onto nearby fields for disposal as fertilizer to prevent lagoons from overflowing. Spraying hog waste can contaminate surface and ground water in normal conditions, but especially after heavy precipitation and hurricanes.[7,26] After heavy rain, the saturated soil cannot uptake vast amounts of animal waste and the runoff can contaminate waterways. Additionally, as most lagoons are uncovered, they are susceptible to flooding and breaching that spreads manure—containing viruses, bacteria, and other contaminants—to nearby and downstream residents. This pathogen-rich manure can contaminate drinking water, especially as many of the residents in rural, southeastern NC who live near hog CAFOs use private wells—unregulated under the Safe Drinking Water Act—for drinking water.[21–24] Environmental Working Group and Waterkeeper Alliance mapped CAFOs in NC and found that of the 4,145 waste pits in NC, 136 are within a half mile of a public well, 170 lie in the 100-year floodplain, and 37 are within a half mile from a school.[13]

In NC, swine CAFOs must be issued a Swine Management System General Permit to operate.[31] These permits must be renewed every five years. The permit prohibits waste from being applied within 100 feet of any well (except monitoring wells) and prohibits hogs from being housed within 100 feet of surface water or a seasonally-flooded area.[31] The permit also prohibits waste from being applied to land during precipitation events or immediately after flooding. In addition, land application of waste must stop within four hours of a Hurricane Warning, a Tropical Storm Warning, or a tropical-storm-associated Flood Watch (as declared by the National Weather Service) for the area where the permitted CAFO is located. The permit requires that the swine CAFOs must be able to contain all swine waste and runoff from a 25-year, 24-hour precipitation event for the location.[31] While permitted hog CAFOs are not legally allowed to violate water quality standards, waste discharge that results from more severe storms does not violate the General Permit. All waste discharge events are required to be reported to the Division Regional Office.

Heavy precipitation can cause a lagoon to be inundated when floodwater rises higher than the lagoon walls and the lagoon walls are still intact. A breach occurs when the lagoon walls collapse and its contents are released. Hog lagoons are required to have a liner (often made of clay or geosynthetic plastics) to prevent or reduce groundwater contamination.[32] NC also requires lagoons' waste levels to be below the specified structural freeboard, which is typically 12 inches from the top of the dam (exceptions are made during extreme weather events).[31] When the waste levels exceed this level, the lagoon owner must notify the North Carolina Department of Environmental Quality (NC DEQ) and report an action plan to reduce the levels within a month. While the Swine General Permit provides some protection to the environment and nearby communities under usual conditions, the protection may be inadequate at preventing the spread of hog waste during hurricanes and other heavy precipitation events. Additionally, some people have documented and reported to DEQ that dozens of hog CAFOs have illegally sprayed their fields with hog manure to partially drain their lagoons before hurricanes, indicating that the protections in place may not be adequately enforced.[33]

Hog waste can contain nutrients, pathogens, veterinary pharmaceuticals, heavy metals, and hormones, including more than 100 microbial pathogens that can cause health problems, such as gastrointestinal illness, for humans.[34,35] NC hogs produce almost 10 million tons of waste each year,[28,36] and fecal bacteria from hog manure can remain in sediment for weeks to months after a large hog lagoon spill.[35] Hog manure also contains harmful gases and vapors, including ammonia, carbon monoxide, hydrogen sulfide, and methane.[28] These gases cause horrible odors and adverse respiratory effects.

Hogs receive antibiotics for microbial infection prevention/treatment and growth promotion. The overuse of antibiotics causes more antibiotic resistant bacteria to evolve, which results in harder-to-treat infections, higher medical costs, and increased mortality.[37] Antibiotics in hog feed are a major contributor to antimicrobial resistance throughout the world.[38] One study found that the percentage of organisms resistant to four antibiotic classes were three times higher inside a hog CAFO compared to upwind from the facility, and concentrations of antibiotic-resistant *Staphylococcus aureus* (MRSA) decreased as distance from the hog CAFO increased.[39] That study, which examined bacterial concentrations during normal weather, found higher numbers of bacteria with multidrug resistance—three orders of magnitude higher—inside the hog CAFO and up to 150 meters downwind of the hog CAFO compared to upwind.

Environmental Justice Issues Surrounding Hog Operations

The health issues caused by hog CAFOs are not distributed equally across NC; industrialized hog operations are often built near minority and low-income communities. In non-urban NC, the proportions of American Indians, Blacks, and Hispanics that lived within 3 miles of a permitted hog CAFO were 2.18, 1.54, and 1.39 times higher, respectively, than the proportion of non-Hispanic Whites in 2014.[16] Many poor and minority communities in eastern NC lack the political power and financial resources to prevent CAFOs from being built in their communities and are often unable to move. The environmental injustice of hog CAFOs encompasses racism, classism, poverty, and the urban-rural divide.[40] Urban areas exploit rural areas for waste disposal and food and energy production, causing pollution and reduced quality of life for rural communities. These environmentally unjust industrial production practices disproportionately harm the health of rural populations while disproportionately benefiting urban populations.[40] Additionally, rural communities near CAFOs frequently have poor healthcare access.[41] Many of the NC counties with a high density of hog CAFOs also have a high percent of uninsured residents, which means reduced access to preventative care and increased risk for health issues.[42]

Health Conditions Associated with Hog Operations

Residents living near hog CAFOs complain that the large amounts of waste produce acrid odors and cause throat, eye, and nose irritation.[15] Long-term exposure to gases from hog manure can lead to bronchitis and asthma.[28] In a study of communities near a cattle CAFO, a hog CAFO, and no nearby CAFOs, the prevalence of self-reported headaches, coughing, sore throat, and diarrhea was highest among residents living near the hog CAFO.[24] Community members living near a hog CAFO also reported worse quality of life and frequently were unable to go outdoors because of the odor. Communities in CAFO-dense areas have also been found to have a greater prevalence of MRSA infections, which can be life-threatening, compared to low density CAFO areas.[43] Hepatitis E, an acute liver disease caused by the hepatitis E virus that can cause AGI, is thought to be spread through contact with infected hogs. However, results are mixed on this. A study in Italy did not find contact with pigs to be associated with an increase in hepatitis E virus exposure, but did find a significant difference in sera IgG anti-hepatitis E virus among workers with long-term exposure to pigs compared to workers with short-term pig exposure.[44] Hepatitis E is typically spread through the fecal-oral route by drinking contaminated water. It can also be transmitted by consuming undercooked meat from infected hogs or deer.[45] Hepatitis E symptoms of fatigue, loss of appetite, nausea, vomiting, and abdominal pains are the same as many AGI symptoms, although hepatitis E is typically uncommon in the United States.

While several studies have examined the association between CAFOs and AGI, the studies have mixed results and no studies have examined this relationship in NC.[46–49] In an ecological study of livestock density and acute gastroenteritis hospitalizations in Quebec, Canada, Febriani et al. observed an increased risk of acute gastroenteritis hospitalizations associated with high intensity farming.[47] They observed modification by age and water source, with a particularly strong association in children under age 5 and in areas that predominantly used private wells and ground water as drinking water. To examine the relationship further, the Febriani et al. group later conducted a cross-sectional telephone survey of 7,006 randomly selected residents in rural municipalities in Quebec, Canada and found living in a municipality with intensive farming to be inversely associated with AGI. They propose that the differences between these studies may be due to ecological vs. individual-level data and severe AGI hospitalizations vs. self-reported AGI. Another study used electronic medical record data from primary care practices in southern Netherlands and found the prevalence of gastrointestinal and respiratory symptoms were similar in the high and low CAFO exposed populations.[48] In the only study that examines this relationship in NC, Wing et al. interviewed 155 residents in eastern NC who lived near a cattle CAFO, a hog CAFO, and no nearby CAFOs, and found self-reported diarrhea, headaches, coughing, and sore throats to be most prevalent among residents living near the hog CAFO.[24] The literature remains mixed on this general subject. Numerous pathogens found in hog manure can cause severe diarrhea, including enterohemorrhagic and enterotoxigenic *Escherichia coli, Salmonella*, *Campylobacter*, *Yersinia enterocolitica*, *Cryptosporidium*, *Giardia* (see Appendix 1).[21] Pathogenic *E. coli* strains are among the more persistent pathogens in manure.[21] While healthy humans are usually able to recover quickly, young children, older adults, and immunosuppressed people are at higher risk for severe illness from exposure to these pathogens.

Hurricane flooding may increase exposure to potentially harmful contaminants, especially in communities near industrial swine operations. Not all fecal bacteria is pathogenic, and fecal indicator bacteria, including fecal coliforms, *E. coli*, and *Enterococcus*, are often used as indicators of recent fecal contamination because they are easier to culture than the various pathogens in fecal waste.[50] A study of 59 wells in southwest Guatemala found recent precipitation to be associated with almost 3-fold higher *E. coli* concentrations, with the strongest association at wells with pigs nearby.[51] Another study of runoff after land application of cattle and swine manure and after simulated heavy rainfall events observed *E.coli* and enterococci concentrations to be significantly higher than control plots with no manure.[23] Runoff from swine slurry-applied fields had the highest concentrations of *E. coli*, *Clostridium,* and

Giardia cysts compared to cattle manure-applied and control fields, possibly because swine manure's liquid state enables microorganisms in the manure to be transported more readily than does cattle manure or chicken litter.[23] Many of the organisms in hog manure can survive for many weeks in relatively warm water, which means that the risk period for illnesses caused by hog manure can extend a month or two after a flooding event. Pathogens (i.e., bacteria, viruses, protozoa) are likely a major cause of gastrointestinal illness in these settings, but hog waste often also contains antibiotics, metals, and nitrates that may also contribute to gastrointestinal illness.[52–54] However, levels of metals and chemicals are often not especially high after floods because the large amounts of floodwater dilutes them.[55,56] Low concentrations of bacteria and other microbes can still be harmful because of replication once they enter a suitable host,[57] while dilute toxic chemicals may have relatively less adverse health effects if they are sufficiently dilute. Chemical pollution sometimes receives a great deal of attention and can indeed cause a great deal of harm, but most water-borne disease outbreaks are caused by bacteria and viruses from sewage.[58]

Recent Hurricanes in North Carolina

Several hurricanes have struck NC over the past few decades, flooding hog lagoons and harming the health of nearby residents.[3,7,59,60] In 1999, Hurricane Floyd caused five hog lagoons to breach and at least 50 lagoons to flood.[3] Numerous lagoons suffered structural damage. Wing et al. found that, according to satellite images and estimates from Hurricane Floyd, African Americans were more likely than Whites to live in areas with flooded CAFOs.[7] This highlights an important environmental justice and climate justice issue, that flooding and related environmental health problems disproportionately harm people of color. Existing environmental injustices often contribute to disaster vulnerabilities.[61] Hurricanes continue to hit NC and hog lagoons continue to flood—potentially spreading fecal contaminants—despite wide discussion of the effects of flooded and damaged lagoons and a ban on building new lagoons in the 100-year floodplain.[3] In 2016, Hurricane Matthew caused at least 14 lagoons to flood and 2 lagoons to breach.[62] At least 110 hog manure lagoons were breached or inundated in NC due to the region's most recent and severe hurricane—Hurricane Florence.[63]

Hurricane Florence was a Category 4 hurricane that came ashore in the Carolinas as a Category 1 hurricane on September 14, 2018 and was responsible for at least 52 deaths.[64,65] It was the wettest cyclone recorded in NC and dropped 8 trillion gallons of water in NC in one week, with parts of the state receiving up to 36 inches of rain.[66] Many areas that received heavy rain and flooding had a high density of hog CAFOs (Figure 1). Hurricane Florence struck only two years after Hurricane Matthew, and these hurricanes flooded many of the same areas. Hurricane Matthew was a Category 5 hurricane that struct NC on October 8, 2016 as a Category 1 hurricane.[67] The maximum rainfall in NC from Hurricane Matthew was reported in Columbus County with 19 inches. While Hurricane Matthew's flooding led to maximum inundation levels of 2-4 feet, the maximum inundation levels from Hurricane Florence flooding reached 5-11 feet above ground level.[65,67]

Heavy precipitation events have been on the rise over the past 30 years in the eastern United States, and autumns have become wetter in this region.[27] The southeast United States experienced a 27% increase of very heavy precipitation events (the heaviest 1% of all daily precipitation events) over the last half century (1958 to 2012).[68] Models project that NC will continue to see an increase of heavy precipitation events.[27] It is important to understand the extent of the environmental and health issues that resulted from these hurricanes, as they will likely reoccur.

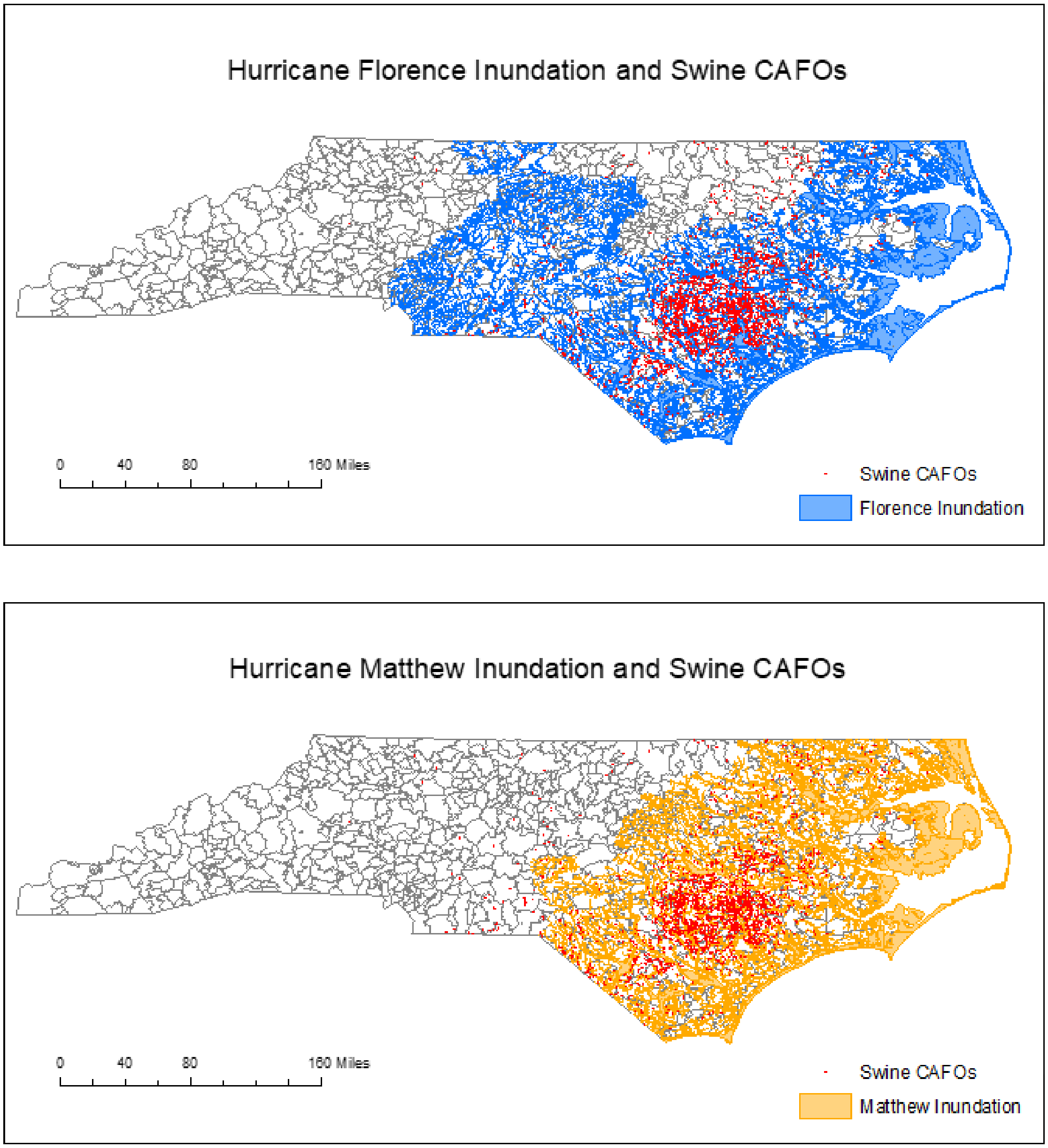

Figure 1. Swine concentrated animal feeding operations (CAFOs) in North Carolina, estimated flood inundation from a) Hurricane Florence and b) Hurricane Matthew, and North Carolina ZIP codes (CAFO data obtained from Environmental Working Group, flood inundation data from North Carolina Department of Public Safety, ZIP code data from NC OneMap GeoSpatial Portal).

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Flooding, Pathogens, and Gastrointestinal Illness

Flooding increases the transport of fecal contaminants because of flooded wastewater treatment plants, landfills, and/or sewage systems.[69,70] Additionally, heavy rainfall events can lead to displacement, which is often associated with an increase in people with inadequate water, sanitation, and hygiene (WaSH) and thus may increase the potential for transmission of infections.[69] Older sewer systems are associated with more leakage and more adenovirus and norovirus contamination in groundwater and tap water, and this increased contamination is associated with increased incidence of acute gastrointestinal illness (AGI; AGI includes non-chronic diarrhea, nausea, and vomiting typically combined with abdominal pain and fever[25]).[71–73] Leaking and flooded sewers are a substantial source of fecal contamination,[74] which can spread bacteria, protozoa, and viruses.[8] Ingesting sewage-contaminated water can cause AGI. Flooding caused by hurricanes regularly spreads sewage and closes roads. For example, after Hurricane Florence, over 22 million gallons of untreated sewage spilled into waterways in New Hanover County, and numerous highways and interstates were closed because of flooding. Almost two million gallons of sewage was discharged in Lumberton and St. Pauls. [75] While unlikely, gastrointestinal illness can also be caused and aggravated by non-pathogenic agents, including antibiotics and metals from coal ash ponds, hazardous waste sites, brownfields, and CAFOs.[76,77] Municipal solid waste landfills can also flood during heavy rain events, releasing chemical and microbial contaminants into the air, soil, and/or floodwater.[70] As Figure 2 indicates, flooded animal waste management systems, septic systems, wastewater treatment plants, landfills, and hazardous waste sites can spread chemicals and pathogens, thus contaminating floodwater, well water, municipal water, and soil. Hurricane survivors may then be exposed to contaminants by direct contact with floodwater, by drinking contaminated water, by contact with surfaces and materials that came in contact with floodwater, or by eating food grown in contaminated soil. These various routes of exposure have different time frames, with direct contact with floodwater affecting AGI within 1-7 days or longer, while eating food grown in contaminated soil affecting AGI weeks, or months, after flooding. This dissertation focuses on effects of floodwater in the 1-3 weeks of hurricanes, thus focusing on exposure via direct contact, contaminated water, and contaminated surfaces. In addition to chemical and microbial exposures, people often deal with stress, depression, trauma, and anxiety after large hurricanes.[78] Stress is associated with increased susceptibility to colonic inflammation, and stressful events may be responsible for the onset or exacerbation of chronic gastrointestinal disorders, although this has not been studied with regard to acute gastrointestinal illnesses.[79,80]

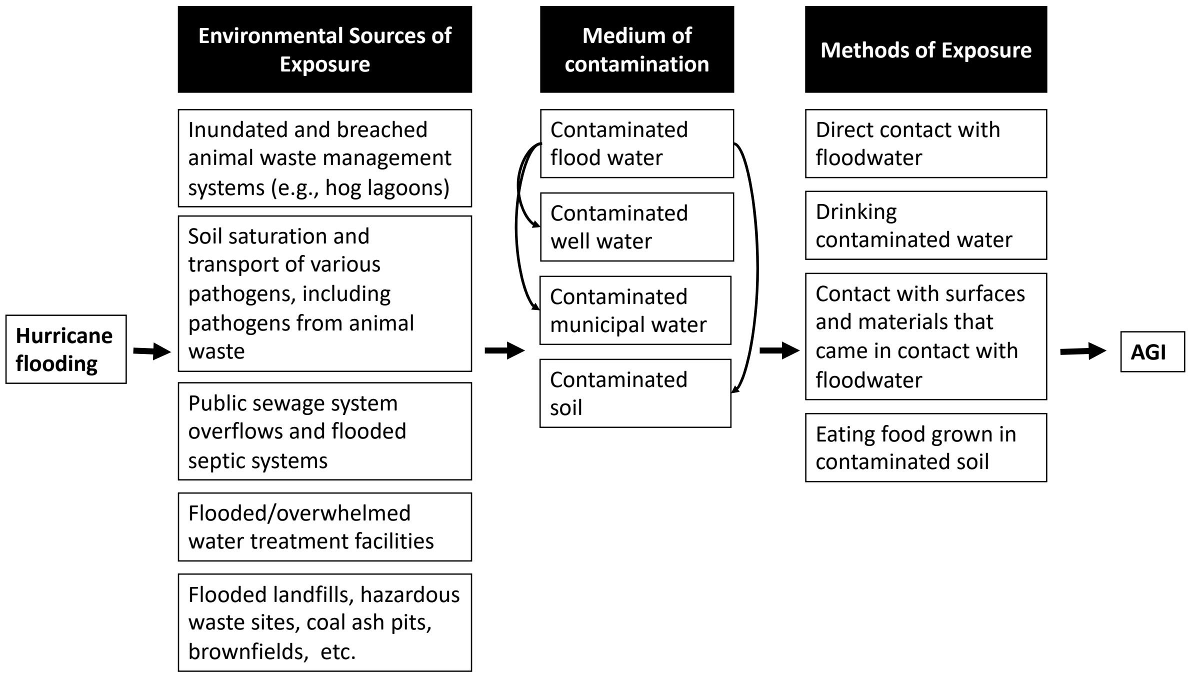


Figure 2. Conceptual diagram for hurricane flooding and acute gastrointestinal illness (AGI), highlighting the environmental sources of exposures, media of contamination, and methods of exposures.

Severe flooding, which often occurs during and after hurricanes, has been associated with stomach upsets, diarrhea, and gastroenteritis, especially in people who come in contact with flood water.[81–84] A case-crossover study in Massachusetts, 2003-2007, found flooding to be associated with increased gastrointestinal (GI) illness-related emergency room visits 0-4 days after flooding.[9] The researchers of this study attributed about 7% of gastrointestinal illness (GI) visits in the four days following the flood to the flooding and projected that this increase was due to contact with contaminated water (possibly contaminated with enteric viruses, due to the short incubation period) during and soon after the flood. This research group also found an increase in *Clostridium difficile* infections—which can spread by water but is most commonly seen in older hospitalized patients—in the

7-13 days after floods, an effect that was stronger in men than women.[10] A time series analysis of weather and AGI (specifically gastroenteritis or diarrhea) ED visits in Wauwatosa, Wisconsin found any rainfall to be associated with an 11% increase in AGI visits four days later.[8] Similar to the Massachusetts case-crossover study mentioned above, these authors also speculated that this may be largely due to viruses (such as rotavirus, norovirus, enterovirus, calicivirus, and adenovirus) that have incubation periods of 1-7 days (Hepatitis A has a longer incubation period of approximately 30 days).[8,85] A similar lag was seen in a case-crossover study in China that found an association between flooding and reported infectious cases of diarrhea in the few days after flooding.[11] The researchers of this study saw the strongest association two days after the flood in Fuyang (about 17 inches of total precipitation, categorized as severe flooding by the Comprehensive Study Group of Major Natural Disasters of the State Science and Technology Commission in China) and five days after the flood in Bozhou (about 11 inches of total precipitation, categorized as moderate flooding). A recent review found that over 70% of 14 published analyses on heavy rainfall and diarrhea found a positive association between heavy rainfall events and diarrhea, especially after dry periods.[69] These 14 analyses were from 10 English language articles published between 1982 and 2014 and examined a fairly even mix of developed and less developed countries, of urban and rural areas, and of survey and medical encounter data.

Many studies look at the association between rainfall or flooding on risk of AGI, but they are often unable to ascertain how subjects came in contact with contaminated water—whether through drinking water or contact with floodwaters. One study surveyed 1,110 Midwestern US residents about their contact with floodwater after a flood and asked them to record their gastrointestinal symptoms in a daily health diary.[86] This study also randomly assigned each household to use an active water treatment device or a similar looking inactive device (placebo). The study found an association between contact with floodwater and GI symptoms that was stronger in children, but no association between tap water consumption and GI symptoms.[86] While these studies indicate that AGI risk increases only in the few days after floods and that AGI is more likely to be due to contact with floodwater than contaminated drinking water, most of these studies focus on small flood events and not large floods—like those experienced after Hurricane Florence—that last for days and are more likely to contaminate wells and public water supplies.

It is often difficult to identify the causes of AGI, as it can encompass a range of enteric illnesses caused by various viruses, bacteria, and protozoa, as well as non-infectious agents.[25] AGI can also be non-infectious in origin, resulting from toxins (in the case of food poisoning), chronic diseases, or antibiotics.[53,87] According to the U.S. Centers for Disease Control and Prevention, norovirus causes 60% of acute gastroenteritis cases with a known cause.[88] Norovirus is spread mainly through the fecal-oral route; however, there have also been many waterborne outbreaks.[88] Norovirus can live on surfaces and in water for days or weeks. One study found an especially strong relationship between water samples with a high proportion of norovirus genogroup I (NoV-GI) and adult AGI.[72] Most viruses have incubation periods from 1 to 7 days, which many studies have found to be the time period after flooding with the greatest increase in AGI.[8,9,11] Thus, some researchers believe viruses (norovirus, as well as rotavirus, enterovirus, calicivirus, and adenovirus) to be the main pathogenic agents of concern related to AGI after flooding.[8,9]

Bacterial agents that cause AGI, including *Campylobacter* (2-3 day incubation period), *Salmonella* (2-3 days), enterohemorrhagic and enterotoxigenic *Escherichia coli* (3-4 days), *Vibrio cholerae* (2-3 days), *Clostridium difficile* (2-3 days), *Shigella* (1-3 days), *Yersinia* (4-6 days), *and Helicobacter pylori* (3-4 days, although more likely to cause a chronic infection than AGI), have similar incubation times (see Appendix 1).[8,89] *Campylobacter* is the main bacteria that causes AGI outbreaks in high-income countries.[89] Studies have found that flooding increases the microbial and chemical load in surface water.[90] A study of surface water contaminants after flooding in the Ohio River found the water to be heavily contaminated with *E. coli*, enterococci, *Salmonella*, and *Campylobacter*.[90] *E. coli* and

Salmonella contamination was found to be elevated in soil after Hurricane Irene flooding in New York.[91] In coastal Maryland, extreme precipitation events have been associated with a 3% increase in campylobacteriosis risk and a 6% increase in salmonellosis risk.[92,93] Salmonella was responsible for the highest number of infections among people who came in contact with floodwater after a flood in Vietnam.[94]

Waterborne protozoa such as *Giardia* (1-14 day incubation period), *Cryptosporidium* (2 days-2 weeks), *Cyclospora cayetanensis* (2-14 days), and *Entamoeba histolytica* (2-4 weeks) cause diarrheal diseases.[89] Most of these protozoa have slightly longer incubation periods, most around 1 or 2 weeks, than do viruses or bacteria. *Giardia* and *Cryptosporidium* concentrations in surface water and catchment areas increase after rainfall and extreme runoff events,[95–97] and *Giardia* and *Cryptosporidium* have also caused disease outbreaks after heavy precipitation events.[8,97]

Gastrointestinal Illness Prevalence

Research suggests that flooding or proximity to hog CAFOs may be associated with gastrointestinal illness and diarrheal diseases,[9,24,47,81–84] which is particularly problematic due to the large hog industry in NC, the increasing number of extreme weather events, and the physical and economic impacts of gastrointestinal illness in humans. Diarrheal diseases are a leading cause of death worldwide, causing 1.3 million deaths annually, including half a million deaths among children under 5 years of age.[98] Most diarrheal diseases are caused by contaminated food and/or water.[99] In developed countries, mortality associated with diarrheal diseases is low, although incidence remains fairly high, especially in children.[25] One study estimated, using U.S. population-based telephone surveys of 52,840 people 1996-2003, that the rate of acute diarrheal illness that impairs normal activity or persists longer than a day was 0.6 episodes/person-year, with the highest rates among children under 5 years.[100] They also projected that only about 20% of people with acute diarrheal illness sought medical care and 6.4%

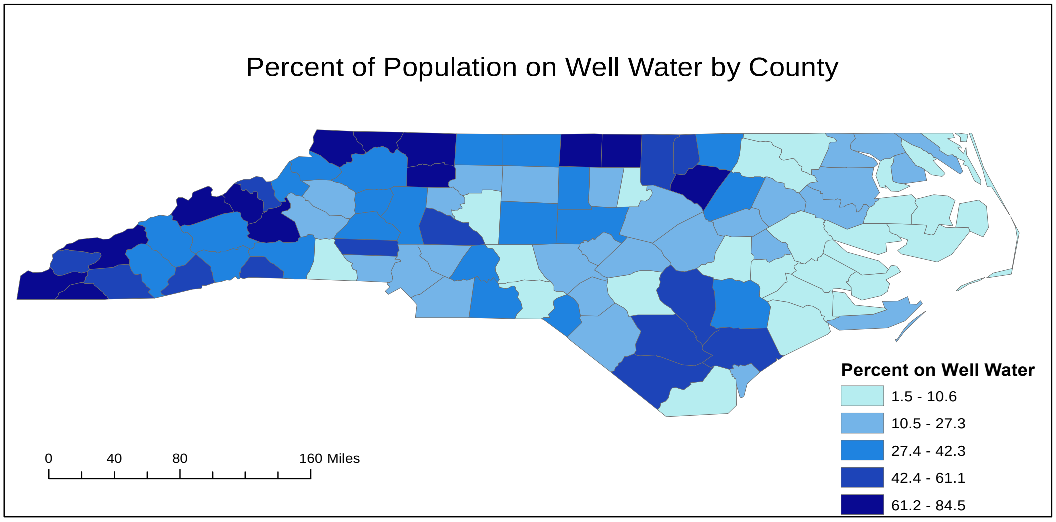
visited an emergency department. While a review of 33 papers on the incidence of AGI in high income countries found a range of 0.1 to 3.5 episodes/person-year, the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet) found that the AGI incidence in the US is approximately 0.65 episodes/person-year.[25] AGI and diarrheal diseases encompass similar symptoms, although AGI is a broader category that includes diarrhea, nausea, and vomiting, which is often combined with abdominal pain and fever.[25] Waterborne enteric illnesses include gastrointestinal illnesses that are caused by waterborne pathogens (as many AGI are caused by contaminated food or linked to other illnesses). In the U.S., approximately 2,330,000 waterborne enteric illnesses occurred in 2014, which incurred about $160 million in direct healthcare costs.[101]

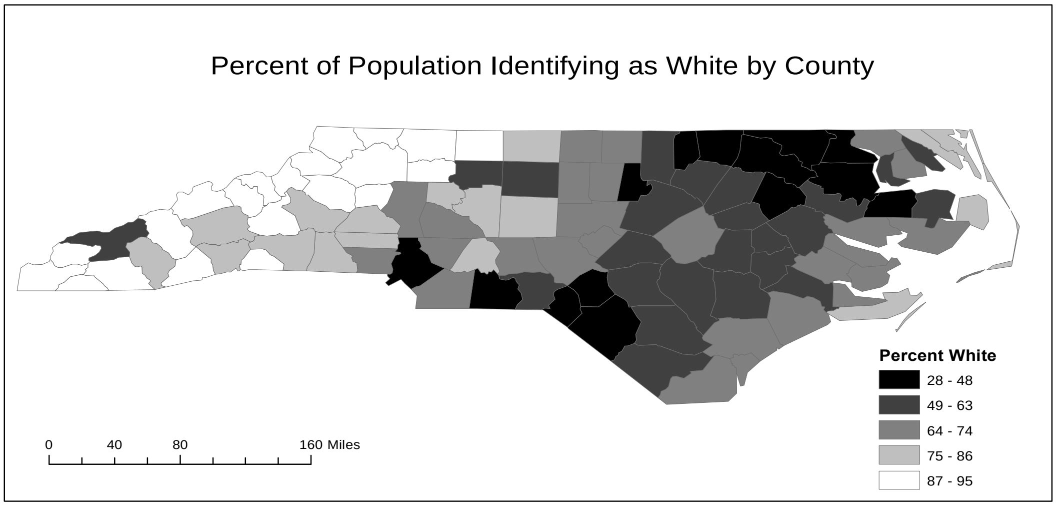
Gastrointestinal Illness and Well Water in North Carolina

Researchers estimate that about a tenth of AGI episodes (or 4-16 million cases annually) are attributable to contamination of public drinking water systems in the U.S.[102,103] Colford et al. used five drinking water intervention population studies in Canada, Australia, and the United States to estimate that the median proportion of risk of AGI that can be attributed to community drinking water systems (i.e., inadequate water treatment or water contamination in surface water) in the U.S. is 12%.[102] They also estimated that 4.26-11.69 million cases of AGI were attributable to contamination in public drinking water systems in the U.S. each year. The U.S. Environmental Protection Agency (EPA) estimates that 8.5% of AGI cases are due to community water systems.[103] In NC, there were approximately 405,000 AGI-related emergency room visits per year in the time period of 2007-2013.[20] Of these, an estimated 7.3% were attributable to microbial contamination, based on a population intervention model, and of these, 99% were linked to private well contamination.[20] The cost of AGI-related emergency department (ED) visits in NC due to microbial contamination in drinking water is approximately $40.2 million annually, with the majority of the cost ($39.9 million) caused by contaminated private wells.[20] This study concludes that extending regulated community water service to just 10% of the people currently on private wells could decrease the annual number of emergency department visits in NC by almost 3,000.

Approximately a third of NC residents obtain their drinking water from household wells or other small residential water systems.[104] The total population of people who drink private well water in NC, 3.3 million, is the second highest in the U.S., after Pennsylvania. Many NC residents who rely on private wells do not have the means or knowledge to properly monitor and maintain their well water, and state- and county-wide programs to advocate for private well water quality lack the necessary funds and integration to improve rates of monitoring and maintenance.[105] Test data for NC private wells show that few well owners regularly test their water.[105]

Private well users are not evenly distributed across NC and do not reflect the demographics of NC as a whole, due to the rurality of many areas and the history and development of community water services. NC municipal boundaries and the development of public water services were affected by racial discrimination. Municipal water lines do not reach some peri-urban, Black communities, which must rely on private wells.[105] This extends the environmental justice issue of flooding and hog CAFOs, as poor Black communities have often been left to live in undesirable, low-lying, flood-prone areas; hog CAFOs continue to be built near low-income communities with a higher percent of people of color than the rest of the state; and Black communities have historically been systematically excluded from regulated public water supplies (Figure 3). In addition to the large number of homes in NC that depend on well water, the EPA estimates that 48% of households in NC rely on septic systems, which is well above the national average of 20%.[106] The most common cause of reported groundwater contamination is from septic tank leachate.[58]





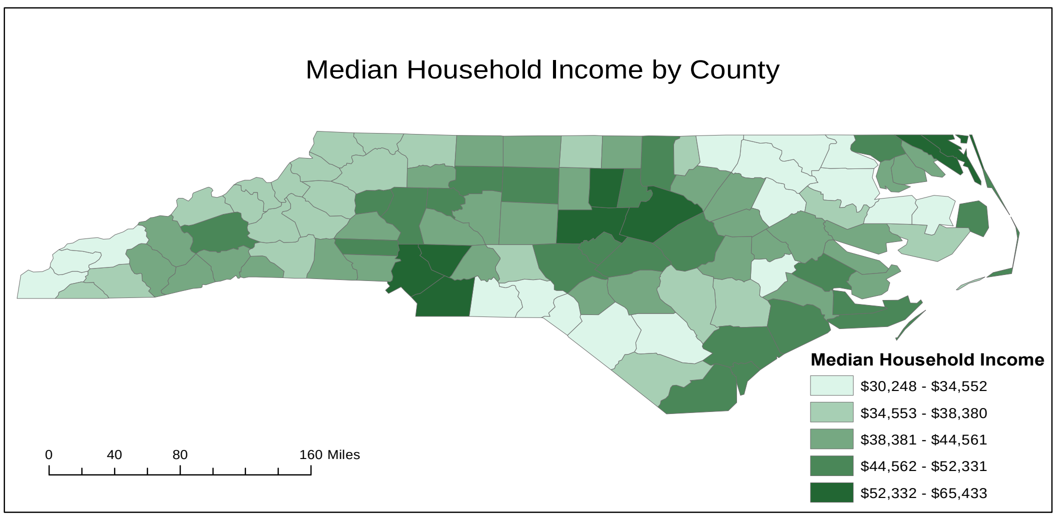


Figure 3. Proportion of population on well water, proportion of population identifying as White, and median household income by county (Well data from U.S. Geological Survey 2015; race and income data from 2015 County Health Rankings).

Gaps in Literature

Despite the frequency and severity of hurricanes in NC, the density of hog CAFOs in eastern NC, and the large number of NC residents on private well water, few studies have examined the effect of flooding and hog CAFOs on gastrointestinal illness in NC. Wing et al. highlighted the environmental justice issues of this relationship by demonstrating that African Americans were more likely than whites to live near flooded hog CAFOs after Hurricane Floyd hit NC.[7] This paper did not specifically examine any health effects, although the differences in risk of exposure by race should be sufficient evidence for removing lagoons from floodplains and from nearby vulnerable communities. Setzer and Domino used Medicaid outpatient data to examine whether Hurricane Floyd was associated with increased waterborne disease-related outpatient visits in eastern NC.[107] They specifically identified outpatient visits related to illness caused by *Cryptosporidium*, *Giardia lamblia*, *Toxoplasma gondii*, *Helicobacter pylori*, *Mycobacterium avium*, and adenoviruses. They examined counties with high concentrations of hogs (>1,000 hogs) and classified the counties on the impact of Hurricane Floyd measured by the Federal Emergency Management Agency's (FEMA) assessment of socioeconomic impact of Floyd (severe, moderate, minor, not affected). The study is somewhat limited by these definitions, as FEMA's designation of hurricane impact is over the entire county and does not consider the proportion of the county affected by the hurricane. Also, considering that some counties have almost 2 million hogs (Sampson County: 1.8 million hogs; Duplin County: 1.7 million hogs) while other counties may have 1,000 hogs in just one or two CAFOs, more categories of hog density would have allowed a more refined analysis of the role of hog CAFOs on gastrointestinal illness.[108] They used difference-in-differences to compare counties severely and moderately impacted by Floyd to unaffected counties and found a small increase in *T. gondii* and adenoviruses outpatient visits after Hurricane Floyd hit compared to unaffected counties. There was an increase in visits for ill-defined intestinal infections in severely and moderately affected counties, compared to unaffected counties. The study did not make any conclusions regarding the combined effect of hurricane flooding and hog CAFOs on gastrointestinal illness, partly because their study not include any counties that were affected by Floyd that did not have a high concentration of hogs.[107] The study was also limited by the use of county-level data. Thus, no known studies have effectively examined the combined effect of hurricane flooding and hog CAFOs on gastrointestinal illness.

The paucity of literature on poultry CAFOs represents another gap in literature. In addition to the dense hog CAFOs in NC, poultry CAFOs are also increasing across the state, especially in eastern NC. Broiler chicken production has been rapidly growing over the past twenty years.[109] NC produced 830.8 million heads of broiler chickens in 2017, making it the fourth-highest-producing state of broilers in the United States.[110] Poultry manure can also spread disease and pollute the water, soil, and air with nitrogen, phosphorus, and arsenic.[17] Poultry litter contains manure, bedding, feathers, and feed, making it a fairly dry waste, especially in comparison to liquid swine waste.[111] Because poultry waste is mostly dry, it is not stored in large lagoons that can breach during heavy precipitation events. Chickens also produce much less waste than large hogs. Nevertheless, research suggests that workers at poultry plants are at increased risk for *Campylobacter* and *Salmonella* infection, as well as eye, skin, and respiratory symptoms.[112,113] This might extend to those who live near poultry operations or are exposed to poultry manure. Swine and poultry waste carry microbes with similar risks for infecting humans; this risk is substantially lower than the risk of infection after exposure to water contaminated with human sewage.[12]

No published research has examined how flooded poultry CAFOs may affect health. Hurricane Florence drowned an estimated 3.4 million chickens and turkeys, in addition to 5,500 hogs.[114] Preliminary estimates indicate that the economic impact of Hurricane Florence on the poultry industry was $40.4 million and the total economic impact on the pork industry was $1.2 million.[115] While flooded hog lagoons appear to be a larger threat because of their liquid waste compared to dry poultry waste, little research has considered how floods may spread poultry waste and affect human health.

Brief History of North Carolina

Over the past three centuries, geography has played a defining role in NC's economic development, affected its industries, and determined who lived where. Many groups of Native Americans thrived in NC for thousands of years. European colonization, however, wiped out entire Native populations by violence and by the spread of smallpox and other diseases. When Europeans began inhabiting North America, most found NC unappealing. NC's numerous sandbars, barrier islands, and powerful fast-approaching Atlantic storms resulted in thousands of shipwrecks with the NC coast being named "the Graveyard of the Atlantic."[116] NC's lack of navigable waterways initially discouraged colonization and made transporting goods and people throughout the state difficult. Poor Whites from Virginia became NC's earliest permanent White settlers, many of whom were freed indentured servants who sought land for themselves. Compared to other colonies (including neighboring South Carolina and Virginia with their deeper ports and rivers), NC remained relatively poor, isolated, politically unstable, and underdeveloped by Whites until the mid-18th century. For many years, outsiders viewed NC as a swampland populated by poor people and misfits.

Wealthy Whites slowly built plantations in eastern NC to produce tobacco, rice, turpentine, tar, pitch, and livestock using slave labor in the 18th and 19th centuries.[116] The enslaved Black population in NC, concentrated on plantations in eastern NC, grew from 6,000 in 1730 to 100,000 in 1790. Small settlements of free Black people in the coastal towns of Edenton, New Bern, and Wilmington also developed during this time. In the 19th century, bright leaf tobacco and cotton were the main plantation crops in eastern NC. As the Civil War raged, many enslaved people fled from plantations to freedom beyond Union lines. New Bern, NC became a sanctuary for former enslaved people (almost 1,000 refugees lived there by the end of the war), especially after Union forces captured the city in March 1862. Nevertheless, years later, in 1893, a local court compelled these Black residents to relocate to an all-Black community, James City. The plantation system remained even after slavery officially ended and Black people were often still tied to the land through sharecropping and tenancy. While many African Americans migrated north from the 1870s to the mid-20th century, many also remained in the areas where their enslaved ancestors had previously lived and worked.[116]

Racist laws that attempted to continue to control African Americans and profit from their exploitation were a large reason that many Black people remained near plantations in eastern NC after the abolition of slavery. Some of these laws, including laws to close the range, were related to hogs. By the 18th century, hogs emerged as the most prevalent type of livestock in NC. Historical records indicate that North Carolinians ate a great deal of fresh pork, but many hogs were also raised to be exported, especially to markets in Virginia and the West Indies.[116] Hogs were easy and inexpensive to raise, and their meat fed the enslaved people whose work in the fields made landowners rich. Before the late 19th century, poor Whites' hogs roamed and grazed freely on the open range. After slavery ended, wealthy White landowners worked to close the range so formerly enslaved Black people would be forced to continue to work for them.[117] Maintaining the open range with unfenced pigs would give freedpeople various subsistence options. The majority of residents in the American South—including the landless and small landowners—continually voted against closing the range, so the powerful, large landowners found undemocratic ways of closing the range (e.g., through petitions, lawsuits, and constant pressure). As part of controlling available resources and eliminating common land, general fish and game laws were also passed.[117] These laws, including requiring hogs to be fenced, were methods of controlling the labor of Black people. Eliminating the range was part of the long transition from traditional, self-sufficient farming practices to a system most concerned with maximizing profits for the wealthy.

In examining the health effects of flooding and hog CAFOs, it is essential to acknowledge that complex historical reasons caused certain groups of people to live in certain areas. Demographic distributions across the United States are not random or happenchance; many people and communities are often unable to move or to live just anywhere. Racial minorities and low-income people have been—and are—regularly left to settle on the least desirable land—whether flood-prone, toxin-filled, or nonarable. For example, the first town incorporated by African Americans, Princeville, NC, was floodplain land unwanted by whites that has since been destroyed multiple times from hurricane flooding.[118] 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 areas heavily populated by African Americans and Native Americans[16]—the same areas where many enslaved Black people resided in the 18th and 19th centuries (Figure 4).[119] Because of many of these historical factors, it is especially important to examine how flooding and hog CAFOs affect Black and Native American communities, as these are communities that have been abused, marginalized, and often forced to live on poor land.

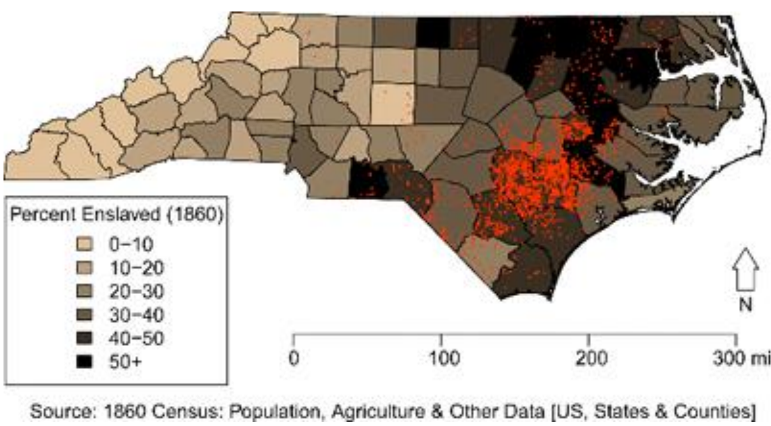


Figure 4. North Carolina enslaved population in 1860 and industrial hog operations re-permitted in 2015 (industrial hog operations marked in red; map created by Nathaniel MacNell).[119]

Critical Race Theory

In order to examine relationships between racism and health disparities relating to hurricanes and CAFOs, I sought to apply critical race theory (CRT), which is a framework that examines and changes the connections between race, racism, and power.[120] While CRT developed among legal scholars and activists in the 1970s, variations of CRT are used now in many fields, including public health. One such variant, Public Health Critical Race praxis (PHCRP), is a broad framework that informs research on the causes of health disparities.[121]

PHCRP consists of four main focuses: 1) *contemporary patterns of racial relations*, 2) *knowledge production*, 3) *conceptualization and measurement*, and 4) *action*. For Focus 1: *contemporary patterns of racial relations*, I considered characteristics of social racialization in NC during the study period of 2016-2019 and the mechanisms in which racism works specific to disasters and consequent exposures during this period. Understanding the history that created the current racial hierarchy is important in this endeavor as discriminatory housing policies and the history of slavery and locations of slave plantations affect where people live today. Communities of people of color (POC) and low-income communities are more likely to live on low-lying land and near hog CAFOs (although the POC communities existed before the hog CAFOs developed around them). Additionally, after disasters like hurricanes, FEMA unequally distributes funds to Black vs. White people, as well as low-income vs. high-income families.[122,123] While not described in this dissertation, I separately conducted focus groups, interviews, and surveys with Hurricane Florence survivors—predominantly POC—to better understand the complex challenges that hurricane survivors face, especially low-income POC survivors recovering within a racist system.

For Focus 2: *knowledge production*, I examined the epidemiological methods I employed to consider if there are factors that are frequently ignored that may bias research findings. For example, epidemiological research on flooding and AGI does not typically consider race and often inadvertently assumes that all people have equal access to care and equal ability to relocate and evaluate. Many epidemiology flood papers seem to assume that floods affect groups similarly (aside from groups based on age, gender, flood severity), or they ignore ways in which floods might affect racial groups differently.

Focus 3: *conceptualization and measurement*, required me to find the best methods to account for the limitations of typical epidemiological methods with regard to racial bias. I considered how race, proximity, and other key measures are constructed and how accurate they are. I examined the limitations of the health data I used from North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), especially with regard to racial categorization and race-related access issues. In each manuscript (aim 1, 2, 3), I described the limitations and missingness of the race data, the factors for which the race variables represent, and I conducted analyses with the most precise race and ethnicity data available. Unfortunately, in aim 1, I had to combine several race and ethnicity categories into an “Other Race” category for analysis because of the small number of AGI cases during the three weeks after the hurricanes. However, in aim 2, I was able to include more race and ethnicity categories in analysis. Additionally, as I described the racial and ethnicity groups that live near hog CAFOs, I broke down the Asian group into several various Asian ancestry groups. Different Asian ancestry populations are distributed differently across NC and combining all groups into a larger “Asian” population can hide differential exposure that may occur for particular Asian ethnic groups.

For Focus 4: *action*, I sought to conduct analyses that examine intervention effects; however, I have fallen short in this area and I will continue to improve my analyses to address interventions. As I continue to work on the aim 3 analyses, I will continue to attempt to estimate the expected change of AGI ED visits if hog CAFOs were removed from areas flooded during Hurricanes Matthew and Florence. This has been especially difficult because there are few areas with heavy hurricane flooding but no hog CAFOs and few areas with many hog CAFOs and no heavy flooding after Hurricanes Matthew and Florence. While I was in touch with two community groups affected by hurricane flooding and hog CAFOs in eastern NC when I started this dissertation, the COVID-19 pandemic has made it difficult for me to continue to attend community meetings and to adequately partner with affected communities. As I continue to develop and finalize the analyses described in this dissertation, I plan to share study limitations, strengths, and results with communities frequently affected by hurricane flooding and hog CAFO exposures. I hope to work with partners to understand how this data and research could be used for action and possibly be converted into accessible education materials and to present to community groups (see Appendix 2). Given the scope of this dissertation, the CRT work has been limited, is incomplete, and is still ongoing. However, the PHCRP has provided an important framework for these research questions.

Innovation

While limited research has highlighted the link between flooding and GI illnesses and between hog CAFOs and AGI symptoms, few studies have examined the association of AGI risk with flooding and hog waste contamination together. It is important to understand the extent to which flooding exacerbates GI illnesses associated with hog waste, as heavy flooding events will continue to occur and are likely to increase in frequency. Previous research has not specifically examined the association between flooding and gastrointestinal illness across several hurricanes while considering hog CAFO exposure. Although the Setzer and Domino study examined the association between Hurricane Floyd flooding and waterborne pathogenic illnesses, that study used categories of FEMA's assessment of the storm's socioeconomic impact instead of flood maps and county-level data instead of ZIP code-level data.[107] Additionally, very few studies have examined the relationship between hog CAFO exposure and health outcomes, and none have specifically looked at AGI ED visits in NC. While several studies have assessed the relationship between flooding and AGI ED visits, very few studies have examined the effect of hurricane flooding on AGI in NC, the third most hurricane-prone US state, and few studies have assessed racial disparities of AGI. Most studies have not examined how these relationships may change in areas with more people of color or more rural areas. This study also benefits from inclusion of two different severe hurricanes, with different pre-hurricane conditions, that affected similar areas. Most studies on flooding and AGI either examine many heavy rain/flooding events or a single hurricane.[8,10,92,107,124–126] As a significant portion of NC's population relies on well water and as the state is such a large producer of hogs, NC is a compelling case study for these questions.

CHAPTER III: METHODS

Overview of Common Methods for Studying Health Effects of Disasters

Researchers use various methods to examine the health effects of hurricanes and similar extreme events and natural disasters. When dealing with a well-defined event (like a hurricane) and an outcome that occurs relatively soon after the event, methods such as case-crossover, difference-in-differences, and interrupted time series are common. These methods compare health outcomes in a geographical area before and after an event, such as a disaster, to see how the event changes the incidence of the health outcome.[127,128] Because each person or each region is compared to itself, these methods control for time-invariant confounders. The case-crossover design compares a case's exposure during the event (or during the few weeks after the event) with the same person's or same geographical area's exposure at a similar reference time before or after the event.[127] Interrupted time series (ITS) is a quasi-experimental method that compares the trend of the outcome after an event, such as a disaster, to the long-term trend in the pre-disaster period within affected area(s).[128] Controlled interrupted time series (CITS) builds on the standard interrupted time series approach by incorporating a control group that was not affected by the disaster (or event or intervention) to compare trends in different areas over time.[129] Difference-in-difference (DiD) estimation examines whether the outcome of a group affected by the disaster significantly differs from its baseline mean by an amount greater than that of the comparison (unaffected) group. All of these methods have advantages and disadvantages, and the ideal method usually depends on the specific data available. For example, unlike CITS and difference-in-difference, the case-crossover design does not use control areas that were unaffected by a disaster because the design requires its cases and controls to have different exposures (e.g., flooded vs.

unflooded exposures). Difference-in-difference estimation is a simplification of CITS and assumes—often incorrectly—that the outcome of the affected and unaffected groups have parallel trends. CITS methods are more rigorous than DiD because CITS better accounts for differing trends of the outcome.[130] However, creating accurate trends requires data from a long period of time, thus, CITS requires more data before the disaster (at least four time points) than DiD.

Studies of flooding have utilized each of these methods. A recent study of flooding and mental health in England used CITS to examine the number of anti-depressant medication prescriptions in the year before and the year after flooding.[131] The researchers were able to compare the prescribing trends in the flooded areas to the prescribing trends in the unflooded areas for five major flood events from 2011 to 2014. Their use of CITS allowed them to account for the increasing trend of antidepressant prescriptions over time in the general population that was independent of extreme weather events. The study found a 0.59% (95% confidence interval (CI): 0.24, 0.94) increase in prescriptions during the post-flood year in primary care practices within 1 km of a flood compared to practices 5-10 km from a flood. The same research team used CITS again to examine the association on mortality and flooding from 319 flood events in England and Wales during 1994-2005.[132] The mortality ratio in the pre-flood year to that of the post-flood year among areas within 5 km of a flood was compared to mortality ratios in areas outside of the flood boundary. The study found a slight decrease in mortality in the year after floods. The unexpected results might be due to flood-caused population displacement or may be because this study failed to account for flood severity. In contrast, a previously mentioned study by Wade et al. employed the case-crossover design to examine the association between flooding and emergency room GI visits in Massachusetts.[9] The study considered only flooded areas and used a time-stratified bi-directional design that matched on the day of the week to select controls, which avoids potential bias caused by temporal trends if controls are only selected after cases. The aforementioned study by Setzer and Domino on waterborne pathogenic illness in NC after Hurricane Floyd used a difference-in-difference method.[107] The method was appropriate for the data available, but using methods that incorporate long-term trends and using geographically finer data would have improved the study by giving more accurate and geographically specific results. All of these types of methods are useful for hurricane and flooding research, and the specific methods used is frequently determined by the nature of the available data. Nevertheless, CITS is a particularly rigorous and appealing method because of its use of a control group and long-term trends, in addition to its ability to control for time-invariant confounders.

Without a control group, ITS analyses sometimes are unable to distinguish the effects of external factors across time from the effects of the intervention or disaster.[133] An appropriate control group with comparable levels and trends of important baseline covariates and the outcome greatly strengthens the interrupted time series method, although determining the appropriate control can be difficult. Inverse probability of treatment weighting (IPTW) can be used to estimate the average treatment effect on the treated (ATT), or, in this dissertation, to estimate the average flooding effect in those who experienced heavy flooding. IPTW controls can be used in CITS to create a control group with covariates that are balanced according to the covariate distribution of the exposed areas, which improve causal inference.[134]

Aim 1 Methods

Aim 1. Determine the relationship between hurricane flooding and rates of AGI ED visits.

Study population and study design

For Aim 1, we used flood and hurricane data from the North Carolina Department of Public Safety (NC DPS) and ZIP code-level data on AGI ED visits from the North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT). We used CITS analysis with an IPTW-ATT control to examine the relationship between hurricane flooding from Matthew and Florence and AGI ED visits on the ZIP code level. Aim 1's study population included people who were released from emergency departments (EDs) in NC with an AGI-related discharge code 2016-2018. CITS was used to compare AGI ED visit trends before vs. during and shortly after hurricanes in areas that were flooded to areas that were not flooded. We created a control pseudo-population of unflooded ZIP codes that had a similar covariate distribution as the flooded ZIP codes with IPTW-ATT.

Exposure

Hurricane flooding. NC DPS created a shapefile of the Hurricane Florence and Hurricane Matthew flood extents in NC based on the effective and preliminary flood maps, observed rainfall, storm surge, Flood Inundation Mapping and Alert Network (FIMAN) flood gauges, and photographs. For the main analysis, we used this DPS data to categorize each ZIP code as flooded or unflooded, based on the amount of ZIP code area flooded. As CITS and ITS methods work best with a dichotomous exposure, we tested different cut points to indicate heavy flooding in a ZIP code. For main analyses, a flooded ZIP code was defined as having a third of its area flooded.

Outcome

Gastrointestinal illness. NC DETECT collects data of emergency department (ED) visits in NC and provided us the de-identified data with patients' ZIP codes. NC DETECT is a surveillance system created and maintained by the NC Division of Public Health and the Carolina Center for Health Informatics. Since 2005, all civilian EDs have been required to send ED data to the state for public health surveillance. This information contains patient age, sex, race, ethnicity, ZIP code, ED arrival date, insurance coverage, chief complaint, triage notes, disposition diagnosis description, and diagnostic codes. The ZIP code provided is the ZIP code of the patient's billing address. For this study, we requested all ED visit data from 2010-

2019 and identified AGI using diagnostic codes from the International Classification of Diseases, Nine and Tenth Revisions (ICD-9 and ICD-10; described below). The following ICD-9 and ICD-10 codes were used to identify AGI cases: intestinal infectious illness (ICD-9: 001-009; ICD-10: A00-A09), unspecified noninfectious gastroenteritis and colitis (ICD-9: 558.9; ICD-10: K52.3, K52.89, K52.9), diarrhea (ICD-9: 787.91; ICD-10: R19.7), and nausea and vomiting (ICD-9: 787.0; ICD-10: R11.10-R11.12). Similar diagnosis codes for AGI have been used by other studies of flooding and AGI ED visits.[8,9,20] All AGI events from diagnosis codes 1-11 were included in our analyses, including repeat visits by some individuals. We considered AGI ED visits as a marker of community infection, although AGI ED visit rate is substantially lower than actual AGI rate, as most AGI cases are self-limiting and do not require medical care. 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.[100]

While we obtained ten years of outcome data, we focused our analysis on 2016-2019 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 ED visits from year to year was always below 10%; however, the number of ED visits in 2015 was over 20% lower than that of 2016 because of systematic changes. For example, some hospitals were added to NC DETECT in 2016.[135] Additionally, some hospitals stopped sending data because of challenges during the ICD-9 to ICD-10 transition and were likely unable to backfill all missing visits. These changes created a discontinuity in the quality and comparability of the data over a longer period.

Covariates

Because aim 1 is a time series analysis where AGI ED visit trends in each ZIP code are compared over time to post-hurricane AGI ED visit trends in the same ZIP code, these analyses only controlled for time-varying confounders, including seasonality by month and year-to-year differences. Generally, time-invariant variables (over this time frame), such as distributions of age, race, and income, do not need to be controlled for in time series models. However, we examined effect measure modification (EMM) by age, race, and health insurance status to understand how these factors might influence AGI ED visit rate.

Month. AGI trends vary by season, with AGI ED visit rates in NC highest in the winter.[20] To account for this seasonal variation, we included month in our models.

Year. ED visit data changes year to year with new facilities opening and closing and with new policy changes that alter access to care. To address these changes, we included year in our models.

Day of week. As ED visit patterns vary depending on the day of the week,[136] we also included day of week in the models.

Precipitation. As heavy precipitation is associated with AGI,[8,69,92,95,96,137] we examined how prior precipitation that is not related to Hurricanes Matthew or Florence may influence the effect of the hurricanes on AGI. We obtained daily precipitation data from the PRISM Climate Group as 4km-by-4km raster data,[138] 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.

Age. Worldwide, diarrheal disease is the second leading cause of death among children under age five.[99] In the United States, rotavirus is the main cause of pediatric diarrhea and there are approximately 136,000 diarrhea-associated hospitalizations in children <5 years of age each year.[139] As children under 5 years of age and adults over 70 years of age are especially vulnerable to AGI,[100,140,141] we examined EMM by age category to examine if young children and older adults have higher rates of AGI following hurricanes than the rest of the population.

Race and ethnicity. NC DETECT data also contains the race (American Indian, Asian, Black, Pacific Islander, White, Other) and ethnicity (Hispanic Origin, Not of Hispanic Origin) of the ED patients. Race in the NC DETECT data should be self-reported, although sometimes receptionists or clinicians make assumptions and indicate a race without asking. It is unknown how frequent this data is self-reported vs. assumed. Race is often used as a proxy for various, unidentified behavioral, economic, historical, environmental, and genetic variables.[142] Race is a social construct that is entrenched in our society and the effect of racist ideas and practices can affect health and biology.[143] While Black and Hispanic children may have higher overall rates of hospitalization due to diarrhea,[144] genetic race differences are likely not responsible for differences in rates of AGI. Race and ethnicity differences in health exist because of racism, white supremacy culture, numerous discriminatory policies, and historical, cultural, and socioeconomic differences, which are difficult to measure. Additionally, disparities in healthcare access, insurance, and trust may account for different reliance in EDs for AGI.[145–148] Black Americans are 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.[149] To attempt to examine how race and ethnicity might affect the relationship between hurricane flooding and AGI, we conducted analyses examining race as an effect measure modifier (EMM).

Rurality. People in rural areas are more likely to rely on well water and septic systems, which put them at increased risk of water contamination and AGI.[20] People in rural areas also have decreased healthcare access.[150] We assessed rurality 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.[151]

Health insurance type. Health insurance type can act as a proxy for income as well as health care access, which may affect whether a person would go to the ED for AGI. A nationwide study found that patients on Medicaid have a higher ED utilization (40% vs. 18%) and were more likely to have barriers to timely primary care than people with private insurance.[147] We examined EMM by health insurance type recorded in NC DETECT data: insurance company (private), Medicare/Medicaid/other government insurance (government), and self-pay (likely uninsured). We used data from the American

Community Survey (ACS) to estimate the percent of uninsured residents in each ZIP code, which was used in IPTW. ACS was also used to estimate the number of people on private health insurance, government health insurance, and no health insurance to serve as the population denominators (i.e., the offset) for these EMM analyses.

Income. Research has found higher AGI rates to be associated with lower median household income.[152,153] ACS data on median household income was used to create the control pseudo-population. To do this, we population-weighted block group-level ACS data to the ZIP code level.

Statistical analyses

For aim 1, we used CITS analysis to examine how daily AGI ED visit trends changed during the 3 weeks after Hurricanes Matthew and Florence, compared to the daily AGI ED visits trends 2016-2019. The interrupted aspect of the time series started on the day the hurricanes struck NC (October 8, 2016 for Hurricane Matthew and September 14, 2018 for Hurricane Florence). Although some areas were underwater for many days, the hazard period began when the flooding begins. We used quasi-Poisson regression, because of overdispersion in the ED data. Our models included variables for including time (year, month, and day of week), a dummy variable indicating pre- or post-hurricane period (0/1), a dummy variable indicating flooded or unflooded area (0/1), interactions between the flooded area variable and all other variables (to control for the change in AGI ED visit rate during this period in unflooded areas), and a population offset. The offset—the yearly estimated ZIP code-level population—enabled us to take into account the changing number of people at risk for AGI over time. This enabled us to obtain a rate ratio, which represents the rate of AGI ED visits during the three weeks after the hurricane over the rate of expected AGI ED visits during this period had the hurricane not occurred (based on previous trends). We estimated yearly ZIP code-level population by aggregating yearly block group-level population estimates from the ACS. To isolate the effect of the large hurricane of interest

(Matthew or Florence), we removed the eight-week periods after other large hurricanes that produced over one foot of maximum precipitation (namely, Hurricanes Hermine, Matthew, and Florence).

To increase the rigor of these methods and the validity of the results, we included an IPTW control group that represents the AGI trend expected in the flooded ZIP codes during the hazard periods of Hurricanes Matthew and Florence if they had not been flooded. To create an appropriate control, unexposed areas were weighted so their pre-disaster characteristics were balanced and comparable to the pre-disaster characteristics of the exposed areas. We created two control pseudo-populations (one for Hurricane Matthew and one for Hurricane Florence) by weighing the unflooded areas to the flooded areas based on the characteristics of the flooded areas that may be confounders or may be associated with AGI ED visit rate (percent White, rurality, median income, percent uninsured, and total number of ED visits). These variables were available from the ACS at the block group level, which we aggregated into ZIP code-level data. While ACS data is available on the ZIP code Tabulation Area (ZCTA) level, ZCTAs are only rough estimations of ZIP code polygons and using ZCTA data for ZIP code data can increase misclassification.[154] Instead, we used population weights to assign block group-level ACS demographic data to block centroids and aggregated all the block centroid data within each ZIP code to create ZIP code level estimates. As ZIP codes change over time, we examined newly created ZIP codes in the 2016-2019 time period, combined ZIP codes that are split over time, and merged the data from the split ZIP codes.

We also examined EMM by race, age, and insurance type to understand how the relationship between hurricane flooding and AGI varies across different demographics. We examined Hurricanes Matthew and Florence separately in their own CITS analyses, and then conducted a random-effects meta-analysis of the rate ratios from the CITS analyses of Hurricanes Matthew and Florence using the DerSimonian-Laird method.[155,156]

Aim 2 Methods

Aim 2. Determine the relationship between hog CAFO exposure and rates of AGI ED visits.

Study population and study design

In aim 2 we examined the relationship between hog CAFO exposure and AGI ED visits on the ZIP code level, using inverse distance weighting to estimate hog CAFO exposure and inverse probability weighting to create appropriate control ZIP codes. We used ZIP code-level data on AGI ED visits from NC DETECT and information on the size and location of hog CAFOs in NC from NC Department of Environmental Quality (DEQ). While the goal of this aim is to examine the general relationship between hog CAFO exposure and gastrointestinal illness across NC, the study population is limited to people who went to an emergency department (ED) in NC and were released with an AGI-related discharge code in 2016-2019.

Exposure

Hog CAFOs. We used the 2014 swine permit data from NC DEQ which included the location, facility name, operational status, type/life stage of animals, lagoon count, allowable animal count, and waste output (gallons/animal/year) of each permitted swine facility. Using this data, we calculated the steady state live weight (SSLW) of each hog CAFO. SSLW is an indicator of the amount of waste produced at each CAFO and has been used in other studies.[16,157] SSLW is calculated with the North Carolina Department of Environment and Natural Resources' formula that incorporates the number of hogs, growth stage of the hogs, and average weight of each growth stage (see Table 1 for list of growth stage/production phase of hogs and mean weight used to calculate SSWL).[158]

Table 1. Weight classes for determining Steady State Live Weight from Pietrosemoli et al., 2012[158]

Production Phase	Initial Weight (lbs.)	Final Weight (lbs.)	Mean Weight (lbs.)
Wean to Feeder	10	50	30
Feeder to Finish	50	220	135
Gild Developing	50	250	135
Boar Stud	250	550	400
Farrow to Wean	-	-	433
Farrow to Feeder	-	-	522
Farrow to Finish	-	-	1417

We estimated case exposure as the inverse distances from each hog CAFO to census block centroids, weighting with Gaussian decay and by hogs per CAFO, then aggregated to the ZIP code using population weights. We compared ZIP codes in the upper quartile of hog exposure ("high hog exposed") to those without hog exposure. Using inverse probability of treatment weighting (IPTW), we created a control with similar demographics to the high hog exposed population and calculated rate ratios using quasi-Poisson models.

Outcome

The outcome of AGI ED visits is the same as the outcome described in Aim 1.

Covariates

Age. As previously mentioned, children and older adults are more susceptible to AGI.[99,139] Because of this, we examined how age modifies the relationship between hog CAFO exposure and AGI.

Race and ethnicity. As previously discussed, AGI ED rates may differ across races and ethnicities,[144] which may be because of discriminatory policies and differences in diet, prior infections, and ED usage. People of color are disproportionately more likely to be frequent ED users than White peope.[145] As hog CAFOs have been built disproportionately near Black and American Indian communities,[16] we described how ZIP code-level race predicts hog CAFO exposure and used a ZIP code-level, ACS-based race variable (percent of population that identifies as White) in IPTW. We also examined how individual-level race and ethnicity (from the ED data) modify the relationship between hog CAFO exposure and AGI ED visit rate.

Income. Research has found higher household income to be associated with lower AGI rates,[152] with low-income women having a higher risk for AGI than high-income women.[153] In NC, high densities of hog CAFOs are also more likely to be located near low-income communities.[15] We examined ZIP code-level, ACS-based median income as an EMM (in adjusted models) and used median income for IPTW (in weighted models).

Rurality. As hog CAFOs tend to be located in rural areas with relatively low population density, we also examined rurality as an EMM and used rurality in IPTW. Rurality was measured using a continuous geographic isolation scale that classifies ZIP codes according to their access to resources.[151] The continuous rurality measure was used in IPTW and the continuous rurality measure was separated into quartiles when examining EMM.

Statistical analyses

For the main analysis, we used IPTW to estimate the average treatment effect on the treated (ATT). To do this, we created a pseudo-population (assumed control) with similar demographics as the high hog exposed population (based on the ZIP codes' median income, rurality, percent of non-Hispanic White residents, and percent of uninsured residents) but with no hog CAFO exposure. We chose to compare areas with high hog CAFO exposure to areas with no hog CAFO exposure because these areas had relatively similar demographics before IPTW; areas with low hog CAFO exposure had higher median incomes and a larger percent of non-Hispanic White residents than NC overall and the high hog exposed areas. We excluded metropolitan ZIP codes from all main analyses by excluding the lowest quartile of the geographic isolation scale (below 5.6; 273 ZIP codes excluded), as urban areas lack hog CAFOs and likely have different ED access and visit patterns than areas with hog CAFOs. More specifically, city political power would not allow miles of a city to smell of hog manure and cities lack the large amounts of open, inexpensive land for CAFOs. We used quasi-Poisson models to account for overdispersion in the ED visit data. When examining EMM, we adjusted for percent uninsured, median income, and rurality, which we had identified as confounders using a directed acyclic graph (see Appendix 3).

Aim 3 Methods

Aim 3. Examine how hog CAFO exposure modifies the relationship between hurricane flooding and rates of AGI ED visits.

Study population and study design

For aim 3, we examined how the change in AGI ED visit rate during/after Hurricanes Matthew and Florence differs in relation to hog CAFOs exposure. These analyses are preliminary and exploratory. We focused on examining the disparities in exposure, outcome, and effect in these areas. We contrasted the demographics between rural areas with hog CAFO exposure and flooding to those with neither. The study population and study design in this aim are the same as for aim 1, with the addition of examining effect measure modification by hog CAFO exposure.

Exposure

The exposure of flooding was the same as described in Aim 1 using the NC DPS data.

Outcome

The outcome of AGI ED visits (2016-2019) was the same as described in Aims 1 and 2.

Covariates

The covariates in the CITS analysis were the same as described in Aim 1. The continuous hog CAFO exposure created in aim 2 was used in this analysis, although the CITS analyses defined high hog CAFO exposure as above the median in this aim (compared to above the 75th percentile) due to small numbers in some of the strata.

Statistical analyses

For aim 3, we examined how the effect of hurricane flooding on AGI ED rate varies across levels of hog CAFO exposure. To examine EMM by hog CAFO exposure, we included a multiplicative interaction term for hog CAFO exposure (high hog CAFO exposure: above the median of hog exposure, low hog CAFO exposure: below the median of hog exposure, no hog CAFO exposure: hog exposure=0) and hurricane flooding in each CITS analysis. We also examined this relationship by comparing the AGI ED visit rate during the three weeks after Hurricanes Matthew and Florence in ZIP codes with no hog CAFOs, in ZIP codes with hog CAFOs farther than 0.1 mile from the flood extent, and in ZIP codes with hog CAFOs within the flood extent or within 0.1 mile of the flood extent to the AGI ED rate in these same areas during the same three-week periods in non-hurricane years (autumns 2017 and 2019, matching by month, day of week, and year). We also described the differences in these demographics by exposures (hurricane flooding and hog CAFO exposure).

CHAPTER IV: HURRICANE FLOODING AND AGI (AIM 1)

Introduction

Hurricanes can be deadly, traumatizing, and can impair human health. 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.[69,84,159] 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.[70] Contact with waterborne pathogens can cause acute gastrointestinal illness (AGI), defined as diarrhea, vomiting, or nausea that often occur with abdominal pain or fever.[25] 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.[98] 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 from AGI.[25,102,103] AGI can encompass a range of enteric illnesses caused by various viruses, bacteria, and protozoa, as well as non-infectious agents.[25] Surface waters have been found to have higher concentrations of *E. coli*, enterococci, *Salmonella*, *Campylobacter*, *Giardia,* and *Cryptosporidium* after extreme rainfall and flood events.[90–94,96] These pathogens may cause AGI or are associated with the presence of other bacteria that may cause AGI 1-14 days after exposure. 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.[81–84] 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.[160]

In the eastern US, heavy precipitation events have risen over the past 30 years, with autumns becoming wetter.[27] Sixteen hurricanes have made landfall in NC in the last 30 years, and heavy precipitation events are expected to increase in the future.[27,161] 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.[20,104,162] 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.[20] Many residents who use private well water live in rural eastern NC, an area frequently flooded from hurricanes. As the second leading hog producer in the US, NC houses 9 million hogs, which are mainly concentrated in its hurricane-prone eastern region.[6,163] These hogs, nearly as many as total statewide human residents, generate more fecal waste than the entire statewide human population concentrated into less than 4,000 feces lagoons.[13] Hurricanes that hit NC may flood these lagoons, transporting fecal bacteria that may cause AGI into nearby waterways.[7] 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.[7,16]

Hurricane Matthew (October 2016) and Hurricane Florence (September 2018) were the two largest, deadliest, and costliest hurricanes to hit 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.[65,67] 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.[66] The maximum rainfall in NC from Hurricane Matthew was 19 inches reported in Columbus County. 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. Hurricanes Matthew and Florence broke high water records on numerous NC rivers and flooded many of the same areas in eastern NC.[65,67]

While many studies have examined the association between 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.[69,107,164,165] 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 civilian ED visits in NC. We calculated AGI ED visit rates at the ZIP code level, the finest geographic level available. 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.[8,9,20] Our main analyses focused on the increase in AGI ED visit rate 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 estimates 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.[166] For race/ethnicity, 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 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.[151]

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, so they 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. Then 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.[154,167] 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 and reporting issues. For example, some hospitals were added to NC DETECT in 2016.[135] Additionally, some hospitals stopped sending data in 2015 because of challenges during the ICD-9 to ICD-10 transition and were unable to backfill all missing visits. 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 ED visit 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, and nearby polluting sources. We added a control group of unflooded ZIP codes to control for the 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 the study period other large hurricanes that produced over one foot of maximum precipitation (namely, Hurricanes Hermine, Matthew, and Florence) and the periods following the other hurricanes for up to eight weeks or until the hurricane of interest, if they occurred less than eight weeks apart (see Figure 5). 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 (see Appendix 4). 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.

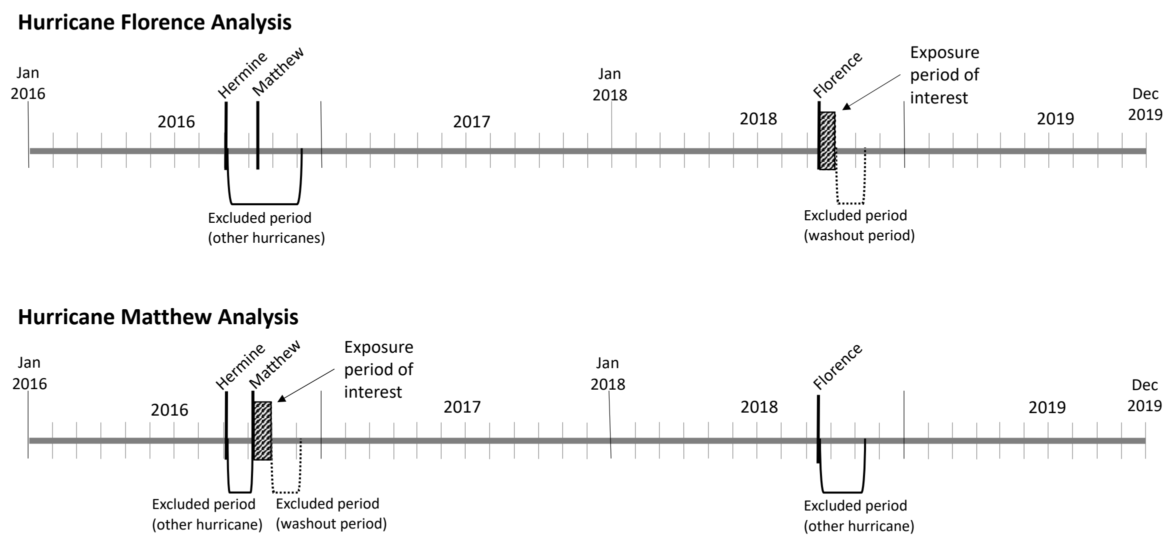


Figure 5. Summary of controlled interrupted time series analysis, including three-week exposure periods of interest (hashed rectangle), 5-week washout periods after the exposure periods (brackets with dotted lines), and excluded periods for other large hurricanes (brackets with solid lines).

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:

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

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 zip code-level 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. 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.[155,156]

We also assessed 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*, pathogenic *E. coli*, *Clostridium difficile*, Giardia, Cryptosporidiosis, Norwalk agent, Rotavirus; see Supplementary Table 4). To understand the effect of our control on our CITS results, we conducted interrupted time series analyses (ITS, with no control area) of the association between various amounts of Matthew and Florence flooding and the change in three-week post-hurricane AGI ED visit rate. Because Hurricanes Matthew and Hermine occurred five weeks apart and Hermine may have influenced the effect of Matthew, we conducted a sensitivity 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). Robust standard errors were used to calculate 95% confidence intervals (95% CI) using the *sandwich* package in R. All analyses were performed in R (Version 3.6.2).[168]

Results

In 2016-2019, there were 868,691 AGI ED visits in NC by residents with a NC ZIP code. 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. 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 9). 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 6). Among all ZIP codes that flooded 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 was 16.5% and the median was 8.6%. However, for analyses, we excluded flooded ZIP codes with <33% flooding. Areas that flooded ≥33% during Hurricanes Matthew and Florence were slightly more rural, with a larger proportion of White non-Hispanics, American Indians, and uninsured residents compared to NC's general population (Table 2).

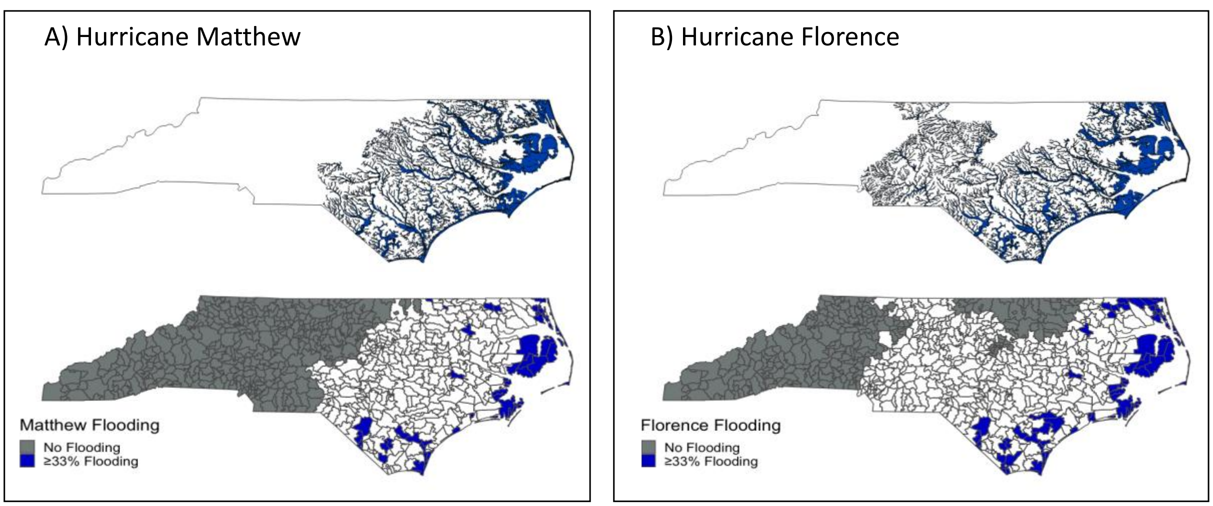


Figure 6. Maps of flood extents. A) Hurricane Matthew flood extent and Hurricane Matthew flooded ZIP codes (at least one third of the ZIP code area flooded after the hurricane, N=81) and unflooded ZIP codes; B) Hurricane Florence flood extent and flooded (N=97) and unflooded ZIP codes. Flood extents created and provided by the North Carolina Department of Public Safety.

Table 2. 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. Demographics are from the 2017 American Community Survey.

		Hurricane Matthew		Hurricane Florence	
	North Carolina Overall	ZIP codes Flooded ≥33%	Unflooded ZIP codes (control)	ZIP codes Flooded ≥33%	Unflooded ZIP codes (control)
Total Population (N)	10,051,041	313,505	5,686,637	392,560	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)
Black, N (%)	2,127,232 (21.2)	44,726 (14.3)	1,018,923 (17.9)	57,483 (14.6)	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)
Hispanic, N (%)	914,745 (9.1)	16,981 (5.4)	496,185 (8.7)	21,995 (5.6)	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)
Number of hogs	12,595,000	176,106	298,533	484,676	271,339
Hog density (hogs/sqmi)	253.0	52.4	12.7	109.0	16.1
Rurality score*	7.19	7.69	6.85	7.68	7.11
Median annual income ($)	48,194	48,306	46,150	47,819	42,861
Area (sqmi)	49,712	3,358	23,491	4,432	16,903
Number of ZIP codes	1082	81	599	97	382

*Higher score indicates more rural area (based on geographic isolation scale)[151]

We observed a 15% increase in AGI ED visit rate (rate ratio (RR)=1.15, 95% CI: 0.97, 1.32, Table 3) after Hurricane Matthew and a 9% increase in AGI ED visit rate (RR=1.09, 95% CI: 0.93, 1.24) after Hurricane Florence compared to the expected AGI ED visit rate based on 2016-2019 trends, controlling for AGI ED visit rate changes after the hurricanes in the unflooded areas (Table 3). The CITS pooled effect estimate for Hurricanes Matthew and Florence together, during the three weeks after each hurricane, was RR=1.11 (95% CI: 1.00, 1.23). When assessing EMM by race, we consistently saw an 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 a large increase in AGI ED rate (RR=2.68, 95% CI: 1.96, 3.41) after Hurricane Florence. 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 visit 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 visit 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 visit rate in areas with a small proportion of residents on private well water (Table 3).

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 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 hurricane (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 7a). For Hurricane Florence, the effect was strongest 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 visit 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 7b). 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 (RR=3.41, 95% CI: 2.75, 4.06; 15 bacterial AGI ED visits in those flooded area during the week; data not shown). The ITS results by flood category illustrate that during the three weeks after Hurricane Matthew, the AGI ED visit rate was substantially 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 8). However, after Hurricane Florence, the AGI ED visit rate increased as percent flooding increased after 33% flooding, with no substantial increase in areas with 0-32% flooding.

Table 3. The association between Hurricanes Matthew and Florence flooding and AGI, main effect and effect measure modification (EMM) 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)			

*In 2016 (Hurricane Matthew), 14.3% of the ED visit data had missing race information, while in 2018 (Hurricane Florence) only 1.4% of the ED visit data had missing race information. As race missingness was not random and was much higher in certain regions, this introduced bias in the Hurricane Matthew race EMM analyses.

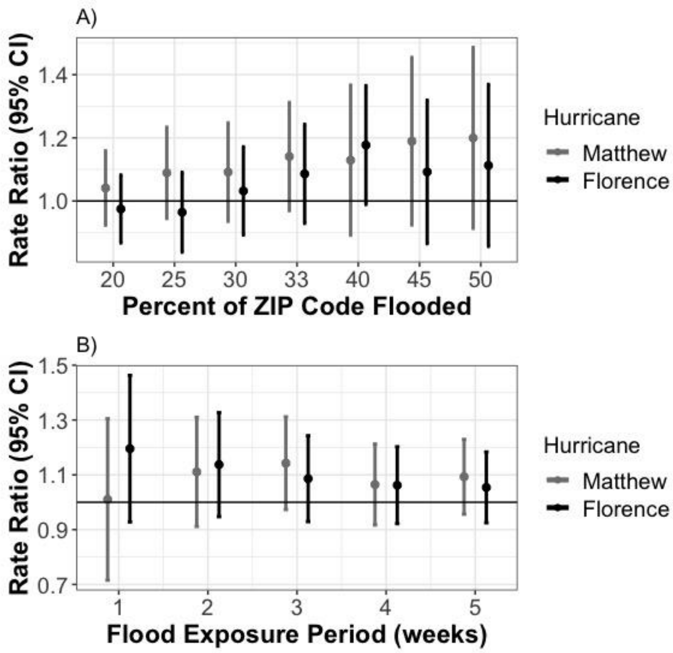


Figure 7. ZIP code AGI ED visit rate ratios generally increased with (A) increasing percent flooding and (B) decreased with longer post-flood exposure period. Flooding cut points (above which ZIP code is categorized as flooded) range from 20% of the ZIP code flooded from the hurricane to 50% of the ZIP 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.

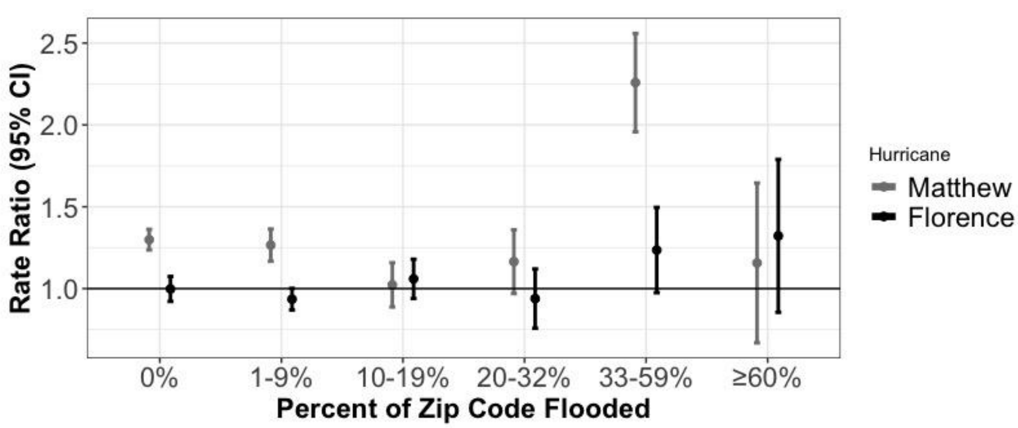


Figure 8. Interrupted time series (ITS, no control group) results show that the increase in AGI ED visit rate during the three weeks among ZIP codes with various amounts of flooding (measured as percent of ZIP code flooded) varied by hurricane. Number of AGI ED visits during the three weeks after hurricane 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.

Results were very similar overall when we conducted the main analysis using Poisson, quasi-Poisson, and negative binomial models (Supplementary Table 5). 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.[169]

Discussion

Overall, 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 ZIP codes with no flooding. We consistently observed an increase in AGI ED visit 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 visit 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 visit 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 are possibly 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 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.[170] 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.[69,170] However, heavy precipitation after a wet period often dilutes pathogen concentration in surface water, decreasing AGI incidence.[170] 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 (Supplementary Figure 10). Hurricane Florence was also substantially wetter than Hurricane Matthew; Hurricane Florence broke rainfall total records in NC, with rainfall up to 36 inches, whereas the maximum rainfall in NC from Hurricane Matthew was 19 inches. 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. However, 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 Supplementary Figure 10). Heavy rain above the 99th percentile of an area's precipitation has been associated with AGI, regardless of flooding.[8,69,170–173] Thus, our CITS analyses could only examine the effect of heavy flooding after hurricanes compared to areas that received heavy rain but no flooding. To further understand the effect of hurricane precipitation on AGI, we conducted supplementary interrupted time series (ITS, no control group) analyses of cumulative six-day hurricane-related precipitation and three-week AGI ED visit rate and 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 6). 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 (Supplementary Figure 10). 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. When we examined the association between hurricane flooding and AGI without a control group (ITS instead of CITS), our results were much stronger, 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). 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.

While many studies use case-crossover, difference-in-difference, and single-group ITS to examine the effect of a disaster or intervention over time, CITS is a more robust method that controls for both time-varying and time-invariant confounders when the pre-event characteristics between the control area and exposed area are comparable.[128,174] While the characteristics of the flooded and unflooded areas were somewhat different in terms of race, income, and rurality, our efforts to use inverse probability of treatment weighting (IPTW) to create a more comparable pseudo-population were unsuccessful due to positivity issues and demographic differences between eastern and western NC (see Supplementary Table 7 and Table 8 for details; IPTW results were similar to unweighted results). 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. Without a control group, ITS analyses may be unable to distinguish the effects of external factors across time from the effect of the event.[133,174]

In addition to the robust CITS methods, this study also benefits from inclusion of two different severe hurricanes, with different pre-hurricane conditions, that affected similar areas. Most studies on this topic either examine many heavy rain/flooding events or a single hurricane.[8,10,92,107,124–126] 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 Hurricane 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. 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 visit rate in areas ≥33% flooded (RR=1.04, 95% CI: 0.87, 1.21).

Our results are generally consistent with other U.S.-based studies that reported a 7-70% increase in AGI rate after flooding, although many of these studies examined less severe flooding.[9,69,86,141,164] 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.[69] 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).[11] 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.[9] 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.[10] As we saw the largest increase in bacterial AGI ED visits and during the first week after Hurricane Florence in ZIP codes flooded ≥33%, 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,[107] 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. Using Medicaid outpatient data and difference-in-differences, they compared counties severely and moderately impacted by Hurricane Floyd to unaffected counties during the year before and the year after Floyd. They observed a small increase in *T. gondii*- and adenovirus-related outpatient visits after Hurricane Floyd. However, *T. gondii* is primarily spread by undercooked meat or food or water contaminated with cat feces and adenoviruses typically spread through and person-to-person contact.[175,176] 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.[177] 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 affected NC four weeks after Florence).[178] 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 as the main outcome, which is one of the broadest indicators of health effects that arise from waterborne pathogens.[103] Our broad all-cause 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, where we observe a stronger association between hurricane flooding and bacterial AGI after Hurricane Florence but no association after Hurricane Matthew. No associations were observed between hurricane flooding and viral AGI for either hurricane. 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.[179] 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.[87] 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.[100]

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 this may be because of the large amount of missing race data in 2016 (during Hurricane Matthew). After Hurricane Florence, we observed a 17% increase in AGI ED visit rate in flooded areas among Black patients and an even higher increase in AGI ED visit rate among American Indians, though we observed no effect among White non-Hispanic patients. Our analysis of racial and ethnic differences in the relationship between hurricane flooding and AGI ED visit rate is limited by the available data. NC DETECT data include race and ethnicity categories of ED patients, but it is unknown how frequently these data are self-reported or are assumed by receptionists or clinicians. Moreover, NC DETECT modified and improved their race variable collection practices in 2016. While we observed that 14.3% of all ED visits were missing a race classification in 2016 (Matthew), this decreased to about 1.5% in 2017-2019. A few regions of the Hurricane Matthew control (unflooded areas in western NC) had an especially high amount of race missingness in 2016, introducing missing-not-at-random (MNAR) bias in the Matthew race EMM analysis.[180] While we report race EMM results for Hurricanes Matthew and Florence, we believe the results from Florence to be more accurate. Although the individual and population-level 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.[142,181]

While several studies find AGI incidence to be higher among White non-Hispanics than Hispanic or Black people,[25,92,100,125,182] other studies have found no difference by race[126] or higher rates of diarrhea-related hospitalization among Black and Hispanic children compared to non-Hispanic Whites.[144] 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, medical trust, and healthcare access, which are caused by structural racism, white supremacy culture, discriminatory policies, and historical differences.[142,143] 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 US town incorporated by Black residents, Princeville, NC, was floodplain land unwanted by Whites that has since been destroyed multiple times from hurricane flooding.[118] For centuries, American Indians 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 American Indian residents[16]—the same areas where many enslaved Black people resided in the 18th and 19th centuries.[119] Black communities have also historically been systematically excluded from regulated public water supplies.[105] Additionally, rural communities in eastern NC frequently have poor healthcare access[41] and have a high percent of uninsured residents, which means reduced access to preventative care and increased risk for health problems.[41,42] 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 9). 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.[145,149] Several studies have also found Hispanic individuals to be less likely to use EDs than non-Hispanic White individuals, due to lack of trust and fear of deportation, which may account for the low ED rate we observed among Hispanics.[183–185]

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. Thousands of people were displaced due to Hurricane Matthew and Hurricane Florence, and it is unknowable, given the available data, 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. To attempt to address this issue, we conducted sensitivity analyses excluding counties with mandatory evacuation orders during the hurricanes, as these are the areas from which people are most likely to be displaced and where assigning their exposure based on their ZIP code might produce the most exposure misclassification. 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), suggesting that displacement may only slightly attenuate the observed association between hurricane flooding and AGI ED visit 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. Eastern NC—predominantly poor, rural areas with high dependence on well water—continues to be hit by devastating hurricanes that spread pathogens and contaminate surface waters. 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 those that did not flood but received heavy rain. This effect was larger among Black and American Indian patients following Hurricane Florence. Our results are supported by data showing high concentrations of pathogens in surface waters after both hurricanes. 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 were also dealing with damage to their homes, relocation, loss of belongings, harmed family and community, 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 disproportionally 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 environmental racism. State, local, and community interventions should consider these equity issues when acting to prevent and respond to such disasters.

Supplementary Tables and Figures

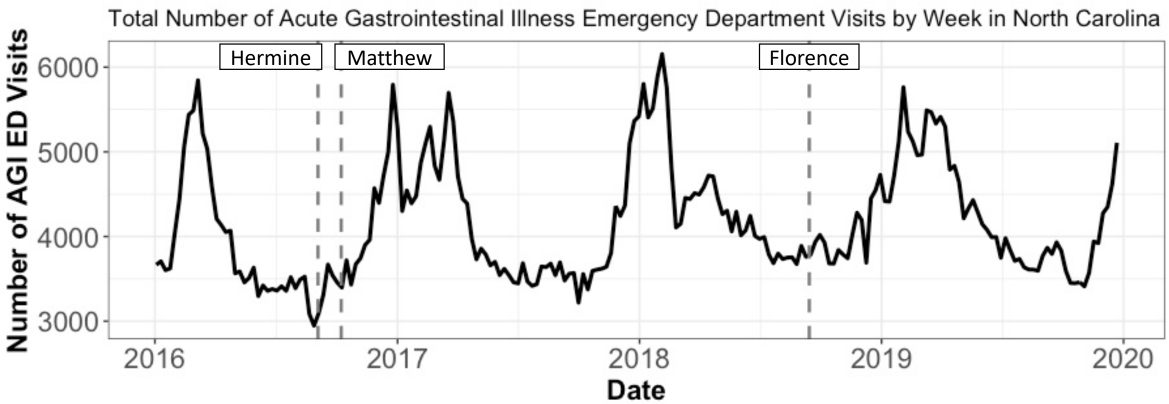


Figure 9. Weekly number of AGI ED visits in North Carolina from 2016-2019.

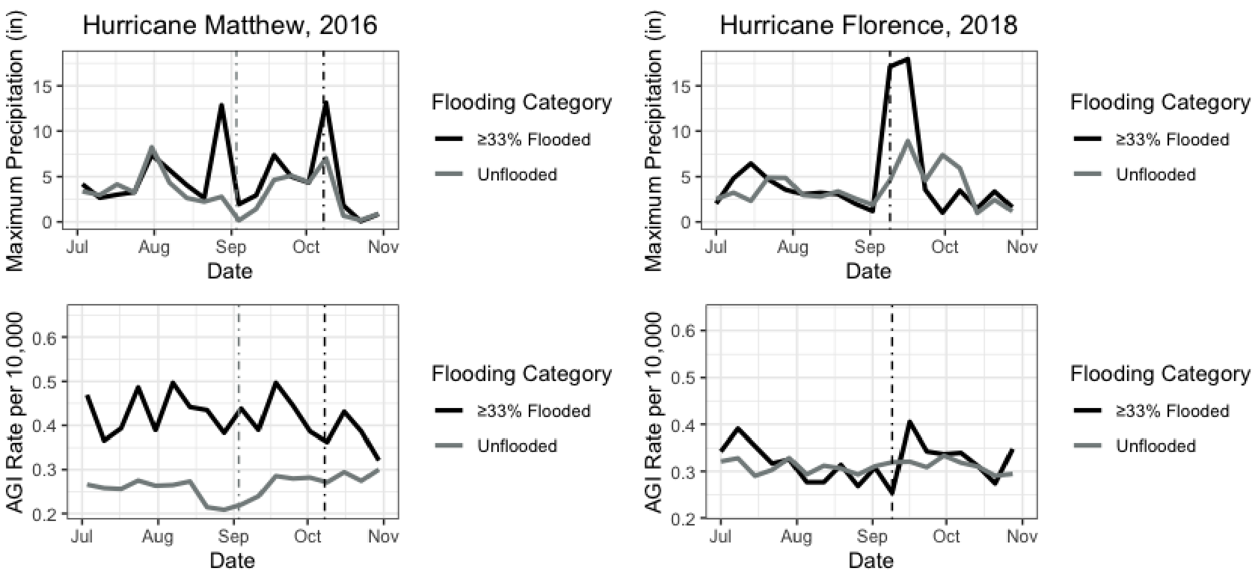


Figure 10. Maximum precipitation and AGI rate per 10,000 people by week by flooding category before and after Hurricanes Matthew and Florence. Precipitation data was provided from the PRISM Climate Group as 4km-by-4km raster data,[138] which we transformed into 1km-by-1km point data then aggregated to 2017 ZIP code polygons, assigning the ZIP code the maximum precipitation recorded in the ZIP code for the day. 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.

Table 4. Names and diagnostic codes of bacterial, protozoal, and viral intestinal infections included in the pathogen-specific analyses. The overall pathogen-specific analysis includes all emergency department visits with any of these codes (bacterial, viral, and protozoal AGI), while the bacterial-specific analysis only includes the codes for bacterial intestinal infections and the viral-specific analysis only includes the codes for viral intestinal infections. The last column indicates the total number of ED visits in North Carolina between 2016-2019 with ICD-10 codes in each category.

Category	**ICD-10 Code and Name**	**Number of cases 2016-2019 in NC**
Bacterial intestinal infections	**A02 Salmonella infections** A02.0 Salmonella enteritis A02.1 Salmonella sepsis A02.2 Localized salmonella infection (meningitis, pneumonia, arthritis) A02.20 Localized salmonella infection, unspecified A02.21 Salmonella meningitis A02.22 Salmonella pneumonia A02.23 Salmonella arthritis A02.24 Salmonella osteomyelitis A02.25 Salmonella pyelonephritis A02.29 Salmonella with other localized infection A02.8 Other specified Salmonella infections A02.9 Salmonella infection, unspecified **A03 Shigellosis** A03.0 Shigellosis due to Shigella dysenteriae A03.1 Shigellosis due to Shigella flexneri A03.2 Shigellosis due to Shigella boydii A03.3 Shigellosis due to Shigella sonnei A03.8 Other shigellosis A03.9 Shigellosis, unspecified **A04 Other bacterial intestinal infections** A04.0 Enteropathogenic Escherichia coli infection A04.1 Enterotoxigenic Escherichia coli infection A04.2 Enteroinvasive Escherichia coli infection A04.3 Enterohemorrhagic Escherichia coli infection A04.4 Other intestinal Escherichia coli infections A04.5 Campylobacter enteritis A04.6 Enteritis due to Yersinia enterocolitica A04.7 Enterocolitis due to Clostridium difficile A04.8 Other specified bacterial intestinal infections A04.9 Bacterial intestinal infection, unspecified	30,524
Protozoal intestinal diseases	**A07 Other protozoal intestinal diseases** A07.0 Balantidiasis A07.1 Giardiasis A07.2 Cryptosporidiosis A07.3 Isosporiasis A07.4 Cyclosporiasis A07.8 Other specified protozoal intestinal diseases A07.9 Protozoal intestinal disease, unspecified	383
Viral intestinal infections	**A08 Viral and other specified intestinal infections** A08.0 Rotaviral enteritis A08.1 Acute gastroenteropathy due to Norwalk agent & other small round viruses A08.11 Acute gastroenteropathy due to Norwalk agent	48,895

	A08.19 Acute gastroenteropathy due to other small round viruses A08.2 Adenoviral enteritis A08.3 Other viral enteritis A08.31 Calicivirus enteritis A08.32 Astrovirus enteritis A08.39 Other viral enteritis A08.4 Viral intestinal infection, unspecified A08.8 Other specified intestinal infections	

Table 5. The increase in AGI ED visits in ZIP codes flooded ≥33% during the three weeks after Hurricanes Matthew and Florence using quasi-Poisson, Poisson, and negative binomial. These rate ratios were calculated using controlled interrupted time series analysis. The dispersion parameter for unweighted quasi-Poisson models=2.4.

Model	Hurricane Matthew	Hurricane Florence
Quasi-Poisson main result	1.14 (0.97, 1.31)	1.09 (0.93, 1.24)
Poisson main result	1.14 (0.97, 1.31)	1.09 (0.93, 1.24)
Negative binomial main result	1.08 (0.91, 1.25)	1.08 (0.94, 1.23)

Table 6. The increase in AGI ED rate during the three weeks after Hurricanes Matthew and Florence among ZIP codes with various amounts of precipitation during the six days after each hurricane arrived in North Carolina, using interrupted time series (ITS, no control group). Total precipitation from PRISM data was broken into quartiles (Q1-Q4). The effect of precipitation among the ZIP codes that received the highest 95th and 99th percentile of precipitation during each storm is also shown.

	Matthew			Florence		
Quartile/ Percentile	**Rate Ratio (95% CI)**	**Number of AGI Cases**	**Inches of Precipitation**	**Rate Ratio (95% CI)**	**Number of AGI Cases**	**Inches of Precipitation**
Q1	1.47 (1.36, 1.58)	1932	0-6.5	0.96 (0.87, 1.06)	2010	0.7-5.5
Q2	1.23 (1.14, 1.32)	3319	6.6-12	1.02 (0.93, 1.10)	3271	5.6-7.4
Q3	1.30 (1.21, 1.38)	2490	12.1-20	0.95 (0.87, 1.03)	3623	7.5-12.9
Q4	1.14 (1.05, 1.24)	2384	20.1-38.1	1.00 (0.91, 1.09)	2640	13-38
P95	1.00 (0.82, 1.19)	493	≥28.6	1.04 (0.84, 1.23)	539	≥27.9
P99	1.05 (0.71, 1.38)	146	≥33	1.17 (0.79, 1.54)	119	≥35.2

Table 7. Comparison of demographics and characteristics of the hurricane-exposed ZIP codes and unflooded ZIP codes, by hurricane flooding and weighting. Because the demographics of the control areas differed slightly from those of flooded areas, we used inverse probability of treatment weighting (IPTW) to weight the unflooded areas to the flooded areas based on the characteristics of the flooded areas that may be confounders or may be associated with AGI ED visit rate (percent White, rurality, median income, percent uninsured, and total number of ED visits). This method enabled us to estimate the average flooding effect in those who experienced ≥33% flooding, the average treatment effect in the treated (ATT). The 2017 American Community Survey (ACS) was selected to estimate ZIP code-level race (percent White), median income, and health insurance (percent uninsured) for IPTW because it captured an appropriate time period for both Hurricane Matthew (2016) and Hurricane Florence (2018). 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.[151] The unflooded ZIP codes that are IPTW-ATT weighted were the implied control for this sensitivity analysis. For Hurricane Florence, IPTW-ATT weighting created a control similar to the Florence flooded areas in terms of percent uninsured and income, but the weighting made the groups more different in their racial distribution and rurality. For Hurricane Matthew, IPTW-ATT weighting created a control similar to the Matthew flooded areas in terms of percent uninsured, percent White, and rurality, but the weighting increased the difference between the groups' median annual incomes.

		Hurricane Matthew			Hurricane Florence		
	North Carolina Overall	ZIP codes Flooded ≥33%	Unflooded ZIP codes - IPTW-ATT weighted	Unflooded ZIP codes - unweighted	ZIP codes Flooded ≥33%	Unflooded ZIP codes - IPTW-ATT weighted	Unflooded ZIP codes - unweighted
Population	10,051,041	313,505	138,967	5,686,637	392,560	285,279	3,019,011
White non-Hispanic, N (%)	6,396,100 (63.6)	233,462 (74.5)	108,460 (78.1)	3,879,033 (68.2)	292,639 (74.6)	192,180 (67.4)	2,227,087 (73.8)
Black, N (%)	2,127,232 (21.2)	44,726 (14.3)	14,147 (10.2)	1,018,923 (17.9)	57,483 (14.6)	45,838 (16.1)	434,559 (14.4)
American Indian, N (%)	109,073 (1.1)	8,594 (2.7)	1,680 (1.2)	25,266 (0.4)	8,851 (2.3)	2,232 (0.8)	19,535 (0.7)
Hispanic, N (%)	914,745 (9.1)	16,981 (5.4)	10,179 (7.3)	496,185 (8.7)	21,995 (5.6)	30,844 (10.8)	219,312 (7.3)
Uninsured, N (%)	1,186,236 (12.1)	44,768 (14.6)	20,108 (14.6)	746,281 (13.3)	54,316 (14.27)	41,404 (14.64)	392,169 (13.2)
Number of hogs	12,812,561	222,418	7917	296,055	611,652	27,538	296,134
Rurality score*	7.19	7.69	7.09	6.85	7.68	6.63	7.11
Median Annual Income ($)	48,194	48,306	42,706	46,150	47,819	48,660	42,861
Number of ZIP codes	1082	81	118	599	97	143	382
Sum of weights	-	81	14.2	599	97	17.5	382

*Higher score indicates more rural area (based on geographic isolation scale)[151]

Table 8. The association between hurricane flooding and AGI, by hurricane with a weighted (IPTW) vs. unweighted control, using controlled interrupted time series where the AGI ED visit rate during the three weeks after each hurricane in zip codes with a third or more of the area flooded after each hurricane was compared to the expected AGI in these areas based on 2016-2019 AGI ED visit trends and controlling for the change in AGI ED visit rate during the event period in areas that did not flood.

	Hurricane Matthew Rate Ratio	n cases	Hurricane Florence Rate Ratio	n cases
Unweighted main result	1.14 (0.97, 1.31)	330	1.09 (0.93, 1.24)	368
Weighted main result (IPTW)	1.10 (0.92, 1.28)	330	1.09 (0.92, 1.26)	368

Table 9. Overall emergency department (ED) rate and all-cause acute gastrointestinal illness (AGI) ED rate per 10,000 people, 2016-2019, by sub-group. This was calculated as ED visits over the total population of the subgroup (based on American Community Survey data).

Category	AGI ED Rate	ED Rate
Race/ethnicity		
American Indian	0.98	14.63
Asian	0.20	3.42
Black	0.99	11.79
Hispanic	0.67	9.08
Pacific Islander	1.20	10.08
White non-Hispanic	0.67	7.50
Other	1.79	25.95
Insurance category		
Public	0.71	15.0
Private	0.13	2.73
Self-Pay	0.48	11.7
Age category		
Under 5	0.97	8.84
Age 5-17	0.25	4.55
Age 18-64	0.30	7.51
Over 64	0.36	8.87

CHAPTER V: INDUSTRIAL HOG OPERATIONS AND AGI (AIM 2)

Introduction

With 9 million hogs, North Carolina (NC) is the second leading hog producer in the United States. Most of the state's hogs are housed, by the thousands, at large concentrated animal feeding operations (CAFOs) in eastern NC.[14] The massive amount of waste produced by these hogs—more fecal waste than the entire statewide human population—is collected in uncovered pits, or lagoons, and sprayed on land as a fertilizer.[13] However, as the land cannot absorb all of the manure, these practices often spread pathogens and chemicals that invariably pollute the air and water.[7] Communities that live near hog CAFOs have reported numerous health problems, including throat, eye, and nose irritation, headaches, diarrhea, methicillin-resistant *S. aureus*-related (MRSA) infections, and reduced quality of life.[15] Drinking water contaminated with waterborne pathogens from hog waste or inhaling the sprayed waste in the air can result in diarrhea, vomiting, nausea, or other gastrointestinal tract distress in humans, known collectively as acute gastrointestinal illness (AGI).[19,24] AGI can be severely painful and can disrupt work and school for several days. In the US, approximately 2,330,000 waterborne enteric illnesses occurred in 2014, which incurred about $160 million in direct healthcare costs.[101] Despite the harm caused by AGI and the potential association between hog CAFOs and AGI, few studies have examined the effect of hog CAFO proximity and density on human AGI.

Numerous pathogens found in hog manure can cause AGI including *Escherichia coli* O157:H7, *Salmonella* spp., *Campylobacter* spp., *Yersinia enterocolitica*, *Cryptosporidium parvum*, *Giardia* spp.[21,22] One gram of raw hog manure can contain 100 million fecal coliform bacteria, and NC hogs produce almost 10 million tons of waste each year.[28,36] Residents who live within two miles of hog CAFOs have reported worse quality of life and higher occurrences of gastrointestinal symptoms, headaches, coughing, and sore throats compared to residents who do not live near a hog CAFO.[24] After heavy rain events, surface water and groundwater near hog farms often have higher concentrations of pathogens, suggesting that the rate of AGI of residents near hog CAFOs may be especially high after heavy precipitation.[23,51] While healthy humans are usually able to recover from AGI in 1-3 days without medical care, young children, older adults, and immunosuppressed people are at higher risk for severe illness.[100,140,141,186]

Hog CAFOs, and the accompanying health issues related to living near hog CAFOs, are not distributed equally across NC; industrialized hog operations have been disproportionally built near communities of people of color (POC) in NC.[16] NC hog CAFOs are densely concentrated in several counties in the flood-prone eastern part of the state that are predominantly rural and are also home to many other harmful exposures like poultry CAFOs and landfills (Figure 11).[16–18] Many of the NC counties with a high density of hog CAFOs also have poor healthcare access and a high percent of uninsured residents, which means reduced access to preventative care and increased risk for health issues.[41,42] Because of the area's rurality, many residents near CAFOs use private wells, which stand at higher risk of contamination than community water supplies.[19,20] Each year, over $40 million are spent in NC on AGI emergency department (ED) visits due to microbial contamination in drinking water.[20] Given that rural POC communities in eastern NC have decreased healthcare access, worse overall health, and a higher risk of private well water contamination than the rest of the state, the disproportionate effect of hog CAFOs on these communities aggregates existing health problems and health inequities.

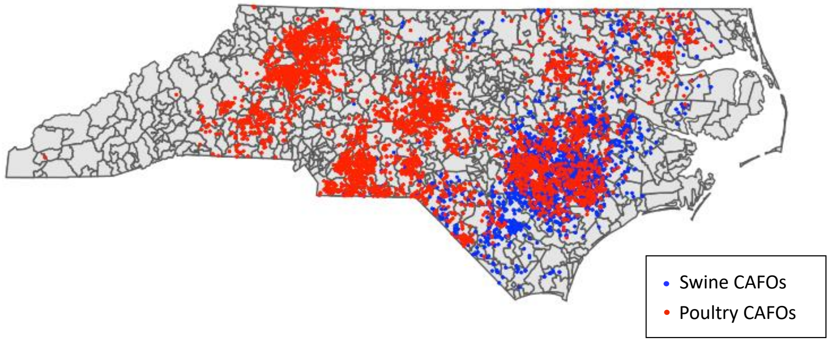


Figure 11. Locations of swine and poultry concentrated animal feeding operations (CAFOs) in North Carolina (NC), according to 2014 NC Department of Environmental Quality swine permit data and poultry estimates from Environmental Working Group and Waterkeepers Alliance.

This is the first study, to our knowledge, that investigates how race may modify the relationship between hog CAFO exposure and AGI ED visit rate. While a few studies have examined the association between CAFO exposure and AGI rates, these studies have mixed results and none have assessed this relationship in NC.[46–49] This paper investigates how the relationship between hog CAFO exposure and AGI ED visit rate varies by race, age, rurality, and precipitation.

Methods

Exposure

We used 2014 swine permit data from the NC Department of Environmental Quality (DEQ), which included the number of animals, type/life stage of animals, and location of each permitted animal facility. We calculated the steady state live weight (SSLW) of each hog CAFO using the North Carolina Department of Environment and Natural Resources' formula that incorporates the number of hogs, growth stage of the hogs, and average weight of each growth stage (see Table 1 for list of growth stage/production phase of hogs and mean weight used to calculate SSLW).[158] SSLW is an indicator of the amount of waste produced at each hog CAFO and has been used in other studies.[16,157]

We measured the distance between hog CAFOs and census block centroids and used inverse distance weighting (IDW) with Gaussian decay (W=$e^{\frac{-distance^2}{\alpha}}$, capped at 10 miles with α=3) to convert distances to weights (see Appendix 5). Our alpha parameter and distance restriction were based on literature that suggests an association between living within half a mile to two miles of hog CAFO and various health outcomes, with weaker associations at three miles and five miles.[43,48,187–189] We multiplied the distance-based weights by each hog CAFO's SSLW to create a block-level exposure measure based on both hog density and distance to CAFOs. We aggregated the block-level hog CAFO exposure estimates to the ZIP code level using population weights created from 2017 American Community Survey (ACS) five-year block group-level estimates, the 2010 block-level census data, and 2017 NC polygon ZIP code boundaries from Esri. Because the hog CAFO exposure measure was highly skewed, we took the natural log of the measure. We categorized ZIP codes in the upper quartile of hog CAFO exposure as high hog CAFO exposed and compared them to ZIP codes with no hog CAFOs within 10 miles (i.e., hog CAFO exposure measure=0), thus excluding areas with low/medium hog CAFO exposure from the main analyses (Figure 12).

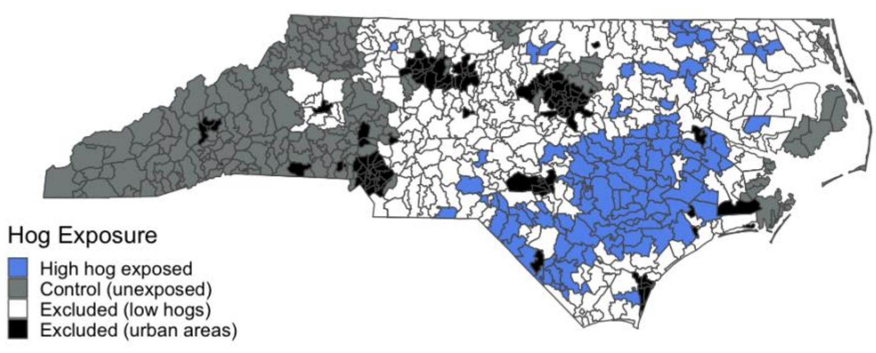


Figure 12. North Carolina ZIP codes with high hog CAFO exposure (>75th percentile of hog CAFO exposure measure), ZIP codes with no hog CAFOs (control areas), and ZIP codes excluded from analyses (urban areas and low hog CAFO exposed areas).

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 civilian ED visits in NC. We calculated 2016-2019 AGI ED visit rates at the ZIP code level, the finest geographic level available. 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 AGI ED visits.[8,9,20] Our main analyses focused on all-cause AGI ED visit rate because specific pathogens are seldom tested for and/or included in the ED discharge report.

Covariates

For the main analyses, we accounted for ZIP code-level rurality, health insurance status, median income, and race. We identified rurality, health insurance status, and median income as the minimally sufficient set of confounders using a directed acyclic graph (DAG; see Appendix 3). We incorporated race when we created our control pseudo-population because race is strongly correlated with the exposure and we found it necessary to include a race variable in order to create balanced groups.[190] Data on median income, number of White residents, number of uninsured residents, and total number of residents were available at the block group-level from the 2017 ACS. We assigned these values to the centroids of each 2010 census block based on the proportion of the block group population within that block and then aggregated these block centroid data to create ZIP code-level population estimates for population, median income, percent of ZIP code population uninsured, and percent of ZIP code population White. Rurality was measured using a continuous geographic isolation scale that classifies ZIP codes according to their access to resources.[151]

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, median income, and well water usage. The 2015 U.S. Geological Survey estimates the number of people in each county on private well water, and we used this data to create ZIP code-level well water usage estimates.[166] For race/ethnicity, 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 analyzed Black, American Indian, Hispanic, and Asian patients separately, but due to insufficient case counts, we combined Pacific Islander patients and Other Race patients into an Other Race category.

We estimated the full population and stratum-specific population (by age category, race/ethnicity, health insurance status) using 2017 ACS block group estimates aggregated to the ZIP code level. We did not use census data at the ZIP code tabulation area (ZCTA) level due to the spatiotemporal mismatch between ZCTAs and ZIP codes.[154,167] We examined all changes in ZIP codes from 2016-2019 and assigned all ZIP codes to the 2017 ZIP code polygon in which they were contained. The continuous geographic isolation scale was split into quartiles when examining EMM by rurality.[151] Data on the location of poultry CAFOs and estimated number of birds at each poultry CAFO was provided by the Environmental Working Group and Waterkeepers Alliance. They identified poultry facility locations with high-resolution satellite data and aerial photograph and estimated number of birds at each poultry CAFO using the NC Agricultural Chemical Manual and the U.S. Department of Agriculture's Ag Census.[30]

Analysis

For the main analysis, we used inverse probability of treatment weighting (IPTW) to estimate the average treatment effect on the treated (ATT, or, in this study, the average exposure effect on the high hog exposed). IPTW creates a synthetic population with no confounding, provided all the confounders have been identified, appropriately measured, and incorporated into the weights.[191] Using IPTW, we created a control group with similar demographics as the high hog CAFO exposed population (based on the ZIP codes' median income, rurality, percent of non-Hispanic White residents, and percent of uninsured residents) but with no hog CAFO exposure. We chose to compare areas with high hog CAFO exposure to areas with no hog CAFO exposure because these areas had relatively similar demographics before IPTW; areas with low hog CAFO exposure had higher median incomes and a larger percent of non-Hispanic White residents than NC overall and the high hog CAFO exposed areas. We excluded metropolitan ZIP codes from all main analyses by excluding the lowest quartile of the geographic isolation scale (below 5.6; 273 zip codes excluded), as urban areas lack hog CAFOs and have different ED visit patterns than areas with hog CAFOs. We used quasi-Poisson models to account for overdispersion in the ED visit data. When examining EMM, we adjusted for percent uninsured, median income, and rurality, which we had identified as confounders using a directed acyclic graph. Robust standard errors were used to calculate 95% confidence intervals (95% CI) using the *sandwich* package in R. All analyses were performed in R (Version 3.6.2).[168]

Sensitivity analyses

While our main analysis examined the effect of high hog CAFO exposure on AGI ED visit rate compared to no hog CAFO exposure using dichotomous categories, in sensitivity analyses we examined the effect between hog CAFO exposure and AGI ED visit rate using alternate methods to categorize hog CAFO exposure. Using our continuous ZIP code-level hog CAFO exposure variable, we created tertiles of all ZIP codes with any hog CAFO exposure and separately compared the AGI ED visit rates in high, medium, and low hog exposed ZIP codes to the hog unexposed ZIP codes, using IPTW and quasi-Poisson models to calculate rate ratios (we created a different control pseudo-population for each tertile of hog CAFO exposure, so each control had similar demographics to the compared exposure tertile). We also examined the association between the continuous hog CAFO exposure (which had been log transformed) and AGI ED visit rate. Additionally, we assessed how changing the distance cap and the alpha for the IDW hog CAFO exposure measure changed the main effect. We also compared our main result that used the IDW hog CAFO exposure variable to results when we used a simpler hog density measure (number of hogs in ZIP code and half-mile buffer around ZIP code, >75th percentile hog density=high hog exposed and 0 hog CAFOs within ZIP code and half-mile buffer=control).

Because hog CAFOs and poultry CAFOs are frequently co-located and living near either type of CAFO may increase one's risk for AGI (Figure 11), we conducted sensitivity analyses where ZIP codes with *any* poultry CAFOs were excluded from the control group and separately where ZIP codes with bird density above the median were excluded from the control group. As poultry CAFOs are located in the majority of areas hog CAFOs are located, we were unable to conduct analyses with poultry CAFOs excluded from the exposed group. We also assessed the association between bird density and AGI ED visit rate to better understand how poultry CAFOs may influence the effect we observed between high hog CAFO exposure and AGI ED visit rate.

To examine how the association between high hog CAFO exposure and AGI rate may vary according to antecedent rain, we conducted restricted analyses according to the ZIP code precipitation during the previous week. We obtained daily precipitation data from the PRISM Climate Group as 4km-by-4km raster data,[138] 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. We identified the days (day 0) and ZIP codes where the precipitation was above the 80th, 90th, 95th, and 99th percentile of daily NC precipitation 2016-2019 (to represent high precipitation time periods and areas) and all AGI ED visits within the next seven days (days 1-7) were included in each analysis of high hog CAFO exposure and AGI ED rate. To represent low precipitation time periods and areas, we identified days and ZIP codes where the precipitation fell below the 50th percentile of daily NC precipitation during the prior seven days and included all AGI ED visits from these days in a separate analysis of high hog CAFO exposure and AGI. We created new IPTWs for each analysis, matching for median income, rurality, percent uninsured, and percent White. Lastly, we examined whether total precipitation over the entire study period by ZIP code was an EMM in the relationship between high hog CAFO exposure and AGI, to assess whether this relationship was stronger in areas that consistently received heavy rain.

We conducted separate analyses restricted to ICD-10 codes that indicated specific pathogens that may be found in hog feces that could cause AGI, including enterotoxigenic or enterohemorrhagic *E. coli*, *Salmonella*, *Campylobacter*, *C. difficile*, and rotavirus. We also examined the effect between hog CAFO exposure and overall bacterial AGI, viral AGI, and protozoal AGI. Additionally, as we observed strong EMM by rurality, we conducted analyses restricted to rural areas (the highest quartile of the continuous geographic isolation scale) where we examined EMM by race, age, and insurance status.

Results

We categorized 111 ZIP codes as high hog exposed and 225 as control ZIP codes (no hog CAFO exposure, see Figure 12). High hog exposed ZIP codes had an average hog density of 1,173 hogs/mile^2 and a median of 50,022 hogs and a maximum of 903,156 hogs (in 213 hog CAFOs) per ZIP code. In 2016-2019, there were 868,691 AGI ED visits in NC by residents with a NC residential ZIP code, with 84,963 AGI ED visits (1030 AGI ED visits per 10,000 people) in high hog exposed ZIP codes and 168,123 (865 AGI ED visits per 10,000 people) in control ZIP codes. High hog exposed areas had higher proportions of American Indian, Hispanic, and Black people and lower proportions of White non-Hispanics and Asians than areas with no hog CAFO exposure (Table 10). Among Asian Americans in NC, high hog exposed ZIP codes have a larger proportion of Filipino, Japanese, and Vietnamese residents and a lower proportion of Indian and Chinese residents compared to ZIP codes with no hog CAFO exposure (Supplementary

Table 18). High hog exposed areas also have a higher proportion of people without health insurance, lower median household incomes, and higher poultry CAFO density than the control. The high hog exposed ZIP codes are also more rural, with a higher overall ED rate than the control. The control and high hog exposed areas likely differ in several unmeasured ways as well. With IPTW, we were able to create a control with similar demographics as the high hog exposed ZIP codes, although the control continues to have a much lower bird density than the high hog exposed area.

Table 10. Comparison of demographics and characteristics of the high hog exposed ZIP codes (>75th percentile of inverse distance weighted hog measure), the unweighted control ZIP codes with no hog CAFO exposure, and the inverse probability of treatment weighted. The control was created using IPTW to match on rurality, percent white, percent uninsured, and median income (data from 2017 American Community Survey).

Characteristic	Unweighted Control	IPT-Weighted Control (assumed control)	High Hog Exposed (>75th percentile)
Total Population	1,943,262	934,302	824,987
White non-Hispanic, N (%)	1,654,190 (85.1)	583,611 (62.5)	511,703 (62.0)
Black, N (%)	168,122 (8.7)	262,983 (28.1)	220,887 (26.8)
American Indian, N (%)	16,338 (0.8)	24,417 (2.6)	37,670 (4.6)
Hispanic, N (%)	121,834 (6.3)	60,883 (6.5)	94,360 (11.4)
Asian, N (%)	27,718 (1.43)	5,907 (0.6)	5,756 (0.7)
Uninsured, N (%)	197,656 (10.3)	95,560 (10.6)	104,552 (13.2)
Median Income	46,185	40,214	38,784
Rurality Score	7.61	8.15	8.09
Hogs, N	0	0	11,254,040
Average Hog Density (hogs/sqmi)	0	0	1173
Birds, N	105,098,131	29,706,726	202,364,566
Average Bird Density (birds/sqmi)	7,714	2,632	21,086
SQMI	13,624	11,287	9,597
Total ED Visits	2,588,820	1,511,287	1,761,909
Total AGI Visits	168,123	82,525	84,963
ED Rate per 10,000 people	3,331	4,044	5,337
AGI ED Rate per 10,000 people	216	221	257
Sum of Weights	225	189	111
Number of ZIP Codes	225	224	111

In high hog exposed areas compared to areas without hog CAFO exposure, we observed a 17% higher (rate ratio [RR]=1.17, 95% CI: 1.08, 1.26, Table 11) in AGI ED visit rate overall. We found strong modification by rurality and observed a rate ratio of 1.24 (95% CI: 1.04, 1.48) in rural areas, while we did not observe an effect of high hog exposure in small towns (RR=1.05, 95% CI: 0.93, 1.19) and micropolitan (RR=0.88, 95% CI: 0.80, 0.97) areas. We observed higher rate ratios in the lowest ($23,600-35,999: RR=1.12, 95% CI: 0.97, 1.28) and highest ($47,900-103,000: RR=1.29, 95% CI: 1.00, 1.66) median income categories and the lowest (1-9.2% uninsured: RR=1.39, 95% CI: 1.13, 1.70) and highest (14.9-32.7% uninsured: RR=1.15, 95% CI: 0.96, 1.37) categories of percent of population uninsured, with no effect in the middle categories (Table 11). We did not observe a positive association between high hog CAFO exposure and AGI ED visit rate in ZIP codes with the highest amounts of precipitation during the study period. We did not observe patterns in the association by well water usage. When assessing the association between high hog CAFO exposure and AGI ED visit rate in all rural, small town, and micropolitan ZIP codes (as we removed urban ZIP codes from main analyses), we observed positive associations for American Indian (RR=1.80, 95% CI: 1.45, 2.14) and Asian (RR=2.21, 95% CI: 1.86, 2.55) patients compared to areas without hog CAFO exposure, but we observed no associations for patients of other races and ethnicities.

Table 11. The association between high hog CAFO exposure (>75th percentile of IDW hog CAFO measure) and AGI ED visit rate (2016-2019). For the main effect, high hog exposed ZIP codes were compared to IPTW control ZIP codes with no hog CAFO exposure (matched on rurality, median income, percent uninsured, percent white). Effect measure modification models do not use IPTW; these models adjust for rurality, median income, and percent uninsured, and they have a product interaction term between the effect measure modifier and the dichotomous hog CAFO exposure variable. Metropolitan ZIP codes were removed from analyses; these analyses include all micropolitan, small town, and rural ZIP codes with high hog exposure or no hog exposure.

Analysis	Rate Ratio (95% CI)	Number of AGI ED Visits in High Hog CAFO Exposed ZIP Codes	Number of AGI ED Visits in ZIP Codes with No Hog CAFO Exposure
Main analysis (hog exposed: >75th percentile)	1.17 (1.08, 1.26)	168,123	84,963
Effect measure modification:			
Rurality[1,2]			
Micropolitan	0.88 (0.80, 0.97)	37,259	81,643
Small Towns	1.05 (0.93, 1.19)	33,036	33,656
Rural	1.24 (1.04, 1.48)	14,668	16,517
Income[1,3]			
$23,600-35,999	1.12 (0.97, 1.28)	39,578	24,286
$36,000-41,599	0.91 (0.78, 1.06)	17,018	56,486
$41,600-47,899	0.99 (0.86, 1.15)	233,45	35,108
$47,900-103,000	1.29 (1.00, 1.66)	5,022	51,198
Percent Uninsured[1,3]			

1.0-9.2%	1.39 (1.13, 1.70)	7,363	42,834
9.3-11.7%	0.89 (0.80, 1.00)	28,045	67,110
11.8-14.8%	0.97 (0.86, 1.10)	23,754	47,266
14.9-32.7%	1.15 (0.96, 1.37)	25,789	9,897
Precipitation (4-year sum of daily rain, inches)[1,4]			
0-19 inches	1.12 (0.71, 1.78)	1,752	3,634
20-51	1.05 (0.66, 1.68)	92,73	10,619
52-105	1.12 (0.98, 1.30)	21,414	31,460
106-361	0.92 (0.85, 1.01)	52,524	121,388
Percent of people on well water[1, 5]			
1-16	0.82 (0.62, 1.03)	15,598	64,408
17-33	0.97 (0.81, 1.13)	22,626	119,315
34-47	1.15 (0.97, 1.32)	28,235	110,864
48-85	0.97 (0.79, 1.14)	16,178	38,023
Race/ethnicity[6]			
American Indian	1.80 (1.45, 2.14)	3,913	505
Asian	2.21 (1.86, 2.55)	285	487
Black	0.89 (0.55, 1.24)	28,420	19,148
Hispanic	0.85 (0.50, 1.20)	6,299	7,900
White non-Hispanic	0.87 (0.53, 1.22)	40,114	123,123
Other	0.43 (0.08, 0.78)	4,636	13,589
Age[6]			
Under 5	1.09 (0.86, 1.39)	12,754	20,188
5-17	1.12 (0.86, 1.48)	9,229	16,424
18-64	1.11 (0.98, 1.25)	48,626	94,670
Over 64	1.00 (0.80, 1.24)	12,331	32,122
Insurance[6]			
Private	1.42 (1.14, 1.77)	17,583	37,826
Public	1.00 (0.87, 1.14)	46,749	82,102
Self-pay/none	1.17 (0.93, 1.48)	16,052	26,452

[1]ZIP code level variables separated into quartiles; [2]Rurality was measured using a continuous geographic isolation scale that classifies ZIP codes according to their access to resources;[151] [3]ZIP code-level estimates created from 2017 American Community Survey data; [4]Precipitation from PRISM Climate Group; [5]Well water data from the 2016 U.S. Geological Survey at the county level; [6]Individual-level data from ED visit data.

Because we observed the effect only in rural areas, we examined EMM by race/ethnicity, age, and insurance status in analyses restricted to rural areas. In these analyses, we found much higher AGI ED visit rates among American Indian (RR=3.62, 95% CI: 3.03, 4.21), Asian (RR=5.54, 95% CI: 4.80, 6.29), and Black (RR=1.54, 95% CI: 1.06, 2.02) patients in rural high hog areas compared to rural areas without hog CAFO exposure (Table 12). We did not observe strong differences by age, although the strongest effect was among adults age 18-64 (RR=1.43, 95% CI: 1.17, 1.69). While we observed a positive association between high hog CAFO exposure and AGI ED visit rate in all insurance categories, the strongest association was found among patients who paid for the ED visit themselves and were likely uninsured (RR=1.79, 95% CI: 1.44, 2.13).

Table 12. The association between high hog CAFO exposure (>75th percentile of IDW hog CAFO measure) and AGI ED rate (2016-2019) compared to areas with no hog CAFO exposure, restricted to rural areas and with various effect measure modifiers (using individual level information from ED visit data).

Effect Measure Modifier	Rate Ratio (95% CI)	Number of AGI ED Visits in High Hog CAFO Exposed ZIP Codes	Number of AGI ED Visits in ZIP Codes with No Hog CAFO Exposure
Race/ethnicity			
American Indian	3.62 (3.03, 4.21)	149	187
Asian	5.54 (4.80, 6.29)	15	16
Black	1.54 (1.06, 2.02)	5377	515
Hispanic	1.06 (0.59, 1.54)	839	588
White non-Hispanic	1.26 (0.92, 1.61)	7197	14505
Other	1.46 (0.83, 2.10)	791	357
Age Category			
Under 5	1.27 (0.91, 1.63)	5117	1881
5-17	1.25 (0.96, 1.54)	1678	1633
18-64	1.43 (1.17, 1.69)	8053	8726
Over 64	1.15 (0.91, 1.39)	2415	3862
Insurance			
Private	1.26 (0.97, 1.55)	2939	3677
Public	1.32 (1.01, 1.62)	8057	8703
Self-pay/none	1.79 (1.44, 2.13)	2537	2169

We observed that the association between high hog CAFO exposure and AGI ED visit rate was higher when restricted to the days and areas when daily heavy precipitation was above the 99th percentile of NC daily precipitation during at least one day during the prior week (RR=1.54, 95% CI: 1.25, 1.83, Table 13). When we restricted our analyses to only include AGI ED visits in areas and during weeks with low precipitation (below the 50th percentile of NC daily precipitation the previous seven days), we did not observe an association between high hog CAFO exposure and AGI ED visit rate (RR=1.03, 95%: 0.37, 1.69).

Table 13. The association between high hog CAFO exposure (>75th percentile of IDW hog CAFO measure) and AGI ED rate (2016-2019) restricted by various daily precipitation measures. All x percentile days (day 0) of daily precipitation were identified and then all AGI ED visits within the next seven days (days 1-7) were included in each analysis. For example, for the "above the 99th percentile of precipitation" analysis, we only included AGI ED visits when the daily ZIP code precipitation was above the 99th percentile of NC daily precipitation during one of the prior seven days. For the "below the 50th percentile of precipitation" analysis, we only included AGI ED visits when the daily ZIP code precipitation was below the 50th percentile of NC daily precipitation during all of the prior seven days. As the 50th percentile was 0 inches, this analysis included only areas and days with no precipitation in the previous week.

Precipitation Restriction	**Rate Ratio (95% CI)**	**Number of AGI ED Visits in High Hog CAFO Exposed ZIP Codes**	**Number of AGI ED Visits in ZIP Codes with No Hog CAFO Exposure**
Below the 50th percentile of precipitation (0 inches)	1.03 (0.37, 1.69)	6,576	15,584
Above the 80th percentile of precipitation (0.3 inches)	1.33 (1.18, 1.48)	57,976	108,703
Above the 90th percentile of precipitation (0.7 inches)	1.33 (1.18, 1.48)	37,557	70,221
Above the 95th percentile of precipitation (1.2 inches)	1.32 (1.17, 1.47)	20,530	40,245
Above the 99th percentile of precipitation (2.4 inches)	1.54 (1.25, 1.83)	4,501	8,495

We also stratified our main IPTW analysis by year and by season and found that the rate ratios have been increasing with time (2016: RR=1.11, 95% CI: 1.01, 1.22; 2019: RR=1.25, 95%CI: 1.17, 1.34; Table 14). While we did not observe much difference by season, the association was slightly stronger in during fall and winter (Table 14). We found that people who lived in high hog exposed ZIP codes were twice as likely to visit an ED due to a *Salmonella* infection compared to those who lived in areas without hog CAFO exposure (RR=2.07, 95% CI: 1.45, 2.95, Table 15). We did not observe any overall positive associations between high hog CAFO exposure and pathogenic *E. coli*, *Campylobacter*, *C. difficile*, and rotavirus ED visits, although when restricted to rural areas we found a rate ratio of 1.54 (95% CI: 1.18, 2.00) between high hog CAFO exposure and *C. difficile* ED visits compared to no hog CAFO exposure.

Table 14. Sensitivity analyses of the association between high hog CAFO exposure (>75th percentile of IDW hog CAFO exposure measure) and AGI ED rate restricted by year and season (2016-2019), compared to areas without hog CAFO exposure (IPTW control).

Sensitivity analysis	Rate Ratio (95% CI)
Year	
2016	1.11 (1.01, 1.22)
2017	1.13 (1.03, 1.23)
2018	1.16 (1.08, 1.26)
2019	1.25 (1.17, 1.34)
Season	
Winter	1.19 (1.10, 1.29)
Spring	1.12 (1.03, 1.21)
Summer	1.15 (1.06, 1.24)
Fall	1.20 (1.11, 1.31)

Table 15. The association between high hog CAFO exposure (>75th percentile of the IDW hog CAFO exposure variable) and alternative AGI case definitions by pathogen or pathogen group, compared to areas without hog CAFO exposure (IPTW control; 2016-2019).

Pathogen	Rate Ratio (95% CI)	Number of AGI ED Visits in High Hog Exposed ZIP Codes	Number of AGI ED Visits in ZIP codes Unexposed to Hogs
All bacteria	0.89 (0.80, 0.99)	2543	6925
All viruses	1.13 (0.97, 1.32)	5401	10242
All protozoa	0.66 (0.38, 1.16)	15	76
Pathogenic *E. coli*	0.16 (0.04, 0.55)	8	186
Salmonella	2.07 (1.45, 2.95)	159	308
Campylobacter	0.41 (0.28, 0.60)	68	547
C. difficile	0.86 (0.77, 0.97)	2017	5487
Rotavirus	0.18 (0.07, 0.44)	15	169
Restricted to rural areas			
C. difficile	1.54 (1.18, 2.00)	336	515
Salmonella	1.79 (0.96, 3.33)	43	30

We did not observe any effect when we examined the continuous association between hog CAFO exposure and AGI ED rate (RR=1.00, 95%CI: 0.99, 1.00; Table 16). When we separated our continuous hog CAFO exposure measure into tertiles and compared each tertile to areas without hog CAFO exposure (using different IPTWs for each tertile), we found a positive association between both medium (RR=1.21, 95% CI: 1.09, 1.35) and high (RR=1.26, 95% CI: 1.14, 1.40) hog CAFO exposure and AGI ED rate, but no association between low hog CAFO exposure and AGI ED rate (RR=1.01, 95% CI:0.90, 1.13;Table 16). In analyses where we excluded all ZIP Codes with poultry CAFOs (within ZIP code or within a half mile from ZIP code boundary) from the control, we found a stronger association between hog density and AGI ED rate (RR=1.30, 95% CI: 1.21, 1.40; Table 17). Similarly, when we examined the association between bird density and AGI ED visit rate, we found a slightly stronger association when areas with hog CAFO exposure were excluded from the control (RR=1.28, 95% CI: 1.18, 1.39) than when we included areas with hog CAFO exposure in the control (RR=1.23, 95% CI: 1.14, 1.33). We did not observe much difference when we conducted our main analysis with the hog CAFO exposure measure created using different alphas and distance caps in the Gaussian decay function (see Supplementary Table 19).

Table 16. The association between hog CAFO exposure and AGI ED rate when examining the IDW hog CAFO exposure variable continuously and when the continuous hog CAFO exposure variable is split into tertiles and compared to ZIP codes with no hog CAFO exposure (IPTW control; 2016-2019).

Hog CAFO exposure Category	**Rate Ratio (95% CI)**
Tertiles	
Low hog CAFO exposure	1.01 (0.90, 1.13)
Medium hog CAFO exposure	1.21 (1.09, 1.35)
High hog CAFO exposure	1.26 (1.14, 1.40)
Continuous	1.00 (0.99, 1.00)

Table 17. The association between hog density (number of hogs within ZIP codes and half mile buffer around ZIP code/area of ZIP code) and AGI ED rate with various poultry restrictions for the control and the association between bird density (number of birds within ZIP codes and half mile buffer around ZIP code/area of ZIP code) and AGI ED rate with various hog restrictions for the control (IPTW control; 2016-2019).

Analysis	**Rate Ratio (95% CI)**
Hog density and AGI	
Overall (control can have poultry CAFOs)	1.02 (0.97, 1.07)
Control excludes ZIP codes with bird density above median	1.02 (0.97, 1.08)
Control areas have no poultry CAFOs	1.30 (1.21, 1.40)
Poultry density and AGI	
Overall (control can have hog CAFOs)	1.23 (1.14, 1.33)
Control excludes ZIP codes with hog density above median	1.22 (1.14, 1.32)
Control areas have no hog CAFOs	1.28 (1.18, 1.39)

Discussion

Overall, we observed a 17% higher (RR=1.17, 95% CI: 1.08, 1.26) all-cause AGI ED rate in high hog exposed areas than in areas without hog CAFO exposure. The effect was stronger in rural areas. When restricting the analysis to rural ZIP codes, we observed EMM by race, where the association between high hog CAFO exposure and AGI ED visit rate was highest among American Indian, Asian, and Black patients. We also observed that the association between high hog CAFO exposure and AGI ED visit rate was stronger during the week after heavy rain (above the 99^{th} percentile of NC daily precipitation). The association between high hog CAFO exposure and AGI ED visit rate was also stronger when ZIP codes with poultry CAFOs were excluded from the control.

Our overall results are consistent with some studies that find increased gastrointestinal symptoms and gastroenteritis hospitalizations near high intensity farming,[24,47] although some other studies found no effect.[46,48] In an ecological study of livestock density and acute gastroenteritis hospitalizations in Quebec, Canada, Febriani et al. observed an increased risk of acute gastroenteritis hospitalizations associated with high intensity farming.[47] They observed modification by age and water source, with a particularly strong association in children under age 5 and areas that predominantly used private wells and ground water as drinking water. Unlike Febriani et al.,[47] we did not find private well water usage or age to be a strong modifier and found the association to be highest among adults 18-64 (although we were limited by the county-level well water data available). To further examine the relationship between intensive farming and AGI, the Febriani et al. group later conducted a cross-sectional telephone survey of 7,006 residents in rural municipalities in Quebec, Canada and found living in a municipality with intensive farming was inversely associated with AGI. They propose that the differences between these studies may be due to ecological vs. individual-level data and severe AGI hospitalizations vs. self-reported AGI. Another study used electronic medical record data from primary care practices in southern Netherlands and found the prevalence of gastrointestinal and respiratory symptoms were similar in the high and low CAFO exposed populations.[48] In the only study that examines this relationship in NC, Wing et al. interviewed 155 residents in eastern NC who lived near a cattle CAFO, a hog CAFO, and no nearby CAFOs, and found self-reported diarrhea, headaches, coughing, and sore throats to be most prevalent among residents living near the hog CAFO.[24] While literature remains mixed on this general subject, our study supports the positive association between hog CAFO exposure and AGI in NC.

Contradictory results on the association between CAFO exposure and AGI rate may be caused by differences in study design, region, precipitation, and type(s) of animals. We observed that the relationship between high hog CAFO exposure and AGI ED visit rate was stronger when a heavy rain event had occurred within the previous week than when the previous week had been dry. These results are supported by studies that have found increased pathogens and/or increased concentrations of fecal indicator bacteria in areas with hogs after heavy rain events. A study of 59 wells in southwest Guatemala found recent precipitation to be associated with almost 3-fold higher *E. coli* concentrations, with the strongest association at wells with pigs nearby.[51] A study of runoff after land application of cattle and swine manure and after simulated heavy rainfall events found *E.coli* and enterococci concentrations to be significantly higher than control plots with no manure.[23] Runoff from swine slurry-applied fields had the highest concentrations of *E. coli*, *Clostridium,* and *Giardia* cysts compared to cattle manure-applied and control fields, possibly because swine manure's liquid state enables microorganisms in the manure to be transported more readily than does cattle manure or chicken litter.[23] Febriani et al. found high precipitation periods in the fall increased AGI risk three weeks later and observed effect modification of high intensity farming and season on the association between cumulative precipitation and AGI four weeks later.[46]

Our study focuses on high hog CAFO exposure, partly because the liquid nature of hog manure allows pathogens to be carried more widely than dry poultry waste. However, as thousands of poultry

CAFOs are co-located with hog CAFOs in eastern NC, it is difficult to isolate the effect of hog CAFOs that is not related to poultry CAFOs in NC. When we include ZIP codes with poultry CAFOs as the control, as we did in our main analyses, our results are attenuated as the poultry CAFO exposure seems to increase the AGI ED visit rate in these areas. When areas with poultry CAFOs are excluded from the control group, the association between high hog density and AGI ED visit rate strengthens. Similarly, the association between high poultry density and AGI ED visit rate is strongest when areas without hogs are not in the control; however, this difference is smaller than that of the high hog density and AGI ED visit rate analysis including and excluding poultry CAFOs from the control. This suggests that the association between high poultry density and AGI ED visit rate might be stronger than between high hog density and AGI ED visit rate, but there are many areas without hog CAFOs and with poultry CAFOs and few areas without poultry areas and with hog CAFOs, so we were unable to adequately tease apart these associations. While some studies that examined industry animal production and AGI, including poultry and hog CAFOs, did not find an association, [46,48] Febriani et al. observed an increasing trend in association between quartile of poultry density AGI. The authors noted that the association between poultry density and AGI in children was predominantly from *Salmonella* infections.[47] Another study found Michigan counties with high poultry density to have a higher incidence of *C. jejuni* enteritis, especially among children, compared with low poultry density counties.[192]

Our restricted analysis of the association between high hog CAFO exposure and AGI ED visit rate by year and season help us understand what factors might be influencing this association. While hog CAFO locations have not changed significantly over the past decade, some CAFOs might have changed in size or become inactive. More significantly, however, is how other nearby exposures (and potential confounders) might have changed, such as the recent increase of poultry CAFOs. The increasing association between high hog CAFO exposure and AGI ED visit rate each year might reflect the increase in poultry exposure, many co-located near hog CAFOs, or the overall increase in ED visit reporting over time. We also observed the association between high hog CAFO exposure and AGI ED visit rate to be slightly stronger during the winter and fall. AGI incidence is typically higher in the winter and lower in the fall, which we observed in our AGI outcome data (see Aim 1's Supplementary Figure 9).[20] The slight seasonal patterns we observed might be related to increased AGI incidence in winter, large hurricanes flooding eastern NC in autumns, and/or varying hog manure spraying patterns.

We observed a stronger association between high hog CAFO exposure and AGI ED visit rate in rural ZIP codes. In analyses restricted to rural areas we found the associations to be particularly strong in American Indian, Black, and Asian patients, as well as in patients who paid for their ED visit out of pocket (self-pay, likely uninsured). Although there were only 15 and 16 cases among Asians in high hog exposed and no hog CAFO exposure ZIP codes, respectively, in the analysis restricted to rural areas, the cases are much higher before the rurality restriction (N=285 in high hog exposed areas, N=487 in no hog exposed areas; see Table 11) and the rate ratio remained high (RR=2.21, 95% CI: 1.86, 2.55). This suggests that the association between high hog CAFO exposure and AGI ED visit rate is increased among Asian patients in NC. While Indian, Chinese, and Vietnamese are the largest Asian ethnic groups in NC, most NC Asians reside in metropolitan area. In high hog exposed ZIP codes, which are the more rural areas of NC, Filipinos are the largest Asian ethnic group, followed by Japanese and Indian (Supplementary Table 18). While we do not observe a positive association between high hog CAFO exposure and AGI ED visit rate among Black patients in the overall analysis, we saw a positive association among Black patients when restricted to rural ZIP codes. As there are several layers of EMM by rurality, race/ethnicity, age, insurance status, and income, the analyses in this study have attempted to disentangle these factors. For the main analysis, IPTW was relatively successful at creating a control pseudo-population with similar levels of rurality, race, insurance status, and median income as the high hog exposed areas. Additional rural restricted EMM analyses were essential to better understand the complex relationship between hog CAFO exposure and AGI in NC. Rural areas in NC have the highest ED rates, the highest amount of uninsured residents, and the lowest median household incomes (Appendix 6). A recent study examining six EDs in Minnesota and South Dakota found rural EDs had a higher proportion of Native American patients and patients below the 200% income poverty level compared to urban EDs.[148] The authors concluded that Native American residents have more barriers obtaining medical care in rural areas than White residents do.[148] Similar medical barriers may exist in rural NC, as we observed an especially strong association between high hog exposure and AGI ED rate among rural American Indians.

This study's strengths include its use of four years of recent data and its use of IDW to incorporate proximity to hog CAFOs, number and density of hog CAFOs, and approximate manure exposure using SSLW. The sensitivity analyses illustrate the results' robustness to changing model specifications and the complexity of the many correlated variables (e.g., race, income, insurance status, rurality, location of hog CAFOs) and co-location of hog and poultry CAFOs. As described in Aim 1, this study is limited by its use of all-cause AGI ED visits as the main outcome, which is a broad indicator of health effects that may arise from pathogens in hog manure. However, AGI has many possible etiologies and comorbidities, including causes unrelated to hog pathogens in hog waste. Our sensitivity analyses restricted to bacterial, viral, and protozoal AGI ED visits, as well as analyses restricted to AGI visits from particular pathogens, attempted to address this limitation, where we observed a positive association between high hog CAFO exposure and *Salmonella* ED rates and viral AGI ED visit rates. However, many AGI-related diagnoses are made without laboratory testing and therefore, do not specify pathogens or specify incorrect pathogens.[179] 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 our effects may be underestimated.[87] Moreover, rural areas—where the stronger association between high hog CAFO exposure and AGI is found—typically have reduced healthcare access.

Residents in high hog exposed ZIP codes are not necessarily exposed to pathogens from hog CAFOs, as exposure depends on topography, drainage, manure spraying patterns, and human actions. As rural ZIP codes can be quite large, residents in one corner of the ZIP code may be highly exposed to pathogens from hog manure while residents in other parts of the ZIP code may be unexposed. We attempted to reduce this misclassification by creating our ZIP code-level continuous hog CAFO exposure using block-level population weights. Thus, if one area of a ZIP code with few people was exposed to large hog CAFOs but the majority of the ZIP code's population resided >10 miles from hog CAFOs, then the ZIP code would be unlikely to be categorized as a high hog exposed ZIP code. While the zip code-level resolution of the AGI ED visit data is better than the county-level resolution used previously, the data and analyses are still limited by the geographic granularity of the data.[107] Additionally, our IPTW methods are limited by the geographical clustering of hog CAFOs in NC.[193,194] The probability of a ZIP code being exposed to CAFOs is affected by various measured and unmeasured factors, including rurality, land price, community resistance and political power, and the location of slaughterhouses and other CAFOs.

Additionally, in attempting to compare high hog CAFO exposed areas to areas without any hog CAFO exposure, we predominantly compared rural eastern NC with dense hog CAFOs to rural western NC without hog CAFOs, which have different populations and different environmental exposures. For example, rural eastern NC has a much higher proportion of Black residents than rural western NC, which has a very high proportion of White non-Hispanic residents. These characteristics are not random; the majority of NC's enslaved Black population in the 18th and 19th century lived in eastern NC. Industrial hog operations in NC expanded during the 1990s and early 2000s in these same areas that continue to be heavily populated by Black people and American Indians.[16,119] The environmental racism of the hog industry makes it difficult to isolate the effect of hog CAFOs on AGI in NC independent of race, income, and rurality, as these factors are strongly correlated with the exposure. In non-urban North Carolina in

2014, the proportions of American Indians, Blacks, and Hispanics that lived within 3 miles of a permitted hog CAFO were 2.18, 1.54, and 1.39 times higher, respectively, than the proportion of non-Hispanic Whites.[16] People living near hog CAFOs report a worse quality of life and are frequently unable to go outdoors because of the strong manure odor, compared to people who do not live near CAFOs.[24] Many low-income and POC communities in eastern NC lack the political power and financial resources to prevent CAFOs from being built in their communities. Lower-income families may not be able to move away from newly sited polluting industries, a challenge exacerbated by the impact of these operations on their property values.[195] The environmental injustice of hog CAFOs encompasses racism, classism, poverty, and the urban-rural divide.[40] Urban areas exploit rural areas for waste disposal and food and energy production, causing pollution and reduced quality of life for rural communities. These environmentally unjust industrial production practices disproportionately harm the health of rural populations while disproportionately benefiting urban populations.[40] NC should reduce the number and density of hog CAFOs and strengthen environmental regulations to improve the health of POC and rural communities.

Conclusions

Results from studies on industrial hog operations and AGI have been inconsistent, possibly due to varying methods, regions, populations, and topography. NC's 9 million hogs are housed predominantly in its hurricane-prone eastern rural region, where many residents use private well water and have limited healthcare access. We observed a 17% higher AGI ED visit rate in high hog exposed ZIP codes than ZIP codes without hog CAFO exposure and 24% higher AGI ED visit rate when restricted to rural areas. We found a higher AGI ED visit rate among American Indians, Black, and Asian American patients in rural high hog areas compared to rural areas without hogs. Hog CAFOs in NC were built in areas with a higher population of Black, Lumbee, and Filipino residents than the rest of the state.

Because hog CAFOs in NC are disproportionally located in and near rural, low-income, POC communities and near poultry CAFOs and in areas with poor water treatment, it is difficult to isolate the effect of hog CAFOs independent from these other factors. We are limited from making causal statements about the effect of hog CAFOs on AGI rate mostly because industries place polluting facilities near other polluters and in under-resourced communities, or sacrifice zones, which often hides harmful effects.[196] However, these highly correlated variables highlight the environmental injustice affecting communities in eastern NC.

Supplementary Tables and Figures

Table 18. Percent of Asians in NC in each exposure or exclusion category by Asian ancestry (Asian ancestry data from the 2017.American Community Survey at the census tract level).

Asian Ancestry	Cities (Excluded)	High Hog Density (Exposed)	Low/Medium Hog (Excluded)	No Hogs (Control)
Indian	34.0	14.0	18.0	22.0
Burmese	2.0	1.0	3.0	0.0
Cambodian	1.0	0.0	2.0	1.0
Chinese	17.0	10.0	13.0	18.0
Filipino	8.0	29.0	16.0	14.0
Hmong	2.0	1.0	8.0	8.0
Indonesian	0.0	0.0	0.0	1.0
Japanese	3.0	14.0	6.0	7.0
Korean	8.0	9.0	9.0	8.0
Malaysian	0.0	0.0	0.0	1.0
Nepalese	2.0	0.0	1.0	1.0
Pakistani	2.0	2.0	3.0	1.0
Taiwanese	1.0	0.0	0.0	0.0
Thai	1.0	2.0	3.0	2.0
Vietnamese	12.0	10.0	10.0	8.0
Other Asian, not specified	4.0	6.0	4.0	4.0

Table 19. The association between high hog CAFO exposure (>75th percentile of IDW hog CAFO exposure variable) and AGI ED visit rate compared to areas with no hog CAFO exposure (2016-2019), using different distance caps and alphas for the inverse distance weighted hog CAFO exposure variable (see Appendix 5).

Inverse distance weighted specifications	Rate Ratio (95% CI)
Alpha=3, cap=10 miles (main analysis)	1.17 (1.08, 1.26)
Alpha=6, cap=10 miles	1.15 (1.06, 1.24)
Alpha=3, cap=5 miles	1.17 (1.08, 1.26)
Alpha=6, cap=5miles	1.15 (1.06, 1.24)

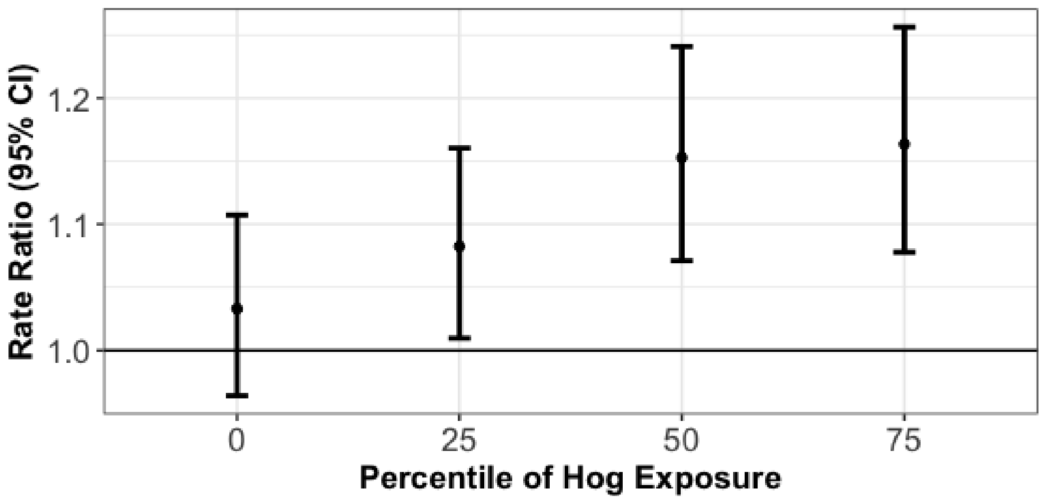


Figure 13.The association between hog CAFO exposure and AGI ED rate with various cut points indicating hog CAFO exposure (2016-2019). The IDW hog CAFO exposure variable was dichotomized using different thresholds: 0^{th} percentile (any hog CAFO exposure=hog exposed), 25^{th} percentile (above the 25^{th} percentile of hog CAFO exposure variable=hog exposed and areas >0 and <25^{th} hog CAFO exposure percentile excluded from analysis), 50^{th} percentile (above the median of the hog CAFO exposure variable=hog exposed and areas >0 and <50^{th} hog CAFO exposure percentile excluded from analysis), and 75^{th} percentile (above the 75^{th} percentile of the hog CAFO exposure variable=hog exposed and areas >0 and <75^{th} hog CAFO exposure percentile excluded from analysis). Separate analyses were run for each cut point and different IPT-weighted controls were created for each cut point of ZIP codes without hog CAFOs.

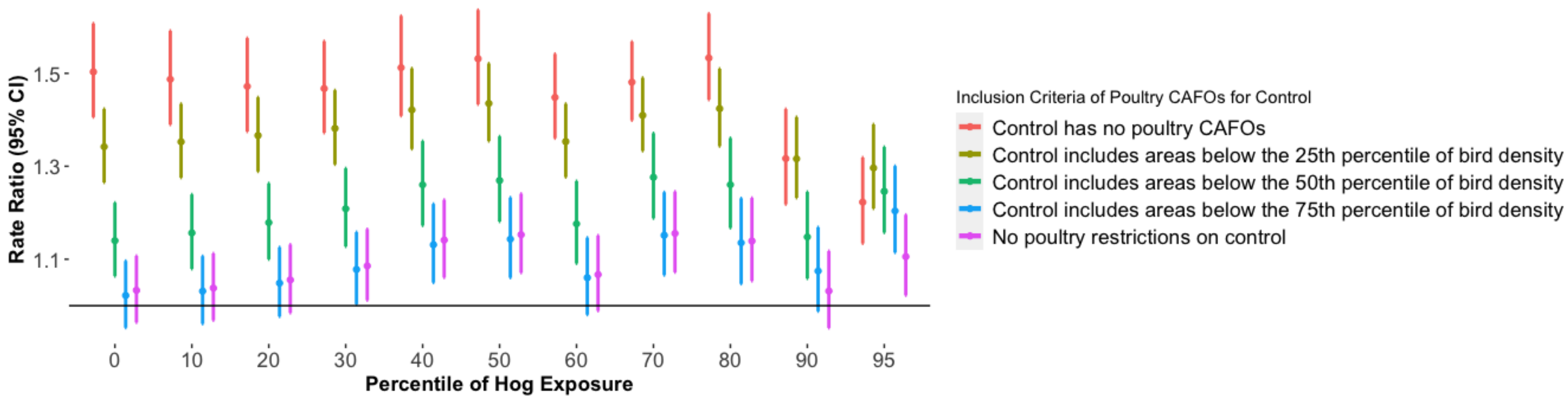


Figure 14. The association between hog CAFO exposure and AGI ED rate (2016-2019) with various cut points indicating hog CAFO exposure and various poultry criteria for control. The IDW hog CAFO exposure variable was dichotomized using different thresholds: 0th percentile (any hog CAFO exposure=hog exposed) to 95th percentile (above the 95th percentile of the hog CAFO exposure variable=hog exposed and areas with hog CAFOs ≤95th percentile excluded from analysis). Separate analyses were run for each cut point and different IPT-weighted controls were created for each cut point of ZIP codes with no hog CAFO exposure. The colors indicate how excluding ZIP codes with various levels of bird density change the effect, as proximity to poultry CAFOs likely also increases one's risk for AGI.

CHAPTER VI: HURRICANE FLOODING, INDUSTRIAL HOG OPERATIONS, AND AGI (AIM 3)

Introduction

Hurricanes can be destructive, deadly, and can lead to perilous health outcomes. In addition to immediate harms inflicted by drowning and being struck from trees and debris, hurricanes can exacerbate environmental health problems when heavy rain and flooding spread chemicals and pathogens from flooded hazardous waste sites, animal manure pits, coal ash ponds, and damaged oil refineries.[1–3,197,198] Environmental contamination aggravated by hurricanes varies by region. As North Carolina (NC) is the second leading producer of hogs in the United States (US) with 9 million hogs and also the third most hurricane-prone US state,[6,160] hurricanes that hit NC may cause illness when floods inundate hog waste pits and fecal pathogens contaminate the waterways.[7] Most of the state's hogs are housed, by the thousands, at large concentrated animal feeding operations (CAFOs) in the eastern, hurricane-prone region of the state.[14] The massive amount of liquid waste produced by these hogs is collected in uncovered pits, or lagoons, and sprayed on land as a fertilizer. However, the land cannot absorb all of the sprayed waste and often spread pathogens and chemicals that pollute the air and water.[7] When NC hurricanes flood hog lagoons, fecal pathogens capable of causing AGI may be transported into nearby waterways.[7] Contact with pathogens from hog waste can result in diarrhea, vomiting, nausea, or other gastrointestinal tract distress in humans, known collectively as acute gastrointestinal illness (AGI).[19,24] AGI causes pain, disrupts work and school, and can be harmful for health, especially in young children and older adults.[25] In the US, approximately 2,330,000 waterborne enteric illnesses occurred in 2014, which incurred about $160 million in direct healthcare costs.[101]

Although news reporters regularly discuss the dangers of flooded CAFOs every time a large hurricane strikes NC, very few studies have examined the effect of flooded hog CAFOs in NC on AGI.[59,199–201]

Heavy rain and flooding have been linked to an increase in gastrointestinal illness rate, because sewer overflows, overwhelmed municipal water systems, and damaged septic systems increase the spread of pathogens.[8–11] Flooded hog CAFOs might exacerbate this effect. Communities that live near hog CAFOs have reported numerous health problems, including throat, eye, and nose irritation, headaches, diarrhea, methicillin-resistant *S. aureus*-related infections, and reduced quality of life.[15] Hog CAFOs are densely concentrated in several counties in eastern NC that are fairly rural, have reduced healthcare access, have a higher percentage of people of color than the rest of the state, and are also home to many other harmful exposures like poultry CAFOs and landfills.[16–18] Because of the area's rurality, many residents near CAFOs use private wells, which, because they are usually not treated, stand at higher risk of contamination than community water supplies.[19,20] Furthermore, AGI-related emergency department (ED) visits in NC due to microbial contamination in drinking water exceed $40 million annually.[20]

Hurricane Matthew (October 2016) and Hurricane Florence (September 2018) were the two largest, deadliest, and costliest hurricanes to hit 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.[65,67] 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.[66] According to news sources, Hurricane Matthew caused at least 14 lagoons to flood and 2 lagoons to breach,[62] and at least 110 hog manure lagoons were breached or inundated in NC due to Hurricane Florence.[63]

This aim preliminarily examines the combined effect of hurricane flooding and hog CAFO exposure on AGI in NC and examines this affect across two different hurricanes—Hurricanes Matthew and Florence. This is the first study to examine how the presence of hog CAFOs in hurricane flooded areas affects all-cause AGI ED visit rates in NC. Climate change models project that NC will continue to see an increase of heavy precipitation events, making it important to understand the connection between flooding, CAFOs, and health to develop appropriate interventions.[27]

Methods

Study Population

This study examines the AGI ED rate among NC residents during 2016-2019. 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

As Hurricane Matthew struck NC on October 8, 2016, we defined Hurricane Matthew exposure as the period from October 8-October 29, 2016 for main analyses. Hurricane Florence struck NC on September 14, 2018, and we defined Hurricane Florence exposure as the period from September 14-October 5, 2018 for main analyses. We chose 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. We obtained flood extent data from the NC Department of Public Safety (DPS), which were based on effective and preliminary flood maps, observed rainfall, storm surge, Flood Inundation Mapping and Alert Network (FIMAN) flood gauges, and photographs. We used flood extents from Hurricanes Matthew and Florence to identify flooded CAFOs. Because of the flood data's mismeasurement and imperfections from incorporating data from various sources, we created a 0.1-mile buffer around the flood extents and identified hog CAFOs within this buffer. For additional analyses, 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 (as described in aim 1).

Outcome

As described in previous aims, acute gastrointestinal illness (AGI) was measured using data from the NC Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), a public health surveillance system containing civilian ED visits in NC. We calculated 2016-2019 AGI ED visit rates at the ZIP code level, the finest geographic level available. 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.[8,9,20] Our analyses focused on all-cause AGI ED visit rate because specific pathogens are seldom tested for and/or included in the discharge report.

Hog CAFO Exposure

We used 2014 swine permit data from the NC Department of Environmental Quality (DEQ), which included the location, number of animals, type/life stage of animals, and lagoon count of each permitted animal facilities (swine CAFO locations shown in Figure 1). We categorized ZIP codes as containing hog CAFOs near flooding if the ZIP code contained >10 hog CAFOs within the flood extent or within 0.1 mile of the flood extent (although we also examined cut points of >0 and >5 hog CAFOs). We included a 0.1-mile buffer because of the imprecision in the flood extent data and the geocoded locations of the hog CAFOs. We categorized ZIP codes as containing CAFOs and no flooding if the ZIP code had no flooding and the continuous IDW hog CAFO exposure variable created in aim 2 was above the median. Lastly, we created a category of ZIP codes with >10% flooding and no hog CAFO exposure (IDW hog CAFO exposure variable=0) (Figure 15).

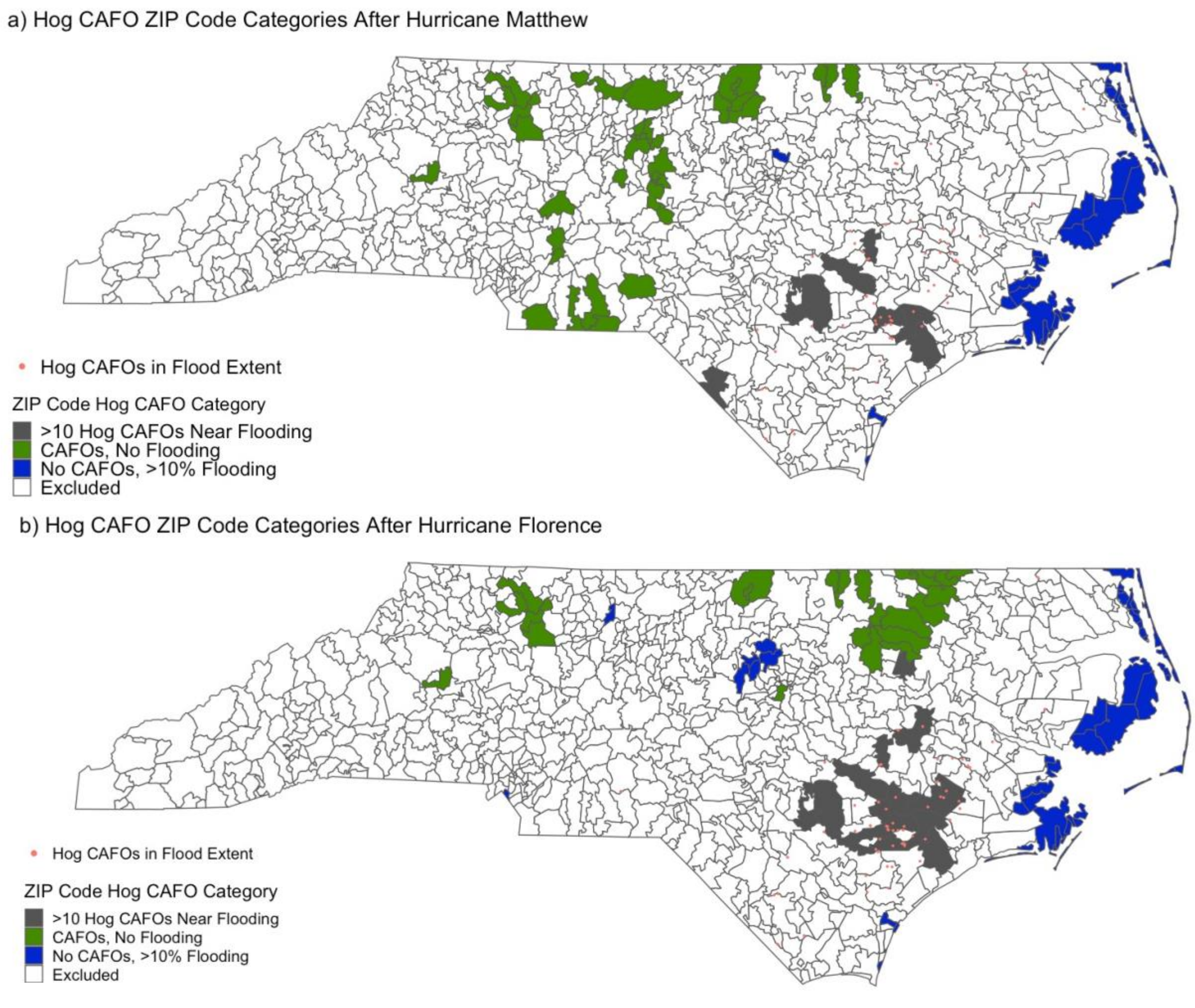


Figure 15. Hog CAFOs within a) Hurricanes Matthew and b) Florence flood extent, ZIP codes with >10 hog CAFOs within 0.1 mile of flood extents, ZIP codes with hog CAFO exposure above the median but no flooding, and ZIP codes with >10% flooding but no hog CAFO exposure (Method 1).

Covariates

Data on number of total number of residents (and other demographics) were available at the block group level from the 2017 American Community Survey (ACS). We assigned these values to the centroids of each 2010 census block based on the proportion of the block group population within that block and then 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.[154,167] We examined all changes in ZIP codes from 2016-2019 and assigned all ZIP codes to the 2017 ZIP code polygon in which they were contained.

Analysis – Method 1

We compared the rate of ED visits for AGI in ZIP codes during the case period to the AGI ED visit rates in same ZIP codes during the control periods.[127] We matched the case and control periods by month, day of week, and year. Case periods were the three weeks after Hurricanes Matthew and Florence and control periods were these same three weeks in 2017 and 2019 (i.e., October 8-October 29, 2017 and October 8-October 29, 2019 for Hurricane Matthew and September 14-October 5, 2017 and September 14-October 5, 2019 for Hurricane Florence). We conducted separate, stratified analyses for each hurricane and each area: >10 hog CAFOs near flooding, hog CAFOs and no flooding, no hog CAFOs and >10% flooding. To conduct these analyses with our over-dispersed ED data, we used conditional quasi-Poisson regression with a population offset.

Analysis – Method 2

Because of the complexity of examining how hog CAFOs affect the relationship between hurricane flooding on AGI ED rate, we used multiple methods to investigate these relationships. For method 2, we used controlled interrupted time series (CITS) to examine how hog CAFO exposure modifies the relationship between hurricane flooding and AGI ED visit rate. In this analysis, we were able to use the flood extent data to categorize ZIP codes as heavily flooded (≥33% of ZIP code area flooded) or unflooded (0% of ZIP code area flooded). Using CITS with EMM, as described in aim 1, we examined EMM of hog exposure with a multiplicative interaction term (hog exposure*flood period*flood group). In this analysis, we described high hog exposure as >50th percentile of the continuous hog CAFO exposure variable created in aim 2, medium hog exposure as >0 and ≤50th percentile of continuous hog exposure variable, and no hog CAFO exposure as continuous hog exposure=0. This this analysis, we excluded ZIP codes with low hurricane flooding (>0 & <33% flooding). We were unable to define hog exposure as ZIP codes with flooded hog CAFOs as unflooded areas obviously did not have flooded hog CAFOs. As described in CITS of Hurricanes Matthew and Florence in aim 1, we excluded period with other large hurricanes from analysis.

Analysis – Method 3

Method 1 and 2 examine the three weeks after the hurricanes as the main exposure and examine how the AGI ED visit rate increases during this period compared to the expected AGI ED visit rate in areas with different levels of hog CAFO exposure. Method 3 examined hog CAFO exposure as the main exposure and how, during the weeks after each hurricane, the effect of hog exposure changed in flooded vs. unflooded areas. In the flooded ZIP codes, we categorized ZIP codes as high hog exposed if the ZIP code contained a hog CAFO within 0.1 mile of each flood extent. As Hurricanes Matthew and Florence flooded slightly different areas, the exact same hog CAFOs were not flooded during both hurricanes, and the high hog exposed ZIP codes differ slightly between hurricanes. Separately for each hurricane, we compared the effect of flooded hog CAFO on AGI to flooded areas with no hog CAFOs, although the demographics of these areas were very different. To increase comparability, we used inverse probability of treatment weighting (IPTW) to estimate the average treatment effect among the treated (ATT). In doing this, we created pseudo-populations (assumed control) with similar demographics as the high hog exposed population (based on the ZIP codes' rurality and percent of non-Hispanic White residents) but with no hog exposure, separately in high flooded areas (≥33% flooding) and unflooded areas during the weeks after Hurricanes Matthew and Florence. We accounted for ZIP code-level rurality and race, which we had previously determined to be the strongest effect measure modifiers between the relationship between hog CAFO exposure and AGI (from aim 2). Because of the differences between the populations and the relatively small number of ZIP codes with heavy flooding and no hog CAFOs, we were unable to use additional variables in the IPTW. We categorized a ZIP codes as heavy flooded when a third of more of its area was flooded after the hurricane, although we also examined other cut points (≥25% and ≥40% flooding). We restricted the analyses to 2 ,4, 6, and 8 weeks after each hurricane to examine how the association might change during the weeks after hurricanes. We conducted analyses separately for Hurricanes Matthew and Florence.

Next, we examined the effect of high hog exposure on AGI in ZIP codes that did not flood during the same time periods. In unflooded ZIP codes, we categorized ZIP codes above the median of hog exposure as high hog exposed and compared them to ZIP codes with no hog CAFOs within 10 miles (i.e., hog exposure measure=0), thus excluding ZIP codes with >0 and ≤50^{th} percentile of hog exposure from the analyses. We excluded metropolitan ZIP codes from all main analyses by excluding the lowest quartile of the geographic isolation scale (below 5.6), as urban areas lack hog CAFOs and have different ED visit patterns than areas with hog CAFOs.[151] We used quasi-Poisson models to account for overdispersion in the ED visit data. Robust standard errors were used to calculate 95% confidence intervals (95% CI) using the *sandwich* package in R. All analyses were performed in R (Version 3.6.2).[168]

Results

Main analysis (method 1)

ZIP codes containing >10 hog CAFOs within the Hurricanes Matthew and Florence flood extent or within 0.1 miles of the flood extent had a higher proportion of uninsured and Black residents and lower median incomes than the state average, especially after Hurricane Florence (Table 20). Additionally, ZIP codes with >10 hog CAFOs near the flood extents have much higher average hog density and bird density than areas with high CAFO exposure and no flooding as well as areas with no CAFOs and >10% flooding. After Hurricane Matthew, there were 85 hog CAFOs within the flood extent and 432 hog CAFOs within 0.1 of the flood extent. After Hurricane Florence, we observed 81 hog CAFOs within the flood extent and 613 hog CAFOs within 0.1 of the flood extent. We categorized 14 ZIP codes as containing >10 hog CAFOs near flooding (<0.1 mile) and 184 AGI visits in these ZIP codes during the three weeks after Hurricane Matthew. For Hurricane Florence, we classified 24 ZIP codes as containing >10 hog CAFOs near flooding (<0.1 mile) and 363 AGI visits in these ZIP codes during the three weeks after Florence (Figure 15). These numbers were larger when we used >5 and >0 hog CAFOs near the flood extents to define flooded CAFO areas.

For both Hurricanes Matthew and Florence, the effect of the three weeks after the hurricanes on the AGI ED visit rate was strongest in ZIP codes with >5 and >10 hog CAFOs within 0.1-mile of the flood extents. During the three weeks after Hurricane Matthew, we observed a weak 15% increase in AGI ED visit rate in areas with >10 hog CAFOs near the flood extent (95% CI: 0.74, 1.78; Table 21) compared to the AGI ED visit rate in these areas during comparable non-hurricane time periods in 2017 and 2019. We did not observe any increase in AGI during this three-week period after Matthew in areas with hog CAFOs and no flooding (RR=0.98; 95% CI: 0.93, 1.03) or in areas with flooding and no hog CAFOs (RR=0.95, 95% CI: 0.64, 1.40; Table 21). After Hurricane Florence, we observed a 25% increase in AGI ED visit rate in ZIP codes with >10 hog CAFOs near the flood extent (95% CI: 1.00, 1.56). During this time, we found a 14% increase in AGI ED visit rate in areas that flooded but did not have hog CAFOs (95% CI: 0.97, 1.35) and no increase in areas with hog CAFOs but no flooding (RR=0.90, 95% CI: 0.72, 1.13). After both hurricanes, we observed that the association between hurricane flooding time period and AGI ED visit rate increased monotonically as the number of hog CAFOs within 0.1 mile of the flood extent increased (from >0, to >5, to >10 hog CAFOs; Table 21).

Table 20. Characteristics of ZIP codes with >10 hogs CAFOs within the flood extent or within 0.1 miles of the flood extent, ZIP codes with hog CAFO exposure above the median but no flooding, and ZIP codes with no hog CAFO exposure and >10% flooding, by hurricane (Method 1).

		Hurricane Matthew			Hurricane Florence		
Characteristic	**NC Overall**	**>10 Hog CAFOs Near Flooding**	**High CAFOs Exposure, No Flooding**	**No Hog CAFO Exposure, >10% Flooding**	**>10 Hog CAFOs Near Flooding**	**High CAFOs Exposure, No Flooding**	**No Hog CAFO Exposure, >10% Flooding**
Total Population	9,934,753	179,178	426,806	159,838	246,670	205,067	354,796
White non-Hispanic, N (%)	6,877,694 (69.2)	116,128 (64.8)	270,002 (63.3)	137,169 (85.8)	153,423 (62.2)	133,400 (65.1)	226,056 (63.7)
Black, N (%)	2,135,974 (21.5)	40,357 (22.5)	129,277 (30.3)	14,358 (9.0)	69,098 (28.0)	53,639 (26.2)	97,431 (27.5)
American Indian, N (%)	117,424 (1.2)	4,699 (2.6)	2,435 (0.6)	544 (0.3)	1,774 (0.7)	3,329 (1.6)	1,237 (0.3)
Hispanic, N (%)	885,107 (8.9)	23,837 (13.3)	31,793 (7.4)	7,565 (4.7)	31,967 (13.0)	13,992 (6.8)	37,487 (10.6)
Asian, N (%)	254,468 (2.6)	2,156 (1.2)	5,621 (1.3)	2,569 (1.6)	2,316 (0.9)	5,776 (2.8)	10,742 (3.0)
Uninsured, N (%)	1289,637 (13.2)	25,811 (15.7)	59,584 (14.2)	20,433 (13.0)	37,521 (16.3)	27,183 (13.6)	49,061 (14.0)
Median Income ($)	45,751	40,364	41,645	49,684	37,742	35,447	50,039
Rurality Score[1]	7.1	7.3	7.3	7.4	7.7	7.7	7.2
Average Percent of ZIP Code Flooded	12.3	14.4	0	65.4	17.8	0	62.4
Hogs, N	12,812,561	2,470,219	226,694	0	4,261,694	284,507	0
Average Hog Density (hogs/sqmi)	258	2,030	84	0	2,123	145	0
Birds,[2] N	281,305,681	18,565,961	33,349,429	0	279,79,984	15,542,091	0
Average Bird Density (birds/sqmi)	5,661	15,260	12,323	0	13,938	7,924	0
Area (sqmi)	49,691	1,217	2,706	16,36	2,008	1,961	1,844
Total ED Visits 2016-2019	15,373,979	254,882	847,489	240,408	408,214	404,429	516,432
Total AGI Visits 2016-2019	868,691	16,497	48,510	9,436	24,538	17,742	25,262
ED Rate per 10,000 people	3,869	3,556	4,964	3,760	4,137	4,930	3,639
AGI ED Rate per 10,000 people	219	230	284	148	249	216	178
Number of ZIP Codes	1082	14	55	57	24	34	65

[1]Rurality was measured using a continuous geographic isolation scale that classifies ZIP codes according to their access to resources.[151]
[2]Data on the location of poultry CAFOs and estimated number of birds at each CAFO was provided by the Environmental Working Group and Waterkeepers Alliance. They identified poultry facility locations with high-resolution satellite data and aerial photograph and estimated number of birds at each poultry CAFO using the NC Agricultural Chemical Manual and the U.S. Department of Agriculture's Ag Census.[30]

Table 21. The increase in AGI ED visit rate during the three weeks after Hurricanes Matthew and Florence in ZIP codes with >10, >5 or >0 hog CAFOs within 0.1 mile of flood extents, in ZIP codes with hog CAFO exposure above the median and no flooding, and in ZIP codes with no hog CAFO exposure and >10% flooding, compared to the AGI ED visit rate during those three weeks in 2017 and 2019 (Method 1).

	Hurricane Matthew			**Hurricane Florence**		
	RR (95% CI)	**ZIP codes (N)**	**AGI cases (N)**	**RR (95% CI)**	**ZIP codes (N)**	**AGI cases (N)**
>10 hog CAFOs <0.1 mi from flooding	1.14 (0.74, 1.78)	14	184	1.25 (1.00, 1.56)	24	363
>5 hog CAFOs <0.1 mi from flooding	1.13 (0.88, 1.44)	47	584	1.17 (1.00, 1.36)	54	801
>0 hog CAFOs <0.1 mi from flooding	1.06 (0.92, 1.22)	132	1370	1.08 (0.99, 1.18)	147	1822
High hog CAFOs, no flooding	0.98 (0.93, 1.03)	55	685	0.90 (0.72, 1.13)	34	242
No hog CAFOs, >10% flooding	0.95 (0.64, 1.40)	57	126	1.14 (0.97, 1.35)	65	398

Method 2

Using CITS, during the three weeks after Hurricane Matthew, we observed a 42% increase in AGI ED rate in areas with low hog exposure (RR=1.42, 95% CI: 1.20, 1.64, Table 22), no increase in AGI ED visit rate in areas with high hog exposure (RR=1.00, 95% CI: 0.73, 1.30), and a slight decrease in AGI ED visit rate in areas with no hog CAFO exposure (RR=0.88, 95% CI: 0.61, 1.15). During the three weeks after Hurricane Florence, we found a 21% increase in AGI ED visit rate in areas with high hog exposure (RR=1.21, 95% CI: 0.93, 1.49), no increase in areas with low hog CAFO exposure (RR=1.05, 95% CI: 0.79, 1.30), and a slight increase in areas with no hog CAFO exposure (RR=1.12, 95% CI: 0.88, 1.36).

Table 22. Effect measure modification of high hog exposure on the association between hurricane flooding and AGI, using CITS. High hog CAFO exposure was defined as above the median of the continuous hog exposure variable (created with IDW) and low hog CAFO exposure was defined as below the median of the hog exposure variable (but above 0). No hog CAFO exposure included ZIP codes where the hog exposure variable was 0. The AGI ED visit rates during the three weeks after the hurricanes were compared to the expected AGI ED visit rates in the same areas based on the areas' AGI trends over time. The changes in AGI ED visit rate in ZIP codes with ≥33% flooding were compared to the changes in AGI ED visit rate in ZIP codes with no flooding (Method 2).

		Hurricane Matthew			**Hurricane Florence**		
Hog CAFO Exposure	**Number of ZIP Codes**	**RR (95% CI)**	**≥33% Flooded ZIP codes (N, AGI cases)**	**Unflooded ZIP codes (N, AGI cases)**	**RR (95% CI)**	**Flooded ZIP codes (N, AGI cases)**	**≥33% Unflooded ZIP codes (N, AGI cases)**
High hog CAFO exposure	294	1.00 (0.73, 1.30)	13 ZIP codes 112 AGI	281 ZIP codes 2607 AGI	1.21 (0.93, 1.49)	21 ZIP codes 157 AGI	273 ZIP codes 2826 AGI
Low hog CAFO exposure	316	1.42 (1.20, 1.64)	18 ZIP codes 157 AGI	298 ZIP codes 3496 AGI	1.05 (0.79, 1.30)	23 ZIP codes 129 AGI	393 ZIP codes 3912 AGI
No hog CAFO exposure	442	0.88 (0.61, 1.15)	50 ZIP codes 73 AGI	392 ZIP codes 4100 AGI	1.12 (0.88, 1.36)	51 ZIP codes 91 AGI	391 ZIP codes 4553 AGI

Method 3

Using Method 3, we attempted to create control pseudo-populations to compare high hog exposed ZIP codes to no hog exposed ZIP codes in flooded areas and unflooded areas during the weeks after the hurricanes. However, our weighting attempts were unable to create an appropriate control. There were only 3 heavily flooded ZIP codes (flooding ≥33%) with high hog exposure after Hurricane

Matthew, and the IPTW method highly weighted one heavily flooded ZIP code without hog CAFO exposure and weighted all other flooded ZIP codes without hog CAFO exposure extremely low (Supplementary Table 23). Because of this, the control pseudo-population has a much lower median income than the exposed group. ZIP codes with high hog exposure that were flooded ≥33% after Hurricanes Matthew and Florence had a higher proportion of Black, American Indian, and Hispanic residents and much lower median income, compared to areas with similar flooding but without hog CAFO exposure (Supplementary Table 24). In this poorly controlled analysis, we observed a strong positive association between high hog CAFO exposure and AGI ED visit rate in heavily flooded areas during the 2, 4, and 6 weeks after the hurricanes and a null or weak association between high hog CAFO exposure and AGI ED visit rate in unflooded areas during these time periods (Supplementary Table 25).

Discussion

Using different methods, we found evidence that areas with flooded hog CAFOs after hurricanes exhibit an increased AGI ED rate compared to areas with hog CAFOs but no flooding and areas with flooding but no hog CAFOs. With method 1, we observed that the ZIP codes with hog CAFOs in the flood extents or within 0.1 mile of them experienced an increase in AGI ED visit rate during the three weeks compared to AGI ED visit rate in these areas during the control years. We did not see an increase in AGI ED visit rate in areas with hog CAFOs but no flooding during these periods. While we observed an increased AGI ED visit rate in flooded areas without hog CAFOs after Hurricane Florence, we observed a larger increase in AGI ED visit rate in areas with >5 or >10 hog CAFOs <0.1 miles from flooding. The strength of the effect between post-hurricane period and increased AGI ED visit rate increased as the number of hog CAFOs in or near flooding increased (especially after Hurricane Florence), suggesting that the effect may be due to the increase in flooded hog CAFOs.

With CITS (method 2), we found hog exposure to be a weak effect measure modifier in the relationship between hurricane flooding and AGI ED visit rate, and observed the association was strongest for ZIP codes with high hog exposure during the three weeks after Hurricane Florence and was strongest for ZIP codes with low hog exposure during the three weeks after Hurricane Matthew. Lastly, we attempted to examine the effect of high hog exposure compared to no hog exposure separately in flooded and unflooded areas, during the weeks after hurricanes. However, the populations we were comparing remained unbalanced despite our efforts to balance their covariates with weighting and the results are too biased to be useful. The analyses for this paper were especially difficult because most heavily flooded areas have high hog CAFO exposure (except for the coast, which has very different demographics) and most unflooded areas do not have high hog CAFO exposure. The challenges in finding or creating an appropriate comparison group highlight the environmental injustice of hurricane flooding and hog CAFO exposure in NC.

Several of our findings in this paper are confirmed by other studies, including our result that areas with flooded hog CAFOs (or hog CAFOs near hurricane flooding) have a higher proportion of Black residents than the rest of NC. In 1999, Hurricane Floyd caused five hog lagoons to breach and at least 50 lagoons to flood in NC.[3] Numerous lagoons suffered structural damage. Wing et al. found that, according to satellite images and estimates from Hurricane Floyd, African Americans were more likely than Whites to live in areas with flooded CAFOs in NC.[7] While this was a powerful paper examining the differential exposure of flooded hog CAFOs, no health outcomes were assessed. The main other study that examined health effects of flooded hog CAFOs, by Setzer and Domino, used Medicaid outpatient data to examine whether Hurricane Floyd was associated with increased waterborne disease-related outpatient visits in eastern NC.[107] They examined counties with high concentrations of hogs (defined as >1,000 hogs) and classified the counties on the impact of Hurricane Floyd measured by the Federal Emergency Management Agency's (FEMA) assessment of socioeconomic impact of Floyd (severe, moderate, minor, not affected). The study is somewhat limited by these definitions, as FEMA's designation of hurricane impact is over the entire county and does not assess which hog CAFOs were inundated or close to the flood extents. Using difference-in-differences, they found an increase in visits for ill-defined intestinal infections in severely and moderately affected counties, compared to unaffected counties. The study did not make any conclusions regarding the combined effect of hurricane flooding and hog CAFOs on gastrointestinal illness, partly because their study did not include any counties that were affected by Floyd that did not have a high concentration of hogs.[107] The study was also limited by the use of county-level data.

While we could not find other studies that examined the health effects of hurricane flooded hog CAFOs, several studies have found increased concentrations of enterotoxigenic and enterohemorrhagic *E. coli*, *Clostridium*, and *Giardia* (which can cause AGI) in surface water and well water after heavy rain events, with stronger associations in areas with swine manure.[23,51] Similarly, Febriani et al. found high precipitation periods in the fall increased AGI risk three weeks later and observed effect modification of high intensity farming and season on the association between cumulative precipitation and AGI four weeks later.[46] In aim 2, we found the relationship between high hog exposure and AGI ED visit rate was stronger when a heavy rain event had occurred within the previous week than when the previous week had been dry. These results in aim 2 support our suggestive findings in this paper that hog CAFO exposure modifies the relationship between hurricane flooding and AGI ED visit rate.

The association between flooded hog CAFOs areas and AGI that we observed differs by hurricane. Using method 1 and 2, we observed a stronger effect of high flooded CAFO exposure and AGI after Hurricane Florence than after Hurricane Matthew. In Aim 1, we also saw a more consistent increase in AGI after Hurricane Florence than after Hurricane Matthew, which we attributed to antecedent rain. The weaker effect after Hurricane Matthew that we observe in this aim may also be related to the extremely wet period that preceded Matthew compared to the dry period that preceded Florence. Additionally, Hurricane Matthew resulted in less overall flooding and we observed fewer AGI cases in the flooded ZIP codes (see Table 21, Table 22), which limits our ability to calculate a precise and accurate effect estimate.

This study's strengths include its use of multiple methods to examine how hog CAFO exposure modifies the relationship between hurricane flooding and AGI. While we hoped to use hog CAFO exposure as the main exposure (method 3), as it may be more intervenable than hurricane flooding, we were limited by the vast differences in populations between areas with flooding and hog CAFOs and areas with flooding and no hog CAFOs. Using methods 1 and 2, we were able to use time to create an effective control of hurricane-exposed areas during non-hurricane time periods. As areas with heavy flooding during Hurricanes Matthew and Florence are regions that tend to flood more than most of NC and may regularly have a higher AGI ED visit rate than other places, and as ZIP codes with high hog CAFO exposure may regularly have a higher AGI ED visit rate than ZIP codes without hog CAFO exposure (see aim 2), CITS methods that compare ZIP codes to themselves over time are especially useful.

Our study was limited by our inability to obtain information on the degrees to which various hog CAFOs flooded, as some hog CAFOs breached, others experienced significant structural damage, and others only flooded. These different ways hog CAFOs can be harmed by flooding can affect the amount of hog waste and fecal bacteria that contaminate the waterways. This information would improve our exposure assessment of flooded hog CAFOs and should be included in future studies. With method 1, we were able to examine the effect of CAFOs that might have flooded; however, separate analyses were required for each group. Using CITS (method 2), we were able to combine the flooding and hog CAFO exposure variables in one model, but we could only examine the interaction of heavy flooding and high hog CAFO exposure and were unable to distinguish flooded CAFOs.

As described in previous aims, this study is also limited by its ZIP code-level AGI ED data. However, as other studies have examined this question on the county level, ZIP code-level analysis is an improvement in geographic granularity.[107] Additionally, while method 1 analysis for Hurricane Florence is two-sided, the Hurricane Matthew analysis is one-sided, as it only uses control periods after the cases/exposure period, which may result in bias due to temporal changes.

As previously described, this study is limited by positivity issues, as there are few AGI cases in heavily flooded areas without hog CAFOs and in unflooded areas with high hog CAFO exposure. This highlights an important environmental justice and climate justice issue, that flooding and related environmental health problems disproportionately harm low-income residents and POC. Existing environmental injustices often contribute to disaster vulnerabilities.[61] Historically, several Black towns, like Princeville, NC, were established in floodplains, as the land was undesirable to White wealthy people.[118]

We plan to continue to build upon these preliminary analyses to examine more fully the effect of hurricane flooding and hog CAFO exposure on AGI. We hope to examine other environmental exposures that flooded during Hurricanes Matthew and Florence, including poultry CAFOs, landfills, wastewater treatment facilities, and sewage systems in a multiple exposure framework. While flooded hog lagoons appear to be a larger threat because of their liquid waste compared to dry poultry waste, little research has considered how floods may spread poultry waste and affect human health. Hurricane Florence drowned an estimated 5,500 hogs and 3.4 million chickens and turkeys.[114] Preliminary estimates indicate that the economic impact of Hurricane Florence on the poultry industry was $40.4 million and the total economic impact on the pork industry was $1.2 million.[115] Large-scale animal production contributes to climate change and harms animals and humans during climate change-caused hurricanes, as well as during non-disaster times.

Conclusions

Hurricanes continue to strike NC and hog lagoons continue to flood and spread pathogens despite wide discussion of the effects of flooded and damaged lagoons and a ban on building new lagoons in the 100-year floodplain.[3] While flooded CAFOs have almost become normalized in NC, the massive release of hog manure during flood events are not natural events. This continual environmental disaster crisis has been created and permitted to continue by NC's lax regulation of CAFOs. While the NC Swine General Permit provides some protection to the environment and nearby communities under usual conditions, the protection is inadequate at preventing the spread of hog waste during hurricanes and other heavy precipitation events. In addition to the human health effects from hog CAFOs flooding, Hurricanes Floyd, Matthew, and Florence drowned tens of thousands of hogs and birds, and lagoon breaches during these storms killed many fish and created algae blooms. While this aim focuses on AGI caused by fecal bacteria, hog manure also contains nitrates and antibiotic residues that also harm the environment and damage health.[52–54] Hurricanes and heavy precipitation events are expected to increase in the future, as the effects of climate change intensify in the coming years. The intersection of hog CAFOs and flooding has created complex environmental and climate justice issues that are exacerbated during every hurricane. Given the increasing frequency and intensity of hurricanes, hog CAFOs should be removed from the 500-year floodplain and the size and density of CAFOs should be drastically decreased in eastern NC.

Supplementary Tables

Table 23. Characteristics of various Hurricane Matthew flooded and unflooded and high hog exposed and no hog exposed ZIP codes, and IPTW-ATT control pseudo-populations, matched on rurality and percent White (Method 3). For the flooded ZIP codes, the weights ranged from 0.0001-5.0, with median=0.002 and mean=0.2. For the unflooded ZIP codes, the weights ranged from 0.004-2.5, with median=0.1 and mean=0.3.

	No Flooding from Hurricane Matthew			≥33% Flooding from Hurricane Matthew		
Characteristic	**No Hog Exposure (unweighted)**	**No Hog Exposure (IPT weighted)**	**High Hog Exposure**	**No Hog Exposure (unweighted)**	**No Hog Exposure (IPT weighted)**	**High Hog Exposure**
Total Population	305,429	1,757,281	301,702	68,503	1,878	46,295
White non-Hispanic, N (%)	237,128 (77.6)	1,504,956 (85.6)	231,521 (76.7)	61,363 (89.6)	1,120 (59.6)	20,875 (45.1)
Black, N (%)	42,472 (13.9)	143,281 (8.2)	52,419 (17.4)	4,623 (6.7)	699 (37.3)	14,707 (31.8)
American Indian, N (%)	8,475 (2.8)	15,374 (0.9)	1,500 (0.5)	249 (0.4)	1 (0.1)	6,673 (14.4)
Hispanic, N (%)	19,598 (6.4)	110,827 (6.3)	23,497 (7.8)	3,115 (4.5)	159 (8.4)	3,737 (8.1)
Asian, N (%)	3,805 (1.2)	25,803 (1.5)	1,943 (0.6)	240 (0.4)	2 (0.1)	427 (0.9)
Uninsured, N (%)	34,748 (11.6)	181,404 (10.5)	32,003 (10.8)	8,200 (12.1)	388 (21.1)	5,498 (12.3)
Median Income ($)	40,965	44,877	43,879	49,568	25,102	33,692
Rurality Score	7.7	7.6	7.7	7.8	8.0	8.2
Average Percent of ZIP Code Flooded	0	0	0	72.6	75.8	45.4
Hogs, N	0	0	222,094	0	0	97,941
Average Hog Density (hogs/sqmi)	0	0	85	0	0	275
Birds, N	104,820,497	65,485,888	24,097,660	0	0	4,089,867
Average Bird Density (birds/sqmi)	9,419	8,976	25,194	0	0	11,478
Area (sqmi)	2,558	11,678	2,599	1,509	53	356
Total ED Visits 2016-2019	3,267	3,317	4,166	3,771	5,539	7,329
Total AGI Visits 2016-2019	32,459	157,501	31,382	4,282	189	6,675
ED Rate per 10,000 people	3,267	3,317	4,166	3,771	5,539	7,329
AGI ED Rate per 10,000 people	266	224	260	156	251	360
Sum of Weights	33	171	32	45	5	3
Number of ZIP Codes	171	171	32	45	45	3

Table 24. Characteristics of various Hurricane Florence flooded and unflooded and high hog exposed and no hog exposed ZIP codes, and IPTW-ATT pseudo control, matched on rurality and percent White (Method 3). For the flooded ZIP codes, the weights ranged from 0-55.3, with median=0.0003 and mean=1.2. For the unflooded ZIP codes, the weights ranged from 0.01-13.8, with median=0.04 and mean=0.3.

	No Flooding from Hurricane Florence			≥33% Flooding from Hurricane Florence		
Characteristic	**No Hog Exposure (unweighted)**	**No Hog Exposure (IPT weighted)**	**High Hog Exposure**	**No Hog Exposure (unweighted)**	**No Hog Exposure (IPT weighted)**	**High Hog Exposure**
Total Population	1,492,926	220,291	149,691	68,503	19,042	80,850
White non-Hispanic, N (%)	1,294,008 (86.7)	117,694 (53.4)	95,867 (64)	61,363 (89.6)	11,172 (58.7)	44,680 (55.3)
Black, N (%)	112,950 (7.6)	21,740 (9.9)	43,601 (29.1)	4,623 (6.7)	7,314 (38.4)	23,320 (28.8)
American Indian, N (%)	14,869 (1)	67,279 (30.5)	2,782 (1.9)	249 (0.4)	10 (0.1)	6,892 (8.5)
Hispanic, N (%)	89,703 (6)	13,175 (6)	9,514 (6.4)	3,115 (4.5)	1,586 (8.3)	5,931 (7.3)
Asian, N (%)	16,242 (1.1)	2,819 (1.3)	673 (0.4)	240 (0.4)	6 (0)	582 (0.7)
Uninsured, N (%)	161,016 (10.9)	44,614 (20.5)	15,971 (11)	8,200 (12.1)	4,156 (22)	9,655 (12.4)
Median Income ($)	42,958	36,653	36,397	49,568	24,193	37,978
Rurality Score	7.7	8.1	8.1	7.8	7.9	8.6
Average Percent of ZIP Code Flooded	0	0	0	74.6	95.1	43.3
Hogs, N	0	0	284,244	0	0	505,597
Average Hog Density (hogs/sqmi)	0	0	147	0	0	425
Birds, N	101,938,433	6,841,155	29,348,514	0	0	16,141,064
Average Bird Density (birds/sqmi)	8,996	1,432	15,162	0	0	13,572
Area (sqmi)	11,332	4,779	1,936	1,509	462	1,189
Total ED Visits 2016-2019	3,515	3,519	5,843	3,771	6,024	6,799
Total AGI Visits 2016-2019	141,303	15,826	15,432	4,282	2,012	10,069
ED Rate per 10,000 people	3,515	3,519	5,843	3,771	6,024	6,799
AGI ED Rate per 10,000 people	237	180	258	156	264	311
Sum of Weights	160	27	24	45	58	11
Number of ZIP Codes	160	160	24	45	45	11

Table 25. The association between hog exposure and AGI during the weeks after Hurricanes Matthew and Florence in areas that flooded (with various cut points, ≥25%, ≥33%, ≥40% of ZIP code area, indicating flooded ZIP code) and areas that remained unflooded (0% of ZIP code flooded). The exposed and unexposed groups were matched on rurality and percent White. Because of the low number of AGI ED cases in the hog exposed ZIP codes that flooded ≥40, we do not present the rate ratios.

		Hurricane Matthew			Hurricane Florence		
Percent of ZIP Code Flooded	Number of Weeks after Hurricane	Matthew Rate Ratio (95% CI)	Number of AGI ED Visits in ZIP Codes with Hog Exposure	Number of AGI ED Visits in ZIP codes Unexposed to Hogs	Florence Rate Ratio (95% CI)	Number of AGI ED Visits in ZIP Codes with Hog Exposure	Number of AGI ED Visits in ZIP codes Unexposed to Hogs
0	2	0.94 (0.69, 1.20)	292	1399	1.09 (0.85, 1.33)	147	1432
0	4	0.96 (0.69, 1.23)	591	2708	1.21 (0.88, 1.54)	297	2802
0	6	0.93 (0.64, 1.21)	872	4129	1.22 (0.86, 1.58)	421	4133
0	8	0.92 (0.64, 1.19)	1223	5789	1.25 (0.91, 1.59)	558	5351
≥25	2	5.72 (4.75, 6.69)	138	33	3.00 (1.32, 4.67)	217	40
≥25	4	4.16 (3.13, 5.19)	229	79	4.32 (2.65, 5.99)	449	89
≥25	6	3.79 (2.87, 4.71)	364	112	5.08 (3.41, 6.75)	646	121
≥25	8	0.99 (0.18, 1.80)	499	158	6.11 (4.44, 7.79)	865	159
≥33	2	13.94 (12.48, 15.4)	68	32	4.43 (2.69, 6.16)	100	40
≥33	4	10.32 (8.75, 11.89)	115	75	4.69 (2.82, 6.56)	195	88
≥33	6	9.96 (8.5, 11.43)	184	108	5.19 (3.32, 7.07)	266	120
≥33	8	0.99 (0.44, 1.54)	257	152	5.83 (3.92, 7.73)	344	157
≥40	2	-	2	27	4.44 (2.78, 6.09)	79	40
≥40	4	-	3	67	4.66 (2.87, 6.44)	155	87
≥40	6	-	4	98	5.09 (3.30, 6.89)	209	117
≥40	8	-	9	139	5.57 (3.74, 7.41)	264	154

CHAPTER VII: CONCLUSIONS

Summary of Findings

In this dissertation, we assessed the relationship between hurricane flooding and AGI ED visit rate, the relationship between hog CAFO exposure and AGI ED rate, and how hog CAFO exposure modifies the relationship between hurricane flooding and AGI ED rate in NC. Overall, we found hurricane flooding to be associated with an increase in AGI ED visit rate, especially when the hurricane was preceded by a dry period. We also observed hog CAFO exposure to be associated with higher AGI ED visit rates than no hog CAFO exposure. The positive association between hog CAFO exposure and AGI ED visit rate was strongest during the week after heavy rain events. We also observed that areas containing hog CAFOs within or near the flood extents experienced an increase in AGI ED visit rate during the three weeks after the hurricanes compared to AGI ED visit rate in these areas during non-hurricane years.

First, we investigated the association between hurricane flooding and AGI in NC, 2016-2019. We observed a 15% increase in AGI ED visit rate (rate ratio (RR)=1.15, 95% CI: 0.97, 1.32) after Hurricane Matthew and a 9% increase in AGI ED visit rate (RR=1.09, 95% CI: 0.93, 1.24) after Hurricane Florence compared to the expected AGI ED visit rate based on 2016-2019 trends, controlling for AGI ED visit rate changes after the hurricanes in the unflooded areas. The effect was particularly strong among American Indian patients and patients over age 64 after Hurricane Florence and elevated among Black patients for both hurricanes. When restricted to bacterial AGI, we found an 85% (95% CI: 1.37, 2.34) increase in AGI ED visit rate after Florence, but no increase after Matthew. In analyses restricted to the first week after the hurricanes struck NC, we observed a 20% increase in AGI ED visit rate (RR=1.20, 95% CI: 0.93, 1.46) after Hurricane Florence but no increase in AGI ED visit rate after Hurricane Matthew. Our sensitivity analyses revealed Florence's effect on AGI to be more consistent than Matthew's effect, possibly because little rain preceded Florence and heavy rain preceded Matthew. The differences in results between the hurricanes may be attributed to differences in antecedent rainfall, 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. Our results are consistent with the concentration-dilution hypothesis, which posits that heavy rainfall following a dry period (e.g., Hurricane Florence) can flush fecal material and other pathogens from soil and surfaces into surface water, increasing AGI incidence.[69,170] However, heavy rainfall after a wet period (e.g., Hurricane Matthew) often dilutes pathogen concentration in surface water and may decrease AGI incidence.

Next, we assessed how proximity to, and density of, hog CAFOs ("hog CAFO exposure") affects AGI ED rates in NC. We estimated a 17% increase (RR=1.17, 95% CI: 1.08, 1.26) in AGI ED visit rate in high hog exposed areas compared to areas without hog CAFO exposure, with a slightly stronger effect in rural areas (RR=1.24, 1.04, 1.48). When restricting the analysis to rural ZIP codes, we observed effect measure modification (EMM) by race, where the association between high hog CAFO exposure and AGI ED visit rate was highest among American Indian, Asian, and Black patients. We found hog CAFOs in NC to be disproportionally located in areas with a higher population of Black, Lumbee, and Filipino residents than the rest of the state. We also found that the association between high hog CAFO exposure and AGI ED visit rate was stronger during the week after heavy rain (above the 99th percentile of NC daily precipitation). The association between high hog CAFO exposure and AGI ED visit rate was stronger when ZIP codes with poultry CAFOs were excluded from the control. We also observed a positive association between high poultry density and AGI ED visit rate.

Lastly, we combined Aims 1 and 2 to examine how hog CAFO exposure modifies the relationship between hurricane flooding and AGI ED visit rate in NC. Using two different methods, we found evidence that areas with flooded hog CAFOs after hurricanes exhibit an increased AGI ED rate compared to areas with flooding and no hog CAFOs and areas with hog CAFOs and no flooding. We observed that ZIP codes with >10 hog CAFOs within 0.1 mile of the flood extents experienced an increase in AGI ED visit rate during the three weeks following hurricanes compared to AGI ED visit rate in these areas during comparable non-hurricane time periods. This increase in AGI ED visit rate in these ZIP codes with hog CAFOs near flooding was larger than the increase in AGI ED visit rate in ZIP codes without hog CAFOs and with flooding or ZIP codes with flooding and without hog CAFOs. Using CITS, we found hog exposure to be an EMM of the relationship between heavy hurricane flooding and AGI ED visit rate, and observed the association was strongest for ZIP codes with high hog CAFO exposure during the three weeks after Hurricane Florence and was strongest for ZIP codes with low hog CAFO exposure during the three weeks after Hurricane Matthew. We also attempted to assess the effect of high hog CAFO exposure compared to no hog CAFO exposure separately in flooded and unflooded areas, during the weeks after hurricanes. However, the populations we were comparing remained unbalanced despite our efforts to balance the covariates with inverse probability of treatment weights (IPTW). We found these analyses to be difficult because most heavily flooded areas had high hog CAFO exposure and most unflooded areas were also unexposed to hog CAFOs. The challenges in finding or creating an appropriate comparison group highlight the environmental injustice of hurricane flooding and hog CAFO exposure in NC, as the populations that live near flooded hog CAFOs have lower incomes and higher proportions of Black and uninsured residents than the state average.

Strengths and Limitations

Strengths

This dissertation uses four recent years of ED data and was able to capture all recorded ED visits 2016-2019, with mostly complete information on race, ethnicity, health insurance, age, and ZIP code.

This surveillance data enabled us to examine the AGI ED rate throughout the entire state of NC. The ED data in this study is standardized and in not subject to recall bias or social desirability bias, as survey data is. Additionally, this dissertation uses both flood extent data and precipitation data to improve our understanding of the effects of heavy rain and flooding on AGI.

In aim 1 and 2, our many sensitivity analyses helped us better interpret the associations of hurricane flooding and hog CAFO exposure with AGI ED visit rate. In sub-analyses, we were able to specifically examine the effects of hurricane flooding and hog CAFO exposure on bacterial AGI, viral AGI, and AGI caused by a few specific pathogens. We were also able to examine EMM by race, age, insurance status, and rurality, which increased our understanding of these complex relationships and the many interconnected factors. Our use of inverse distance weighting enabled us to create a hog CAFO exposure variable that incorporated proximity to hog CAFOs, number and density of hog CAFOs, and approximate manure exposure (using the steady state live weight calculation). This is a more precise estimation of exposure to pathogens from hog exposure than the simple, commonly used hog density.

Aim 1 and 3 benefit from their examination of two different severe hurricanes, with different pre-hurricane conditions, that affected similar areas. Most studies on hurricanes either examine many heavy rain/flooding events or a single hurricane. We were able to examine, describe, and compare the AGI effects of Hurricanes Matthew and Florence. Aims 1 and 3 also use robust methods (controlled interrupted time series) that control for time-invariant confounders by comparing AGI ED visit rates in ZIP codes after hurricane flooding to the expected AGI ED visit rate had no hurricane occurred. Lastly, in aim 3, we explored three different methods to examine how hurricane flooding and hog CAFO exposure jointly affect AGI ED visit rate in NC.

Limitations

This dissertation was limited by our outcome data's geographic specificity, which indicated the ZIP code of the patient's billing address but did not identify the ED's location, whether the patient was displaced prior to or during the hurricane, or whether the patient lived downstream from hog CAFOs. We were also limited by the broadness of the AGI category that we used in the main analyses. Because AGI has many possible etiologies and comorbidities, including causes unrelated to waterborne pathogens, many of the AGI ED visits in this dissertation were unrelated to flooding and hog CAFO exposure. Our sensitivity analyses examining bacterial AGI, viral AGI, and AGI caused by a few specific pathogens attempted to address this limitation. Additionally, our outcome data consist only of AGI episodes that resulted in ED visits (possibly the more severe AGI), which represent a small proportion of total AGI in the population, suggesting that the true effects may be underestimated.

We were also limited by the available flood inundation data. The NC DPS hurricane flood extent shapefiles incorporate data from various sources, but the inundation heavily relies on flood gauges and may have missed some smaller, localized flooding that occurred away from rivers. However, this flawed flood inundation data from NC DPS was the best available data and it was the main flood data used by the state to determine hurricane-affected areas in need of assistance.

While aims 1 and 3 were able to use time to create appropriate controls, aim 2 analyses were limited by the available data from the U.S. Census Bureau and American Community Survey (ACS) and likely suffer from residual confounding. Additionally, residents in high hog CAFO exposed ZIP codes are not necessarily exposed to pathogens from hog CAFOs, as true exposure depends on topography, drainage, manure spraying patterns, and human actions. Aim 2 and 3 analyses were limited by large demographic differences between ZIP codes with high hog CAFO exposure and no exposure, as well as ZIP codes with flooding and no hog CAFOs and those with flooding and flooded hog CAFOs. Additionally, we were unable to obtain information on the degrees to which the hog CAFO lagoons flooded, as some lagoons breached, others experienced significant structural damage, and others only flooded. These different ways in which hog lagoons are damaged by flooding likely affect the amount of hog waste and fecal bacteria that contaminate the waterways.

Public Health Significance

As NC is the third most hurricane-prone US state and the second leading hog producer, understanding how flooded hog CAFOs affect health is essential for disaster mitigation and improved public health in eastern NC. Microbial contamination in drinking water costs approximately $40 million in AGI-related ED visits in NC each year and results in millions of AGI cases in the US.[20,100] Many AGI cases are painful, debilitating, and disrupt work and school, but resolve themselves in a few days. However, AGI in young children, older adults, and the immunocompromised can result in serious health problems or death. Extreme rain events, which appear to increase AGI rates, are expected to become more frequent and severe in the coming years. Climate change in NC—and possibly throughout the world—will likely disproportionately harm the health of lower-income people and people of color (POC).

The results from this dissertation expose how racist policies harm the health of POC and how disasters often exacerbate existing health inequities. When politicians do not hold polluting industries accountable for their actions, the health of nearby residents (often low-income and POC) suffers. When disaster aid disproportionally benefits wealthier White residents, while providing inadequate funds to low-income disaster survivors, low-income families are often forced to continue living in mold-infested homes. As observed during major hurricanes and the COVID-19 pandemic, disasters disproportionately harm the health and livelihood of low-income and POC communities while many large industries and stockholders get richer. Environmental policies and disaster response continue to be affected by structural racism, white supremacy culture, and discriminatory policies.

This dissertation highlights the large impact that hurricane flooding and hog CAFOs have on rural areas in NC. The association between hurricane flooding and AGI ED visit rate was especially strong in rural areas after Hurricane Florence (aim 1). Similarly, the positive association between high hog CAFO exposure and AGI ED visit rate was strongest in rural areas, compared to less rural areas (aim 2). Additionally, ZIP codes with hog CAFOs near flood extents were more rural than the state average (aim 3). Hurricane flooding, hog CAFO exposure, and their joint effect exacerbates the urban-rural divide. Urban areas continually exploit rural regions for food production and waste disposal, which often causes pollution, health problems, and reduced quality of life for rural communities.

The issue of hog CAFOs and hurricane flooding disproportionately harming POC in eastern NC emphasizes the vulnerability of many of these communities as they are *exposed* to multiple social and environmental stressors, many are *sensitive* to exposure of pathogens (especially young children, older adults, and the immunocompromised), and many lack *adaptive capacity* (e.g., resources, health insurance) to manage and recover from illness and disasters.[202] To reduce the health effects from hog CAFOs and hurricanes, all hog CAFOs within the 500-year floodplain should be relocated to areas unlikely to flood and away from communities of people of color. We identified 85 hog CAFOs within Hurricane Matthew's flood extent and 81 hog CAFOs within Hurricane Florence's flood extent (about 4% of total hog CAFOs in NC) which should be relocated because of their flood risk. Additional interventions might include educating residents in flood-prone areas about precautions to take regarding drinking water after hurricanes and providing resources to establish better and more systematic water testing after heavy flooding (especially when preceded by a dry period). State, local, and community interventions must focus on equity when acting to prevent and respond to disasters.

Directions for Future Research

Future research on hurricane flooding and AGI should further examine how the conditions before hurricanes (wet vs. dry period, temperature) affect changes in AGI rate. Further work on CAFOs and AGI rate should examine the combined effect of swine, poultry, and cattle CAFOs and may consider creating an animal density measure based on the number and weight of animals ("animal units"), as described by Booth et al.[203]. Additional research should use a multiple exposure framework to examine more fully the effect of hurricane flooding and environmental exposures on AGI by examining various flooded industries that release pathogens, including poultry and hog CAFOs, landfills, wastewater treatment facilities, and sewage systems. Future research should use precipitation, flood, elevation, and topography data to model how flood water travels and to identify the specific areas or watersheds that are exposed to floodwaters downstream of hog CAFOs. As AGI is only one of many potential health effects caused by flooded hog CAFOs, studies should examine flooded CAFOs' effects on other health outcomes, such as methicillin-resistant *S. aureus* (MRSA) infections. Because many people are displaced after hurricanes and many AGI cases do not result in ED visits, a useful future study may survey hurricane-affected people asking about their contact with floodwater, their proximity to various environmental contaminants, their movement or displacement during/after the storm, their experience requesting and receiving disaster assistance, and their health outcomes.

Conclusions

Eastern NC—a predominantly poor, rural region with high proportions of Black, Hispanic, and American Indian residents, high dependence on well water, and high hog CAFO exposure—continues to be hit by devastating hurricanes that spread pathogens and contaminate surface waters. Hurricanes Matthew and Florence were powerful storms with record-breaking flooding, but climate change projections predict that such extreme weather events will increase in frequency and intensity in the coming years. Large-scale animal production significantly contributes to climate change, due to its massive emissions of greenhouse gases. Climate change increases extreme weather events, which in turn flood animal production facilities and transport disease-causing pathogens into the environment and to nearby communities.

In this dissertation, we found high hog CAFO exposure to be associated with a higher AGI ED visit rate, especially in rural areas and in American Indian, Asian, and Black patients. We also observed hurricane flooding to be associated with an increase in AGI ED visit rate, although the strength of effect may depend on antecedent rainfall. The AGI ED visit rate in areas with flooded hog CAFOs increased more after hurricane flooding than the AGI ED visit rate increased in flooded areas without hog CAFOs. Areas with flooded hog CAFOs have lower median incomes and higher proportion of Black residents than the state average. These results are evidence of continued environmental racism by animal production industries and policymakers. The intersection of hog farms and flooding has created entangled environmental and climate justice issues in NC that must be ameliorated by the removal or relocation of all CAFOs in the 500-year floodplain, stricter environmental regulations on CAFOs, and equitable disaster response.

APPENDIX 1: TABLES OF PATHOGENS

Appendix 1a. Potential pathogens in flood water[8,9,89,91–94]

Pathogen	Survival Time in Warm Water (days)	Incubation Time (days)	Health Effects
Viruses:			
Norovirus	>108	1-2	Vomiting, diarrhea, nausea, stomach pain; lasts 1-3 days
Rotavirus	10	1-3	Diarrhea, fever, vomiting, stomach pain; lasts 3-10 days
Enterovirus	56	3-10	Fever, runny nose, sneezing, cough, skin rash, breathing problems, mild abdominal pain and diarrhea; lasts 7-10 days
Calicivirus	>21	1-2	Nausea, vomiting, diarrhea, stomach pains, low fever; lasts 1-3 days
Adenovirus	>108	5-6	Fever, sore throat, acute bronchitis, diarrhea
Bacteria:			
Campylobacter spp.	<2	2-5	Diarrhea (bloody), abdominal pain, fever, nausea, vomiting; lasts 1 week
Salmonella spp.	45-154	1-3	Diarrhea, nausea, vomiting, abdominal cramps, fever, headache; lasts 10 days
Yersinia enterocolitica	10	1-14	Diarrhea, fever, abdominal pain, joint pain; lasts 2-3 weeks
Escherichia coli O157:H7	49-84	1-10	Bloody diarrhea, abdominal cramps; last 5-10 days
Vibrio cholerae		2-3	7-14 days
Clostridium difficile	months	2-3	Severe diarrhea, fever, stomach pain, nausea; lasts 1-2 weeks
Shigella spp.	11	1-3	Bloody diarrhea, severe stomach pain, fever; lasts 5-7 days
Helicobacter spp.		3-4	Abdominal pain, nausea, loss of appetite, bloating; lasts 1-2 weeks with treatment
Protozoa:			
Giardia spp.	14	1-14	Diarrhea, fatigue, abdominal cramps, nausea; lasts 2-6 weeks
Cryptosporidium spp.	70	2-14	Diarrhea, fever, nausea, stomach pain; lasts 1-2 weeks
Cyclospora cayetanensis	7-60	2-14	Watery diarrhea, loss of appetite, weight loss, stomach pain, bloating and gas, nausea; lasts 2-30 days
Entamoeba histolytica	months	14-28	Watery or bloody stools, abdominal cramping, loss of appetite, fatigue

Appendix 1b. Potential pathogens in human sewage[204,205]

Pathogen	Survival Time in Warm Water	Incubation Period	Health Effects
<u>**Bacteria**</u>:			
Campylobacter spp.	<2 days	2-5 days	Diarrhea (bloody), abdominal pain, fever, nausea, vomiting; lasts 1 week
Salmonella spp.	45-154 days	12-72 hours	Diarrhea, nausea, vomiting, abdominal cramps, fever, headache; lasts 10 days
Yersinia spp.	10 days	1-14 days	Diarrhea, fever, abdominal pain, joint pain; lasts 2-3 weeks
Escherichia coli O157:H7	49-84 days	1-10 days	Bloody diarrhea, abdominal cramps; lasts 5-10 days
Enterotoxigenic Bacteroides fragilis			Diarrhea, especially in children (cognitive deficits in children); lasts 2-11 days
Shigella	11 days	12-96 hours	Bloody diarrhea, especially in children, lasts about a week
<u>**Protozoa:**</u>			
Giardia spp.	14 days	1-14 days	Diarrhea, fatigue, abdominal cramps, nausea; lasts 2-6 weeks;
Cryptosporidium spp.	70 days	2-14 days	Diarrhea, fever, nausea, stomach pain; lasts 1-2 weeks; can be life-threatening for people with compromised immune system

Appendix 1c. Potential pathogens in hog manure[21–23]

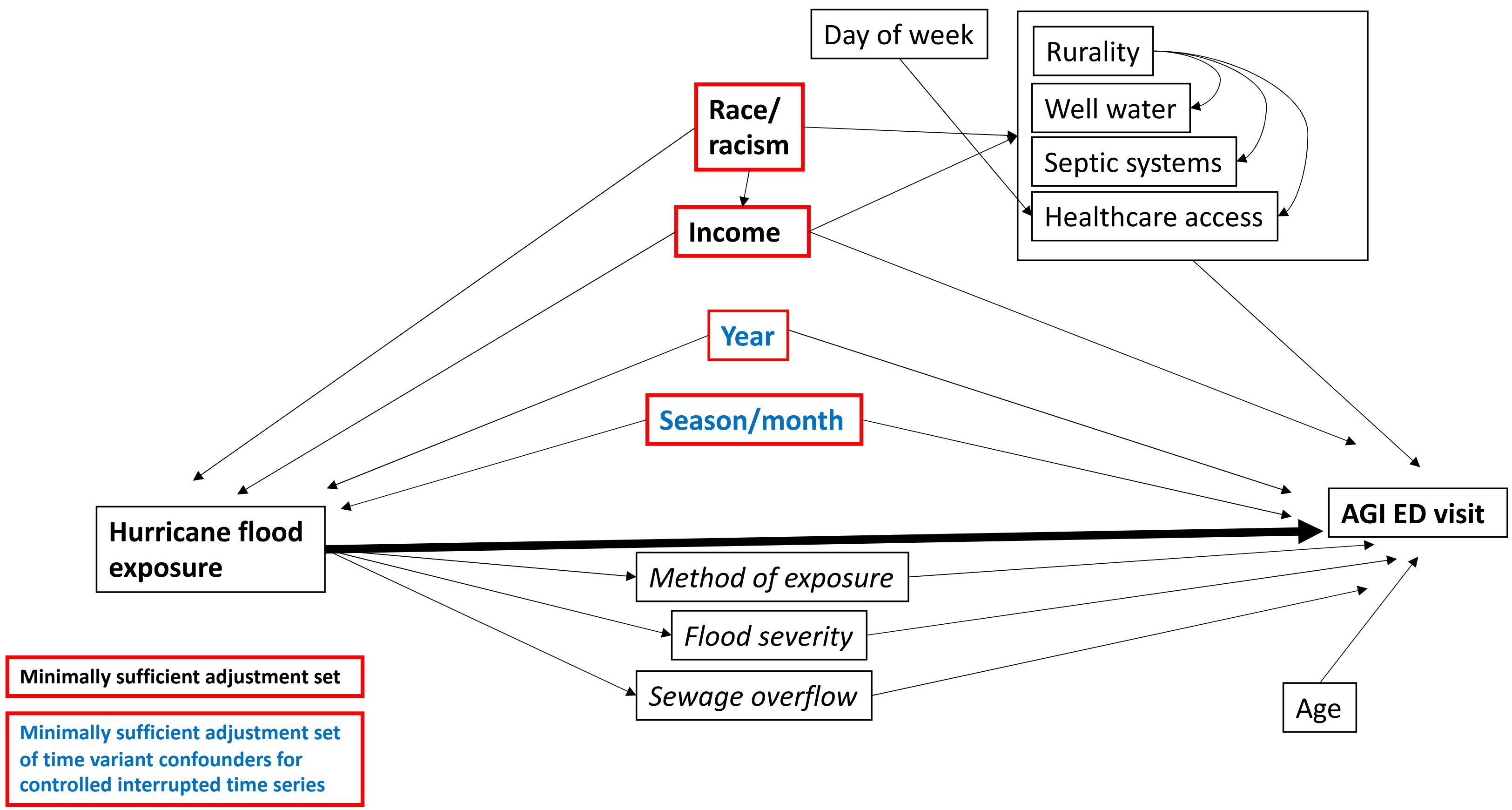
Pathogen	**Survival Time in Warm Water**	**Incubation Period**	**Health Effects**
Bacteria:			
Campylobacter spp.	<2 days	2-5 days	Diarrhea (bloody), abdominal pain, fever, nausea, vomiting; lasts 1 week
Salmonella spp.	45-154 days	12-72 hours	Diarrhea, nausea, vomiting, abdominal cramps, fever, headache; lasts 10 days
Yersinia enterocolitica	10 days	1-14 days	Diarrhea, fever, abdominal pain, joint pain; lasts 2-3 weeks
Escherichia coli O157:H7	49-84 days	1-10 days	Bloody diarrhea, abdominal cramps; lasts 5-10 days
Protozoa:			
Giardia spp.	14 days	1-14 days	Diarrhea, fatigue, abdominal cramps, nausea; lasts 2-6 weeks;
Cryptosporidium spp.	70 days	2-14 days	Diarrhea, fever, nausea, stomach pain; lasts 1-2 weeks; can be life-threatening for people with compromised immune system

APPENDIX 2: TABLE OF PUBLIC HEALTH CRITICAL RACE PRAXIS MAIN FOCUSES

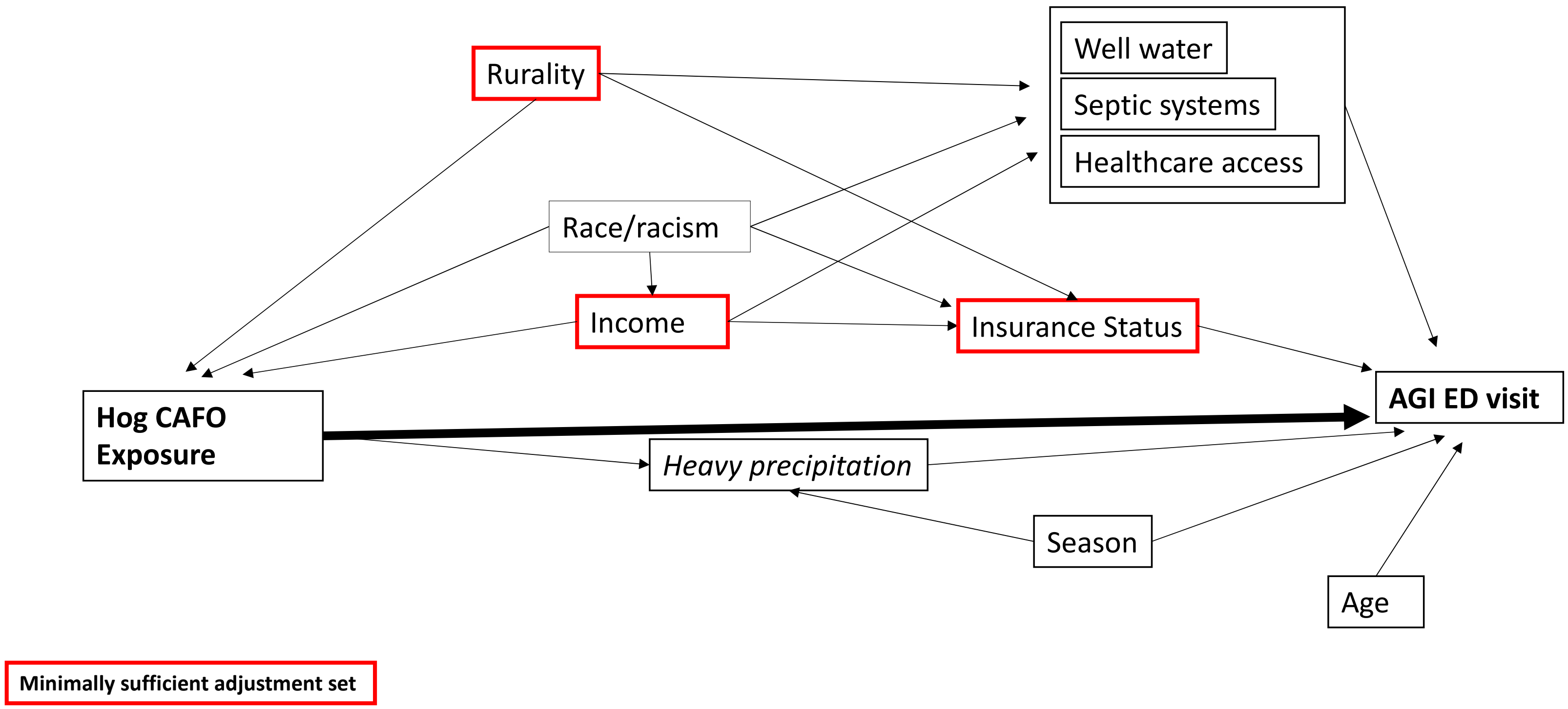
Public Health Critical Race Praxis Main Focuses[121]	**Examples of My Completed Work or Future Work**
Contemporary patterns of racial relations	- I examined inequities in hog CAFO exposure and hurricane flood exposure - I interviewed hurricane survivors to understand complex challenges BIPOC survivors face, recovering within a racist system - I continue to examine inequities in disaster relief funds
Knowledge production	- I continue to examine epidemiological methods employed to consider biases in methods and results
Conceptualization and measurement	- I considered limitations of the race data (sometimes self-reported, sometimes assumed by clinicians in NC DETECT data) - I conducted analyses with the most precise race and ethnicity data available and examined specific American Indian and Asian groups residing near hog CAFOs
Action	- I will continue to conduct analyses that examine intervention effects - I will continue to work with community groups to share results - I will work with justice-orientated lawyers to use these results to advocate for environmental justice

APPENDIX 3: DIRECTED ACYCLIC GRAPHS (DAGS)

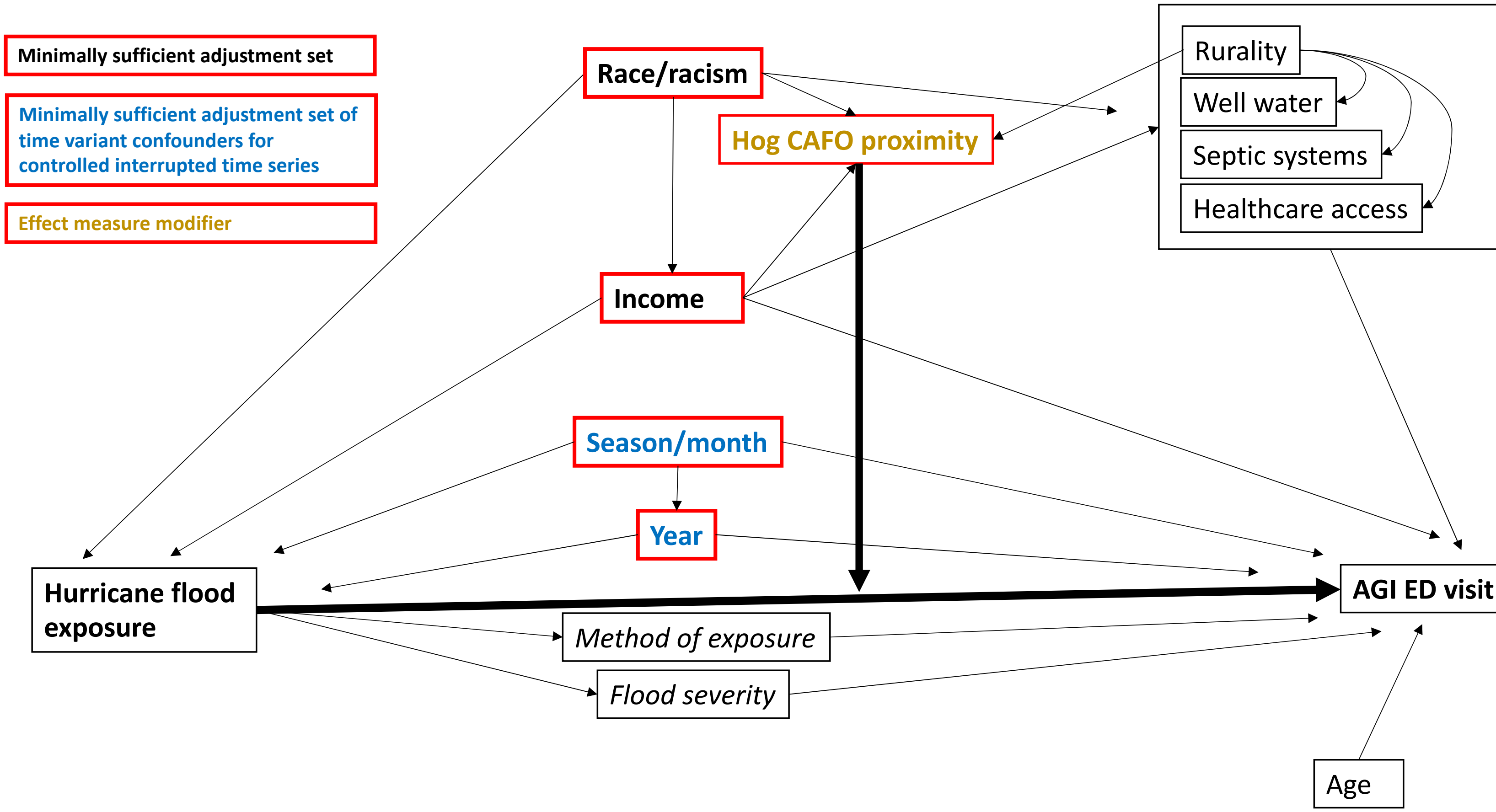
Appendix 3a. Aim 1 DAG



Appendix 3b. Aim 2 DAG

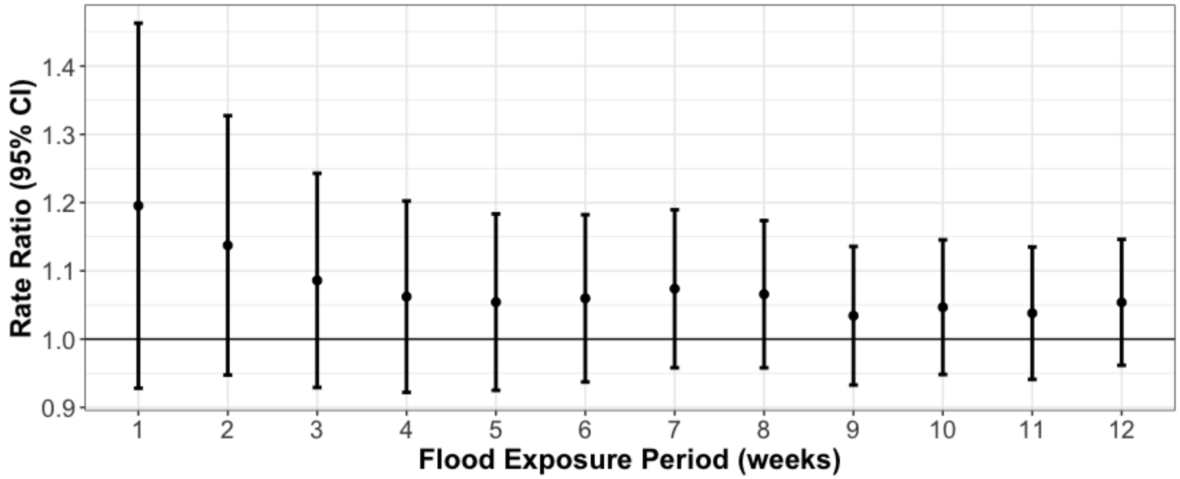


Appendix 3c. Aim 3 DAG



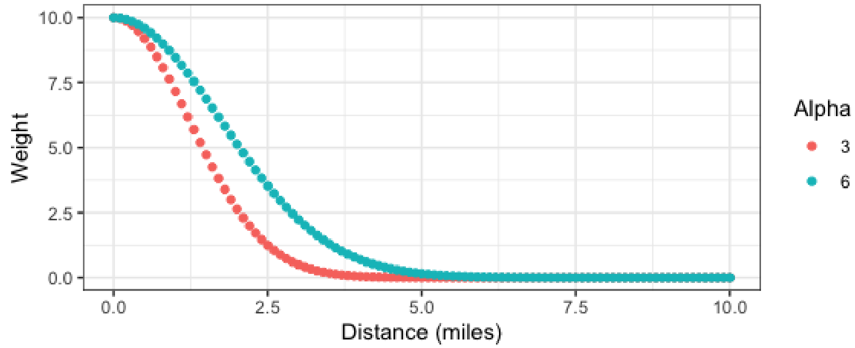
APPENDIX 4: GRAPH OF THE AGI RATE INCREASE AFTER HURRICANE FLORENCE BY WEEK

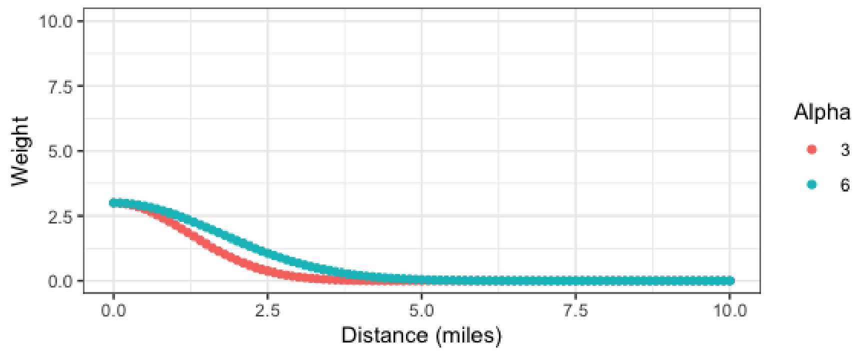
AGI ED visit rate after Hurricane Florence remained slightly elevated for approximately eight weeks after the hurricane struck North Carolina. Graph shows the rate ratios from the controlled interrupted time series analyses with various lengths of exposure period (1 week to 12 weeks).



APPENDIX 5: GRAPHS OF GAUSSIAN CURVE USED IN AIM 2

Graphs showing the Gaussian curve used in aim 2 analyses. We primarily used an alpha of 3, but we conducted sensitivity analyses with an alpha of 6. The top graph shows the distance-weight curve for a large hog CAFO with a large steady state live weight while the bottom graph shows the curve for a small hog CAFO with a small steady state live weight.





APPENDIX 6: CHARACTERISTICS OF NORTH CAROLINA BY RURALITY

Characteristics of metropolitan areas, micropolitan areas, small towns, and rural areas in North Carolina, using the geographic isolation scale ZIP code-level data broken into quartiles for rurality;[151] 2017 American Community Survey for race, ethnicity, insurance status, and income data; hog CAFO, landfill, wastewater treatment facility, brownfields, dry cleaning facility data from NC DEQ,[206] ED rate and AGI ED rate from NC DETECT, flooding data from NC DPS; and poultry CAFO data from Environmental Working Group.[30]

Characteristic	**Metropolitan**	**Micropolitan**	**Small Towns**	**Rural**
Population	5,005,092	3,020,535	1,373,083	535,495
Number of Hogs	142,163	2,417,801	5,418,532	4,834,065
Number of Lagoons	71	981	2,110	1,845
Number of Pre-regulatory Landfills	319	349	278	221
Number of Active Landfills	219	217	196	189
Number of Birds	5,944,758	69,524,195	117,512,876	88,323,852
SQMI	5,704	13,680	14,469	15,834
Number of Wastewater Treatment Facilities	530	610	452	339
Brownfields	1,303	323	216	193
Dry cleaning Facilities	516	221	186	186
ED Rate per 10,000	3,500	3,935	4,594	5,079
AGI ED Rate per 10,000	191	246	253	235
Percent White	64	75	74	72
Percent Black	25	17	18	22
Percent American Indian	0	1	3	2
Percent Hispanic	10	8	8	5
Percent Asian	4	1	1	0
Percent Uninsured	12	14	15	16
Median Income ($)	55,901	48,181	41,669	39,185
Average Bird Density (birds/sqmi)	1,042	5,082	8,122	5,578
Average Hog Density (hogs/sqmi)	25	177	374	305
Average percent flooding during Hurricane Florence	8	13	12	16

DISCLAIMERS

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.

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

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