ASSOCIATIONS BETWEEN HURRICANE WEATHER EXPOSURE AND PREGNANCY OUTCOME: DEMONSTRATION OF ECOLOGICAL AND INDIVIDUAL-LEVEL METHODS

Shannon C. Grabich

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology in the Gillings School of Global Public Health.

Chapel Hill
2015

Approved By:

Stephanie Engel

Jennifer Horney

Charles Konrad II

David Richardson

Whitney Robinson

ABSTRACT

Shannon C. Grabich: Associations between hurricane weather exposure and pregnancy outcome: demonstration of ecological and individual-level methods
(Under the direction of Whitney Robinson)

The impacts related to natural disasters are influenced by population growth, increasing coastal settlement, and global climate change. Socially vulnerable groups, including pregnant women, may be disproportionately affected by hurricane-related health effects. The limited literature on this topic is comprised primarily of pre-post ecological studies that may have biases due to confounding. The results of current studies, although mixed, have suggested that adverse fetal outcomes, including preterm delivery, may increase with hurricanes exposure.

We assessed hurricane exposure in 2004 with pregnancy outcomes using a cohort of Florida pregnancies constructed from 2003-2005 using vital statistics records. We first utilized a difference-in-differences modeling technique to assess the county-level association between hurricane exposure and birth rates. We then conducted an individual-level analysis using time-to-event modeling to investigate hazard rates of single and multiple hurricane exposures on preterm delivery stratified by race/ethnicity.

In county-level analysis the difference-in-differences method consistently produced estimates that suggested no association between hurricane and live birth rate, while the results from generalized linear model sensitivity analysis were inconsistent across exposure methods. The consistency of the difference-in-differences method suggests potential ability to control for time-invariant confounders.

In individual-level analysis we found evidence of association between hurricane exposure and increased hazard of extremely preterm delivery (<32 weeks gestation) but no association with overall preterm delivery (<37 weeks gestation). Suggested associations appeared driven by white Hispanic and black Hispanic subgroups although we found limited evidence of statistical interaction. We did not find evidence of increasing hazards of preterm delivery with exposure to multiple hurricanes.

This work provides examples for confounding control for future research to reduce biases. Although we found no association between hurricane exposure and live birth rate, we demonstrated a potential increase in hazard of extremely preterm delivery with hurricane exposure consistent with some of the current literature. As coastal populations and hurricane severity increases, future research is needed to understand the impacts of hurricane exposure on reproductive health, with a potential focus on the heterogeneity among race/ethnicity subgroups for targeting interventions, such as messages about evacuation or education about the importance of prenatal care during and after a disaster.

ACKNOWLEDGEMENTS

This dissertation would not have been possible without the help, guidance, and support of many people. I would like to thank my committee members who have guided me through the dissertation process. I would like to first thank my adviser, Dr. Whitney Robinson, for her support, advice and encouragement through the academic and dissertation process. I would like to thank my mentor Dr. Jennifer Horney for her support, knowledge and friendship through the doctoral career. I would also like to thank Dr. Stephanie Engel, Dr. Charles Konrad and Dr. David Richardson for their comments, suggestions and support which greatly improved the quality of this work and continued my educational experience at UNC Chapel Hill.

I would also like to gratefully acknowledge the significant contributions of the following affiliations and personnel. Hurricane Weather Data was provided by Dr. Charles Konrad through his efforts with the (CDC's) BRACE study and the Florida Department of Health. Vital statistics data and consulting were provided by the Florida Department of Health, Vital Statistics Division. Special thanks to Yasmin Serrano, a Research Associate at the Florida Bureau of Vital Statistics, who served as my point of contact and assisted greatly with data management. Also, to the Odum Institute for their statistics and Arc Map 10 support, specifically Phillip MacDaniel GIS Librarian. I also am thankful to Danelle Lobdell who has created a supportive working environment through my ORISE fellowship and has been both a mentor and friend through this process.

Funding and guidance towards my doctoral degree were provided primarily by the Clendenin family through The Clendenin Fellowship and Oak Ridge Institute for Science as well as through an Education Fellowship at the Environmental Protection Agency. Both fellowships have provided mentoring as well as financial support for me and my family.

I would also like to thank my friends and family for their invaluable support. I am especially grateful to my mom who has always been very supportive and encouraging not only during the course of my education but for all my life. Finally, many thanks to my husband, James, and son, Aaron, who supported me and kept my spirits high; I love you both and appreciate everything you do.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BD	birth defect
BRACE	Building Resilience against Climate Effects
BW	birth weight
CDC	Center for Disease Control and Prevention
DAG	Directed Acyclic Graph
DID	difference-in-differences
EPA	Environmental Protection Agency
EQI	Environmental Quality Index
EXP	exponentiated
FEMA	Federal Emergency Management Agency
FIPS	Federal Information Processing Standard
FL	Florida
GIS	geographic information system
GLM	generalized linear models
HR	hazard ratio
HRD	Hurricane Research Database
IPCC	Intergovernmental Panel on Climate Change
km	kilometers
LBW	low birth weight
mph	miles per hour
NCHS	National Center for Health Statistics
NHC	National Hurricane Center

NOAA	National Oceanic and Atmospheric Administration
NS	non-significant
PTB	preterm delivery
PTSD	post-traumatic stress disorder
RR	risk ratio
UNC	University of North Carolina
US	United States
VPTB	very preterm delivery

CHAPTER 1: BACKGROUND

Introduction to Hurricanes and Reproductive Health

The impacts and losses related to natural disasters have grown as populations in vulnerable areas and the severity of large-scale disasters have increased. Specifically, hurricane hazard vulnerability is influenced by population growth, urbanization, increasing coastal settlement, and global climate change. The eastern seaboard region of the United States (US), which along with the US Gulf coast, is the area where hurricanes most often make landfall, is home to over 50% of the nation's population, and its proportion of the US population is projected to exceed 55% by 2015. Suggested hurricane-related health effects include mortality, injury, economic distress, excessive stress and disruption of health care. Federal Emergency Management Agency (FEMA) defines pregnant women as a socially vulnerable populations disproportionately affected by disaster-related health effects. Hormone fluctuation during pregnancy may influence stress related reactions while potential lapses in access to health care could impact reproductive outcomes.

Published studies investigating associations between hurricane exposure and adverse pregnancy have often had mixed results. Studies have predominantly shown that adverse fetal outcomes, including preterm delivery, increase with exposure to natural disasters; however, results of research on the association between exposure to natural disaster and birth or fetal death rates have been mixed. Due to increased vulnerabilities during the perinatal period and the increasing hazard vulnerability, understanding the potential adverse consequences of hurricanes on fetal events is necessary.

Published research on this topic is comprised primarily of ecological studies conducted after the hurricanes make landfall, using surrounding areas as controls. These case studies are not generalizable to other areas impacted by storms of differing magnitudes, and have not yet addressed the impact of being exposed to multiple hurricanes during a single hurricane season. Also, the use of the surrounding areas as controls may induce confounding by county-level differences as well as other environmental differences. Past studies have also used different definitions for what constitutes hurricane exposure, making it difficult to compare studies and possibly leading to the heterogeneity of effects seen in the literature.

To investigate potential associations between hurricane exposure during pregnancy and reproductive health outcomes, we propose to construct a population-based cohort of Florida pregnancies occurring between 2003-2005 using combined birth certificates and fetal death records. This unique timeframe includes a variety of exposures: a non-hurricane control year, 2003, when no hurricanes made landfall; and 2004, when four hurricanes made landfall in Florida - Charley (August 13th), Frances (September 5th), Ivan (September 21st) and Jeanne (September 25th) (Figure 1.1). In general, hurricanes are categorized by the maximum strength of their maximum wind speeds based on the Saffir-Simpson Hurricane scale (Table 1.1).

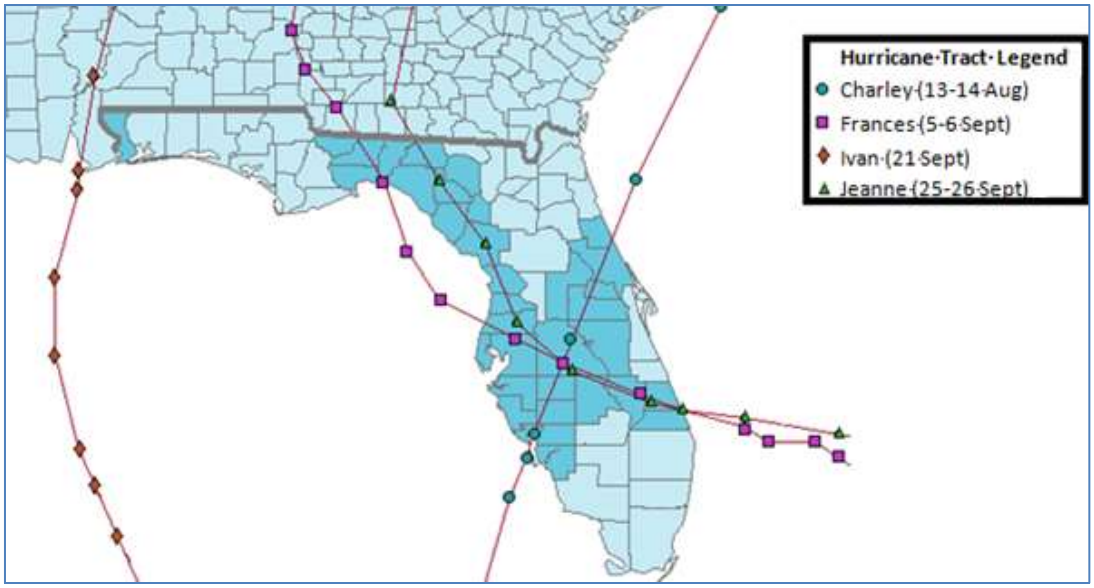

Figure 1.1 2004 Florida Hurricane Track County Map with Counties on Track Highlighted

Charley, a category 4 hurricane, was the strongest hurricane to strike the US since Hurricane Andrew in 1992 and was relatively small but intense. Charley travelled northeastward through central and northeast Florida, through the heart of the Florida Peninsula. Frances, a category-2 hurricane, was not as strong as Charley, but was much larger and responsible for over 100 tornadoes and massive floods. Frances traveled northwest through Florida, hitting central Florida and the western coast towards the panhandle. Hurricane Ivan, a category 3 hurricane when it hit Alabama and Florida, was both strong and large leading to flooding and tornadoes, but only affected a small area of the Florida panhandle. The final hurricane of the 2004 season, Jeanne, a category 3 hurricane, followed a very similar path to that of Frances and affected many of the same counties. Jeanne, however, was not as powerful as Frances but was more slow–

Table 1.1 Saffir-Simpson hurricane wind scale definitions

Hurricane Category	**Sustained Winds (miles per hour (mph))**
1	74-95 mph
2	96-110 mph
3	111-129 mph
4	130-156 mph
5	157 mph and higher

moving, dropping several inches of rain over the already saturated flooded region of Florida just hit by Frances. The 2004 hurricane season was the worst in Florida's history, with four hurricanes causing at least 47 deaths and over $45 billion in damages.

First, we show preliminary analyses which explore methods of quantifying hurricane exposure. Next, we will use a novel application of the difference-in-differences method to describe the association between 2004's hurricane-related weather exposure and county-level live birth rates. Lastly, we will conduct individual-level analysis to investigate the effect of hurricane exposures on preterm delivery, defined as births before 37 total gestational weeks, using time-to event models. The proposed research will be conducted using novel meteorological modeling of hurricane wind speed in comparison to previous published methods. Our results will both demonstrate efficient analytic methods to control confounding and provide insight regarding the potential effect of hurricane-related weather exposure on reproductive health outcomes. The findings may be generalizable to Florida pregnancies during other hurricane seasons and used to make inference to similar coastal populations.

Literature Review

A growing body of literature suggests that hurricane-related exposures may impact maternal and fetal health; however, many of the currently published reports were either anecdotal in nature or clinician recommendations as opposed to systematic studies (1, 2). Systematic studies of natural disaster and reproductive health outcomes are primarily focused on single disasters of large economic consequence including Hurricane Agnes (1972), Hurricane Gilbert (1988), Hurricane Hugo (1989), Hurricane Andrew (1992) and Hurricane Katrina (2005). Several mechanisms have been hypothesized for the way in which hurricane exposure can impact reproductive health. Currently proposed mechanisms include maternal or fetal death, injury, disruption of health care, economic distress and psychosocial stress. These mechanisms include both long term (e.g., post-traumatic stress disorder [PTSD]), and short term (e.g., power outages) exposures. Much of the literature on post-disaster outcomes hypothesizes maternal psychosocial stress as either a primary exposure or the proposed mechanism influencing fetal outcomes. These mechanisms are thought to be similar across various types of natural disasters.

This review includes literature describing potential mechanisms related to natural disasters on reproductive health as well as the current state of the literature concerning the effects of disaster exposure on reproductive health outcomes including birth rates, fetal death rates, maternal depression, PTSD, birth weight and gestational age. First, we discuss the effects of biological mechanisms of exposure on public health and vulnerability of pregnancy and reproductive health outcomes. Next, we review the current literature on hurricanes and other natural disaster exposures and reproductive health outcomes. Two recent systematic review articles of disaster and reproductive outcomes have included both manmade and natural disasters (1, 2). Our review has been limited to natural disasters since we are primarily interested in the impacts of hurricane exposure. Hurricanes are unlike spontaneous manmade disasters in that populations often receive advance warning when a hurricane threatens their area, giving them opportunity to evacuate from unsafe locations.

Mechanisms of Health Outcomes from Hurricane Exposure

Hurricanes are some of the world's most catastrophic disasters and have a wide range of public health implications (2-4). Severe storms have lasting implications, including economic crisis, infectious disease, injury, psychosocial stress, and disruption of health care services (3, 5-7). Evacuation may mitigate some of these negative outcomes, such as mortality and injury;

however, psychosocial stress and PTSD are a continuing problem, both in populations who directly experience a hurricane and in those who evacuate (8-10).

Injury/Mortality

Injuries attributed to hurricane can occur before, during, or after the actual hurricane landfall. Prior to the storm, injuries such as falls, strains, and fractures can occur during storm preparation. Motor vehicle accident related injuries also tend to increase with mass evacuations During hurricanes, physical injury represents the major cause of death and the primary cause of morbidity (3). Major injuries during the storm are often caused by structural collapse, wind borne debris, and fallen trees and power lines. The direct impact of hurricanes can include contact with hurricane force winds, rain, and flood. Minor trauma is common, including lacerations, abrasions, sprains, and fractures (11-15). After the hurricane, injuries are more likely due to fire, carbon monoxide poisoning, injury from chainsaws, and falls sustained in repairing storm damages (3, 16).

Prior to the implementation of evacuation and shelter systems, drowning from storm surge flooding accounted for 90 percent of hurricane attributable mortality (3, 5). Likewise, before 1990, the majority of deaths attributed to hurricanes making landfall in the US occurred at the time of impact and were attributed to drowning in storm surges (11). Advances in construction, forecasting, and evacuation have decreased hurricane-related mortality in the US (17-20). Improvements in forecasting and evacuation have shifted hurricane mortality trends in two ways (21). First, storm-surge drowning deaths have decreased, and thus the majority of deaths during the most violent part of the storm are now due to injury by high-velocity winds (16, 22). Second, most of the storm-related mortality and much of the morbidity now occurs in the post-impact period after hurricane rain and winds have ceased. Prominent causes of death and injury during the storm are now electrocutions from downed power lines, chain-saw injuries, blunt trauma from falling trees, and motor vehicle fatalities while after the storm flooding is the major cause of death (23). Specifically, flooding in part due to hurricanes, accounts for 40% of the natural disasters reported and is the leading cause of death associated with natural disasters in the US (37, 116).

Pregnant women may be more vulnerable to some types of injuries due to changes in balance, increased blood flow, and pregnancy related comorbidities such as fractures due to falls(24). Some studies of pregnancy trauma have found increased fetal loss and poor outcomes in mothers who experience other types of trauma, such as vehicular accidents and severe falls (25, 26), but, to our knowledge, none of the published disaster literature has specifically investigated hurricane injury and related morbidity in pregnant women.

Infectious Disease

In general, outbreaks of infectious disease following hurricanes are rare in the US and other developed countries. In these nations, increases in gastrointestinal disease and respiratory illness are reported occasionally, which are generally shelter associated (17, 21, 27, 28). No notable post storm increases in communicable diseases have been captured by the post-disaster surveillance systems in use in developed nations (16, 28).

In the developing world, occurrences of infectious disease outbreaks are more common after hurricanes (16, 21, 28). Increases in both acute respiratory infection and severe gastrointestinal disease have been noted (27). Factors unique to developing nations that are more likely to lead to outbreak of disease include high endemic rates of disease, low immunization rates, poor access to clean water , poor sanitation, prolonged crowding in shelters, and inadequate nutrition (29). Prolonged disruption of routine public health-care services is more likely to occur in developing countries and contributes to an increase in disease (16). Additionally, interruption of public health-care service and antimalarial spraying have contributed to several outbreaks of malaria after hurricanes in Central America, South America, and Haiti (30).

Pregnant women are more susceptible to some communicable diseases and may have a more severe reaction due to a compromised immune system during pregnancy; however no published reports to date have focused on reproductive health and outbreaks of infectious disease due to hurricanes (31-33). Since hurricane-related outbreaks of infectious disease are not a problem in developed nations, we do not expect this to be an active mechanism in our hurricane reproductive health analysis.

Economic/Property Loss and Disruption of Care

Hurricanes are among the costliest weather-related natural disasters. NOAA reports all of the billion-dollar weather related disaster in the US and since 1980, hurricanes have accounted for the vast majority of these disasters (34). From 1970-2009, seven of the ten most costly global natural disasters, in terms of insured losses - a total of $164 billion - were hurricanes that struck the Gulf of Mexico and Atlantic coasts of the US (4). Previous research into long-term trends in hurricane-related damage along the US coast has suggested that damage has been quickly increasing within the last three decades, even after adjusting for inflation. To best capture the year-to-year variability in hurricane damage, consideration must also be given to coastal population changes and changes in wealth (35). Much individual property loss is driven by location and housing type (36) - for instance, mobile homes and homes not retrofitted for hurricanes are more likely to have increased damages (28, 37).

Structural damage together with a loss of power, water, and communication are to be expected from severe hurricane weather. Lack of access to medical care may occur due to high winds, rain, and flooding during and after the hurricanes and floods (38). The windows of health care facilities may be shattered from a hurricane's high winds or the premises may be flooded with water, prompting the evacuation of patients and staff to safer areas of the hospital. Additional nursing staff, family members, and high need patients (e.g. pregnant women, dialysis patients, ventilator patients) contribute to hospital overcrowding and need for additional resources (39). In addition to crowding, health care facilities may be understaffed or have some staff working long hours due to road damage and infrastructure problems that limit workers' ability to commute to work (40, 41).

Factors that influence individual property loss and health care facilities could have a major impact on pregnancy outcomes. Case studies have reported increases in Caesarian delivery around the time of disaster occurrences (42, 43). If women are unable to get to the hospital during labor, it may take emergency services longer to respond. Also, if services are lost or health facilities are disabled, pregnant women may delay routine checkups or may not receive adequate prenatal care. The effects of economic, structural, and other sources of disruption of health care may differ depending on the timing of exposure during pregnancy as well as the severity of hurricane weather.

Psychosocial Stress

Behavioral health effects due to fear, injury, economic loss, and other psychosocial stresses are among the most debilitating long-term outcomes of hurricane exposure (3, 9, 10, 44-46). Studies have consistently shown increased levels of stress, anxiety, and depression among victims of natural disasters (47-50). In the four years after a natural disaster, the incidence of suicide increases by 13.8 percent generally, and by 31 percent in counties affected by hurricanes (2, 51). Even exposure to moderate-scale disasters with a small number of deaths and injuries has been linked to increased stress, especially for women. Hospital and public health services may be compromised by other physical damage and stress to personnel (3, 7, 52, 53). Psychosocial stress and the disruption of health care often act in tandem to create an unstable environment for populations highly dependent on health care services, including pregnant women (1, 43).

While the exact biological mechanism that links increased levels of maternal stress and poor fetal outcomes like preterm delivery and low birth weight is not precisely known, studies suggest excess stress in the fetal environment is caused by excessive maternal psychosocial stress disrupting the maternal hypothalamus and adrenal systems (54-57). Clinical data has shown that the increased production of neuropeptide corticotrophin-releasing hormone during periods of anxiety can play a role in initiating labor. Studies have found women with elevated blood levels of corticotrophin-releasing hormone in the second trimester or early third trimester were at a greater risk of preterm delivery (57-61). Maternal stress measured at different gestational ages has been found to correlate significantly with corticotrophin-releasing hormone measured at the same time, and including levels of corticotrophin-releasing hormone in analyses has been found to mediate the relationship between maternal stress and preterm delivery (61). Stress during pregnancy is a suggested risk factor for many adverse reproductive outcomes including distressed delivery, low birth weight and preterm delivery (55, 56, 62).

A published review of stress and reproductive health studies published between 1966 and 2001 reported that pregnant women with (generally self-reported) high stress and anxiety levels are at an increased risk for spontaneous abortion, preterm labor, low birth weight, and the delivery of a malformed or growth-restricted baby(56). These findings may be limited due to confounding by omitted variables and biased by other factors that correlate with both stress and birth outcomes, e.g., poverty or poor health (56). A more recent review of prenatal maternal psychological distress and adverse reproductive outcomes found that, in general, elevated levels of depression and anxiety were found to be associated with poorer obstetric outcomes (e.g. obstetric complications, pregnancy symptoms and preterm delivery), which had implications for fetal and neonatal well-being and behavior (63).

Pregnancy Vulnerability

Vulnerability to natural hazards is not based solely on the event itself, but also on the social, economic, and political environment in which populations face hazards (64). In general, the term "vulnerable populations" refers to individuals who are either physically, psychologically, or socially disadvantaged compared to the average individual in the population (65). Studies have shown that racial and ethnic populations in the US are more vulnerable to natural hazard events due to "language, housing patterns, building construction, community isolation and cultural insensitivities" (66). Although not well studied, it is suggested that pregnancy may encompass both physical and psychological vulnerabilities for the mother and fetus, which increase the effects of natural disaster exposure (67, 68).

Pregnant women and fetuses may be disproportionality vulnerable to disruptions in health care due to the physical status and psychosocial stresses during hurricane exposure (2). Pregnant women not only require routine medical care throughout pregnancy, but also immediate medical services throughout pregnancy and during delivery (40, 43). Studies of disasters and stress indicate that women need disaster psychotherapy more often than men (45) and pregnant women may be even more vulnerable (2, 9, 69, 70). Factors related to natural disaster stress exposure contribute to a very unique stress experienced by persons living in areas with frequent and severe hurricane exposure. Several studies of pregnancy and disaster-related stress find that pregnant women with disaster exposure experience PTSD, depression and anxiety after delivery more often than women not exposed to hurricanes (9, 43, 67, 71).

While there are many hurricane exposure mechanisms that could have an influence on preterm delivery, the assumed stress mechanism is well supported in the literature. This exposure may be ubiquitous in individuals living in Florida, regardless of evacuation, in areas that are routinely and severely affected by hurricane weather. We are not directly able to test anxiety and stress in the proposed cohort, but do acknowledge this as an avenue for potential intervention to improve post-disaster outcomes in the future.

Review of Hurricanes and Reproductive Health

The current body of literature pertaining to hurricane exposure and reproductive health outcomes is primarily based on hurricanes that made landfall in the United States. The majority of these are individual case studies of hurricanes that made landfall with destructive large scale consequences, including Agnes (1972), Gilbert (1988), Hugo (1989), Andrew (1992) and Katrina (2005). A single study by Currie (2013) investigated major hurricanes (categories 3, 4, or 5), which made landfall in Texas between 1980-2008, to look at the overall effect of hurricane exposure on reproductive health. Most studies have focused on the association between hurricane exposure and adverse birth outcomes in areas directly impacted by hurricanes in comparison with surrounding areas without hurricane exposure. Many of these studies either assume psychosocial stress is or measure it as the primary mechanism between disaster exposure and outcomes. Table 1.2 summarizes each study's exposure, outcome and results.

Birth and Fetal Death

Several ecological studies have investigated birth and fetal death after hurricane exposure. These studies have mixed results but suggest an increase in birth and fetal death rates the year following hurricane exposure.

A study by Cohan and Cole (2002) examined the change in marriage, birth, and divorce rates following Hurricane Hugo from 1975 to 1997 for all counties in South Carolina. Time-series analysis indicated that in the year following the hurricane, birth rates increased in the 24 counties declared disaster areas compared with the 22 other counties in the state(72). Hamilton (2009) also investigated county birth rates in the Gulf Coast states following Hurricane Katrina. This study had mixed results, with births declining in most counties and parishes of Louisiana and Mississippi and rising in the counties of Alabama. Overall, birth rate trends were inconsistent across counties although these trends declined most in non-Hispanic black populations (51). A study conducted of deeply flooded areas after Hurricane Agnes found that fetal death rates increased the year after severe flooding in highly affected areas (73).

Maternal Stress

Many of the currently published studies on hurricanes and reproductive health outcomes measure maternal psychosocial exposures or outcomes and all of them were conducted after Hurricane Katrina. These studies assessed PTSD, depression, or general psychosocial stress in pregnant or postpartum women post disaster. Overall, these studies consistently found an increased incidence of PTSD and depressive symptoms in women exposed to the storm as compared to those unexposed or with less exposure. Differences were particularly profound among postpartum women.

In a study of 301 Louisiana women, Xiong et al. (2010) found that measured psychological trauma after Hurricane Katrina was not associated with low birth weight or preterm delivery. The authors did find an association between low birth weight and greater hurricane exposure, i.e., reporting three or more of eight severe hurricane experiences (9). A subset of this cohort was utilized by Harville (2010) to analyze hurricane-related threat, illness, loss, and damage. Overall, two or more severe hurricane experiences was associated with an increased risk for both depression and PTSD. These associations were found to be strongest in black women and women with less education (74). Savage (2010) used a cross-sectional, exploratory study of 199 postpartum /expectant mothers to describe perinatal moods and complementary alternative therapy (CAT) use among childbearing women living in New Orleans, LA, after Hurricane Katrina. This study found that women who sought alternative therapies and health behaviors had decreased self-perceived anxiety and depression (75).

Fetal Distress

A single study explored an indicator of fetal distress using birth records and monthly time series spatial models to examine the effects of Hurricane Andrew in Florida. Increased fetal distress was found when comparing the hurricane exposure period to the non-exposure periods in areas of severe hurricane damage. Exposure during the second and third trimester was associated with increased odds of fetal distress compared to first trimester exposure or no exposure. Similar to Harville et al. (2010), this study found that black mothers were more likely to have birth distressed infants (76).

Low Birth Weight and Gestational Age

Several studies have explored the effect of hurricane exposure on low birth weight and gestational age, and these studies have found an increase in low birth weight (68, 74) but mixed results for gestational age. Xiong (2008) also found a higher frequency of low birth weight and preterm delivery in women with greater hurricane exposure. The study concluded that women who had greater hurricane exposure were at an increased risk of having poor infant outcomes (68). Harville et al. (2010) concluded that while the risk of low birth weight and preterm delivery remained higher in black compared to white women, the storm did not appear to have exacerbated health disparities (74). Another study of Hurricane Katrina investigated birth rates and poor fetal outcomes in the Gulf Coast states, including Louisiana and Alabama (51). This study found lower rates of very preterm deliveries and very low birth weight in exposed parishes of Louisiana following Hurricane Katrina, as well as higher rates of very preterm deliveries in exposed counties of Alabama.

A single study used Texas birth records over a twelve year period to look at the effect of multiple hurricanes between 1996-2008 (Currie and Rossin-Slater 2013). This study found that exposure to a hurricane during pregnancy increased the probability of abnormal conditions of the newborn, such as being on a ventilator and meconium aspiration syndrome. Also, exposure in the third trimester, but not first or second trimester exposure, increased the risk of low birth weight. The authors concluded that exposure to stressful events like natural disasters during pregnancy can influence fetal outcomes, although the effects may be subtle and sensitive to statistical analysis method.

Birth Defects

Two studies have investigated birth defects after hurricane occurrence. Duff (2004) conducted a case control study (17 cases, 51 controls) of neural tube defects in Jamaica after Hurricane Gilbert. An increase in neural tube defects was noted after Hurricane Gilbert, thought to be due to decreased folic acid intake after crop destruction (77). Janerich and colleagues conducted a study after Hurricane Agnes of highly flooded areas and found that fetal death rates were higher the year after severe flooding in highly affected areas; however, change in birth defect rates were not significant (73).

Table 1.2 Literature review of hurricanes and reproductive health outcomes

Hurricane	Author	Pub Date	Outcomes: Life Events	Outcomes: Maternal Stress	Outcomes: Fetal Outcome	Major Findings
Agnes(1972)	Janerich	1981	X		X	Increase fetal death, BD NS
Gilbert(1988)	Duff	1994				Increase BD
Hugo(1989)	Cohan and Cole	2002	X	X		Increase birth rates
Andrew(1992)	Zahran	2010		X		Increase fetal distress
Katrina(2005)	Xiong	2008		X		Increase LBW, PTD NS
	Hamilton	2009	X	X		Conflicting birth rates by county. Decrease VPTD, PTD LBW NS
	Harville	2009		X		Increase PTSD
	Harville	2010			X	Increase LBW, PTD NS
	Xiong	2010			X	Increase PTSD/Depression
	Savage	2010		X		Increase PTSD/Depression
Texas(1980-2008)	Currie	2013			X	BW and PTD NS

NS – non-significant, PTD- preterm delivery, VPTB – very PTD, BW – birth weight, LBW – low birth weight, BD- birth defect

Review of Other Natural Disasters and Reproductive Health

Given that the biological mechanisms could be similar across various types of natural disasters, it is necessary to briefly review literature on reproductive outcomes following other types of natural disasters, including earthquakes, floods, and ice storms. This literature is more extensive than the current published hurricane literature and includes domestic and international studies. These studies may provide additional insight on the relationship between disasters and preterm delivery, as well as timing of disaster exposure during pregnancy.

Earthquake

Several systematic studies have been conducted following earthquake events. Overall, these studies show that earthquake exposure increases the risk of maternal psychosocial stress and that the exposure timing in pregnancy can affect fetal outcomes including gestational age and birth weight.

For example, a study of the Northridge Earthquake in California showed that the mean gestational age was lowest in pregnancies exposed to earthquake in the second and third trimester (78). A study by Torche used individual-level data on measured shaking from earthquake to study the effects of the 2005 earthquake in Chile, and found that exposure to the shaking during the first trimester of pregnancy increased the risk of low birth weight and short gestation (79). Another study of a 2010 earthquake in Chile found a reduction in the overall birth rate, but an increase in the rate of early preterm deliveries (<34 weeks), premature rupture of membranes (PROM), macrosomia, small size for gestational age, and intrauterine growth restriction (IUGR). Women exposed to the earthquake during the first trimester were more likely to deliver smaller newborns and preterm infants compared to those exposed at third trimester (80). A study in China by Tan and colleagues used birth records to investigate birth outcomes as a consequence of a major 2008 earthquake. Significant low birth weight, greater ratio of low birth weight, preterm delivery and low Apgar scores were all observed in the post-earthquake group (81). One study of birth outcomes after an earthquake in Israel found a significant increase in delivery rate 48 hours following the earthquake, and a significant increase of preterm delivery (82). These studies consistently suggest increased adverse birth outcomes after earthquake exposure.

Several earthquake exposure studies have investigated maternal psychosocial stress. A study of an earthquake in Taiwan investigated the prevalence of minor psychiatric morbidity in a group of women who were pregnant during or immediately after a major earthquake. Overall, maternal history of abdominal injury, death of a spouse, and instability in living conditions were significantly correlated with low birth weight (142). A study in Japan demonstrated that psychological impact and stress resistance were associated with exposure during pregnancy. During pregnancy, postnatal depression was a significant predictor of a physical abnormality during pregnancy or childbirth (83).

Flood

While floods often co-occur with hurricane, there is no literature specifically addressing this type of flooding on health. Studies of overall flood exposure in the US and in Poland have been conducted to investigate potential associations with reproductive health outcomes. These studies suggest an increase in preterm delivery and birth complications after disaster, but inconsistent results with regard to birth rates.

A study of the 2009 North Dakota Red River Floods explored changes in birth rates, birth outcomes, and pregnancy risk factors. The study used county-level birth files and found that the crude birth rate and the direct-adjusted fertility rate decreased significantly following floods. Compared to pre-disaster figures, there were significant increases in poor maternal outcomes as well as significant increases in low birth weight and preterm deliveries (249). Two studies were conducted by Neuberg (1998, 2010) in Poland after a flooding disaster in the Klodzko region: One study explored maternal stress and fetal outcomes (84) and another investigated birth rates

(85). The first, a small study of women injured in flood, found injured women to have an increased risk of pregnancy loss, preterm delivery, birth asphyxia, premature rupture of membranes and intrauterine growth retardation. The second study found an increase in birth rates in the year after the flood (84, 85).

Ice Storm

A single study of an ice storm in Canada found that gestation lengths and predicted birth weights were smaller among participants exposed to the ice storm during early to mid-pregnancy, compared to third trimester and pre-pregnancy exposure. High objective prenatal maternal stress levels predicted smaller head circumferences in early pregnancy, however, these effects decreased in later pregnancy (86).

Non-Specific Natural Disasters

In a large-scale study, Simeonova (2009) used county-level data on all births in the US in 1968–1988 to investigate a range of natural disasters. Exposure to disaster during pregnancy increased the likelihood of a preterm delivery but not low birth weight. This study also found that mothers affected in the second trimester of pregnancy suffered the largest negative impact on preterm deliveries and low birth weight (87).

Outcome Review: County-level Live Birth Rate

Live birth rates are defined as live births per 1,000 persons in the population at midyear, indicating the number of births respective to the entire population. The birth rate is usually the dominant factor in determining the rate of population growth. It depends on both the level of fertility and the age structure of the population (88). Since 2010, the number of births and the fertility rate either declined or were unchanged for most races and Hispanic origin groups in the US; however, both the number of births and the fertility rate for Asian or Pacific Islander women rose. The birth rate for teenagers 15-19 years was down 6 percent (29.4 births per 1,000 teenagers 15-19 years), with rates declining for younger and older teenagers and for nearly all race and Hispanic origin groups (88). The literature of hurricane exposure and birth rates is inconsistent, with some evidence of declining birth rates the year after disaster (51, 72).

Outcome Review: County-level Fetal Death Rate

Fetal death rates are computed as the number of fetal deaths at 20 weeks of gestation or more per total 1,000 live births and fetal deaths (89). Fetal death is defined as the intrauterine death of a fetus at any gestational age (90). Much of the concern surrounding reproductive loss has focused on infant mortality, due in part to a lesser understanding of the incidence, etiology, and prevention strategies for fetal death. Although the vast majority of fetal deaths occur very early in pregnancy, it is customary in research to only consider fetal deaths after 20 weeks of completed gestation because of the lack of information on loss before 20 weeks (91). Most states in the US only report fetal deaths at 20 weeks of gestation or more, and statistics on fetal death exclude data for induced terminations of pregnancy. Even when only fetal deaths at 20 weeks or more are considered, nearly as many fetal deaths as infant deaths occur in the US each year (89, 92).

Outcome Review: Preterm Delivery

Preterm deliveries, which are defined as births before the 37th week of gestation, are one of the major health problems of industrialized societies (93). The 37-week cut point has been established because several organ systems mature between 32 and 37 weeks, and the fetus is thought to reach adequate maturity by the end of this period (94). One of the main organs greatly affected by premature birth is the lungs. The lungs are one of the last organs to mature; because of this, many premature babies spend the first days or weeks of their life on a ventilator. Close to 13 percent of all births in the US in 2006 were preterm (54, 57, 95). While the frequency of low birth weight (<2,500 g) infants declined somewhat in the US between 1970 and 1980, this decline appears to have occurred primarily among full-term as opposed to preterm infants (96).

The neonatal and long-term health care costs of preterm infants impose a considerable economic burden both on individual families and the nation (97). A recent March of Dimes report estimates that the average cost of care for a premature baby is $49,000, as compared to $4,551 for a full-term birth without complications. The costs of prematurity are almost five times higher than for any other complication of birth and delivery, resulting in at least $26.2 billion in societal costs each year (93).

Preterm delivery is the single most important cause of perinatal mortality in the United States (97). Preterm deliveries are the leading cause of infant mortality and are associated with substantial neurocognitive, pulmonary, and ophthalmologic problems later in life. Death rates among extremely preterm infants (less than 32 weeks of gestation) are more than 150 times higher than among full term babies (90). Also, the risk of neurologic and developmental impairment during childhood is substantially elevated for the youngest gestational age survivors. Despite reductions in infant mortality, the rate of preterm delivery in the US remains considerably higher than the rates in many other industrialized countries. It is unlikely that there will be further substantial improvement in infant survival in the US unless a reduction in births of preterm infants can be accomplished (97).

While clinical measures can be taken to delay birth and drugs can be used to facilitate maturation of the lungs, understanding the underlying mechanism of preterm delivery has been difficult (93). Preterm delivery as a consequence of excessive stress at any time point in pregnancy is supported in the animal and epidemiological literature (54, 56, 57, 98, 99). Many studies imply an underlying stress mechanism in the analysis of natural disaster exposure and adverse fetal outcomes including preterm delivery. The association between hurricane exposure and preterm delivery has been inconsistent; however, studies of other disaster exposure have consistently demonstrated increased risk of preterm delivery (1, 2, 43, 51, 55, 70, 76, 100, 101). Current studies on the relationship between maternal hurricane exposure and preterm delivery suggest a dose response relationship with severity of exposure, and potential differences by exposure trimester; however, these studies are limited to case reports and single disaster cases (3, 9, 17, 51, 76). Disaster-related stress, injury, clinical disruption and economic loss could all play an important role in preterm delivery risk.

Preterm Delivery and Race/Ethnicity

Studies of preterm delivery consistently find significant differences by race (91, 97). In the US, black women are consistently reported to be at higher risk of preterm delivery compared to other minorities or white women. Preterm delivery rates are in the range of 16–18% in black women compared with 5–9% for white women. Black women are also three to four times more likely to have a very early preterm delivery than women from other racial or ethnic groups (102, 103). Part of the discrepancy in preterm delivery rates between the US and other countries might be explained by the high rate of preterm deliveries in the US black population (104). Over time, the disparity in preterm delivery rates between black and white women has remained largely unchanged and unexplained, and contributes to a cycle of reproductive disadvantage with far-reaching social and medical consequences (105).

Clustering and diversity of race/ethnicity groups in Florida created a unique environment to look at subgroups in the relationship between hurricane exposure and preterm delivery (106). Published studies of hurricane and reproductive health effects show that African

Americans have increased risk of adverse fetal health outcomes compared to other minorities and white women (66, 74). In contrast, regarding the assumed stress mechanism, a recent study of stress and preterm delivery across 19 states using the Pregnancy Risk Assessment and Monitoring System found that no significant interaction effects between race-ethnicity and stress on preterm delivery (107). With our large racial and ethnically diverse cohort, we will investigate differences between race and ethnic subgroups.

Hurricane Exposure Measurement

A hurricane is often defined by its wind speed and force. The Saffir-Simpson Hurricane Wind Scale classifies hurricanes into 5 distinct categories of severity: Category 1 (74-95 mph), 2 (96-110 mph), 3 (111-129 mph), 4 (130-156 mph), and 5 (157 and higher mph). Category 3-5 hurricanes are considered major hurricanes in which buildings and resources can be damaged or unavailable for days or weeks.

Appendix A describes our preliminary analysis of 2004 hurricane exposure measurement. The current disaster literature focuses primarily on two methods of assigning disaster exposure: 1) Federal Emergency Management Agency (FEMA) Presidential Disaster Declarations and 2) exposure using spatial data on the specific storm trajectory. We compared the use of these two methods and an additional novel wind speed measure based on Saffir-Simpson hurricane intensity scale. Hurricane wind exposure was defined by residence from the birth certificate in a hurricane affected county as determined using several maximum wind speed categorizations.

In summary this paper highlights that FEMA disaster declaration, spatial data based on storm trajectory, and meteorological severity of wind speed displayed clear heterogeneity of exposure assignment when assessing the four hurricanes of the 2004 hurricane season. The number of counties classified as exposed varied greatly between methods, with the largest margin of difference for Hurricane Ivan, which impacted the far western Florida panhandle. The disaster declaration method consistently assigned a higher number of counties as exposed to hurricanes when compared to other exposure methods, supporting the assertion that the use of this method, developed for providing federal assistance to affected jurisdiction, likely over assigns county-level hurricane exposure. We found no statistically significant associations between counties designated as exposed using the disaster declaration method and reproductive health outcomes.

For increased comparability between studies, a more objective, quantitative method of exposure such as wind speed may be preferred over the less specific assignment of disaster exposure like the FEMA disaster declaration. Meteorological wind speed modeling provides a new and reproducible approach to better characterize hurricane exposure and its effect on health. For these reasons the binary wind speed classifications were chosen for the primary exposure classification method in this research. For the difference-in-differences analysis the spatial buffer was also used to assess consistency across exposure methods.

Study Significance

The potential impacts of global climate change on health are not yet well understood. More frequent and more intense weather events may be one result of climate change. In particular, variability in climate has been demonstrated by the increasing intensity of hurricanes in the US (9, 42). With increasing scientific evidence of climate change and its subsequent potential impact on severity of hurricanes, a better understanding of the growing health consequences is needed. Some populations, including the elderly, racial and ethnic minorities, and pregnant women may be more vulnerable to health effects of natural hazards (66). We will investigate pregnancy outcomes and multiple hurricane events using methods to reduce methodological biases and

Climate Change and Disasters

Much of the social and economic costs associated with climate change may result from related health consequences and the shifts in the frequency and severity of extreme weather events (108). This is illustrated by a large number of costly weather disasters in 2011, which tied 2005 as the warmest year globally since 1880 (108). In 2011, overall damages from major natural disasters exceeded $55 billion, five times the costs incurred in the average year (35). Some effects of climate change include increasing temperature, changes in patterns and amount of precipitation, rising sea level, and increasing number of global natural disasters. Global climate change can affect interannual variability in the climate system, such as El Niño, which influences disaster probabilities (109, 110). While we cannot state that climate change has directly caused a specific disaster event, there is evidence that increases in temperature influence the weather in unexpected ways and the occurrence of hazardous weather events.

Climate Change and Public Health

There are many mechanisms by which climate can affect health, including temperature (e.g., heat waves) and rainfall (e.g., floods and droughts), which have both immediate and long term effects (111). Often the most severe hurricane weather includes high winds and heavy rains that can lead to severe flooding. Populations that have experienced flooding may suffer from sustained increases in mental illness such as depression and anxiety (112). Disruption in ecology from excessive rainfall also can affect the distribution of disease vectors, such as mosquitoes (111). Climate can also affect levels of air pollutants. For example, studies suggest ozone pollution are higher in some areas of Europe, and lower in others but the mechanisms are not well understood (113). There is also the potential of environmental degradation associated with climate change, which can lead to population displacement as well as economic or property loss (47).

Increases in natural disaster severity are the most widely hypothesized economic and health risk attributable to climate change. Losses from disasters have grown exponentially as populations have increased in vulnerable areas and the severity of large-scale disasters has increased (114, 115). The current literature suggests that natural disaster exposure is related to injury, infectious disease, psychosocial stress and mortality (3).

Climate change effects of warming tropical sea surface temperatures are argued to be increasing the intensity and longevity of tropical cyclones. Since 1980, hurricanes have contributed to more billion-dollar weather disasters than any other natural hazard (4). Specifically, flooding in part due to hurricanes, accounts for 40% of the natural disasters reported and is the leading cause of death associated with natural disasters in the US (37, 116). Along the Atlantic Coast, almost 60% of the land that is within a meter of mean sea level is planned for further development despite inadequate information on the potential rates and amount of sea level rise (35). Climate change and increases in temperature may be increasing severity of hurricane occurrences and related hazardous weather events.

Hurricane Burden and Trends

NOAA reports that the average number and intensity of hurricanes has increased by in the US over the last 20 years, and the economic burden of each major hurricane (category 4, or 5) has increased from $7 to $22 billion(3, 4, 7, 44, 45, 110, 117, 118). Specifically the number of Category 4 and 5 hurricanes had increased 80% in the past 30 years (117). The Intergovernmental Panel on Climate Change (IPCC) also predicts a steady increase in tropical cyclone wind intensities and mean and peak precipitation intensities, as well as an increased intensity of mid-latitude storms (119). In the past, North Atlantic storms have made landfall once every few years, but recent occurrences have included single hurricane seasons where multiple storms have made landfall (118, 120, 121). In our study period, during the 2004 hurricane season, four storms made landfall in Florida, causing destructive flooding, high winds, and tornados (4, 110, 117, 118, 122). Some of the climate models currently used by IPCC predict that major cities in Europe and Northern America will experience more frequent and more severe hurricanes over the next century (123). This effect is a current focus area of climatological and epidemiological research into the related health consequences. While we cannot prevent hurricanes, we can respond to the increasing burden caused by these storms by understanding the public health implications and increasing emergency preparedness measures.

Hurricanes are increasing in severity while US populations are steadily increasing in coastal areas. In the US, hurricanes most frequently make landfall along the Outer Banks of North Carolina, southern Florida and southern Louisiana. Landfalls of hurricanes of Category 3 and higher are most frequent in south Florida and along the eastern Gulf Coast. Additionally, adverse weather effects, including severe wind and rain, have extended as far inland as Kansas and Nebraska (3, 4). The US southeast is most often and hardest hit by hurricanes; it is also the most developed, and home to 50% of the nation's population (124, 125). Florida's population density of 654 persons per square mile is more than double that of any other region of the US and continues to increase daily (118, 124). Between 2000 and 2010, Florida, along with Georgia and North Carolina, had the highest percent increase (approximately 18%) in population(25).The health consequences related to hurricane exposure are an increasing public health concern, given the increasing coastal populations and increasing hurricane severity.

Hurricanes and Reproductive Health

Increasing storm severity has lasting public health implications, including economic crisis, infectious disease, injury, psychosocial stress, and disruption of health care services (3, 5-7). Evacuation mitigates some of these negative outcomes, such as mortality and injury; however, psychosocial stress and PTSD are a continuing problem, both in populations who directly experience hurricane and those who evacuate (8-10).

Behavioral health effects due to fear, injury, economic loss, and other psychosocial stresses are among the most long term and debilitating outcomes of hurricane exposure (3, 9, 10, 44-46). Studies have shown increased levels of stress, anxiety, and depression among victims of natural disasters (47-50). In the four years after any natural disaster, the incidence of suicide increases by 13.8 percent generally and by 31 percent in counties affected by hurricanes. Even exposure to moderate-scale disasters with a small number of deaths and injuries has been linked to increased stress, especially for women. Studies of disaster and stress indicate that women need disaster psychotherapy more often than men, (45) and pregnant women may be even more vulnerable (2, 9, 69, 70).

Psychosocial stress and disruption of health care act in tandem to create an unstable environment for populations highly dependent on health care services, including pregnant women (1, 43). Not only do pregnant women experience stress, but necessary public health services can be affected through both employee stress and physical damages, potentially compromising the health care infrastructure (3, 7, 52, 53). Women require routine medical care throughout pregnancy, but also immediate medical services for acute conditions and delivery (40, 43). Case studies of delivery during disaster suggest that labor and delivery method may be driven by staffing shortages and storm related complications (40, 43). These reports of medical services during disaster and pregnancy are typically limited to the impressions of relief workers (126, 127) and clinicians rather than systematic studies (100, 128). The lasting health effect on pregnant mothers could affect reproductive health even after hurricane occurrence and effect fetal birth and death rates (51, 72, 74).

Disruption of health care coupled with disaster-related stress during pregnancy is a suggested risk factor for many adverse reproductive outcomes including distressed delivery, adverse birth outcomes, and preterm delivery (55, 56, 62). Pregnant women and their fetuses may be disproportionately vulnerable to adverse health outcomes, including fetal death and preterm delivery, from disruption of care and lasting psychosocial effects of hurricane exposure. These hurricane-related effects increase the risk of delivery complications, and may influence birth and fetal death rates and have lasting health outcomes for both the mother and fetus.

Previous studies have investigated, often with mixed results, the associations between hurricane exposure and adverse pregnancy outcomes. Hormone fluctuation during pregnancy may influence stress related reactions while potential lapses in access to health care could greatly impact reproductive outcomes at many time points during pregnancy Studies have shown that adverse fetal outcomes, including preterm delivery, may increase with exposure to natural disasters. Research on county-level birth and fetal death rates have shown mixed results. Pregnant women may be disproportionately affected by hurricane-related health effects and with current mixed exposure methods and research results more studies are warranted.

CHAPTER 2: METHODS

Specific Aims

Birth rates, fetal death rates, and preterm deliveries are important reproductive health outcomes for assessing population health. With a growing coastal populations and increases in hurricane severity, there is a need to better understand potential population changes in reproductive health after hurricanes. US coastal states where hurricanes often make landfall, like Florida, have the ideal populations to examine hurricane health effects.

To investigate the potential associations between hurricane exposure during pregnancy and pregnancy outcomes, we proposed to construct a cohort of Florida pregnancies between 2003 and 2005 using vital statistics records. This unique timeframe includes a non-hurricane control year, 2003, when no hurricanes made landfall, as well as 2004, when four hurricanes made landfall. First, we conducted county-level analyses on the association hurricane exposure (defined previously as residence in a hurricane affected county) and birth rates and fetal death rates in 2003 and 2004 focusing on the use of the difference-in-differences method for confounding control. Second, we conducted an individual-level analysis using time-to-event modeling to investigate the effect of hurricane exposure on preterm delivery, stratified by race/ethnicity subgroups. The proposed research was conducted using data from NOAA's Hurricane Research Database (HRD) on maximum wind speed merged with Vital Statistics Records from the Florida Department of Public Health.

AIM 1: Apply the difference-in-differences method for confounding control to conduct a county-level analysis of hurricane-related weather exposure and A) live birth rates B) fetal death rates

Hypothesis: Counties with exposure to hurricane-related weather in the 2004 hurricane season (June-November) will have increased fetal death rates and decreased birth rates compared to the 2003 hurricane season in which no hurricanes made landfall. The difference-in-differences method allowed us to explore the association while controlling for unmeasured confounding in county-level analysis. Fetal death rates analysis was considered supplemental due to limited the statistical power to interpret estimates.

Rationale: Changes in access to health care and stress during pregnancy or around the time of delivery may have adverse effects on fetal death rates. Current disaster literature suggests an increase in fetal deaths the year after severe natural disaster occurrence (1, 2, 73). Studies have estimated inconsistent population effects after natural disasters. Increases in birth rate (suggested as "baby boom") are suggested to be attributable to hurricane-related economic disruption and disruption of health care, which possibly limit access to birth control (2, 51, 72). Psychosocial stress, job loss, injury and economic struggle are suggested to decrease birth rates after natural disasters (51, 129). Most of the current hurricane reproductive health literature uses aggregate data which may not fully control for confounders. The difference-in-differences method controls for static level confounding without the covariates being collected. We feel this method could assist in reconciling some of the inconsistencies in the literature when compared to a standard adjusted generalized linear model.

AIM 2: Investigate hurricane-related weather exposure on individual-level pregnancies to estimate preterm delivery hazard ratios.

SUB AIM 2: Stratify by race/ethnicity subgroup to investigate heterogeneity of hazards.

Hypothesis: We expected to see an increase in preterm delivery with hurricane exposure. We hypothesized the hazard ratios comparing exposed to unexposed person time will be highest in black non-Hispanic women and black Hispanic women.

Rationale: Excessive stress, similar to disaster events, at any time during pregnancy is a well-supported risk factor for preterm delivery in animal and epidemiological literature (54, 56, 57, 98, 99). The relationship of hurricane exposure to preterm delivery has been inconsistent (risk ratios (RR) range 0.8-2.3) while other natural disasters show a consistent increased risk of preterm delivery (RR range 1.2-2.3) (1, 2, 43, 51, 55, 70, 76, 100, 101). Non-disaster studies have consistently shown that black women are three to four times more likely to have a very early preterm delivery than women from other racial or ethnic groups (102, 103). Current hurricane literature suggests that racial and ethnic minorities may be more vulnerable to the health effects of disaster, including reproductive health outcomes (51, 74).

Population

Source Population

This study used a retrospective cohort of Florida live births and fetal deaths to conduct county and individual-level analysis. We used this Florida population because of the unique advantage of measuring multiple hurricane exposures during single pregnancies in a large diverse population. The state of Florida has the most annual hurricane landfall events in the US and over 200,000 births annually. Our source population, taken from birth and fetal death records, is a population of all recorded Florida pregnancies that completed 20 weeks gestation.

We used a subset of data from 2003-2005. The specific timing and population definitions varied by each aim and outcome. Subsets of maternal demographic variables from 2004 births are shown in Table 2.1 The cohort of Florida pregnancies is diverse thus may provide insight into racial and ethnic differences in an increasingly diverse US Florida has a slightly higher proportion of black and Hispanic mothers but otherwise is similar to the total US population in 2004 in terms of other maternal characteristics such as age and educational attainment. We would like to use our study to make inferences to other similar coastal populations in the continental US.

Table 2.1 Comparison of Florida and US 2004 maternal characteristics**.**

Characteristic	**Florida Pregnancies**		**US Pregnancies**	
	N	%	N	%
Maternal Race				
White	160,132	73	3,222,938	78
Black	46,998	22	616,074	15
Other	10,479	5	292,960	7
Maternal Ethnicity				
Hispanic	58,513	27	1,439,101	23
Non-Hispanic	158,787	73	4,694,628	77
Maternal Age				
<=15	1418	1	25054	1
16-19	22386	10	595,160	10
20-24	56378	26	1,554,648	25
25-29	56378	26	1,670,283	27
30-34	49693	23	1,441,009	23
35-44	31419	14	8,731,967	14
45+	335	0	9,390	0
Maternal Education				
<High School	45287	21	1,011,428	22
High School Diploma	69609	32	1,386,421	30
Some College/ Associates	54237	25	981,238	21
College Degree	46659	22	1,262,161	27
TOTAL	218,045		4,112,052	

Unknown covariates have been excluded from this Table 2.1 to easily compare US and Florida populations.

Exclusion Criteria

The study population included all live births to Florida residents that completed 20 weeks gestation. Fetuses born before 20 weeks gestation are excluded since they were never at risk of preterm delivery (95, 130-132). We also excluded mothers less than 15 and over 45 years of age at the start of the risk period (20 weeks gestation) due to increased risk of preterm delivery independent of the mechanisms proposed by our investigation (e.g., young mothers may have pregnancy loss or preterm delivery due to different mechanisms than other women and older women are more likely to undergo fertility treatment (133-138). Additional records were excluded if there is missing data for any one of the following: maternal age, maternal residence, Florida residency, plurality or gestational age at delivery. We expected less than 5% of records to be missing these criteria.

Study Population

The source population for the historical cohort included all resident Florida pregnancies conceived between January 2003 and October 2004, or approximately 500,000 births. The study population is defined by inclusion criteria and conception time. To be included in the study population, births and fetal deaths must have been born to a mother with Florida residence, have gestational age recorded, and have plausible gestational age when reconciled with last menstrual period and birth weight. Estimates of the total number of the pre-study expected Florida resident live births, fetal death and preterm deliveries are shown in Table 2.2

Table 2.2 2003-2005 Florida Vital Statistics population numbers **(139)**

Year	Live Births	Fetal Deaths	Preterm Delivery
2003	212,243	1,604	27,933
2004	218,045	1,701	29,842
2005	226,219	1,650	32,352

For Aim 1 fetal death analysis we created a study population to estimate county-level fetal death rates of fetuses conceived before or during the unexposed (2003) and exposed (2004) hurricane season. Separately, for birth rate analysis data included conception dates during or shortly after the 2004 and 2005 hurricane seasons. This difference is due to different hypothesized biological mechanisms, in which hurricane exposure may influence fetal death in utero, but only influence birth rate preconceptionally.

The individual-level analysis of preterm delivery in Aim 2 study population included all pregnancies which were at risk for preterm delivery and exposure to the 2004 hurricane season. These methods are explained in more detail for each Aim below. The risk period for all three outcomes begins at 20 completed weeks gestation because pregnancies which result in early loss, or are medically ended due to fetal or maternal adverse health in early pregnancy would not be captured in our data. Pregnancies terminated before 20 weeks gestation in the majority of cases would not be recorded in vital records. Details on this topic are addressed later.

Aim 1

Aim 1 was conducted to apply the difference-in-differences method to estimate county-level birth rates and fetal death rates. The full cohort included pregnancies in which date of conception was less than 20 weeks before January 1, 2003. The restriction of 20 weeks completed gestation is specified due to the fact that birth records and fetal death records are not accurately captured before this cutoff (90). For example, a pregnancy at 30 weeks completed gestation on January 1, 2003 could have resulted in a preterm delivery or fetal death before the calendar date cut off. These observations would be left censored and not appropriately accounted for in our data. These specifications were further refined for fetal death rates and birth rates to define exposure time periods for each outcome.

For Aim 1's birth rate analysis, the difference-in-differences model included women who conceived during or shortly after the 2003 hurricane season when no hurricanes made landfall and women pregnant during or shortly after the 2004 hurricane season. Since we assumed birth rates to be influenced during conception (after hurricane occurrence), women who conceived before the first hurricane of 2004 would not be eligible to have a hurricane influenced conception. Therefore, the exposed cohort in the 2004 hurricane season included women whose date of conception falls after the first hurricane in 2004 (August 13, 2004) through conception approximately one month after the last hurricane on September 26, 2004. We considered one month a conservative estimates of when conception could be influenced by hurricane exposure since often community resources can be disabled for one or more months after major hurricanes. Using these specifications, women estimated to have conceived between August 14, 2004 and October 31, 2004 were included in the exposed cohort. We compared these women to those who conceived a year prior (August 14, 2003 to October 31, 2003) during the 2003 hurricane season when no hurricanes made landfall.

Figure 2.1 graphically displays the sample selection used to identify the live birth study population for Aim 1's birth rate analysis. Overall, 92,398 live births were identified for the exposed cohort while 45,607 live births were identified for the unexposed cohort.

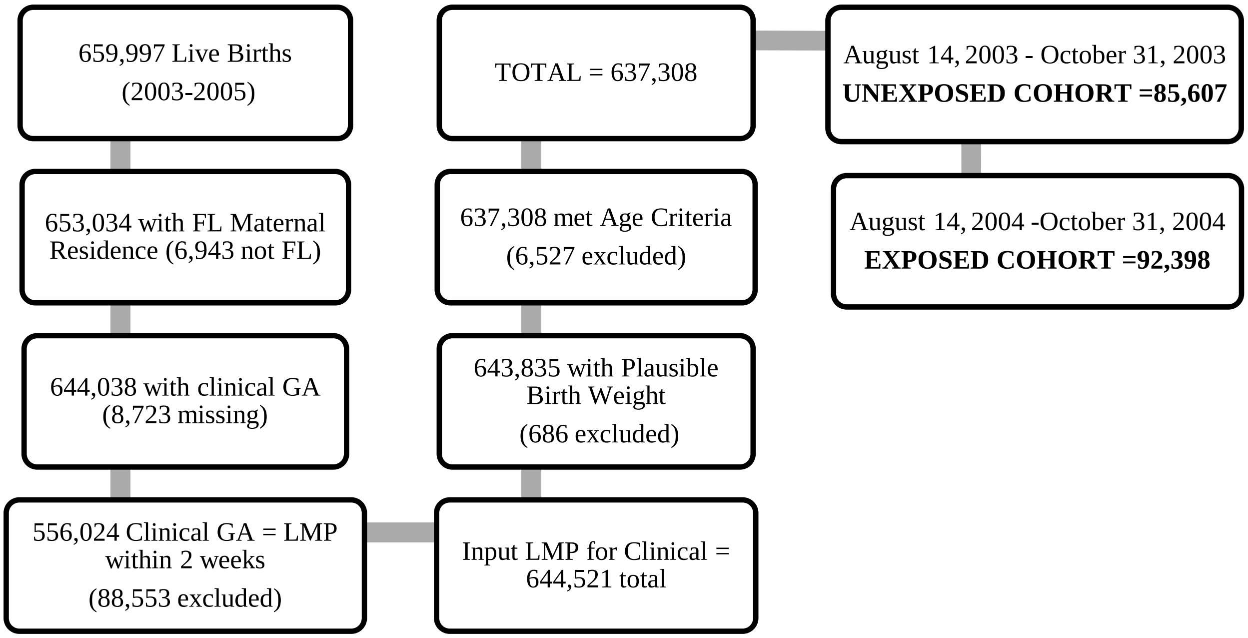

Figure 2.1 Sample selection of live births for Aim 1. birth rate analysis

In the analysis of fetal death rates, we included women pregnant during the 2004 hurricane season and women pregnant during the 2003 hurricane season when no hurricanes made landfall. The exposed cohort in the 2004 hurricane season included women whose date of conception falls between November 9, 2003 and October 4, 2004. These dates encompass 42 weeks before the first hurricane occurrence on 2004(August 13, 2004) through one week after the last hurricane (September 26, 2004). Pregnancies conceived more than 42 weeks before the first hurricane event on August 13, 2004 would have a very low probability of hurricane exposure since only approximately 5% of pregnancies go beyond 42 weeks gestation (140). Women in this exposed time period were compared to women who conceived during the same time period (November 9, 2002 through October 4, 2003) in the previous year. By using the same window of time we control for potential seasonal effects and contribute the same amount of calendar time into the unexposed and exposed cohort definitions.

Figure 2.2 and Figure 2.3 graphically display the sample selection used to identify the study population of the total number of fetal deaths and live births used in the fetal death rate for Aim 1. Overall, 959 fetal deaths and 187,116 live births were identified for the exposed cohort while 1,316 fetal deaths and 193,309 live births were identified for the unexposed cohort.

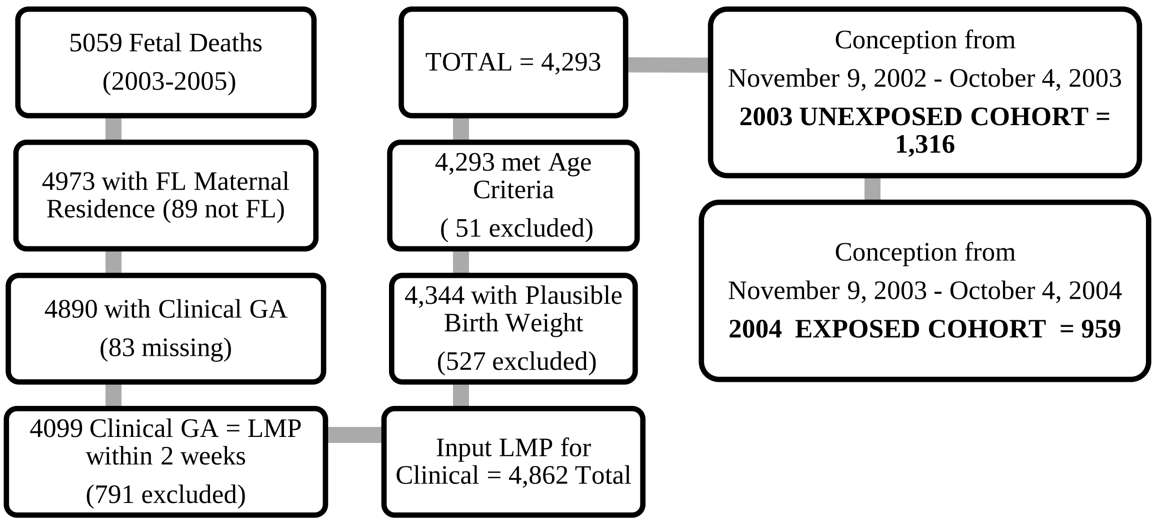

Figure 2.2 Sample selection of fetal deaths for Aim 1. fetal death analysis

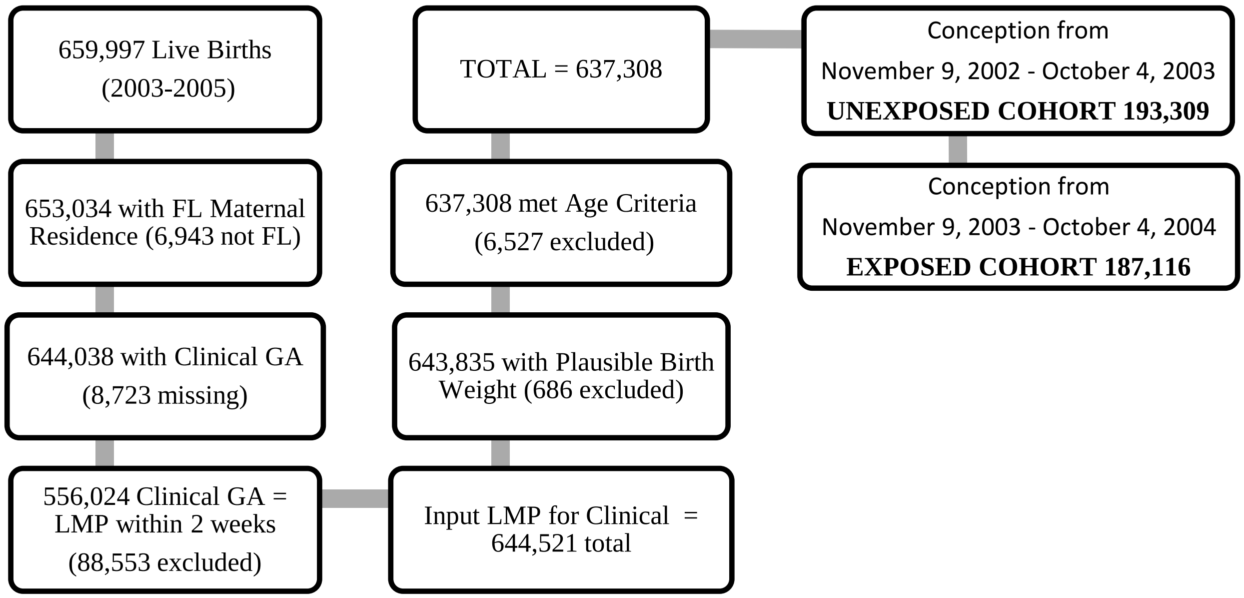

Figure 2.3 Sample selection of live births for aim 1. fetal death analysis

Aim 2

The sub cohort for Aim 2, preterm delivery hazard, is systematically different from that of Aim 1. To be considered, all pregnancies have to be at risk of preterm delivery within the 2004 hurricane season. The first pregnancies included in the cohort are those with an estimated date of conception 37 weeks prior to the first hurricane occurrence in order to be at risk of being born at or before 37 weeks completed gestation. Similarly, to be at risk of hurricane exposure and preterm delivery, the last pregnancies included would have a date of conception on the week of the last hurricane occurrence. Similar to Aim 1, time at risk begins at 20 weeks completed gestation to avoid biases due to left censoring of pregnancies lost before 20 weeks. This approximate calendar time period at risk of hurricane exposure and preterm delivery thus would include pregnancies with a date of conception from December 7, 2003 through October 1, 2004. This time period will differ for each of the individual hurricane analyses such that the study period would begin 37 weeks before hurricane occurrence and would end the week of hurricane occurrence. Details on the timing and Cox models are described in the Statistical Analysis section.

Data Sources

Exposure Data

To improve upon the previous methods used to assign exposure to hurricanes, we used a third method of calculated maximum wind speed to create a more specific measure of exposure. This weather driven method is both quantitative and reproducible, as data on these occurrences is collected by NOAA and the NHC. This method relies on the fact that hurricanes are generally defined by wind speed and force. Traditionally the Saffir-Simpson Hurricane Wind Scale categorizes hurricanes into 5 distinct categories of severity (Table 1.1). These levels include Category 1 (74-95 mph, 2 (96-110 mph), 3 (111-129 mph), 4 (130-156 mph), and 5 (157 mph and higher) (25). Tropical Storm wind speeds are classified as 39-73 mph. In general, Category 1 wind speeds are dangerous and produce some damage and potential power outages for a few days. Category 2 winds are extremely dangerous, more likely to cause structural damages and complete power loss to areas for up to a week. Category 3-5 hurricanes are considered major hurricanes which are likely to cause severe damage to both the built and natural environment as well as power and water loss, potentially for weeks. Utilization of wind speed and tropical cyclone severity scales allows us to explore a quantitative, reproducible method of assigning hurricane weather exposure based on currently applied thresholds of hurricane wind effects. Similar methods are used in climatology to predict areas affected by inland hurricane storm surges (141, 142). Further description of different exposure methods is documented in a preliminary exposure paper found in Appendix A.

Data was extracted on county maximum wind speeds during hurricane from NOAA, Hurricane Research Division (HRD) public databases. The wind speeds and data used in our analyses were developed and constructed by Dr. Charles Konrad. Details of the data collection and the HRD real-time hurricane wind analysis system have been previously published (26).

We categorized maximum wind speed using two binary categorizations based on the Saffir-Simpson hurricane wind: $\geq$ 39 mph to indicate tropical storm winds speed and $\geq$ 74 mph to indicate hurricane wind speed. Exposure to each hurricane was defined based on maternal county of residence as indicated through Vital Statistics' records.

In the 2004 hurricane season, four hurricanes made landfall in Florida: Charley (August 13th), Frances (September 5th), Ivan (September 21st) and Jeanne (September 25th). These hurricanes showed much variation in their size and strength. Charley was the strongest hurricane to strike the US since Hurricane Andrew in 1992 and was a relatively small but intense hurricane. Charley travelled northeastward through central and northeast Florida, through the heart of the Florida Peninsula. Frances was not as strong as Charley but much larger and responsible for over 100 tornadoes and massive floods. Frances traveled northwest through Florida hitting central Florida and the western coast towards the panhandle. Hurricane Ivan was both strong and large but in terms of our Florida population only affected a small area of the Florida panhandle. Ivan struck the same counties just hit by Frances and led to massive flooding and many tornados. The final hurricane of the 2004 season Jeanne followed a very similar path to that of Frances. Jeanne was not powerful but was slow-moving, dropping several inches of rain over the already saturated flooded region of Florida. These four hurricanes exemplify the heterogeneous nature of hurricane force and size. An example map of the 67 Florida counties and dates of landfall is shown in Figure 1.1.

Outcome Data

We obtained data on gestational age, maternal demographic, fetal demographic and reproductive health from Florida fetal death and birth certificates from 2003 through 2005. The Florida State Department of Health supplied Florida birth certificate data with maternal county of residence in concordance with the Data Use Agreement. Per the Data Use Agreement, for the proposed study no subjects were contacted, nor will ever be contacted. (139, 143).

Aim 1

For Aim 1, we constructed county-level birth rates and fetal death rates for 2003 and 2004 using individual vital statistics records. Live births and fetal deaths were defined as recorded on the respective birth or death record. Studies have shown that reliability of these records is generally good; however, some show an underreporting of fetal deaths at early gestational ages (90, 144, 145). The pregnancies included in the cohort will be identified based on the calculated date of conception as described in the Analysis Plan.

Aim 2

Aim 2 investigated maternal prenatal exposure to hurricane and risk of preterm delivery stratified by race/ethnicity subgroups. Preterm delivery status is not directly reported on birth certificates. Preterm status was estimated based on clinical estimate of gestational age. Births that occur before 32 completed weeks of gestation are extremely preterm and births before 37 weeks of gestation are considered overall preterm. We used the National Center for Health Statistics (NCHS) method to increase validity of gestational age measures by excluding observations in which gestational age measurement and birth weight are implausible based on published criteria (146, 147). This criterion is described in more detail in the Analysis Plan.

Unlike Aim 1, all pregnancies in the Aim 2 individual analysis must be at risk of hurricane exposure in the 2004 hurricane season; therefore all pregnancies conceived by December 7, 2004 and before October 31, 2004 are included. The 2003 pregnancy data was not included in this analysis. These dates were calculated based on the definition of preterm delivery of 37 completed weeks gestation (63, 96). Pregnancies conceived more than 37 weeks before the first hurricane event on August 13, 2004 would not be at risk of preterm delivery after hurricane occurrence. These dates and risk periods varied slightly specific to individual hurricane models and outcome timing.

Data Linkage

Hurricane weather exposure and birth certificate data, including outcome and covariates, were linked using Federal Information Processing Standard (FIPS) geocodes of mother's county of primary residence as noted on the birth certificate. The FIPS county code is a five-digit code which uniquely identifies counties and county equivalents in the US. This method was used to reduce errors which might have occurred if linking had been done by county name due to clerical or data entry errors.

Variable Measurement

Exposure

We primarily defined county-level exposure based on hurricane exposure in the county of maternal residence as indicated in vital records. Pregnancies classified as exposed in the study population were selected based on the specified analysis inclusion criteria and maternal county hurricane exposure level. Pregnancies from the study population in counties with no maternal hurricane exposure, or delivered before a hurricane made landfall in specific counties, were classified as unexposed.

There is currently no gold standard to measure hurricane exposure. We used several different exposure methods to describe sensitivity of current methods as well as a novel wind exposure method. Each aim is described separately below in term of exposure metrics. A preliminary paper on hurricane exposure metrics can be found in Appendix A.

Timing of hurricane exposure during pregnancy was determined by estimates of date of conception and the date of hurricane landfall. Due to potential inaccuracy of vital statistics records, we applied exposure to the closest week of conception, as opposed to day. Exposure time was defined from the time that the maximum measure of wind speed was recorded during the hurricane.

Aim 1

For Aim 1, counties in the unexposed time period in 2003 were all assigned an exposure value of "0", indicating no exposure in difference-in-differences models. Counties in 2004 were assigned a binary value based on the Saffir-Simpson hurricane wind: ≥ 39 mph to indicate tropical storm winds speed and ≥ 74 mph to indicate hurricane wind speed. To describe sensitivity of the difference-in-differences we also conducted analysis using the 60 km buffer.

Aim 2

Aim 2 used the identified county-level hurricane exposures with individual-level pregnancy outcomes. We categorized maximum wind speed using two binary categorizations based on the Saffir-Simpson hurricane wind: ≥ 39 mph to indicate tropical storm winds speed and ≥ 74 mph to indicate hurricane wind speed. Each method of exposure was defined as a time dependent covariate by gestational weeks (weeks after conception). Exposure status was assigned on the first day a hurricane made landfall in the county of residence. Since classification was made by gestational week, not day, if exposure occurred mid-week, e.g. 20 weeks and 2 days, exposure was rounded down and assigned at 20 weeks gestation. This classification is often used for reproductive gestational age estimation as estimation of completed weeks. If the hurricane was slow moving and was within the county boundaries for more than one day, exposure status was still assigned based on the first day of hurricane exposure.

The exposure timing was applied to each hurricane independently to appropriately estimate unexposed and exposed time. Exposure status was assigned to a pregnancy upon first exposure in county of residence and time remained exposed for the remainder of pregnancy time in hazard rate models. This exposure definition was used to look at the single and multiple hurricane exposures. For each of the four hurricane events, a pregnancy was classified as either exposed to hurricane = 1 or unexposed to the specific hurricane = 0. In this exposure classification, a pregnancy could be considered exposed in one or more of the four combinations and unexposed in others. We compared the effect of exposure to each hurricane individually to help understand the conditional status of rapidly occurring hurricane events. Figure 2.4 shows the approximate trimester when exposure would begin based on conception window.

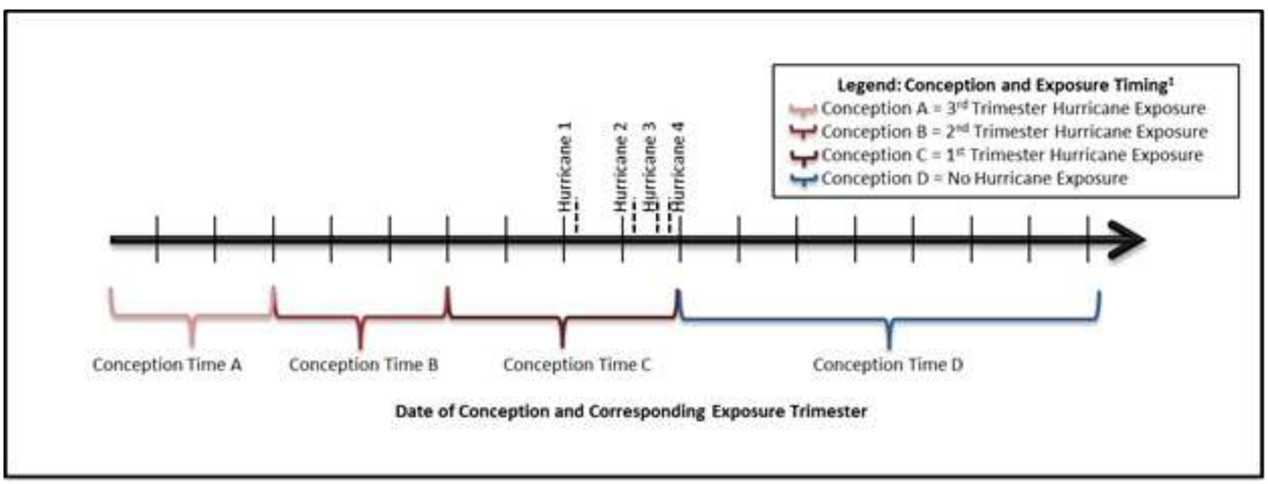

Figure 2.4 Hypothetical exposure trimester timing by date of conception (which result in live birth and hurricane exposure) for Aim 2 analysis

Outcomes

Live Birth

A live birth is defined as a fetus who after expulsion or extraction from its mother, irrespective of the duration of pregnancy, shows any evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether the umbilical cord has been cut or the placenta is attached. Heartbeats are to be distinguished from transient cardiac contractions; respirations are to be distinguished from fleeting respiratory efforts or gasps (148, 149). In the US, birth records include births outside of the clinical setting and can be recorded after the live birth of a child and as late as the first infant pediatric visits (146). Although live births are recorded regardless of gestational age, for our analysis, we excluded pregnancies reported before 20 completed weeks of gestation. Crude live birth rates from vital records were calculated as:

$$Live\ Birth\ Rate = \left(\frac{Number\ of\ live\ births}{Total\ population\ at\ midyear}\right) * 1{,}000.$$

To calculate the 2004 and 2003 county live birth rates for Aim 1, we used the number of live births during our specified calendar period and divided by the total population for the year of interest. While this is not comparable to a full-year birth rate calculation, this does create a comparison equal for the unexposed year (2003) to the exposed year (2004) for the difference-in-difference modeling.

Supplemental Outcome: Fetal Death

Fetal death (i.e., fetal mortality) is defined as death prior to the complete expulsion or extraction of a fetus from its mother, not including an induced termination of pregnancy (148). The death is indicated by the fact that, after such expulsion or extraction, the fetus does not breathe or show any other evidence of life. Federal guidelines recommend reporting fetal deaths whose birth weight is greater than 12.5 oz. (350 g) or those whose gestational age is greater than 20 weeks. Forty-one US states use a definition very similar to the federal definition, thirteen areas use a shortened definition of fetal death, and three areas have no formal definition of fetal death (89). Some states often use the term 'stillbirth' synonymously with late fetal death; however they are split as to whether stillbirths are "irrespective of the duration of pregnancy" or some age or weight constraint is to be applied (90). For the purpose of this study, we excluded any fetal deaths recorded before 20 weeks gestation or when gestational age was missing. Fetal death rates from vital records were calculated as:

$$Fetal\ Mortality\ Rate = \left(\frac{N\ fetal\ deaths}{Total\ population\ of\ births}\right) * 1{,}000$$

$$where\text{:}\ Total\ population\ on\ births = fetal\ deaths + live\ births.$$

To calculate the 2004 and 2003 county fetal death rates for Aim 1, we used the number of fetal deaths during our specified calendar period and divided that value by the sum of the fetal deaths and live births over the same period of interest. This time specification will create a comparison for the 2003 to the 2004 year in the difference-in-difference modeling without problems of comparing different calendar seasons.

Preterm Delivery

The most often used definition of preterm delivery is a birth before a gestational age of 37 complete weeks (150). This cut point has been used because most organ systems mature between 32 and 37 weeks, and the fetus reaches adequate maturity by the end of this period. A dichotomous cut point of preterm may not be sufficient since the risk of complications, morbidity and mortality increase with decreasing gestational age. Several studies and experts in the field of reproductive epidemiology have suggested either using additional discrete points of gestational age or modeling gestational age as a continuous measure (91, 150-152).

We choose to utilize preterm delivery rather than birth weight because birth weight is thought to have many different etiologies. Also both high and low birth weight can be considered negative infant outcomes which would be hard to interpret with our exposure. Preterm delivery and gestational age may not be as accurately measured on birth certificates as birth weight, but we felt that the stress and healthcare mechanisms were most biologically plausible with the preterm delivery outcome.

We considered three methods of classification to determine the most appropriate choice for modeling and understanding the potential heterogeneity of risks across the continuum of gestational age. A measure of gestational age will be calculated using the estimation of conception method described on the next page. To evaluate heterogeneity of the estimates of gestational age, we estimated hazards of delivery among overall preterm (<37 gestational weeks) and extremely preterm (<32 weeks) deliveries. Further details on the classification of preterm delivery modeling are discussed in the Statistical Analysis.

Analysis Plan

Estimation of Conception

Before beginning analysis, we estimated the calendar timing of date of conception for each pregnancy in order to properly estimate exposure timing. NCHS recommends a method for estimating gestational age in the US vital statistics reports that relies primarily on self-reported last menstrual period (104, 149). We felt that exposure could be associated with potential recall of last menstrual period, consequently we primarily used gestational age as designated by the clinician. If clinical gestational age was missing or implausible when compared to birth weight then the pregnancy was excluded from analysis (153, 154). We expected <1% of pregnancies to be excluded based on this method of calculating day of conception.

Although we used an analytical method to reconcile the clinical estimate of conception with birth weight, gestational age is often miss-specified on the birth certificate (149, 155). The misspecification can be due to heterogeneity in growth as well as biological variation of follicular phase length. One reason not to use last-menstrual period is the tendency to produce an asymmetrical error in gestational age, resulting in more false "late" deliveries than false "early" deliveries (91). Partly due to these reasons, we investigated two cutpoints of gestational age in the preterm analysis for Aim 2.

Statistical Analysis

AIM 1: Describe the difference-in-differences method for confounding control in the county-level analysis of hurricane-related weather exposure and A) live birth rates B) fetal death rates

For Aim 1, we first conducted ecological analysis of live birth and fetal death rates for exposed and unexposed counties using generalized linear models to estimate crude rate differences before conducting difference-in-differences analysis. We used individual data to estimate the county fetal death rate and birth rates over the specified calendar time periods. Generalized linear models were used for the 2004 hurricane season to estimate the rate difference when comparing adjacent exposed and unexposed counties. We reported both crude and adjusted models for county-level social and environmental characteristics. Next, we used the difference-in-differences method to compare the difference between the rates in the unexposed and exposed time periods (156). We used each of the eight defined exposure categorizations for both the fetal death rate and the birth rate analyses as well as the supplemental analysis of low birth weight.

Difference-in-Differences

Difference-in-differences is a statistical technique which attempts to mimic experimental research study design using observational data by estimating the effect of exposure (treatment) on an outcome as the difference in the average change over time in the exposed group and the unexposed group. By assigning a value in the 2003 unexposed period, we calculated the difference-in-differences by looking at the change in slope from one year to the next. Since a portion of counties will be unexposed in both hurricane seasons, this allows for control of both measured and unmeasured static county-level confounders as shown in Figure 2.5. This does not adjust for confounders which changed between 2003 and 2004. This difference- in-differences technique is often used in econometrics to measure the effect of an exposure at a given period in time (157).

Proper confounding control using the difference-in-differences approach rests on the assumption of parallel trends. This means that no exposure group specific trends should bias the estimates of exposure effects (157, 158). Covariates identified from the birth certificate data were compared between 2003 and 2004 to verify we met the model assumption of no covariate change over the time period (Supplemental Appendix Table S1).

We conducted analysis of the difference-in-differences method using PROC GLM with the ABSORB statement in SAS 9.2 to estimate the rate difference between the 2003 and 2004 within-county live birth rates. This is similar to the rate difference generated in a generalized linear model with the background rate removed, estimating the marginal within-county rate difference as shown using model parameters in Figure 2.5. The 2003 period in these models is used to obtain the baseline covariate distributions to control for county-level static differences.

Generalized Linear Model

We illustrate the sensitivity of results to confounding by also fitting generalized linear models with a continuous outcome of county live birth rate and imply a normal distribution (15).We conducted unadjusted and adjusted linear regression generalized linear models using PROC REG in SAS 9.2 to estimate the rate differences of the association between hurricane exposure and live birth rates in the 2004 at-risk period. For example, counties affected by wind speeds equal to or over 74 mph were considered exposed and compared to counties with wind speed less than 74 mph for a given storm.

To demonstrate a typical approach to confounding control in aggregate analyses, crude models were then adjusted for county-level 2000 US Census covariates, including percent renter-occupied units, median household income, percent of persons who speak English less than well and percent of adults with more than high school education. These variables have been used previously in developing social indices and controls in county-level studies (159-161). The chosen covariates were determined *a priori* based on a literature review of natural disasters and public health. Selected results are described in Chapter 3.

<u>Model Parameters</u>

- y_{it} IS response variable (e.g. fetal death rate) for county *i* at time *t*.
- z_i is a column vector (covariate) which <u>does not</u> vary over time *t*.
- x_{it} is a column vector (covariate or hurricane exposure) which <u>does</u> vary over time *t*.
- μ is the model intercept.
- β and γ are row vectors while ε is the random error.

Unexposed 2003 Model: $y_{i0} = \mu_0 + \beta\, x_{i0} + \gamma\, z_i + \varepsilon_{i0}$

Exposed 2004 Model: $y_{i1} = \mu_1 + \beta\, x_{i1} + \gamma\, z_i + \varepsilon_{i1}$

Differenced model: $y_{i1} - y_{i0} = (\mu_1 - \mu_0) + \beta\, (x_{i1} - x_{i0}) + (\varepsilon_{i1} - \varepsilon_{i0})$

Figure 2.5 Descriptions of model parameters and form for difference-in-differences Aim 1. analysis

AIM 2: Investigate hurricane-related weather exposure on individual-level pregnancies to estimate preterm delivery hazard rates.

SUB AIM 2: Stratify by race/ethnicity subgroup to investigate heterogeneity of hazards.

To address Aim 2, we estimated relative hazards using Cox proportional hazard regression using weeks of exposure time (>20 weeks) during pregnancy as a time varying exposure. Cox models were chosen for the ability to handle left-truncated data and better evaluation of a time varying exposure in an open cohort. Pregnancies terminated or delivered before 20 weeks of gestation were not captured on fetal birth and death records and therefore are not at risk for the outcome. We used Cox regression to estimate rates between independent hurricane exposures for each of several cut-points for gestational age. In each model, we tested the proportional hazards assumption using exposure-by-gestational age interaction terms.

Using Cox regression, we first investigated exposure dichotomously and compared relative hazard rates of overall preterm deliveries (<37 weeks gestation) between exposed and unexposed groups at each person-time for each hurricane in four independent models. Next, we built an additional model for each hurricane to look at the continuum of gestational age using extremely preterm (<32 weeks gestation). Each pregnancy contributed a specified number of pregnancy-weeks after 20 completed weeks as either unexposed time, exposed time or both unexposed and exposed time. For example, a woman with no hurricane exposure in her county who delivers at 36 weeks would contribute 16 weeks of *unexposed* time while similarly a woman who delivers at 36 weeks in a county exposed to hurricane before her 20th week of pregnancy would contribute 16 weeks of *exposed* time in hazard calculations. Some women who experienced a hurricane between 20 weeks and delivery will contribute the time before the

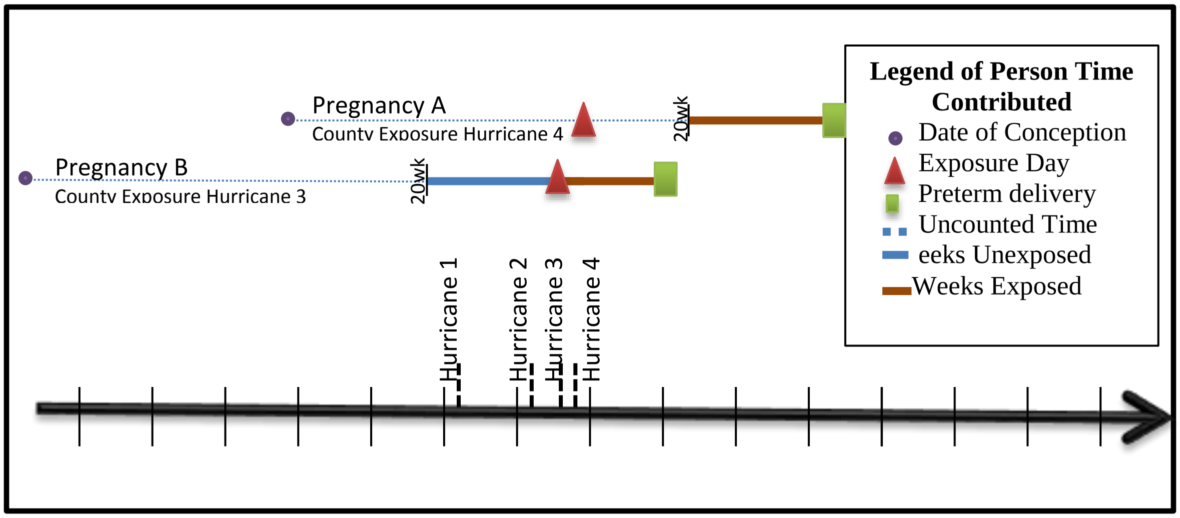

Figure 2.6 Example pregnancies in cohort: exposure timing by date of conception

hurricane as unexposed time, and time after the hurricane as exposed time. This time varying exposure method was used so that exposure time is not inflated.

Figure 2.6 displays how exposure time is designated based on date of conception. For example, Pregnancy B would contribute all time after 20 weeks as unexposed (blue line) until being exposed to Hurricane 3, at which time the remaining exposure through 37 weeks would be counted as exposed time (red line).

The Cox model is used to estimate and compare the rate at the time of the event in the exposed and unexposed pregnancy time. An exponentiated beta value greater than the null value of 1.0 suggests that the hazard of experiencing the outcome (preterm, early-preterm or term birth) in the exposed individuals is different from the hazard of experiencing the event in the reference category. Often this is interpreted as a percent higher or lower hazard when comparing the two groups. In our analysis, with a time varying exposure, we were in essence comparing exposed to unexposed persons; however, we have more accurately defined the person-time at risk by using exposure classifications based on when the hurricane made landfall during each individual's pregnancy. We calculated crude models as well as multivariate models to adjust for potential confounders. Figure 2.7 below describes the model parameters and form of the proportional Cox model used to estimate hazard ratios.

Model Parameters

- *h*(*t*) is the underlying hazard function(which is not necessarily specified)
  - $h_1(t)$ would be the hazard in the exposed and h_0 the unexposed
  - *Exp* $(X_1 \beta_1)$ is sometimes referred to as the relative hazard function as it is used to estimate the relative hazard or hazard ratio.
  - In our models when we exponentiate the estimates we get the hazard ratio of exposed rate to unexposed rate.
  - Proportional hazards regression: $h(t|X) = h(t) \exp(X_1 \beta_1 + \ldots. + X_p \beta_p)$
- Cox model : $HR = h_1(t) / h_0(t)$
  - When we add covariates $\exp(\beta_x)$ *is the HR for a unit difference in x (x=exposure) holding the covariate constant at ANY level.*

Figure 2.7 Description of model parameters and form for Cox hazard ratio Aim 2. analysis

To properly assess the pregnancies at risk for preterm delivery, person-time after 37 weeks gestation was not counted for the initial preterm delivery analysis (in the two additional analyses this cutoff was set at 32 weeks). After a pregnancy has completed 37 weeks of gestation, by definition it can no longer end in preterm delivery and therefore is outside of the risk set. These pregnancies contribute time in analysis but are considered right censored. Similarly, pregnancies that end in a competing risk, including fetal death, will contribute time to analysis but will be included as censored events. A nearly universal feature of survival data is censoring, the most common form of which is right-censoring. One of the most useful functions of Cox proportional hazard regression for survival data is the ability to handle censored values in the computation of the likelihood function and therefore making them useful in analysis. Censored observations contribute time to the exposure time but not to the numerator (event count) used to calculate the hazard function.

We conducted stratified race/ethnicity subgroup analysis for Sub Aim 2. We felt that the effect of confounding factors on preterm delivery could vary in difference racial/ethnic stratum and therefore could be better described in stratified models. In order to discuss racial/ethnic differences we additionally performed models with and interaction term for race/ethnicity and exposure to statistically quantify potential differences. We used an *a priori* criteria for an effect measure modifier of a Wald heterogeneity test p-value < 0.20 (162). Subgroup analysis focused on racial/ethnic groups defined by combinations of black/white race and Hispanic ethnicity because of limited statistical power for other subcategories.

Covariates

Covariates from Vital Statistics records, including maternal socio demographics, pregnancy characteristics and fetal characteristics, were analyzed using the following criteria as potential confounders and effect measure modifiers. For analysis of Aim 1, static level confounders were controlled by the use of the difference-in-differences method. We compared potential confounders in Aim 1 in the unexposed to exposed cohorts to ensure these covariates remained relatively static between years. Supplemental Appendix Table S2 displays the full list of covariates considered as candidates for confounding or modification from Vital Statistics records.

Confounders

<u>Potential Measured Confounders</u>

Potential confounders were selected based on previous studies and evaluation of Directed Acyclic Graphs (DAG) (161, 163). Each potential confounder was assessed for logical temporality (i.e. could the covariate occur before the exposure and the outcome) and for plausible direct effect on the exposure or outcome. While none of the covariates would directly affect or influence hurricane exposure, if a variable was thought to influence maternal residence, stress, clinical disruption or economic change caused by a hurricane, they were considered as a potential confounder. Some considered variables included maternal age, smoking, education and maternal comorbidity.

For Aim 2, when controlling for confounding was necessary, we used both an *a priori* and a statistical approach to fully understand potential nuisance effects. The complex and unknown biological processes under consideration make it difficult to fully capture confounding using only *a priori* theory and DAGs. Consequently, after identification of potential confounders from DAG analysis, we used a combined approach utilizing both a change in estimate method with an *a priori* 0.10 cut off, and an exploratory analysis of the associations of the covariate with the exposure and outcome to determine which confounders would be used in each model. While using a more statistically driven approach, we kept in mind potential colliders, backdoor paths and mediators identified in our DAG analysis. In this study, model constraints and power were also taken into consideration. Figure 2.8 displays one example potential DAG in the relationship between hurricane exposure and preterm delivery.

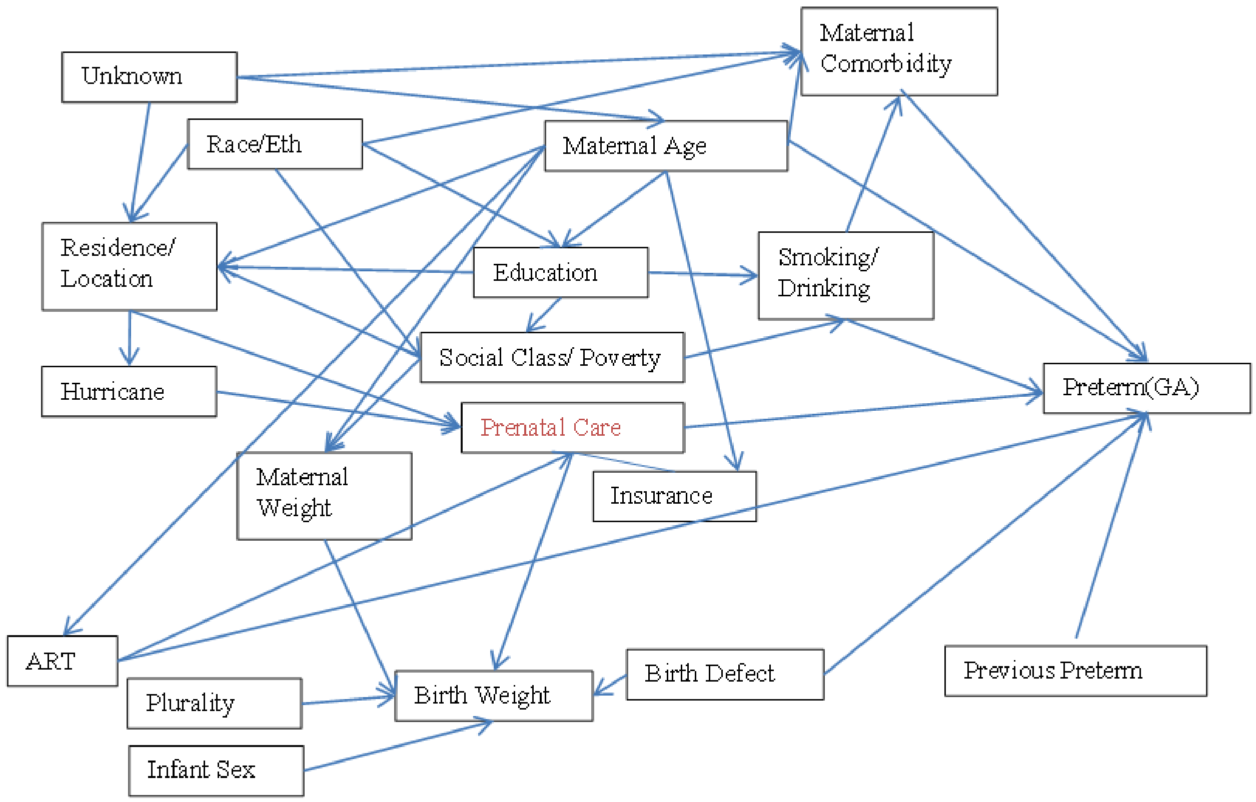

Figure 2.8 Example Directed Acyclic Graph (DAG) of hurricane exposure and preterm delivery association

Unmeasured Confounders

We would like to also acknowledge covariates that were unmeasured in the study but could influence the relationship between exposure and outcome. Some unmeasured covariates in the study could include genetic information, individual evacuation information, English proficiency and type of home. Specifically, housing type and English proficiency could influence vulnerability to disaster and could have combined effects on pregnancy outcomes. Type of home has been shown to be a strong predictor of evacuation in many studies and can also influence whether or not an individual returns to the home after the hurricane occurs (19, 20, 164).

Effect Measure Modifiers

In the Aim 2 individual analysis of preterm delivery modification by maternal ethnicity and maternal race were assessed by stratifying and comparing exposed and unexposed individual hazard rates and 95% confidence intervals. We examined the exposure-outcome relationship while adjusting for one covariate at a time in each model. Each covariate was added into the model as the interaction with the main exposure.

Assessing differences by race/ethnicity was a primary part of Aim 2. After conducting analysis of race/ethnicity as a modifier we felt that confounding structures may differ between race/ethnicity groups and therefore published fully stratified estimates. These estimated, shown in Chapter 4, no longer describe modification in the full Florida cohort but instead describe the main effect of hurricane and preterm delivery in each race/ethnicity stratum separately. This allows us to better control confounding within the individual subgroup analyses.

Missing Data

Outcome or covariate data on date of conception, prenatal care, smoking, maternal race/ethnicity, education and maternal infection were evaluated for missingness. Since the difference-in-differences analysis does not require individual variable adjustment, we are only concerned with covariates for the Cox analysis of births occurring during the 2004 exposed period. *A priori*, we decided that if less than 5% of these data items are missing, then we would exclude the affected pregnancies and perform a complete case analysis. If more than 5% of the outcome or covariate data are found to be missing, data was assessed for covariate patterns of the missing data and imputed using chained equations variables (165). We acknowledge that some covariate data available from birth certificates may have a high proportion of missing data or be unreliable (e.g. maternal smoking, prenatal care and education) and we explored the appropriateness of using these variables in modeling. Supplemental Appendix Table S9 displays the proportions of covariates with missing data for both the 2003 and 2004 Florida populations.

CHAPTER 3: AIM 1 RESULTS[1]

County-Level Hurricane Exposure and Birth Rates; Application of Difference-In-Differences Analysis for Confounding Control

Summary

Epidemiological analyses of aggregated data are often used to evaluate theoretical health effects of natural disasters. Such analyses are susceptible to confounding by unmeasured differences between the exposed and unexposed populations. We demonstrate difference-in-differences as a method to control for time-invariant confounders investigating hurricane exposure on live birth rates. Our population included all recorded Florida live births that reached 20 weeks gestation and conceived after the first hurricane of 2004 or in 2003 (when no hurricanes made landfall). Hurricane exposure was categorized using ≥ 74 mile per hour hurricane wind speed as well as a 60 km spatial buffer based on weather data from the National Oceanic and Atmospheric Administration. The effect of exposure was quantified as live birth rate differences and 95% confidence intervals (RD [95% CI]). To illustrate sensitivity of the results, the difference-in-differences estimates were compared to generalized linear models adjusted for census-level covariates. Difference-in-differences analysis yielded consistently null associations across exposure metrics and hurricanes for the post hurricane rate difference between exposed and unexposed areas (e.g., Hurricane Ivan for 60 km spatial buffer (-0.02 births/1,000 individuals [-0.51, 0.47]). In contrast, generalized linear models suggested a positive association between hurricane exposure and birth rate (Hurricane Ivan for 60 km spatial buffer

[1] A revised version of Chapter 3 was submitted to the journal *Epidemiology* in 2015 with the following co-authors: Whitney Robinson, Stephanie Engel, Charles Konrad, David Richardson, Jennifer Horney

(2.80 births/1,000 individuals [1.94, 3.67]) but not all models. Ecological studies of associations between environmental exposures and health are susceptible to confounding due to unmeasured population attributes. Here we demonstrate an accessible method of control for time-invariant confounders for future research.

Background

Ecological analyses, often used in environmental and natural disaster epidemiology, are sometimes defined by administrative units where exposure and outcomes are measured at an aggregate level. The purpose of ecological analyses can be the estimation of ecological associations or the inference of individual risks. While ecological research may be more practical when individual exposures and outcomes are difficult to define, there are many methodological challenges surrounding its use. Some concerns may include ecological bias, exposure misclassification and proper control of measured or unmeasured confounders. Confounding control may be a particular concern in disaster research. Challenges inherent to the timely collection of post-disaster data or reliance on surveillance data often leads to unmeasured or inadequately measured confounding.

To assess the health impacts of hurricanes, and inform the policies needed to mitigate adverse effects, epidemiologists often conduct analyses of aggregated data (2, 11). The findings of the current literature on hurricane exposure and reproductive health outcomes are generally mixed (9, 51, 71, 74, 75). These inconsistencies may be in part the result of the limitations associated with the use of ecological data. Methods like difference-in-differences fixed-effects modeling can be applied to control confounding in ecological pre-post or county-level level analysis (166-168).

Difference-in-differences methods have a long history in disciplines outside of epidemiology (25, 26, 156); however, their use is relatively less common in epidemiology, with the exception of the case-crossover design, which may be viewed as a variant on this approach. Difference-in-differences analysis methods can be applied to any model where outcomes are observed in a minimum of two groups (e.g., treatments or exposure categories) at two different time points. This can be applied in individual or aggregate analysis. The exposed group must have an exposure status which changes across the two time points, while the referent group remains unexposed in both time periods. The estimate in the unexposed group is then subtracted from that of the exposed group. This removes biases resulting from static population characteristics between the two time points. A commentary by Kaufman (2008) discusses the application of similar fixed-effects methods in epidemiology to reduce bias and derive more valid estimates(14). This method is a relatively simple yet powerful technique to address confounding inherent in comparing aggregate populations that may not have the same baseline characteristics.

To demonstrate an application of this method in aggregate analysis, we assessed the association between hurricane exposure and live birth rates. Live birth rates are often anecdotally assumed to be influenced by natural disaster occurrences, with some reports suggesting a "baby boom" following severe weather events (51, 72). In other words, live birth rates may increase after disaster occurrence through increased conception rates. We compared an adjusted generalized linear model approach, where rate differences from affected and unaffected counties are compared, to results obtained by a difference-in-differences analysis to illustrate the method's application in disaster epidemiology.

Methods

Study Population

We used a retrospective cohort of 2003 and 2004 Florida live births to demonstrate the difference-in-differences method on the relationship between county-level hurricane exposure and live birth rates. Four hurricanes made landfall in Florida during the 2004 hurricane season, exposing the majority of the 67 counties to hurricane weather. No hurricanes made landfall during the 2003 season. Our source population, from vital records data, included all documented Florida pregnancies conceived in 2003 and 2004 that completed a minimum of 20 weeks gestation.

The 2004 cohort used in both the difference-in-differences models and generalized linear models included women who conceived between August 14, 2004 and October 31, 2004. This window of exposure falls from just after the first hurricane occurrence through three months after the last hurricane occurrence. This exposure window aligned with the conception-based "baby-boom" hypothesis. For the difference-in-differences analysis, we also used pregnancies conceived in the previous year, from August 14, 2003 and October 31, 2003, to calculate 2003 unexposed live birth rates.

Exclusions

We excluded births to non-Florida residents, as they did not have a residential address to link to Florida hurricane exposure. Additionally, births with gestational age less than 20 weeks and of mother less than 15 years at delivery or greater than 45 years of age were also excluded. Our assumed risk period begins at 20 completed weeks' as earlier pregnancies are not fully captured in Vital Statistics data. Of the 94,593 total eligible births, 92,398 remained in the analytic population after exclusion criteria were applied.

Hurricane Exposure

We focused on two of the four 2004 hurricanes which made landfall in Florida: Charley (August 13, 2004) and Ivan (September 21, 2004) (Figure 1). Charley was chosen because it was the first and strongest hurricane of the season, hitting many Florida counties with diverse population groups. In contrast, Ivan hit the Florida panhandle, which contains a very homogeneous sub-population and therefore provides a unique opportunity to explore issues with unmeasured confounding. Counties were classified with respect to hurricane exposure using two previously published methods. The first method applied exposure based on maximum wind severity according to the Saffir-Simpson Wind Scale (169). Counties affected by winds ≥74 mph were considered exposed and compared to counties with wind speeds less than 74 mph (unexposed). The second method was defined by a 60 km symmetrical spatial buffer around the storm track. Any county within the 60 km buffer, including partial counties, was considered exposed and compared to the counties completely outside of the buffer (unexposed) (170, 171). We compared the two methods of classifying exposure to assess the consistency of the results, since a standard hurricane exposure metric has not been established.

Statistical Methods:

We calculated county-level live birth rates for 2003 and 2004 as the number of live births in a county divided by the total county population at midyear times 1,000. Live births are defined as fetuses which show any evidence of life following delivery (148, 149). All analyses were conducted in SAS 9.2 (Cary, NC) and an example SAS program of difference-in-differences methods is provided in the online appendix. This research was approved by the Institutional Review Boards at the Florida Department of Health (#H13049) and the University of North Carolina at Chapel Hill (#13-0784).

Difference-in-Differences

Difference-in-differences is a statistical technique which attempts to mimic experimental research study design for analyses of observational data. The effect of exposure (treatment) on an outcome is calculated as the difference of the average change in the exposed group minus the change in the unexposed group. In this hurricane exposure example, we are estimating the difference in live birth rate differences in exposed counties from the 2003 to 2004 time periods as shown in the hypothetical diagram Figure 3.2. The change in birth rate labeled “Difference from hurricane effect (β)” graphically illustrates the rate estimated using the difference-in-differences analysis.

We conducted analyses of the difference-in-differences method using PROC GLM with the ABSORB statement in SAS 9.2 to estimate the rate difference between the 2003 and 2004 within-county live birth rates. This is analogous to the rate difference generated in a generalized linear model with the previous unexposed year rate difference removed, estimating the marginal within-county rate difference (Figure 3.3). The 2003 period in these models stands in for the baseline covariate distributions to adjust for county-level time-invariant differences.

Generalized Linear Models

We illustrate sensitivity of results by fitting generalized linear models to estimate the association between hurricane exposure and county-specific live birth rates in 2004 (15).We conducted unadjusted and adjusted generalized linear models using PROC REG in SAS 9.2 software to estimate rate differences.

To demonstrate a regression approach to control confounding in aggregate analyses, the models were adjusted for county-level 2000 United States Census covariates, including percent renter-occupied units, median household income, percent of persons who speak English less than well and percent of adults with more than high school education. These variables have been used previously in developing social indices and controls in county-level studies (159-161). The chosen covariates were determined *a priori* based on a literature review of natural disasters and public health.

Results

The first hurricane of 2004, Charley, moved northeast through central Florida impacting a wide variety of socioeconomic and racial groups. Pregnancies affected by Charley had no previous hurricane exposure. In contrast, Hurricane Ivan made landfall in Alabama and Florida, affecting only a small area of the Florida panhandle. The Florida counties exposed to Hurricane Ivan had lower median incomes, less education and a higher proportion of renter occupied units than the unexposed counties (not shown).

The number of exposed and unexposed counties varied with the specific hurricane (Table 3.1). For example, using the 60 km buffer, twenty three counties were classified as exposed to Hurricane Charley while only two were exposed to Hurricane Ivan. Associations in Table 3.1 are reported as Rate Differences (RD) with 95% Confidence Interval (95% CI). Overall, there was no evidence of an association between hurricane exposure and live birth rates using difference-in-differences models. However, generalized linear models did suggest an association between Hurricane Ivan and birth rates.

Generalized linear models were adjusted for several census characteristics (Table 3.2). In the 67 Florida counties, 7 (10.4%) had more than 35% renter occupied units and 4 (6.0%) had more than 5% persons who do not speak English. Four (6.0%) had less than 65% of the population with at least a high school education. The median household income in 47 counties (70.1%) was less than the state median of $38,819.

For Hurricane Charley, neither the difference-in-differences nor the generalized linear models identified an association between hurricane and live birth rates. The 95% confidence intervals produced by the difference-in-differences method exhibited greater statistical precision as shown by the tighter confidence intervals. The associations found for Hurricane Ivan differed from Hurricane Charley. Prior to Hurricane Ivan, this part of Florida had no prior hurricane exposure in the 2004 season; however, since two hurricanes made landfall before Ivan, the reference unexposed counties may have had prior hurricane exposure. The difference-in-differences model did not suggest an association between hurricane exposure and live birth rates. In the generalized linear models, live birth rates were consistently positively associated with both the 60 km buffer (2.80 births/1,000 individuals [1.94, 3.67]) and the wind speed ≥74 mph (RD=2.23 births/1,000 individuals [1.47, 2.99]). This may indicate residual uncontrolled confounding present in the generalized linear models.

Discussion

To assess the health impacts of environmental exposures including natural disasters, epidemiologists often conduct analyses of aggregated data. Such approaches may have methodological limitations, including incomplete confounder control, exposure misclassification and lack of group level covariate information. We sought to demonstrate an application of the difference-in-differences method in estimating the effect of county-level hurricane exposure on live birth rates. While still potentially suffering from bias due to residual confounding and migration, this method overcomes some of the limitations of conventional approaches by addressing confounding by unmeasured time-invariant attributes. It has become increasingly common in epidemiologic and public health research to perform aggregate level analysis (e.g., at the level of the county, ZIP code or census track) and to use aggregate indices or census variables to control for confounding (160). Results from the difference-in-differences analyses demonstrate a method to improve control of confounding due to time-invariant variables in aggregate analyses.

The rate differences of the difference-in-differences and of generalized linear models have different interpretations. For the difference-in-differences model, the rate difference measured the increase or decrease in the within-county live birth rate difference from 2003 to 2004 attributable to hurricane exposure. In contrast, the generalized linear models rate difference measured the increase or decrease in birth rates comparing women with 2004 residence exposure to the surrounding unexposed counties, controlling for census covariates. These estimates are not directly comparable; however, the direction of association can be compared and consistency across models can be assessed.

There is no current consensus on the impact of hurricane exposure on reproductive health, with associations widely varying across studies (1, 2). These mixed findings are potentially the result of varied mechanisms of exposure (e.g., stress, economical, injury etc.), variations in exposure definitions, dissimilar study populations, incomplete confounding control and potential heterogeneity in hurricane effects. Our analysis applied several exposure metrics over multiple hurricanes to examine some of these potential inconsistencies. All difference-in-differences models yielded null associations for both hurricanes and for all exposure metrics. In contrast the generalized linear model yielded some potential associations with Hurricane Ivan. In supplemental analyses of the other two hurricanes of the 2004 season (Frances and Jeanne), generalized linear models varied in magnitude and direction from the fairly consistent null associations using the difference-in-differences approach (Table 3.3). The consistency of the difference-in-differences method suggests the integrity of this method over the generalized linear models to better control for confounding.

Suggested associations between hurricane exposure and live birth rates are largely anecdotal, including clinical observations and media reports. Two studies have focused on birth rates after hurricane occurrence. Cohan and Cole (2002) investigated live birth rates in twenty four South Carolina counties in a time-series analysis before and after Hurricane Hugo and found that before the hurricane live birth rates decreased, while after the hurricane live birth rates increased (72). Hamilton (2009) investigated county live birth rates in the Gulf Coast states (Louisiana, Mississippi and Alabama) following Hurricane Katrina and had mixed results depending on state (51). While both studies controlled for measured population characteristics, the difference-in-differences approach (which additionally accounts for unmeasured factors) may more fully adjust for differing population characteristics.

The resulting rate difference from the difference-in-differences is no longer a between-county estimate, but rather a within-county estimate with the baseline difference from the previous time period removed. In our example, this can be thought of as an absolute within-county rate difference. Difference-in-differences models have the same assumptions as the underlying model form with additional assumptions regarding parallel trends in county attributes. This implies that within-county characteristics, e.g., median income, are invariant between time periods. If this assumption completely holds, then difference-in-differences removes confounding by these static covariates. If this assumption is violated, there will be residual confounding by factors that change between study years. These assumptions can in theory be evaluated to the extent that all confounders' distributions are available in both time periods. A review of the current literature suggests that the parallel trend assumption was likely met as hurricanes are thought of as an exogenous occurrence likely uncorrelated with population characteristics (172). Like many environmental studies, our exposure was defined by county of residence and therefore secular trends influencing birth rate may differ by county. Researchers should consider these assumptions in the application of the difference-in-differences method.

While the difference-in-differences model may have improved control of unmeasured confounder bias, other biases such as ecological bias, residual confounding, and migration may persist in both methods. Specific limitations of the difference-in-differences method include a lack of knowledge of individual-level confounders, and potential underestimation of standard errors. Several articles have criticized the use of difference-in-differences methods using large datasets, where biased small standard errors can incorrectly indicate significant relationships (12, 173). This can be a particular problem if outcomes are non-independent between subjects. Our difference-in-differences models showed tighter 95% confidence intervals than the generalized linear models, indicating smaller standard errors; however, we assume individual changes in conception are independent. Additionally, difference-in-differences estimates are not exempt from ecological bias. Ecological biases can occur when some confounding may be controlled but unmeasured effects of the population are directly contributing to the outcome (12).

Supplement analysis were conducted investigating county fetal death rates (Table 3.4). Fetal deaths rates were defined as deaths prior to the complete expulsion or extraction from its mother, excluding induced abortions (Kowaleski 1997) and calculated as the proportion of fetal deaths out of 1,000 total births in a given county. Only two US studies have investigated the relationship between hurricane and fetal death. The first study by Janerich (1981) looked at four New York counties in a pre-post analysis after Hurricane Agnes and found no association (Janerich, Stark et al. 1981). A recent paper by Zahran (2014) found a strong association between damage from Hurricane Katrina and proportion of fetal death (Zahran, Breunig et al. 2014). While other literature has shown an association between hurricane and fetal death in developing countries the limited domestic studies do not provide enough evidence to confirm this in the United States. Difference-in-difference analysis did yield some negative associations indicating a decrease in fetal death with hurricane exposure; however, the analysis was too low powered to imply true relationships. While this was an original Aim of the dissertation, this was excluded from the published manuscript as to not be misconstrued. Future studies should when possible investigate the potential relationship between hurricane and fetal losses and focus on mechanism of loss.

There were also several limitations with our study methods. A major limitation of our study is that the four hurricanes hit Florida in 2004 in rapid succession, limiting our ability to understand independent hurricane effects. We choose to primarily investigate Hurricane Charley, the first hurricane of 2004, because it is the only residence exposure not potentially influenced by other hurricanes. Additionally, the number of counties exposed changed by the method of exposure categorization, thus rendering comparisons across method or hurricane difficult, especially using generalized linear models (Table 3.1). The county-fixed effects which are used in the difference-in-differences approach better allows for comparisons across models; however, the statistical power using either method will differ for each storm. This complexity of the changing referent is both a limitation of our analysis and relevant to environmental aggregate analyses where multiple levels of exposure in different regions may be compared. The Ivan-unexposed counties are still affected by exposure to other hurricanes, which could bias our estimates. Moreover, our reliance on Vital Statistics data prevents us from understanding the impact of early pregnancy loss, provides extremely limited covariate information, and results in an open cohort without information on migration into or out of our study population.

Changes in live birth rates can be influenced by increases in the number of conceptions, migration into or out of the study area, and changes in fetal loss rates. While we are assuming migration into and out of our Florida cohort is equal, we have no way to document births that occurred outside of the state of Florida due to relocation or evacuation. Studies of the 2004 hurricane season estimate that between one-quarter and one-third of Florida's population evacuated their homes prior to at least one hurricane; and many were evacuated several times (164). We assume the relocation of potentially exposed individuals could bias associations toward the null since people returning to exposed counties would have actually received no direct exposure by evacuating heavily influenced areas. Given the trauma and stress of evacuation or if their property was damaged while they were evacuated, they still might have been exposed to disaster-related stressors. Maternal exposure was defined based on residence at the time of delivery as listed on the birth certificate; however, we acknowledge that residence in a county throughout pregnancy has not been verified.

Conclusions

In summary, we illustrate a method of inference for aggregate analyses to account for time-invariant confounding. Our analysis differs from much of the current epidemiological application of differences-in-differences method by demonstrating its application with aggregate level data. The inconsistency of the literature on hurricanes and reproductive health may be in part due to biases inherent in aggregate pre-post or county-level comparisons. This example can aid future researchers in applying these methods to future studies. While difference-in-differences is not commonly applied in the epidemiologic literature, the ability to better control confounding by unmeasured factors is rationale for future application.

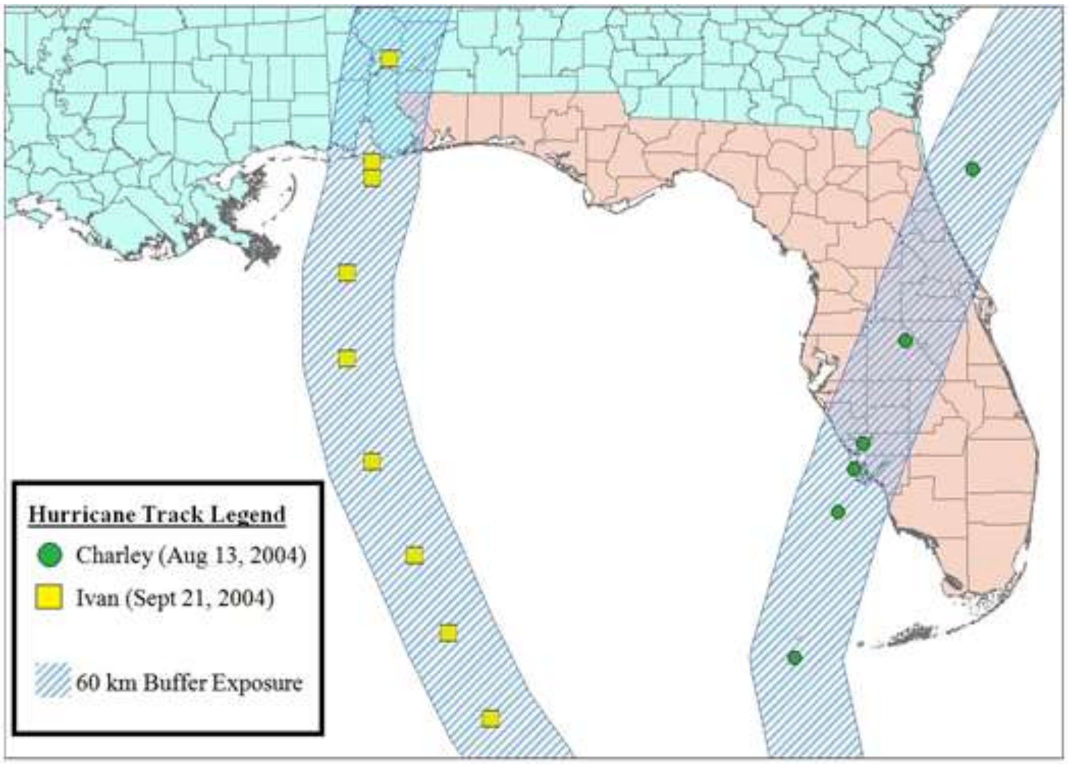

Figure 3.1 2004 Florida hurricane track map with 60 km buffer (n=67 counties)

Table 3.1 Florida 2004 census adjusted[1] generalized linear models (GLM) and difference-in-differences models of hurricane exposure and live birth rates (n=67 counties)

Exposure Method	*Hurricane Charley Exposure* N exposed[2]	Estimate (95% CI)			*Hurricane Ivan Exposure* N exposed[2]	-Estimate (95% CI)		
60 km buffer								
Within County Difference-in-Differences Model	23	0.02	(-0.16	0.20)	2	-0.02	(-0.51	0.47)
Across County GLM Adjusted Model		-0.30	(-0.72	0.13)		2.80	(1.94	3.67)
Wind Speed ≥ 74 mph								
Within County Difference-in-Differences Model	5	0.18	(-0.13	0.49)	3	0.05	(-0.34	0.44)
Across County GLM Adjusted Model		0.06	(-0.67	0.78)		2.23	(1.47	2.99)

Abbreviation: CI, confidence interval; GLM, generalized linear model

[1] Adjusted models include percent renter-occupied units, median household income, percent of persons who do not speak English and percent of persons with more than high school education.

[2] N exposed column indicates the number of exposed counties given indicated exposure method and hurricane out of 67 total counties

Table 3.2 Florida 2004 census adjusted[1] generalized linear models (GLM) and adjusted analysis (n=67 counties)

	Number of counties	
Census Variable	**N**	**(%)**
Renter Occupied Units		
<15%	5	7.5%
15-<25%	43	64.2%
25-<35%	12	17.9%
35+%	7	10.4%
Median Household		
< Median ($38,819)	47	70.1%
>Median ($38,819)	20	29.9%
Percent persons do not speak English		
<1%	45	67.2%
1-<3%	17	25.4%
3-<5%	1	1.5%
5+%	4	6.0%
Percent persons with >= HS education		
<65%	4	6.0%
65-<75%	26	38.8%
75-<85%	26	38.8%
85+%	11	16.4%

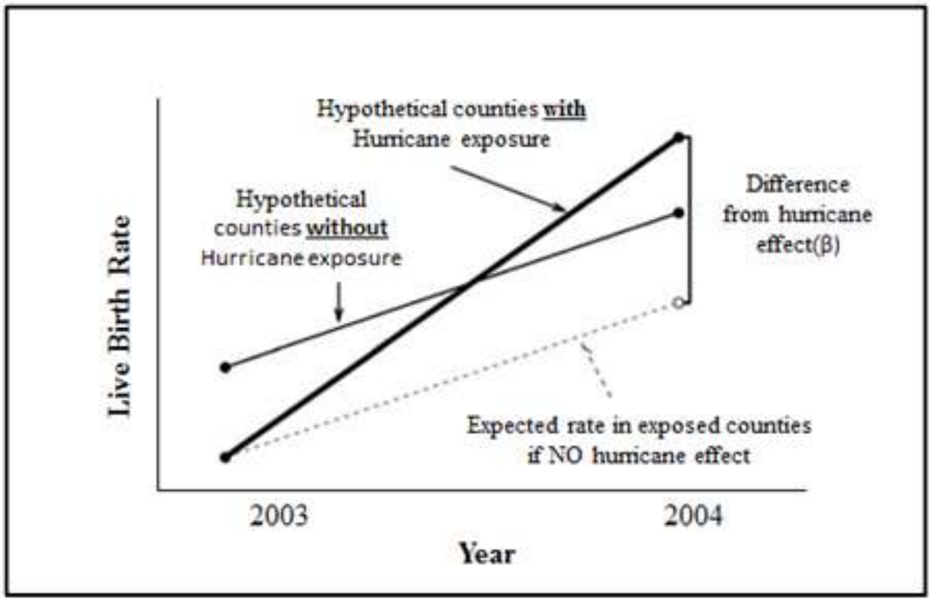

Figure 3.2 Hypothetical illustration of difference-in-differences method

Model Parameters

y_{it} is response variable (e.g. live birth rate) for county i at time t.

z_i is a column vector (covariate) which does not vary over time t.

x_{it} is a column vector (hurricane exposure) which does vary over time t.

μ is the model intercept.

β and γ are row vectors while ε is the random error.

Generalized Linear Model

2003 Model(time 0): $y_{i0} = \mu_0 + \beta\, x_{i0} + \gamma_{\,zi} + \varepsilon_{i0}$

2004 Model(time 1): $y_{i1} = \mu_1 + \beta\, x_{i1} + \gamma_{\,zi} + \varepsilon_{i1}$

Differenced model: $y_{i1} - y_{i0} = (\mu_1 - \mu_0) + \beta\,(x_{i1} - x_{i0}) + (\varepsilon_{i1} - \varepsilon_{i0})$

Figure 3.3 Model description for generalized linear and difference-in-differences models

Table 3.3 Florida 2004 census unadjusted and adjusted[1] generalized linear models (GLM) and difference-in-differences analysis of hurricane exposure and live birth rates (n=67 counties)

Exposure Method	**Any Hurricane Exposure** Estimate (95% CI)	**Hurricane Charley Exposure** Estimate (95% CI)	**Hurricane Frances Exposure** Estimate (95% CI)	**Hurricane Ivan Exposure** Estimate (95% CI)	**Hurricane Jeanne Exposure** Estimate (95% CI)
60 km buffer					
Unadjusted Model	-0.05 (-0.23 0.13)	-0.39 (-0.80 0.02)	-0.06 (-0.45 0.33)	2.62 (1.98 3.60)	0.03 (-0.38 0.44)
Adjusted Model	-0.02 (-2.08 2.05)	-0.30 (-0.72 0.13)	-0.52 (-2.67 1.61)	2.80 (1.94 3.67)	0.09 (-0.31 0.49)
Difference in Diff Model	0.002 (-0.08 0.08)	0.02 (-0.16 0.20)	-0.04 (-0.22 0.14)	-0.02 (-0.51 0.47)	0.03 (-0.15 0.21)
Wind speed $\geq$ 39 mph					
Unadjusted Model	-0.16 (-1.00 0.68)	-0.23 (-0.64 0.18)	0.45 (-0.08 0.98)	-0.61 (-1.10 -0.12)	-0.45 (-0.72 -0.18)
Adjusted Model	0.05 (-0.78 0.88)	-0.36 (-0.81 0.10)	0.48 (-0.04 1.01)	-0.63 (-1.13 -0.13)	-0.65 (-1.17 -0.13)
Difference in Diff Model	-0.14 (-0.49 0.21)	0.02 (-0.16 0.20)	-0.40 (-0.64 -0.16)	-0.15 (-0.37 0.07)	0.008 (-0.17 0.18)
Wind Speed $\geq$ 74 mph					
Unadjusted Model	0.28 (-0.17 0.73)	0.04 (-0.72 0.80)	-0.11 (-0.76 0.54)	2.01 (1.83 2.19)	-0.17 (-0.70 0.36)
Adjusted Model	0.34 (-0.78 0.88)	0.06 (-0.67 0.78)	-0.02 (-0.48 0.43)	2.23 (1.47 2.99)	-0.17 (-0.69 0.35)
Difference in Diff Model	-0.05 (-0.25 0.15)	0.18 (-0.13 0.49)	-0.10 (-0.37 0.17)	0.05 (-0.34 0.44)	-0.18 (-0.40 0.04)

[1] Adjusted models include percent renter-occupied units, median household income, percent of persons who do not speak English and percent of persons with more than high school education.

Table 3.4 Florida 2004 census unadjusted and adjusted[1] generalized linear models (GLM) and difference-in-differences analysis of hurricane exposure and fetal death rates (n=67 counties)

	Any Hurricane Exposure			**Hurricane Charley Exposure**			**Hurricane Ivan Exposure**			**Hurricane Frances Exposure**			**Hurricane Jeanne Exposure**		
Exposure Method	Estimate (95% CI)			Estimate (95% CI)			Estimate (95% CI)			Estimate (95% CI)			Estimate (95% CI)		
60 km buffer															
Unadjusted Model	0.30	(-0.44	1.04)	-0.38	(-2.30	1.54)	-0.96	(-6.33	4.41)	0.64	(-1.18	2.46)	1.46	(-0.34	3.26)
Adjusted Model	0.36	(-0.48	1.19)	0.22	(-1.88	2.31)	-0.16	(-5.60	5.29)	0.09	(-1.84	2.03)	1.05	(-0.89	2.99)
Difference in Diff Model	0.43	(-0.71	1.57)	-1.30	(-4.24	1.64)	-3.72	(-11.91	4.47)	0.75	(-2.05	3.55)	2.74	(0.00	5.48)
Wind Speed ≥39 mph															
Unadjusted Model	0.54	(-3.32	4.40)	-0.38	(-2.26	1.50)	-0.17	(-1.64	1.30)	-0.17	(-1.64	1.30)	-0.20	(-1.99	1.69)
Adjusted Model	1.30	(-2.72	5.32)	-0.25	(-2.52	2.02)	-0.04	(-2.67	2.58)	-0.86	(-1.36	0.35)	0.91	(-1.76	3.57)
Difference in Diff Model	-0.8	(-6.76	5.08)	-0.68	(-3.56	2.20)	-2.24	(-5.98	1.50)	0.97	(-2.58	4.52)	-0.20	(-2.95	2.65)
Wind Speed ≥74 mph															
Unadjusted Model	0.21	(-1.89	2.31)	-0.34	(-1.30	0.62)	-1.27	(-5.70	3.16)	0.21	(-2.79	3.21)	0.63	(-1.84	3.10)
Adjusted Model	0.48	(-1.67	2.64)	-0.33	(-3.86	3.20)	-0.40	(-3.93	3.13)	0.87	(-2.22	3.96)	0.71	(-1.86	3.28)
Difference in Diff Model	-0.50	(-3.70	2.72)	-0.95	(-6.28	4.38)	-2.70	(-9.44	4.04)	1.37	(-3.20	5.94)	0.46	(-3.32	4.24)

[1]Adjusted models include percent renter-occupied units, median household income, percent of persons who do not speak English and percent of persons with more than high school education.

Variables

y_{it} is response variable (e.g. live birth rate) for county i at time t.
z_i is a column vector (covariate) which does not vary over time t.
x_{it} is a column vector (hurricane exposure) which does vary over time t.
μ is the model intercept.
β and γ are row vectors while ε is the random error.

Differenced model: $y_{i1} - y_{i0} = (\mu_1 - \mu_0) + \beta\,(x_{i1} - x_{i0}) + (\varepsilon_{i1} - \varepsilon_{i0})$

Starting point model each year separately:

```
PROC REG DATA=data;
MODEL outcome0=exposure0;  /* unexposed or timepoint 0*/
MODEL outcome 1 = exposure 1;  /* unexposed or timepoint 1*/
RUN;
```

Manual differencing technique:

```
DATA diff;
        SET data;
outcomediff=outcome1-outcome0;
exposurediff=exposure1-exposure0;
PROC REG DATA=diff;
MODEL outcomediff=exposurediff;
RUN;
```

Alternatively if you have repeated measures for county at time 0 and time 1;

```
PROC GLM DATA=data;
ABSORB county; /*ABSORB tells SAS not to generate the coefficient of change for each county but still uses said coefficients in the model*/
MODEL outcome= exposure time;
RUN;
```

If the data is properly set up the two methods will give you the same overall model estimate.

Figure 3.4 Annotated SAS code for difference-in-differences example

CHAPTER 4: AIM 2 RESULTS[2]

Hurricane Charley Exposure and Hazard of Preterm Delivery, Florida 2004

<u>Summary</u>

Objective: As coastal populations and hurricane severity increase in the United States, public health impacts will likely intensify. Although the reproductive period is likely vulnerable to hurricane-related effects, the evidence to date between hurricane exposure and preterm delivery is sparse. We used time-to-event analyses to examine the association between exposure to Hurricane Charley and the hazard of preterm delivery. *Methods:* We used data on 342,942 singleton births from Florida Vital Statistics Records 2004-2005 to capture pregnancies at risk of delivery during the 2004 hurricane season. Maternal exposure was assigned based on maximum wind speed in maternal county of residence. We estimated hazards of overall preterm delivery (< 37 gestational weeks) and extremely preterm delivery (< 32 gestational weeks) in Cox regression models, adjusting for maternal and pregnancy characteristics. To evaluate heterogeneity of the hurricane-preterm delivery association among racial/ethnic subgroups, we assessed for statistical interaction and ran models stratified by race/ethnicity. Models were also conducted to investigate multiple hurricanes exposure. *Results:* There was a positive association between Hurricane Charley exposure and hazard of extremely preterm delivery. Associations appeared to be of largest magnitude among black Hispanic and white Hispanic mothers although we found limited evidence of interaction. Hazard of preterm delivery was not greater with multiple hurricane exposure compared to Hurricane Charley alone. *Discussion:* This study provided evidence that

[2] A revised version of Chapter 4 will be submitted to the *Maternal and Child Health Journal* in 2015 with the following co-authors: Whitney Robinson, Stephanie Engel, Charles Konrad, David Richardson, Jennifer Horney

hurricane exposure may increase hazard of extremely preterm delivery with possible differences by race/ethnicity. As coastal populations and hurricane severity increase in the United States, the associations between hurricane exposure and preterm delivery should continue to be studied.

Background

Health related consequences related to hurricane exposure are increasing as coastal populations and hurricane severity are increasing in the United States (US). The US southeast is most often and hardest hit by hurricanes and Florida had the highest percent increase (approximately 18%) in population between 1990 and 2010 (4, 37). The adverse impacts of hurricane exposure on health outcomes such as injury, psychosocial stress and loss of community resources have been well documented (37). However, relatively few studies have evaluated reproductive health outcomes such as preterm delivery.

Preterm delivery is associated with a variety of factors including sociodemographic, genetic and environmental factors (134, 150, 174, 175). Although the mechanisms by which hurricanes could adversely influence pregnancy are uncertain, one potential route is for stress to trigger early labor and delivery (2, 54, 56).Other mechanisms could include immediate effects such as injury or cumulative effects such as potential lapses in access to health care or prenatal care, both of which could increase the risk of preterm delivery (2). Children who are born preterm are more likely to experience many negative health consequences including increased respiratory illnesses and lower cognitive abilities (176). Death and disability rates among extremely preterm infants (< 32 weeks) are more than 150 times higher than among term babies (104). In the US, black women are consistently reported to be two to three times more likely to have a preterm delivery and three to four times more likely to have an extremely preterm delivery compared to other minorities or white women (91, 96, 174).

Current disaster literature suggests a potential association between natural disasters and preterm delivery (2); however, the results of studies investigating hurricane exposure and preterm delivery have been mixed (51, 68, 74, 171). Several studies explored the effect of Hurricane Katrina exposure on preterm delivery and while some suggested associations with extremely preterm delivery (<32 weeks), findings were mixed with regard to overall preterm delivery (<37 weeks) (51, 68, 74). Currie and Rossin-Slater (2013) evaluated county exposure to any hurricanes from 1996-2008 impacting Texas and found no association with preterm delivery (171). Only one study has evaluated racial differences (74) and no hurricane reproductive health study to date has evaluated differences by ethnicity.

The aim of this study is to determine the association between hurricane exposure and hazards of preterm delivery overall and looking at racial/ethnic subgroups, using a time-to-event analysis of individual-level Florida birth data.

Methods

Birth Cohort

Data on singleton live births from 2003-2005 were obtained from the Florida Department of Health, Vital Statistics Department. The study population included births with an estimated date of conception between October 24, 2003 and September 26, 2004. Therefore, the study period encompasses births that were conceived before the first hurricane occurrence in 2004 (on August 13, 2004) and the last hurricane of 2004 (September 26, 2004). We excluded births to non-Florida residents as they did not have an address to link to Florida hurricane exposure. Additionally, congenital anomalies, births with gestational age less than 20 weeks and births of mother less than 15 years old at delivery or greater than 45 years of age were also excluded.

Exposures

Hurricane exposure was classified by the maximum wind speed during hurricane occurrence in a specific Florida county extracted from National Oceanic and Atmospheric Administration, Hurricane Research Division public databases (169). The Saffir Simpson Hurricane Scale categorizes hurricanes into five distinct categories of wind severity: Category 1 (74-95 miles per hour (mph)), 2 (96-110 mph), 3 (111-129 mph), 4 (130-156 mph), and 5 (157 and higher mph) while tropical storm wind speeds are classified as 39-73 mph (170). We categorized maximum wind speed using two binary categorizations based on the Saffir-Simpson wind scale: ≥ 39 mph to indicate tropical storm winds speed and ≥ 74 mph to indicate hurricane wind speed.

The 2004 hurricane season in Florida was unique, as four hurricanes made landfall. This provided the opportunity to look at both individual and multiple hurricane exposures. Our analysis was primarily focused on the first hurricane of 2004, Hurricane Charley, to assess exposure with no potential biases related to previous hurricane occurrence. We additionally performed analysis on multiple hurricane occurrences. To compare multiple hurricane exposures, hazard ratios of Hurricane Charley only exposure to no exposure were compared to hazard ratios Hurricane Charley plus subsequent hurricane exposure compared to no exposure.

Outcomes

We assessed two outcomes: extremely preterm delivery (< 32 completed gestational weeks) and overall preterm delivery (< 37 completed gestational weeks). Gestational age was determined based on clinical estimate of gestational age as reported on vital statistics record. Although the National Center for Health Statistic(NCHS) recommends that gestational age be estimated by self-reported last menstrual period (92, 149), we assumed that hurricane exposure could be differentially associated with self-reported recall of last menstrual period. Validity of estimate was assessed using the NCHS method of comparing gestational age with birth weight, and was excluded when implausible (149).

Covariates

Maternal and infant characteristics were available from vital statistics records. The following variables were chosen for adjustment using *a priori* approach based on the current literature and variable availability: maternal age (18-24, 25-34, 35-39 or 40-45), maternal education (< high school degree, high school degree, some college/associates, bachelor's degree or graduate/professional degree), maternal race (black, white, Asian/pacific islander and other/multiracial), maternal ethnicity (Hispanic or non-Hispanic), marital status (legally married or not legally married), maternal tobacco consumption during pregnancy (yes or no) and maternal gestational diabetes (yes or no). Maternal age was categorized as a categorical variable due to non-linear association with the outcome. We created a composite race/ethnicity variable for analysis of white non-Hispanic, white Hispanic, black non-Hispanic, black Hispanic and Asian/Pacific Islander subgroups to better understand cultural groups in our Florida population.

Statistical Analysis

We estimated the hazard of preterm delivery among women who conceived between October 24, 2003 and September 26, 2004 and who successfully carried the pregnancy to 20 weeks. For all outcomes, the risk period begins at 20 completed weeks gestation because pregnancies that resulted in early before that point are not captured in vital statistics data. The hazards of extremely and overall preterm delivery were modeled individually using Cox proportional hazards with gestational age in weeks as the time-scale (177). Pregnancies were right censored at 32 and 37 weeks for each outcome respectively. PROC PHREG (SAS 9.2 Cary, NC) was used to estimate hazards with time-varying hurricane exposure. A tabular method was used so that each pregnancy had two records, one unexposed and one exposed, with a variable to describe the amount of pregnancy-weeks contributed to each timeframe. For instance, a woman who delivered at 36 weeks residing in a county with hurricane Charley exposure at 34 weeks and 5 days gestation would have 13 weeks unexposed (from 20 - 33 weeks) and 3 weeks exposed (34 - 36 weeks). In contrast women who delivered at 28 weeks in a county unexposed to hurricane Charley would have 0 weeks exposed and 8 weeks unexposed. Exposure prior to 20 weeks gestation would be counted only from the start of the 20 week risk period. Individual analyses were conducted for each exposure (≥ 34 mph wind speed and ≥ 79 mph wind speed) to estimate the hazard of extremely and overall preterm delivery comparing exposed pregnancy-weeks to unexposed pregnancy-weeks.

We estimated hazard ratios (HRs) and 95% confidence intervals (95% CI) of Hurricane Charley exposure and early preterm adjusting for maternal age, maternal education, maternal race/ethnicity, marital status, maternal tobacco use and maternal gestational diabetes. To investigate race/ethnicity differences we conducted individual stratified model by each race/ethnicity subgroup and performed formal statistical tests of the exposure by race/ethnicity interaction. We used an a priori criteria for an effect measure modifier of a Wald heterogeneity test p-value < 0.20 (162).In adjusted multiple hurricane models (Hurricane Charley and subsequent hurricane occurrence) we estimated the hazard of multiple exposures to no exposure and compare to single Hurricane Charley estimates.

All analyses were conducted in SAS 9.2 (Cary, NC). This research was approved by the Florida Department of Health Institutional Review Board (IRB) (#H13049) and the IRB of the University of North Carolina at Chapel Hill (#13-0784).

Results

Descriptive Data

Table 4.1 displays covariate distributions by preterm delivery outcomes in our study population. The mean maternal age at the time of childbirth was 32 years. The racial/ethnic distribution of the diverse Florida cohort included non-Hispanic white (45%), Hispanic white (28%), non-Hispanic black (17%), and Hispanic black (4%). There was little difference in the maternal and delivery covariates between the extremely preterm (< 32 weeks) and preterm (< 37 weeks) deliveries. Each covariate used in adjusted analysis had less than 2% missing information with a total of 15,740 out of 342,942 records excluded from the starting study population in Cox regression due to missing information on one or more covariates.

Hurricane Charley Cox Proportional Hazard Models

Overall, a positive association was observed between hurricane occurrence and hazard of extremely preterm delivery, but not for preterm delivery (Table 4.2). This was observed for both ≥ 39 mph and ≥ 74 mph exposures (HR=1.09, 95% CI [1.03, 1.16] and HR=1.21, 95% CI [1.06, 1.38] respectively).

In stratified analysis of race/ethnicity, the ≥ 39 mph wind speed models suggested associations between hurricane and extremely preterm delivery among white Hispanics and black Hispanics (HR=1.14, 95% CI [1.01, 1.27] and HR=1.49, 95% CI [1.17, 1.87] respectively) (Table 4.3). Associations did not appear to be present among white non-Hispanic and black non-Hispanics in the analysis of the ≥39 mph wind speed (HR=1.06, 95% CI [0.96, 1.19] and HR=1.02, 95% CI [0.90, 1.14] respectively). The race/ethnicity stratified ≥ 74 mph wind speed models suggested an association between hurricane and extremely preterm delivery among white Hispanic but no association in black Hispanic, white non-Hispanic and black non-Hispanic subgroups (HR=1.32, 95% CI [1.04, 1.69], HR=1.56, 95% CI [0.85, 2.85], HR=1.18, 95% CI [0.97, 1.45] , HR=1.03, 95% CI [0.76, 1.40] respectively). In additional models, we did not find evidence of modification by racial/ethnic subgroups with the exception of the ≥39 mph wind speed extremely preterm black Hispanic subgroup (p-value 0.05; ref: White non-Hispanics).

In race/ethnicity stratified analysis of hurricane and overall preterm delivery there was no evidence of an association in either ≥ 39 mph wind speed or ≥ 74 mph wind speed models. We did not find evidence of modification by racial/ethnic subgroups with the possible exception of the ≥74 mph wind speed overall preterm black non-Hispanic interaction (p-value 0.18; ref: White non-Hispanics).

Multiple Hurricane Cox Proportional Hazard Models

Of the 67 Florida counties, 37 counties were exposed to multiple hurricanes (Hurricane Charley and one or more subsequent hurricanes) when categorized by ≥ 39 mph wind speed, and 8 counties were exposed when applying the ≥ 74 mph wind speed (Table 4.4). In all models, there was no evidence of an increased hazard of extremely preterm or overall preterm delivery with exposure to more than one hurricane (Table 4.5). For example, compared to no exposure to no hurricanes, the hazard ratios of extremely preterm and preterm delivery among those exposed to ≥ 74 mph winds were similar when assessing only Hurricane Charley exposure and when assessing exposure to Charley plus a subsequent hurricane (extremely preterm (HR=1.21, 95% CI [1.06, 1.38] and HR=1.20, 95% CI [0.98, 1.46], respectively; overall preterm (HR=1.06, 95% CI [1.00, 1.12] and HR=1.07, 95% CI [1.04, 1.10], respectively).

Discussion

To our knowledge, our Florida-based study population is the only example of evaluating associations between hurricane and preterm delivery in ethnic subgroups and is only the second study to evaluate hurricane influence on a full state population of births. While some hurricane studies are done at aggregate levels, we were able to control for individual-level confounders in our analysis using Vital Statistics data. Overall we found that pregnant women living in a county exposed to Hurricane Charley experienced increased hazard of extremely preterm delivery (< 32 weeks) but not preterm delivery (< 37 weeks) in Florida during the 2004 hurricane season.

Our results for Hurricane Charley are similar to several preterm delivery studies that focused on Hurricane Katrina. A smaller study conducted after Hurricane Katrina examined how demographic characteristics affected birth outcomes in Louisiana, and the effect of the hurricane on racial disparities using pre-post comparisons of counties. Similar to our study, overall preterm delivery rates did not increase in the two years after Katrina and the risk of preterm delivery remained higher in black compared to white women(74). But in general race did not interact with hurricane exposure. In another study investigating poor fetal outcomes in US Gulf Coast states after Katrina, higher rates of extremely preterm delivery were reported in Alabama (51).

In contrast to our Hurricane Charley results, Hamilton (2009) found lower rates of extremely preterm delivery in Louisiana after Hurricane Katrina (51). In addition, a study by Xiong (2008), collected data in New Orleans and Baton Rouge after Hurricane Katrina related to hurricane "experiences" (e.g. feeling that one's life was in danger or having a loved one die). This study found a higher frequency of overall preterm delivery in women with three or more subjective hurricane experiences versus women with less than three, but did not explore extremely preterm delivery (68). The only non-Katrina hurricane study, Currie (2013), investigated Texas birth records over a twelve year period and found that exposure to a hurricane during pregnancy, as determined by disaster declaration, was not associated with gestational age at delivery (171).

Prior research demonstrates that socially vulnerable populations, including women and members of racial/ethnic minorities, suffer disproportionately from disasters (178, 179). However, our study is the first to have investigated the hazard of preterm delivery among understudied racial/ethnic subgroups including Asians and Hispanics. Published studies of hurricane exposure and reproductive health show that black women may have an increased risk of adverse reproductive outcomes that are persistent but not necessarily exacerbated by hurricane exposure. These studies have not evaluated differences by ethnicity. In our race/ethnicity analysis it appeared that there may be some differences in race/ethnicity subgroups. We felt that the effect of confounding factors on preterm delivery could vary in different racial/ethnic strata and therefore multivariable-adjusted associations could be better described in stratified models. Additionally, two of our interaction models did suggest multiplicative interactions comparing black Hispanic and black non-Hispanic to white non-Hispanic subgroups. Overall, more research is needed on racial/ethnic subgroups to better target vulnerable groups for public health intervention where appropriate.

Although underpowered, due to the racial and ethnic diversity of the State of Florida, we were able to describe more associations among racial/ethnic groups than other published analyses. Supplemental modification analyses performed for the dissertation for race and ethnicity separately and as a composite variable are shown in supplemental Appendix Tables S8-S13. This subgroup analysis may help Florida public health officials better prepare for future hurricanes, as well as better understand the hazards of preterm delivery in particularly vulnerable population subgroups.

Current disaster reproductive health literature has not investigated the association of multiple hurricanes on delivery outcomes. Four hurricanes made landfall in Florida in rapid succession between August 13, 2004, and September 26, 2004. Hurricane Charley was the first hurricane of the 2004 hurricane season and therefore is the only hurricane not potentially biased by prior evacuation and changes in residence from previous hurricanes. In our analysis, we found that the hazard of preterm delivery did not differ when comparing multiple hurricane exposure to only Hurricane Charley exposure. In addition, we conducted analyses to examine the interaction between Charley and each subsequent hurricane. Because of power limitations, only interaction between Charley and the second hurricane of the 2004 season, Frances, could be described (Appendix Tables S6). We found no evidence of interaction between Hurricane Charley and Frances. We also investigated each hurricane of the 2004 season independently and found similar results to the Hurricane Charley analysis presented here (Appendix Tables S7).

The current literature on hurricane and preterm delivery uses mostly pre-post analyses of county-level preterm delivery rates. Findings from these studies have been mixed, possibly due to biases inherent to pre-post analysis such as ecological fallacy. In addition, a strength of our analysis is the use of the individual-level outcomes and covariates. Our analyses used of Cox proportional hazard models to conduct a fetus-at-risk approach to evaluate preterm delivery. This method has been advocated as more appropriate in perinatal epidemiology, as opposed to cohorts of births when investigating time varying exposure and pregnancy-time dependent outcomes like gestational age (160, 180, 181). Since the risk of delivery increases with gestational age, a model using traditional dichotomous (yes/no) exposure and not time contributed to exposure, may inflate the risk of delivery as it becomes imminent. This method also can account for fetuses-at-risk of hurricane exposure and the preterm delivery event, creating a better counterfactual contrast. Future research using time-to-event analysis on disaster exposure and preterm delivery could benefit by using a cohort design with time-varying confounders to account for changes in care or comorbidities during the course of pregnancy.

Our study had several limitations. Using vital statistics data, we could not distinguish spontaneous preterm delivery from other subtypes. Fetal deaths, although rare, were not included in adjusted analysis due to a lack of complete covariate information. Although overall missingness was not a concern, many potential confounders were not available from fetal death records (Appendix Tables S14). Fetal deaths made up less than 1% of total births and when included in crude analysis did not show a difference in estimate from adjusted analysis. The addition of fetal deaths which occur after 20 weeks gestation in future analysis would strengthen the fetus-at-risk approach using time-to-event modeling. Additionally, hurricane exposure was determined based on residence reported at time of delivery. Women may have moved out of exposed areas if barriers to access to care or other damages occurred in their community. This would likely bias associations towards the null.

Another limitation is the current lack of ability to target the mechanisms that influence the hurricane to preterm delivery causal pathway, which may not be the same for extremely and overall preterm delivery. One hypothesis for the consistent association in the < 32 week deliveries is the possibility that pregnancy at this stage could be more vulnerable to some short-term mechanisms, including access to care or injury. Additionally, unmeasured confounding may be a larger issue in this extremely preterm analysis, where less reliable or unknown variables may have a greater impact compared to the overall preterm analysis. An additional possibility is that pregnant women are more likely to evacuate at later stages of pregnancy. This could drive the association in the overall preterm analysis toward the null if they move from exposed to unexposed areas. Also, using residence at delivery as a proxy to assign hurricane exposure could lead to exposure misclassification in our study. While research has not been done on evacuation trends during pregnancy, during the 2004 hurricane season 1 in 4 individuals of the total Florida population evacuated their primary residence during one or more hurricane events (164). Individuals most often relocate or return to the same county within a relatively short period of time (182).

Conclusions

Associations between hurricane exposure and preterm delivery need to be better understood as coastal populations and hurricane severity increase in the United States. Preterm children, in particular extremely preterm, are more likely to experience negative consequences such as respiratory and cognitive impairment. We found that Hurricane Charley exposure in Florida in 2004 was consistently associated with the hazard of extremely preterm delivery (< 32 weeks gestation). This association with extremely preterm delivery is shown with other published research, although limited to few studies. These results should potentially be considered by public health leaders in recommendations for evacuation procedures or prenatal care. Future studies of hurricane and preterm delivery should further evaluate race/ethnicity subgroups and use individual-data with methods such as time-to-event analysis to provide more accurate estimates than ecological and pre-post analysis.

Table 4.1 Descriptive characteristics of study population 2004 and 2005 live births by extremely preterm (<32 weeks), and preterm (32-36 weeks) status (n= 342,942)

	Total Cohort		<32 weeks (n=11,681 (3.4%))		32-36 weeks (n=29,344 (8.6%))	
	N	%	N	%	N	%
Maternal Age						
<18	10035	2.9%	589	5.0%	1051	3.6%
18-25	114002	33.2%	4210	36.0%	10049	34.2%
25-35	167904	49.0%	5015	42.9%	13502	46.0%
35-45	50593	14.8%	1845	15.8%	4696	16.0%
Missing	408	0.1%	22	0.2%	46	0.2%
Maternal Education						
High School Diploma	72172	21.0%	3072	26.3%	7097	24.2%
Some College/Associates degree	86601	25.3%	4153	35.6%	9750	33.2%
Bachelor's Degree	110093	32.1%	2680	22.9%	7072	24.1%
Professional/Graduate Degree	70898	20.7%	1543	13.2%	5131	17.5%
Missing	3178	0.9%	233	2.0%	294	1.0%
Maternal Race/Ethnicity						
White Non-Hispanic	155736	45.4%	3957	33.9%	11959	40.8%
White Hispanic	94875	27.7%	2913	24.9%	7918	27.0%
Asian/Pacific Islander	9276	2.7%	249	2.1%	781	2.7%
American Indian	7494	2.2%	220	1.9%	632	2.2%
Other/Multiracial[1]	762	0.2%	23	0.2%	93	0.3%
Black Non-Hispanic	59044	17.2%	3474	29.7%	6445	22.0%
Black Hispanic	12476	3.6%	679	5.8%	1226	4.2%
Missing	3279	1.0%	166	1.4%	290	1.0%
Maternal Marital Status						
Married	201441	58.7%	5380	46.1%	15956	54.4%
Single	141002	41.1%	6260	53.6%	13333	45.4%
Missing	499	0.1%	41	0.4%	55	0.2%
Maternal Tobacco						
Yes	24341	7.1%	1064	9.1%	2294	7.8%
No	311961	91.0%	10322	88.4%	26455	90.2%
Missing	6640	1.9%	295	2.5%	595	2.0%
Gestational diabetes						
Yes	12949	3.8%	385	3.3%	1467	5.0%
No	328860	95.9%	11182	95.7%	27752	94.6%
Missing	1133	0.3%	114	1.0%	125	0.4%

[1]Other/Multi Racial includes mothers whom selected multiple races or other on the birth certificate.

Table 4.2 Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Charley wind exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery

		Outcome			
		<32 weeks		<37 weeks	
		HR	(95% CI)	HR	(95% CI)
Wind Speed Exposure	*Model Description*				
≥ 39 mph					
	1a. Unadjusted	1.12	(1.06 1.19)	1.05	(1.02 1.07)
	1b. Adjusted	1.09	(1.03 1.16)	0.99	(0.96 1.01)
≥ 74 mph					
	2a. Unadjusted	1.18	(1.04 1.35)	1.07	(1.01 1.13)
	2b. Adjusted	1.21	(1.06 1.38)	1.06	(1.00 1.12)

[1] Adjusted for gestational diabetes, maternal age, maternal race, maternal ethnicity, maternal education, and maternal pregnancy tobacco use.

Table 4.3 Florida 2004 adjusted[1] hazard ratio (HR) of Hurricane Charley race/ethnicity stratified hurricane wind exposure on extremely preterm (< 32 weeks) and overall preterm (< 37 weeks) delivery and p-value for interaction in exposure by race/ethnicity model term.

		Outcome							
		< 32 weeks			Interaction	< 37 weeks			Interaction
		HR	95% CI		p-values[2]	HR	95% CI		p-values[2]
Wind Speed Exposure	*Race/Ethnicity Stratified Models*								
≥ 39 mph									
	Model 3a.White Non-Hispanic	1.06	(0.96	1.19)	Referent	0.99	(0.95	1.04)	Referent
	Model 4a. White Hispanic	1.14	(1.01	1.27)	0.52	0.98	(0.98	1.02)	0.26
	Model 5a. Asian/Pacific Islander	0.97	(0.60	1.57)	0.76	0.90	(0.77	1.07)	0.27
	Model 6a. Black Non-Hispanic	1.02	(0.90	1.14)	0.35	0.98	(0.93	1.04)	0.32
	Model 7a. Black Hispanic	1.49	(1.17	1.87)	0.05	1.06	(0.94	1.18)	0.80
≥ 74 mph									
	Model 3b. White Non-Hispanic	1.18	(0.97	1.45)	Referent	1.08	(0.99	1.17)	Referent
	Model 4b. White Hispanic	1.32	(1.04	1.69)	0.50	1.07	(0.96	1.18)	0.82
	Model 5b. Asian/Pacific Islander	1.50	(0.55	4.08)	0.71	1.09	(0.74	1.63)	0.88
	Model 6b. Black Non-Hispanic	1.03	(0.76	1.40)	0.37	0.95	(0.82	1.10)	0.18
	Model 7b. Black Hispanic	1.56	(0.85	2.85)	0.43	1.33	(0.99	1.79)	0.22

[1] Adjusted for gestational diabetes, maternal age, maternal race, maternal ethnicity, maternal education and maternal pregnancy tobacco use.

[2] Interaction p-values were generated by conducting models which included interactions between the five race/ethnicity subgroups explored in Table 4.3 with the main effect of exposure. Reported p-values are from a single model for each exposure outcome relationship.

Table 4.4 Florida 2004 sample size description for multiple hurricane exposures hazard ratio models.

Exposure	*≥39 mph exposure* N of Counties	<32 week events	<37 week events	*≥74 mph exposure* N of Counties	<32 week events	<37 week events
0 Hurricane Exposure	4	259	1433	50	9902	50054
1 Hurricane Exposures	26	2391	11844	9	1206	6534
2 Hurricane Exposures	11	3737	17999	7	2171	10855
3 Hurricane Exposures	26	7355	39845	1	185	1110

Table 4.5 Florida 2004 adjusted[1] hazard ratio (HR) of multiple hurricane exposure and single Hurricane Charley exposure to no hurricane exposure on extremely preterm (< 32 weeks) and overall preterm (< 37 weeks) delivery

		Outcome			
		<32 weeks gestation		*<37 weeks gestation*	
Wind Speed Exposure	*Multiple Hurricane Models*	HR	95% CI	HR	95% CI
≥39 mph					
	Model 8a. Hurricane Charley to no exposure	1.21	(0.99 1.49)	0.99	(0.91 1.08)
	Model 8b Charley with subsequent hurricane to no exposure	1.20	(0.98 1.46)	1.08	(1.00 1.17)
≥74 mph					
	Model 9a. Hurricane Charley to no exposure	1.12	(1.02 1.23)	1.09	(1.05 1.13)
	Model 9b. Charley with subsequent hurricane to no exposure	1.13	(1.06 1.22)	1.07	(1.04 1.10)

[1] Adjusted for gestational diabetes, maternal age, maternal race, maternal ethnicity, maternal education, maternal pregnancy tobacco use

CHAPTER 5: DISCUSSION

Overall Study Aims, Findings and Interpretation

The goals of this project were to evaluate the associations between hurricane-related weather exposure and reproductive outcomes, as well as to highlight methods that may prove useful in similar epidemiological analyses. In summary, Aim 1 demonstrated the use of the difference-in-differences method in county-level analysis of live birth rates and Aim 2 evaluated the individual-level association between hurricane and preterm delivery using a time-to-event approach.

Aim 1: Difference-in-differences Analysis Method

We demonstrated an application of the difference-in-differences method for controlling time-invariant confounders by investigating the effect of hurricane exposure on county-level live birth rates. This method was contrasted with generalized linear models, which controlled for confounding using selected census-level covariates. All difference-in-differences models yielded null associations for both hurricanes and exposure metrics while the generalized linear model yielded some potential associations with Hurricane Ivan. The consistency of the difference-in-differences method suggests the potential integrity of this method over the generalized linear models to better control for time-invariant confounders.

There is no current consensus on the impact of hurricane exposure on reproductive health with reported associations varying across studies (1, 2). These mixed findings are potentially the result of varied mechanisms of exposure (e.g., stress, economical, injury), differences in exposure definitions, dissimilar study populations, incomplete confounding control or potential heterogeneity in hurricane effects. Our analysis applied several exposure metrics over multiple hurricanes to examine some of these potential inconsistencies. Our analysis differs from much of the current epidemiological application of difference-in-differences by demonstrating its application with aggregate-level data. While difference-in-differences is not commonly applied in the epidemiologic literature, the ability to potentially better control confounding may be a sufficient reason for its use in future applications.

Aim 2: Hazard of Preterm Delivery with Race/Ethnicity Subgroup Analysis

Results of the analysis related to Hurricane Charley suggested a positive association between exposure and extremely preterm delivery. Estimates for overall preterm deliveries did not suggest an association. There was some evidence of modification in the association between hurricane exposure and extremely preterm delivery and overall preterm delivery by race/ethnicity. White Hispanics and black Hispanics were most at risk of extremely preterm delivery after exposure to Hurricane Charley. Overall, there was no evidence of an increased hazard of extremely preterm or preterm delivery with exposure to more than one hurricane compared to the single hurricane occurrence.

Our results suggest that hurricane exposure may have a stronger effect on delivery in earlier pregnancy; however, the etiology and adequacy of confounding control using vital statistics in the extremely preterm delivery analyses must be taken in consideration. In our race/ethnicity analysis it appeared that associations in the full population were being driven by black and white Hispanic subgroups. Additionally, two of our interaction terms did suggest multiplicative interaction comparing black Hispanic and black non-Hispanic to white non-Hispanic subgroups. Overall, more research is needed on racial/ethnic subgroups to better target vulnerable groups for public health intervention where appropriate. Since current research is limited to a few hurricanes and ecological analysis, more studies are needed to understand the relationship between hurricane and preterm delivery for the general population, as well as for specific racial/ethnic subgroups to better target vulnerable groups for public health intervention where appropriate.

Methodological Considerations

In addition to the limitations and strengths discussed in the Aim 1 and Aim 2 manuscripts, there are additional methodological considerations relevant to research into the effects of hurricane exposure on reproductive health.

Clarity of exposure assessment can pose challenges in natural disaster studies. Currently, the few studies specifically examining hurricane exposure and reproductive health use different ways of defining hurricane exposure, making comparisons difficult to interpret. We investigated a novel objective method of exposure assessment in order to reduce exposure misclassification and compared its sensitivity to that of two commonly-used exposure classification methods. In preliminary analysis, we found that county-level FEMA disaster declarations do not necessarily quantify exposure as consistently as methods using a symmetrical buffer of hurricane track or our novel wind speed method. We suggest future researchers clearly define exposure methods that best answer the research questions of interest.

We advocate the use of maximum wind speed as an exposure metric. In our study, exposure was defined by the maternal county of residence indicated on the birth certificate. This is a major limitation, given that that residence may not coincide with the actual residence during hurricane occurrence. We also had no way of documenting births that occurred outside of the state of Florida due to relocation or possible evacuation. Studies of the 2004 hurricane season estimate that between one-quarter and one-third of Florida's population evacuated prior to at least one hurricane, and many evacuated several times (164). Individuals most often relocate or return to the same county within a relatively short period of time. An estimated 20% of homes throughout Florida were damaged by these hurricanes, and 124 persons died. No literature to date indicates that the evacuation response in pregnant women will differ from the general population.

In this research we use a difference-in-differences method in county-level birth rate analysis and a time-to event model in individual-level preterm delivery analysis. Environmental studies which measure exposure and/or outcomes at an aggregate level may have unique challenges with population level confounding. Both methods we applied may have advantages over current disaster studies which often use pre-post analysis and may not fully control confounding. While still potentially suffering from bias due to residual confounding and migration, the differences-in-differences method overcomes some of the limitations of conventional approaches by addressing confounding by unmeasured time-invariant attributes. The Cox proportional hazard models did not only include individual-level reproductive health attributes but also allowed for the application of a time varying exposure. The use of a time varying exposure has been advocated as more appropriate in perinatal epidemiology when investigating time varying exposure and pregnancy-time dependent outcomes such as gestational age, and covariates to create a better counterfactual contrast.

To our knowledge, our study is the only analysis to examine multiple hurricane exposures during a single year in a single state. No study to date has investigated the public health outcomes associated with multiple maternal hurricane exposures during pregnancy. In the last 10 years, it has become increasingly common for multiple storms to make landfall on the U.S. Atlantic or Gulf coast in a single hurricane season (118, 120, 121). Therefore, it is important to investigate both the independent and combined effects of hurricane exposure on reproductive health. The effect of multiple hurricane exposures on pregnancy could be synergistic with respect to stress or further disable healthcare systems, with each added event increasing risk through multiple pathways. Since the four hurricane events occurred close together in time, we did not make inference on individual hurricanes occurring after Hurricane Charley due to a possible lack of independence. In the analysis of effects of multiple hurricanes, we did not find any indication that exposure to multiple hurricanes increased the risk of preterm delivery compared to individual hurricane exposure.

Natural disaster exposure is a complex event with many potential mechanisms which could influence a population. Much of the current literature and proposed mechanisms for poor outcomes involve psychosocial stress; however, we know that other disaster-related mechanisms including injury, infectious disease, and access to care could also affect reproductive outcomes. This study does not isolate a single mechanism and therefore it will be difficult to devise interventions from our findings. Hurricane exposure itself is not preventable, but we hope that this study can add to the current literature of the effects of hurricanes, even without the ability to isolate a mechanism for prevention.

Future Approaches

The literature on hurricane exposure and reproductive health outcomes shows mixed associations and uses a variety of exposure definitions and analytic methods. Our study explored the associations between hurricane and reproductive health as well as highlighted epidemiologic methods to potentially improve upon confounding control. Future methods should consider the proper control of confounding and possibly explore some of the methods suggested. Despite some evidence indicating that there may be an association between hurricanes and adverse fetal outcomes, such as preterm delivery, the lack of a detailed validated mechanisms and full individual reproductive information limits current interpretations. Future studies which target mechanisms and potential interventions would help to clarify this multifactorial exposure. In addition, further attention to differences in racial and ethnic subgroups as well as social contributors to health would provide a more complete picture of disparities and the relationship with hurricane occurrence.

A limitation of our analysis that can be addressed in future studies was the use of vital statistics to determine exposure, covariates and outcomes. Exposure was defined based on residence from vital statistics records that may not have reflected county of residence during hurricane exposure. While prospective analysis of hurricane impacts cannot easily be conducted due to the unpredictable nature of natural disaster, quick response grants and post-disaster evacuation studies should be conducted on pregnant women to collect and analyze perishable data.

Conclusions

Coastal regions are attractive places to live and work, but are increasingly exposed to some of the most powerful storms on earth. The persistent movement of people to these areas and rapid development in coastal regions has been the main driver of the growth in disaster losses for much of the past century. This trend will likely accelerate as the destructive potential of these events increases due to climate change and a concomitant rise in sea levels. Achieving a more comprehensive understanding of the influence of hurricanes on pregnant women and their fetuses should be a priority in natural disaster research since these populations may be disproportionately vulnerable to long-term health consequences.

In the evaluation of hurricane exposure on reproductive health, we found no associations between hurricane exposure and live birth rates in county-level analysis. We were unable to determine associations with fetal deaths due to a limited sample size. We did find some evidence of association between hurricane exposure and extremely preterm delivery, but not necessarily with overall preterm delivery. Black and Hispanic women have a higher baseline risk of preterm delivery, which we found may have persisted with hurricane exposure. While our research did not target a specific mechanism between hurricane exposure and preterm delivery, our results do suggest that women exposed to hurricanes, particularly women of certain race/ethnicity subgroups, may be at higher risk of early delivery.

Our study demonstrated methods useful in limiting biases and more effectively exploring the associations between hurricane weather and reproductive health. In aggregate-level analysis, the difference-in-differences method can be applied to control for unmeasured or unreliably measured confounders. Our Aim 1 findings demonstrate the utility of this method and attempt to highlight its strengths for future research. When individual-level data is available, methods such as time-to-event analysis should be considered, as we did in our analysis for Aim 2. Specifically when evaluating preterm delivery, the chance of delivery increases with gestational age, therefore a model using traditional dichotomous exposure and not time contributed to exposure may inflate the estimates of the effects of exposure on the hazard of delivery.

In summary, this work provides insight into methods for future natural disaster research as well as suggests potential increase in the rate of preterm delivery due to hurricane exposure. This knowledge will provide an example for future disaster studies and help those working in public health preparedness to understand better the potential impacts of hurricane exposure in pregnancy.

APPENDIX A: PRELIMINARY PAPER 0 RESULTS.[3]

Title: Measuring the Storm: Methods of Quantifying Hurricane Exposure in Public Health

<u>Summary</u>

Increasing coastal populations and storm intensity may lead to more adverse health effects from tropical storms and hurricanes. Exposure during pregnancy can influence birth outcomes through mechanisms related to healthcare, infrastructure disruption, stress, nutrition, and injury; however, accurate estimation of health effects may be limited by non-specific exposure definitions that create potential misclassification. Two predominant hurricane exposure assignments are: 1) county of Federal Emergency Management Agency Presidential disaster declaration and 2) specified area within a storm track. We propose a third method, meteorological severity of wind speed. Based on Saffir-Simpson categories, wind speed was examined through binary and quartile comparisons. We compared all three methods of exposure classification by examining associations with county-level preterm delivery and low birth weight rates among Florida women pregnant during the 2004 hurricane season. To control for county-level environmental factors, we used the county-level Environmental Quality Index developed by the Environmental Protection Agency. Although models yielded unexpected negative results and non-significant rate differences, descriptive and mapping analysis of exposure methods showed clear heterogeneity of county exposure.

<u>Background</u>

Natural disasters' impacts and related losses have grown with increasing populations in vulnerable areas and with severity of large-scale disasters (109). Specifically, future vulnerability

---

[3] A revised version of Appendix A is Under Review at the journal *Natural Hazards Review* Since July 2014 with the following co-authors: Whitney Robinson, Danelle Lobdell, Charles Konrad, Jennifer Horney

to hurricanes is influenced by coastal population growth, urbanization and global climate change. The United States(US) Atlantic and Gulf coasts, where hurricanes most often make US landfall, are home to over 50% of the nation's population, and projected to exceed 55% by 2015 (183). This additional population vulnerability is likely to lead to an increase in the health effects of tropical storms and hurricanes. Potential health effects include mortality, injury, economic distress, psychosocial stress, and disruption of health care (3). Vulnerable populations, including pregnant women, may be disproportionately affected by hurricane-related health effects. Hormone fluctuation during pregnancy may influence stress related reactions around hurricane occurrence, while potential lapses in access to health care could greatly impact reproductive outcomes.

Many studies have examined different types of health outcomes related to hurricanes; however, the exposure definitions employed vary greatly across published studies (3, 17, 43, 68, 72, 76, 77, 170, 171). Assigning exposure at the appropriate level to measure health outcomes related to hurricanes may be difficult. For example, stress from natural disasters is likely to be widespread throughout communities, counties, or even larger geographies (2) while injury and economic loss may only affect a smaller subset of individuals. The current disaster literature focuses primarily on two methods of assigning disaster exposure: 1) Federal Emergency Management Agency (FEMA) Presidential disaster declarations (37, 47, 76, 184, 185) and 2) spatial data on the specific storm track trajectory (171). Additionally, some studies investigate clinic-based populations or more subjective geographic assignment of exposure (24, 67, 74). We will demonstrate and discuss a novel method of using meteorological data to define exposure to hurricanes in order to accurately understand health effects of hurricanes.

Methods

Hurricane Exposure Measurement

Three different methods assessing hurricane disaster exposure were considered: 1) FEMA Presidential disaster declarations (185) ; 2) assigning exposure using spatial data on the specific storm trajectory (26) and 3) a novel meteorological measure based on Saffir-Simpson hurricane intensity scale.

Data on disaster declarations was extracted from FEMA presidentially declared disaster archives (185). Presidential disaster declarations are requested by the Governor of an affected state and, when approved, release aid from the federal government to provide supplemental assistance to state and local governments, families, and nonprofits to assist with disaster recovery (185). When used as a research exposure measure, counties exposure is classified base on if aid was released in a county for a given disaster event.

The spatial storm trajectory method utilizes Geographic Information System (GIS) mapping of inland storm tracks and applies a symmetrical buffer to identify severely affected geographic areas. Like the disaster declaration method, this method often is used to identify exposed counties, although smaller geographic units could be specified. Current literature using spatial methods often apply several buffer distances, ranging from 30 to 100 kilometers (km), to better categorize potential exposure (171). The eye of a major storm is typically 30 to 60 km wide, and the eye is surrounded by the strongest winds (25). Historical track data for North Atlantic hurricane systems is derived from National Oceanic and Atmospheric Association's (NOAA) Atlantic Hurricane Database in the form of geographic points and lines which can be imported into ArcMap 10 GIS software (186, 187).

Our novel meteorological method relies on the fact that hurricane intensity is defined by maximum wind speed. The Saffir-Simpson hurricane wind scale categorizes hurricanes into 5 distinct categories of severity: category 1 (74-95 miles per hour (mph)), 2 (96-110 mph), 3 (111-129 mph), 4 (130-156 mph), and 5 (157 and higher mph) (25). Tropical storm wind speeds are classified as 39-73 mph. In general, Category 1 wind speeds are dangerous, producing some damage and power outages for a few days. Category 2 are extremely dangerous, more likely to cause structural damages and complete power loss to areas for up to a week. Category 3-5 hurricanes are considered major hurricanes in which there is likely to be severe damage to both the built and natural environment, as well as power and water loss, potentially for weeks (4). To be consistent with the previously discussed methods, we used maximum wind speed at the county-level at the exposure metric. Utilization of the Saffir-Simpson hurricane intensity scale allows us to explore a quantitative and reproducible method of assigning hurricane exposure based on the currently applied thresholds of hurricane wind effects.

The use of meteorological data increases the sensitivity of exposure between hurricanes and is regularly collected in hurricane monitoring. Measures of both maximum and average county wind speeds, which are easily reproducible by other researchers and can vary by hurricane size and strength, are utilized to assess exposure to hurricane weather. Wind speeds were extracted from NOAA's Hurricane Research Division (HRD) public databases. Details of the data collection and the HRD real-time hurricane wind analysis system have been published elsewhere (26).

2004 Hurricane Season Study Population

The three exposure methods were compared using reproductive health data from the 2004 hurricane season in Florida. The 2004 hurricane season was the worst in Florida's history, with four hurricanes making landfall and causing at least 47 deaths and $45 billion in damages (164). Using the 2004 hurricane season allows us to investigate several different exposure methods across four hurricanes in a single year. Florida has 67 counties and over 200,000 births annually. Figure 1.1 displays the hurricane tracks of four storms that made landfall in Florida during the 2004 hurricane season.

In the 2004 hurricane season, four hurricanes made landfall in Florida: Charley (August 13th), Frances (September 5th), Ivan (September 21st) and Jeanne (September 25th). These hurricanes were systematically different. Charley was the strongest hurricane to strike the US since Hurricane Andrew in 1992 and was a relatively small but intense hurricane. Charley travelled northeastward through central and northeast Florida, through the heart of the Florida Peninsula. Frances was not as strong as Charley but much larger and responsible for over 100 tornadoes and massive floods. Frances traveled northwest through Florida hitting central Florida and the western coast towards the panhandle. Hurricane Ivan was both strong and large but in terms of our Florida population only affected a small area of the Florida panhandle. Ivan saturated the same counties just hit by Frances and led to massive flooding and many tornados. The final hurricane of the 2004 season Jeanne followed a very similar path to that of Frances. Jeanne was not powerful but slow moving dropping several inches of rain over the already saturated flooded region of Florida. These four hurricanes exemplify the heterogeneous nature of hurricane force and size.

Mapping and Analysis

To compare the three exposure methods, descriptive and mapping comparisons were made. We also assessed the three exposure methods in relation to several reproductive health outcomes using Florida birth certificate data. We compared eight exposure contrasts for each of the 2004 hurricanes: FEMA disaster declaration, three symmetrical spatial buffers (30 km, 60 km, and 100 km), and four meteorological maximum wind speed methods (continuous, categorical (based on the Saffir-Simpson wind scale), and two binary (≥ 39 mph and ≥ 74 mph)) of maximum wind speed (Table 2.4). Each exposure method was first contrasted visually using ArcMap 10.0 (Redlands, CA) and descriptively by comparing the number of exposed counties and calculating percent differences.

To further contrast exposure methods we modeled hurricane exposure with several reproductive health indicators, including county preterm delivery and low birth weight rates. We used county-level Vital Statistics data obtained from the Florida Department of Health to calculate county specific rates of low birth weight and preterm delivery for women pregnant during the 2004 hurricane season.

We focused on reproductive health indicators as previous studies have shown pregnant women and fetuses may be disproportionality vulnerable to disruptions in health care, psychosocial stresses, and injury and mortality during hurricane exposure (2). Preterm delivery babies are live births born after 20 weeks completed gestation and before 37 weeks completed gestation. Low birth weight babies are live births born after 20 weeks completed gestation and weighing less than 2,500 grams (5.5 pounds) (133, 151).

We modeled county-level hurricane exposure and county-level preterm delivery and low birth weight rates using linear models. Both preterm delivery and low birth weight are indicators of poorer health; therefore, we hypothesized a positive association between increasing hurricane exposure and each reproductive health outcome. We calculated county-level rates using the mother's primary residence as indicated on Vital Statistics records. Exclusions included all Florida births where the mothers' primary residence was outside of Florida, as well as births <20 weeks completed gestation as these should not be recorded in Vital Statistics records and are not properly captured in birth records. Preterm delivery rates were calculated as the number of county preterm deliveries (births less than 37 weeks completed gestation) divided by the total number of Florida resident births multiplied by 100. Similarly, low birth weight rates were calculated as the number of county low birth weight births (births less than 2,500 grams) divided by the total number of Florida resident births multiplied by 100.

To adjust for county-level differences in both population and environmental characteristics, we applied the county-level Environmental Quality Index (EQI) developed by the Environmental Protection Agency (159). The EQI includes five environmental specific indices: air, water, land, built and sociodemographic, as well as an overall environmental domain (the EQI). We compared crude and adjusted estimates to adjust for potential confounding by social and environmental factors. All analyses were conducted in SAS 9.2 (Cary, NC). This research was approved by the Florida Department of Health Institutional Review Board (IRB) (#H13049) and the IRB of the University of North Carolina at Chapel Hill (#13-0784).

Results

Descriptive Results

Of the 67 Florida counties, the number of counties classified as exposed to hurricanes using each of the described methods (e.g., disaster declaration, buffer, and binary wind speed measures) is shown in Table S1 Each method yielded a different number of exposed counties. The disaster declaration method consistently assigned a higher number of counties exposure to hurricanes when compared to the four categorizations of maximum wind exposure. For example for Hurricane Ivan, the disaster declaration method identified 44 exposed counties, while other methods yield 11 counties or less, a 120% difference in exposed counties.

Table S.1 Number of counties exposed by exposure method and hurricane (n=67 total counties)

Exposure Method	Charley	Frances	Ivan	Jeanne	All 4 Hurricanes
Disaster Declaration	26	66	44	52	66
30 km buffer	16	19	1	27	38
60 km buffer	23	36	2	37	43
100 km buffer	32	47	2	47	47
Max Wind Speed[1] (continuous)	137 mph	102 mph	104 mph	106 mph	137 mph
Saffir-Simpson[2] (4 categories)	3	2	1	3	14
Wind Speed >=39 mph (binary)	26	54	11	35	63
Wind Speed >=74 mph (binary)	5	7	3	11	17

[1]For Maximum Wind Speed Exposure category, maximum wind speed over the 67 counties for each storm is displayed.
[2]For Saffir-Simpson 4 category, counties classified in the high category displayed in table.

The geographic spatial buffer exposure method yielded different results than either the disaster declaration method or the binary maximum wind speed exposure classifications. For all hurricanes except Hurricane Ivan, the 60 km and 100 km buffer identified a similar number of counties as the binary 39 mph wind speed categorization. For Hurricane Ivan, which affected only the far west panhandle of Florida, the number of counties exposed to both the 60 km and 100 km buffer was less than any of the other methods. Compared to the counties exposed using the dichotomous ≥ 74 mph maximum wind speed, there was a 138% difference in number of counties exposed. While the spatial buffer categorized a similar number of counties exposed as the binary wind speed methods, the heterogeneity across storms is shown, particularly for Hurricane Ivan.

Maps were generated to visually compare the number of counties designated as exposed using each exposure method. For example, Figures S1a and S1b show comparisons of Hurricane Ivan based on the 100 km buffer around Ivan's storm track which identifies 2 counties as exposed (Figure S1a) and the 4-category Saffir-Simpson categorization of exposure by maximum wind speed in the county (Figure S1b). Maps of Hurricanes Charley, Frances, and

Jeanne displayed similar graphical results (not shown). Overall, the number of counties categorized as exposed using the 100 km buffer and maximum wind exposure methods were similar, while the disaster declaration method designated more counties as exposed, including many that were away from the storm track, and areas of highest maximum wind speed.

Statistical Results: Preterm Delivery

Linear regression modeling was conducted to determine the association between each hurricane exposure method and county preterm delivery rates. Overall, the crude associations between hurricane exposure and preterm delivery were negative, indicating a decrease in preterm delivery rates with increasing hurricane exposure; however, the majority of these associations were not statistically significant. Results including model estimates for exposure and corresponding p-values for significance ($p<0.05$) for all analyses with exception to the 60 km spatial buffer are shown in Table S2 Results for the 60 km buffer were similar to the 100 km buffer estimates and were therefore excluded.

Models were adjusted for county-level environmental and socio-demographic characteristics using the EQI. In 30 of 40 models the addition of the EQI adjusted the model towards the expected direction (more positive association), indicating that a portion of the unexpected directionality may be due to county-level population differences. Overall, in adjusted models, the association between hurricane exposure and county preterm delivery rate was found to be negative, with the exception of Hurricane Ivan.

Associations between the disaster declaration method and preterm delivery rates were negative and non-significant across all adjusted models. The strongest negative estimates were seen in models of Hurricane Charley (-0.88, p=0.09). Hurricane Frances was the least significant in models of preterm delivery, with an adjusted estimate of -0.16 (p=0.94).

Spatial buffering methods had mixed results over hurricanes with some negatively associated significant results for Hurricane Charley (100 km: -1.67, p=0.002) and All Hurricanes (100 km: -0.42, p=0.04). Estimates over all three spatial buffer distances were positive for Hurricane Ivan although non-significant (30 km: 1.57 p=0.45; 60 km: 0.86 p=0.56; 100 km: 0.86 p=0.56).

Directionality and significance of results were highly variable using the maximum wind speed exposures. Unadjusted and adjusted models using continuous maximum wind speed were statistically significant for each hurricane; however, estimates were smaller in magnitude than in other models due to the continuous nature of the exposure data. Exposure to Hurricane Ivan using continuous wind speed was positively associated with preterm delivery (0.47, p= 0.29). Saffir-Simpson category models for the other three hurricanes were negatively associated (Charley: -0.64, p=0.05; Frances: -0.95, p=0.02; Jeanne: -0.91 p=0.003) Binary wind speeds of greater than or less than 79 mph (i.e. hurricane wind speed) were negatively associated with preterm delivery for Hurricane Jeanne (-1.60, p=0.02), Hurricane Ivan (-0.06, p= 0.96), and for All Hurricanes and (-1.42, p= 0.01)). Binary wind speeds greater than 39 mph (tropical storm wind speed were negatively associated with preterm delivery for Hurricanes Charley (-1.15, p= 0.03), Jeanne (-1.42, p=<0.001), and Frances (-1.34, p=0.03).

Across the eight potential exposure methods, the relationship between exposure and preterm delivery rates was unexpectedly negative for all hurricanes except Hurricane Ivan. Of all exposure methods, only the continuous measure of maximum hurricane wind speed of Hurricane Ivan was statistically significant and positively associated with preterm delivery (0.03, p=0.04). The continuous maximum wind speed exposure method yielded significant negative associations for the other three hurricanes. The association between the disaster declaration method of exposure classification and preterm delivery was inconsistent and non-significant across all hurricanes. Overall, none of the exposure methods were consistently associated with preterm delivery.

Statistical Results: Low Birth Weight

Additional linear models were constructed to determine the association between each method of assigning hurricane exposure and county rates of low birth weight. Similar to the analysis of preterm delivery rates, the overall association between hurricane exposure and low birth weight was negative, indicating a decrease in low birth weight rates with increasing hurricane exposure. The majority of these associations were not statistically significant. Results including model estimates for exposure and corresponding p-values for significance for all analyses are shown in Table 3.3.

After adjustment for environmental and socio-demographic characteristics using the EQI, 32 of 40 models had estimates adjusted towards the expected direction (more positive association). This indicates that a portion of the unexpected directionality may be due to county-level population differences. Overall, in most adjusted models the association between hurricane exposure and county low birth weight rate was found to be negative with exception to Hurricane Ivan.

Associations between the disaster declaration method and low birth weight rates were inconsistent and non-significant for Hurricanes Charley (-0.47, p=0.32), Jeanne (-0.21, p=0.70), Ivan (0.53, p=0.29), Frances (0.61, p=0.75) and all hurricanes (0.61, p=0.74). The spatial buffering methods also had inconsistent results over each hurricane and no statistically significant results. There was an increased rate of low birth weight in the counties exposed at the 30km buffer for Hurricanes Charley (0.03, p=0.95) and Ivan (1.48, p=0.43) and at the 100 km buffer for Hurricane Frances (0.14, p=0.78). Estimates over all three spatial buffer distances (30 km, 60 km, and 100 km) were similarly positive but not significant for Hurricane Ivan.

Unadjusted models using continuous maximum wind speed exposure were close to significant for each hurricane; however, in the adjusted models, they were no longer significant. The four category Saffir-Simpson exposure models were negatively associated with low birth weight for Hurricane Frances (-0.98, p= 0.007) and all hurricanes (0.35, p= 0.02). Adjusted estimates for binary hurricane wind speed (79 mph) and Hurricane Charley (0.03, p=0.97) and Ivan (0.35, p=0.75) were positively associated with low birth weight and while adjusted estimates for binary tropical storm wind speed (<39 mph) were negatively associated for Hurricane Frances (-1.68, p= 0.003) and all hurricanes (-2.37, p=0.01).

Across the eight exposure methods, the associations with low birth weight rates were mostly negative. Hurricane Ivan was the exception, with positive associations with low birth weight across all eight exposure methods; although none were statistically significant. Overall, none of the positive associations were statistically significant. Significant negative associations were found for Hurricane Frances when using both the four category maximum wind speed method and the binary > 34 wind speed method (-0.98 p=0.007 and -1.68, 0.003 respectively).

<u>Discussion</u>

Descriptive analysis and mapping of three different exposure methods – FEMA disaster declaration, spatial data based on storm trajectory, and meteorological severity of wind speed – displayed clear heterogeneity of exposure assignment. The number of counties classified as exposed varied greatly between methods, with the largest margin of difference for Hurricane Ivan, which impacted the far western Florida panhandle. The disaster declaration method consistently assigned a higher number of counties as exposed to hurricanes when compared to other exposure methods, supporting the assertion that the use of this method, developed for providing federal assistance to affected jurisdiction, likely over assigns county-level hurricane exposure. We found no statistically significant associations between counties designated as exposed using the disaster declaration method and reproductive health outcomes. While this could be due to heterogeneity of exposure and limited statistical power, consistent null findings support our hypothesis of exposure misclassification.

Using disaster declarations to classify exposure to disaster may over-represent exposed areas since declarations are not intended for research use, but rather for the provision of assistance. If the disaster declaration method is misclassifying counties as exposed that do not have a high enough exposure to cause health effects, this would be considered exposure misclassification. We would expect potential misclassification to mask the health effects of hurricane exposure by assigning some less exposed populations as exposed, biasing results towards the null. Given the descriptive and statistical findings, we feel that there is fairly clear evidence that counties that are not as severely exposed are being assigned exposure, therefore yielding findings biased towards the null.

The spatial hurricane track with symmetrical buffer exposure method had more similar results to our maximum wind speed exposure method. Descriptively, maps of each storm showed that a similar number of counties were exposed. For example, exposure was similar for the 60 mph buffer and the binary 39 mph (tropical storm) wind speed. A major difference between the two methods was the exposure status of counties located to the upper right side of each storm track, where the maximum wind speed method identified much higher exposure than to the left of the storm track. Symmetrical buffers cannot account for the rotation and pattern of hurricane winds. These differences were not supported by the statistical analysis, the vast majority of which were non-significant. For example, in the birth weight analysis, positive non-significant associations were found between the spatial analysis and Hurricanes Ivan and Frances, whose track was up Florida's west coast. For these two storms in particular, the spatial method may suggest an association if we had more statistical power.

The spatial buffer method takes into account the difference between areas closer to and farther from the storm track; however, it neglects the fact that hurricane force (and damage) is generally not symmetrical around the storm track. The maximum weather effects of a hurricane are usually felt within the right-front quadrant, often the northeast corner of the hurricane, where winds are usually strongest, storm surge is highest, and the possibility of tornadoes is greatest (4). Therefore, the use of a symmetrical buffer around the storm track could misclassify counties in the left-lower quadrant of the storm as exposed when exposure is actually greater in counties in the right-front quadrant. Also, each storm is unique in terms of both severity and size, so employing the same buffer over multiple storm systems may lead to exposure misclassification due to the expected natural variation in hurricane size and strength.

While one of the strengths of the spatial method is that it can take into account the areas potentially affected by more severe hurricane weather on one side of the track, another possibility is that this method may effectively be estimating predicted impact or perceived stress. We would expect individuals along the storm track to have prior knowledge of the cone of the storm due to improvements in meteorological modeling and forecasting. These individuals may be exposed to the stress effects of a hurricane, but may not actually suffer damages or loss of infrastructure. Several studies have shown that pregnant women with high (generally self-reported) stress and anxiety levels are at an increased risk for many poor pregnancy outcomes including spontaneous abortion, preterm labor, and low birth weight (55, 56, 62). In studies specific to researching hurricane-related perceived stress and predicted knowledge of storm, the symmetrical spatial buffer may be adequately addressing this question.

Of the four categorizations of maximum wind speed, none appeared to perform superiorly and in most cases the direction of effect in modeling was unexpected. Statistical significance was most often achieved using a continuous measure of maximum wind exposure, but this is likely due to higher statistical power. A limitation of the meteorological data was that wind speeds under 25 mph were imputed as 0 mph. This would imply that categorical measures would likely be more accurate than the continuous measure. This imputation for continuous models would likely have little effect for a storm like Charley, which only had two counties with a maximum wind speed of 0 mph, but may have inflated results for the other three storms. Of the categorical methods, the four category Saffir-Simpson method shows the most graphical exposure contrasts but in statistical testing the low power of 67 counties may have influenced statistical significance. Results of the two binary cut points for maximum wind speed appeared to be very storm dependent. This would make sense given that the number of counties affected by very high wind speeds was relatively low with exception to counties affected by Hurricane Charley.

We adjusted for environmental and sociodemographic county-level characteristics using the EPA developed EQI. While both the crude and adjusted associations in the majority of models were negative, the EQI adjusted models were towards the expected positive direction. These adjustments may indicate that a portion if not all of the unexpected directionality may be due to county-level population differences. The EQI may be adjusting out some effects; however, many population characteristics as well as pregnancy characteristics were not controlled for in these models.

To attempt to better control for baseline population characteristics, we performed a supplemental difference-in-difference analysis, holding population characteristics constant and analyzing change in preterm delivery and low birth weight from 2003 to 2004. Since no hurricanes made landfall in Florida in 2003, this is an ideal baseline to control for static county-level nuisance population variables. In this analysis, the majority of maximum wind speed models of both preterm delivery and low birth weight were positively associated with Hurricane Frances and Jeanne. The association with Hurricane Ivan was no longer positive and Hurricane Charley had mixed results depending on method; however, these results similarly to the EQI adjusted results were mostly statistically non-significant. While these results do not change our reported results based on exposure methods, they do indicate that more confounding control should be conducted in order to properly estimate the association between hurricane exposure and our health outcomes. The EQI uses many sources of available county-level sociodemographic and environmental variables for confounding control.

We did consider some additional meteorological models to define hurricane exposure (141). In our analysis, we choose county-level specificity in order to reduce potential misclassification of more finite geographic units and consistency with the currently described methods. One limitation of this geographic level is the range of Florida county sizes, which vary from 240 to 2034 square miles (188); however, smaller geographic areas (e.g. zip code, census block) also vary in size at approximately the same relative magnitude. It may also be harder to obtain wind speed meteorological data at these smaller geographies. Another alternative could be to apply both wind speed and precipitation or flooding to better understand the meteorological effects. We explored several sources of data for precipitation measures including digitizing images of rainfall associated to hurricanes produced by NOAA. This data was not available for hurricanes before 2005 but should be considered as an additional meteorological component for future analysis.

Conclusions

Decisions on which method is most appropriate to use when assigning hurricane exposure should be dependent on the question and scope of the research. For increased comparability between studies, a more objective, quantitative method of exposure may be preferred over the less specific assignment of disaster exposure like the FEMA disaster declaration. While hurricane exposure and reproductive health has been studied, the heterogeneity of exposure methods makes comparability across geographic areas and individual storms difficult. The use of heterogeneous methods of assigning exposure in the current literature may also be contributing to the overall inconsistency of results in the current disaster and public health literature.

As populations continue moving toward coastal regions and storms intensify, the need to understand the effect that hurricane exposure may have on health is growing. Studies after major hurricanes in the US like Andrew, Katrina, and Sandy have demonstrated the potential lasting health impacts on vulnerable populations such as women pregnant during the storm. It will be difficult to more fully understand the impact of hurricanes and other disasters on reproductive health until exposure methods are more comparable so that the impacts of hurricanes can be more clearly understood. Meteorological wind speed modeling provides a new and reproducible approach to better characterize hurricane exposure and its effect on health.

Table S.2a Hurricane exposure by declaration and spatial buffer and preterm delivery crude and adjusted rate linear models for all Florida counties (n= 67 counties)[1]

Hurricane Model		Declaration		30 km		60km		100 km	
		Est	**p-val**	**Est**	**p-val**	**Est**	**p-val**	**Est**	**p-val**
Charley	Crude	-1.10	0.04	-1.32	0.03	-1.65	0.01	-1.95	<0.001
	Adjusted	-0.88	0.09	-0.90	0.14	-1.27	0.04	-1.67	0.002
Jeanne	Crude	-1.02	0.10	-0.40	0.45	-0.49	0.39	-0.49	0.39
	Adjusted	-0.85	0.16	-0.64	0.22	-0.48	0.38	-0.48	0.38
Ivan	Crude	-0.12	0.85	0.97	0.65	0.97	0.65	0.34	0.83
	Adjusted	0.48	0.40	1.57	0.45	1.57	0.45	0.86	0.56
Frances	Crude	-0.87	0.69	-0.85	0.14	-0.30	0.63	-0.12	0.83
	Adjusted	-0.16	0.94	-0.7	0.21	-0.23	0.72	-0.45	0.43
All Hurricanes	Crude	-0.87	0.69	-0.48	0.08	-0.55	0.05	-0.47	0.02
	Adjusted	-0.16	0.94	-0.48	0.06	-0.53	0.07	-0.42	0.04

[1]Adjusted models used the EQI to control for county-level environmental and socio-demographic characteristics.

Table S.2b Hurricane exposure by maximum wind speed method and preterm delivery crude and adjusted rate linear models for all Florida counties (n= 67 counties)[1]

Hurricane Model		Max MPH		Saffir-Simpson		Binary >79		Binary >34	
		Est	**p-val**	**Est**	**p-val**	**Est**	**p-val**	**Est**	**p-val**
Charley	Crude	-0.03	0.00	-0.76	0.03	-0.94	0.35	-1.4	0.007
	Adjusted	-0.02	0.01	-0.64	0.05	-0.78	0.42	-1.15	0.03
Jeanne	Crude	-0.03	<0.001	-1.08	<0.001	-1.75	0.01	-1.75	<0.001
	Adjusted	-0.03	0.01	-0.91	0.003	-1.6	0.02	-1.42	<0.001
Ivan	Crude	0.02	0.03	0.45	0.33	-0.54	0.67	1.12	0.11
	Adjusted	0.02	0.04	0.47	0.29	-0.06	0.96	0.96	0.16
Frances	Crude	-0.05	0.00	-1.15	0.4	-1.48	0.08	-1.51	0.02
	Adjusted	-0.04	0.01	-0.95	0.02	-0.98	0.25	-1.34	0.03
All Hurricanes	Crude	-0.02	<0.001	-0.58	<0.001	-1.62	0.006	-2.18	0.05
	Adjusted	-0.02	0.005	-0.5	0.002	-1.42	0.01	-1.72	0.11

[1]Adjusted models used the EQI to control for county-level environmental and socio-demographic characteristics.

Table S.3a Hurricane exposure by declaration and spatial buffer and low birth weight rate crude and adjusted linear models for all Florida counties(n= 67 counties)[1]

Hurricane Model		Declaration		30km		60km		100km	
		Est	**p-val**	**Est**	**p-val**	**Est**	**p-val**	**Est**	**p-val**
Charley	Crude	-0.62	0.19	-0.31	0.57	-1.16	0.008	-1.13	0.01
	Adjusted	-0.47	0.32	0.03	0.95	-0.98	0.05	-0.90	0.06
Jeanne	Crude	-0.33	0.56	-0.1	0.83	-0.19	0.78	-0.10	0.84
	Adjusted	-0.21	0.7	-0.26	0.58	-0.11	0.80	-0.09	0.86
Ivan	Crude	0.11	0.82	1.08	0.57	1.08	0.57	0.28	0.84
	Adjusted	0.53	0.29	1.48	0.43	1.48	0.43	0.64	0.63
Frances	Crude	0.12	0.95	-0.26	0.62	0.21	0.67	0.34	0.50
	Adjusted	0.61	0.75	-0.15	0.76	0.04	0.80	0.14	0.78
All Hurricanes	Crude	0.12	0.95	-0.1	0.67	-0.15	0.39	-0.17	0.37
	Adjusted	0.61	0.74	-0.08	0.75	-0.10	0.50	-0.13	0.47

[1]Adjusted models used the EQI to control for county-level environmental and socio-demographic characteristics.

Table S.3b Hurricane exposure by maximum wind speed method and low birth weight rate crude and adjusted linear models for all Florida counties(n= 67 counties)[1]

Hurricane Model		Max MPH		Saffir-Simpson		Binary >79		Binary >34	
		Est	**p-val**	**Est**	**p-val**	**Est**	**p-val**	**Est**	**p-val**
Charley	Crude	-0.02	0.05	-0.36	0.30	-0.08	0.93	-0.9	0.06
	Adjusted	-0.01	0.14	-0.27	0.37	0.03	0.97	-0.73	0.12
Jeanne	Crude	-0.02	0.02	-0.69	0.01	-0.93	0.14	-1.16	0.01
	Adjusted	-0.02	0.06	-0.56	0.05	-0.82	0.18	-0.94	0.06
Ivan	Crude	0.02	0.06	0.18	0.66	0.02	0.98	0.3	0.63
	Adjusted	0.02	0.09	0.19	0.63	0.35	0.75	0.19	0.76
Frances	Crude	-0.03	0.03	-1.1	0.002	-1.1	0.14	-1.78	0.002
	Adjusted	-0.02	0.11	-0.98	0.007	-0.77	0.31	-1.68	0.003
All Hurricanes	Crude	-0.01	0.03	-0.41	0.03	-0.6	0.26	-2.64	0.005
	Adjusted	-0.007	0.12	-0.35	0.02	-0.46	0.38	-2.37	0.01

[1]Adjusted models used the EQI to control for county-level environmental and socio-demographic characteristics.

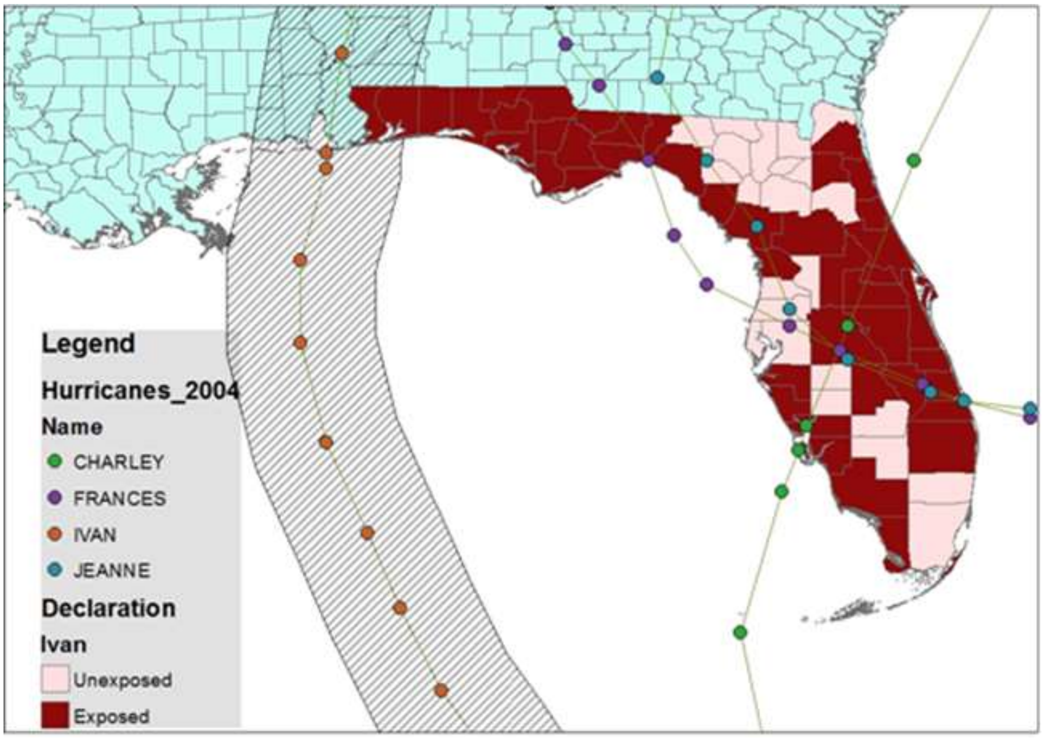

Figure S.1a 2004 Florida hurricane tracks with 100 km buffer and declaration shown for Hurricane Ivan

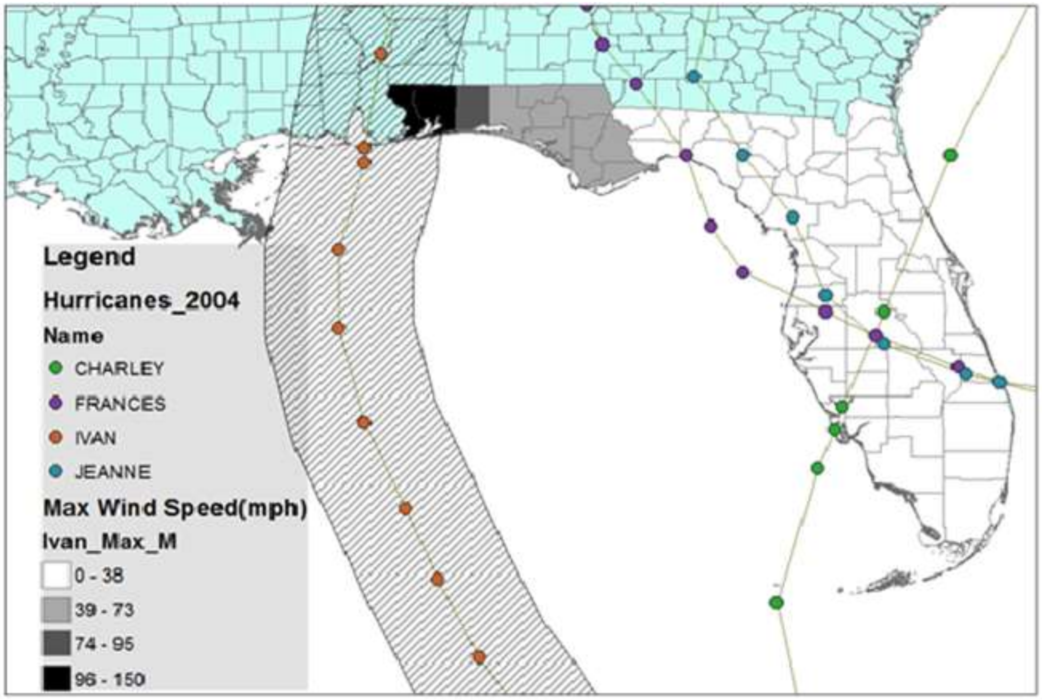

Figure S.1b 2004 Florida hurricane tracks with 100 km buffer and 4 category maximum wind speed for Hurricane Ivan

APPENDIX B: SUPPLEMENTAL TABLES

Table S.4 Comparison of the 2003 and 2004 Florida birth record covariate distribution

Covariates		Unexposed (2003) N (%[1])	Exposed (2004) N (%[1])
Maternal Age			
	<18	5,627 (2.9)	5,272 (2.8)
	18-24	63,431 (32.6)	61,554 (32.8)
	25-34	95,845 (49.3)	92,800 (49.4)
	35-44	29,409 (15.1)	28,204 (15.0)
	Missing	313	245
Maternal Race			
	White	139,977 (72.0)	123,149 (65.6)
	Black	42,605 (21.9)	40,835 (21.8)
	Other	11,707 (6.0)	23,775 (12.7)
	Missing	336	316
Maternal Hispanic Ethnicity			
	Yes	29,336 (30.2)	58,206 (31.2)
	No	67,747 (70.8)	128,204 (68.8)
	Unknown/Missing	97,542	1,665
Maternal Education			
	< High School (0-11)	24,386 (19.3)	37,990 (20.4)
	High School Degree (12)	43,352 (34.3)	59,530 (32.0)
	Some College or Degree (13-16)	47,655 (37.7)	77,115 (41.4)
	Graduate Degree (17)	10,957 (8.7)	11,471 (6.2)
	Unknown/Missing	68,275	1,969
Maternal Marital Status			
	Married	118,598 (61.5)	111,525 (59.7)
	Not Married	74,362 (38.5)	75,218 (40.3)
	Other	5 (0.00)	10 (0.01)
	Unknown/Missing	1,660	1,322
Child Sex			
	Female	95,087 (48.8)	91,868 (48.9)
	Male	99,524 (51.2)	96,197 (51.1)
	Unknown	14	10
Gestational Age			
	20-24	1,070 (0.6)	737 (0.4)
	25-30	2,647 (1.4)	2,053 (1.1)
	31-36	21,434 (11.0)	20,039 (10.7)
	37-40	147,276 (75.7)	143,529 (76.3)
	41-44	22,198 (11.4)	21,717 (11.6)
Birth Weight			
	<1000 grams	2,040 (1.1)	1,441 (0.9)
	1000-1999 grams	4,750 (2.4)	4,132 (2.5)
	2000-2999 grams	46,587 (24.0)	22,689 (13.7)
	3000-3999 grams	126,990 (65.3)	124,097 (74.0)
	>4000 grams	14,123 (7.3)	13,636 (8.2)
	Missing/Unknown	135	80 (0.0)
Plurality			
	1	183,991 (96.9)	181,727 (97.1)
	2	5,571 (2.9)	5,159 (2.8)
	3	262 (0.1)	219 (0.1)
	4+	10 (0.01)	10 (0.01)
	Missing/Unknown	4,789	960
Prenatal Care			

	Yes	63,062 (98.9)	174,191(98.7)
	No	715 (1.1)	2,343(1.3)
	Missing/Unknown	130,848	11,541
Alcohol use			
	Yes	765 (0.9)	503(0.3)
	No	89,075 (99.1)	185,588(99.7)
	Missing/Unknown	4,985	1,984

[1] Percentage calculation excludes missing/unknown data.

Table S.5 Description of available covariates from vital statistics records considered for confounding and modification in preterm delivery Aim 2 analysis**.**

Covariate from Vital Records	Potential Confounder	Potential Modifier	Notes
Marital status	X	X	Indicator of Social Support
Maternal education	X	X	Part of SES
Maternal Hispanic ethnicity		X	
Maternal race		X	
Paternal education	X	X	Possibly high number of missing
Paternal Hispanic ethnicity		X	Possibly high number of missing
Paternal race		X	Possibly high number of missing
Place where birth occurred(hospital/birthing center)		X	
Date of first prenatal care	X		Prenatal Care should be a time varying covariate
Total number of prenatal visits	X		
Did mother receive WIC	X	X	Part of SES
Cigarette smoking before/during	X	X	
Date of last live birth(spacing)	X		
Gestational diabetes	X		
Pre-pregnancy diabetes	X		
Gestational hypertension	X		
Pre-pregnancy hypertension	X		
Pregnancy from fertility treatment	X		
Infection during this pregnancy	X		
PROM		X	Stratify on methods of preterm, possible consideration
Induced labor		X	Stratify on methods of preterm, possible consideration
Augmentation of labor		X	Stratify on methods of preterm, possible consideration
Delivery method		X	Possible consideration
Birth weight	X	X	Birth weight related to gestational age, need to consider
Sex infant		X	

Table S.6 Florida 2004 adjusted beta of Hurricane Charley wind exposure on very preterm (<32 weeks) and preterm (<37 weeks) delivery with interaction by subsequent Hurricane Frances exposure.

			Outcome							
			<32 weeks				<37 weeks			
			Beta	(95% CI)		p-value	Beta	(95% CI)		p-value
Wind Speed Exposure	*Hurricane*	*Model Description*								
≥39 mph										
	Hurricane 2. Charley*Frances									
		Main Effect	-0.10	(-0.16	-0.04)		0.06	0.04	0.08	
		Previous Hurricane	0.09	(0.01	0.17)		-0.09	-0.13	-0.05	
		Interaction	0.03	(-0.07	0.13)	0.36	-0.03	-0.07	0.01	0.20
≥74 mph										
	Hurricane 2. Charley* Frances									
		Main Effect	0.09	(-0.01	0.19)		0.01	-0.03	0.05	
		Previous Hurricane	0.28	(0.16	0.40)		0.07	0.03	0.11	
		Interaction	-0.26	(-0.61	0.09)	0.18	-0.02	-0.16	0.12	0.79

[1] Adjusted for gestational diabetes, maternal age, maternal race, maternal ethnicity, maternal education, maternal pregnancy tobacco use

Table S.7 Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of hurricane wind exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery for each 2004 hurricane

			Outcome			
			<32 weeks		<37 weeks	
			HR	(95% CI)	HR	(95% CI)
Wind Speed Exposure	*Hurricane*	*Model Description*				
≥ 39 mph						
	Charley					
		1a. Unadjusted	1.12	(1.06 1.19)	1.05	(1.02 1.07)
		1b. Adjusted	1.09	(1.03 1.16)	0.99	(0.96 1.01)
	Frances					
		2a.Unadjusted	1.19	(1.14 1.24)	1.02	(1.00 1.04)
		2b. Adjusted	1.11	(1.05 1.17)	0.90	(0.89 0.92)
	Ivan					
		3a. Unadjusted	1.28	(1.12 1.46)	1.12	(1.06 1.19)
		3b. Adjusted	1.29	(1.12 1.49)	1.12	(1.05 1.19)
	Jeanne					
		4a. Unadjusted	1.17	(1.12 1.23)	1.04	(1.02 1.06)
		4b. Adjusted	1.12	(1.06 1.18)	0.95	(0.93 0.97)
≥ 74 mph						
	Charley					
		5a. Unadjusted	1.18	(1.04 1.35)	1.07	(1.01 1.13)
		5b. Adjusted	1.21	(1.06 1.38)	1.06	(1.00 1.12)
	Frances					
		6a. Unadjusted	1.29	(1.17 1.43)	1.09	(1.05 1.14)
		6b. Adjusted	1.30	(1.17 1.44)	1.07	(1.02 1.12)
	Ivan					
		7a. Unadjusted	1.16	(0.98 1.37)	1.05	(0.98 1.13)
		7b. Adjusted	1.20	(1.01 1.43)	1.06	(0.98 1.13)
	Jeanne					
		8a. Unadjusted	1.21	(1.10 1.32)	1.06	(1.02 1.11)
		8b. Adjusted	1.21	(1.10 1.33)	1.04	(1.00 1.08)

[1] Adjusted for gestational diabetes, maternal age, maternal race, maternal ethnicity, maternal education, and maternal pregnancy tobacco use.

Table S.8a Florida 2004 unadjusted and adjusted[1] Hazard Ratio(HR) of Hurricane Charley and Frances ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including Interaction by race

			Hurricane Charley Exposure				**Hurricane Frances Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	White	unexposed	ref				Ref			
		exposed	1.26	(1.08	1.47)	n/a	1.12	(1.05	1.21)	n/a
	Black	unexposed	2.05	(1.93	2.19)		1.53	(1.49	1.58)	
		exposed	2.58	(2.17	3.08)	0.19	1.72	(1.59	1.87)	0.74
	Other[1]	unexposed	1.11	(0.97	1.29)		1.18	(1.12	1.25)	
		exposed	1.40	(1.13	1.74)	0.63	1.33	(1.21	1.46)	0.88
<37 weeks										
	White	unexposed	ref				Ref			
		exposed	1.08	(1.01	1.15)	n/a	1.06	(1.01	1.12)	n/a
	Black	unexposed	1.53	(1.49	1.58)		1.53	(1.49	1.57)	
		exposed	1.65	(1.54	1.78)	0.26	1.62	(1.52	1.73)	0.53
	Other[1]	unexposed	1.17	(1.11	1.24)		1.17	(1.11	1.24)	
		exposed	1.27	(1.16	1.38)	0.19	1.25	(1.15	1.35)	0.67

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.8b Florida 2004 unadjusted and adjusted[1] Hazard Ratio(HR) of Hurricane Ivan and Jeanne ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including Interaction by race

			Hurricane Ivan Exposure				**Hurricane Jeanne Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	White	unexposed	ref				ref			
		exposed	1.13	(0.90	1.42)	n/a	0.91	(0.89	0.93)	n/a
	Black	unexposed	2.05	(1.93	2.18)		1.56	(1.51	1.61)	
		exposed	2.31	(1.82	2.95)	0.18	1.42	(1.35	1.49)	0.06
	Other[1]	unexposed	1.11	(0.97	1.28)		1.18	(1.11	1.26)	
		exposed	1.25	(0.96	1.65)	0.65	1.08	(1.00	1.16)	0.58
<37 weeks										
	White	unexposed	ref				ref			
		exposed	1.04	(0.95	1.14)	n/a	1.15	(1.02	1.30)	n/a
	Black	unexposed	1.54	(1.49	1.58)		2.04	(1.92	2.17)	
		exposed	1.59	(1.45	1.75)	0.87	2.35	(2.03	2.71)	0.07
	Other[1]	unexposed	1.18	(1.12	1.24)		1.11	(0.97	1.28)	
		exposed	1.23	(1.10	1.36)	0.26	1.28	(1.06	1.55)	0.45

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.9a Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Charley and Frances ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by Hispanic ethnicity

			Hurricane Charley Exposure				**Hurricane Frances Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.13	(0.95	1.33)	n/a	1.29	(1.13	1.46)	n/a
	Hispanic	unexposed	1.00	(0.94	1.07)		1.02	(0.95	1.08)	
		exposed	1.12	(0.93	1.35)	0.34	1.31	(1.12	1.52)	0.76
<37 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.03	(0.97	1.11)	n/a	1.09	(1.02	1.14)	n/a
	Hispanic	unexposed	1.00	(0.98	1.03)		1.00	(0.98	1.03)	
		exposed	1.04	(0.96	1.12)	0.32	1.09	(1.02	1.16)	0.04

Abbreviation: p-val, p-value for interaction; ref, referent

Table S9b Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Ivan and Jeanne ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by Hispanic ethnicity

			Hurricane Ivan Exposure				**Hurricane Jeanne Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.20	(1.00	1.44)	n/a	0.90	(0.88	0.92)	n/a
	Hispanic	unexposed	1.02	(0.96	1.08)		1.02	(0.99	1.06)	
		exposed	1.22	(1.00	1.49)	0.97	0.92	(0.88	0.97)	0.63
<37 weeks										
	Non-Hispanic	unexposed	ref	ref				ref		
		exposed	1.06	(0.98	1.15)	n/a	1.23	(1.09	1.37)	n/a
	Hispanic	unexposed	1.00	(0.98	1.03)		1.03	(0.96	1.09)	
		exposed	1.06	(0.98	1.16)	0.61	1.26	(1.10	1.44)	0.76

Abbreviation: p-val, p-value for interaction; ref, referent

Table S.10a Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Charley and Frances ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by race/ ethnicity

			Hurricane Charley Exposure			**Hurricane Frances Exposure**		
Outcome	**Race/ Ethnicity**		HR	95% CI	p-val	HR	95% CI	p-val
<32 weeks								
	White Non-Hispanic	unexposed	ref			Ref		
		exposed	1.21	(0.98 1.48)	n/a	1.20	(1.01 1.42)	n/a
	White Hispanic	unexposed	1.06	(0.98 1.15)		1.08	(1.00 1.17)	
		exposed	1.28	(1.02 1.61)	0.50	1.29	(1.06 1.58)	0.57
	Asian/Pacific Islander	unexposed	1.11	(0.90 1.37)		1.15	(0.94 1.41)	
		exposed	1.34	(1.00 1.81)	0.71	1.38	(1.04 1.81)	0.70
	Other/Multi Racial	unexposed	1.16	(0.94 1.42)		1.18	(0.97 1.44)	
		exposed	1.40	(1.04 1.88)	0.43	1.41	(1.08 1.86)	0.81
	American Indian	unexposed	1.50	(0.93 2.43)		1.69	(1.05 2.73)	
		exposed	1.82	(1.07 3.07)	0.88	2.02	(1.21 3.38)	0.47
	Black Non-Hispanic	unexposed	2.16	(2.00 2.32)		2.18	(2.02 2.34)	
		exposed	2.60	(2.07 3.26)	0.17	2.60	(2.13 3.18)	0.11
	Black Hispanic	unexposed	1.88	(1.66 2.14)		1.89	(1.66 2.15)	
		exposed	2.27	(1.77 2.91)	0.44	2.26	(1.81 2.84)	0.25
<37 weeks								
	White Non-Hispanic	unexposed	ref			Ref		
		exposed	1.09	(1.00 1.18)	n/a	1.06	(0.99 1.13)	n/a
	White Hispanic	unexposed	1.20	(1.02 1.42)		1.18	(1.00 1.38)	
		exposed	1.31	(1.08 1.57)	0.81	1.24	(1.04 1.48)	0.78
	Asian/Pacific Islander	unexposed	1.20	(1.11 1.30)		1.21	(1.12 1.31)	
		exposed	1.30	(1.16 1.46)	0.99	1.28	(1.15 1.42)	0.96
	Other/Multi Racial	unexposed	1.22	(1.11 1.34)		1.20	(1.09 1.32)	
		exposed	1.32	(1.17 1.50)	0.15	1.27	(1.13 1.43)	0.63
	American Indian	unexposed	1.42	(1.16 1.75)		1.46	(1.17 1.81)	
		exposed	1.55	(1.24 1.93)	0.67	1.54	(1.22 1.93)	0.23
	Black Non-Hispanic	unexposed	1.62	(1.57 1.68)		1.61	(1.56 1.67)	
		exposed	1.76	(1.61 1.93)	0.18	1.71	(1.58 1.85)	0.17
	Black Hispanic	unexposed	1.52	(1.28 1.81)		1.52	(1.28 1.79)	
		exposed	1.66	(1.37 2.01)	0.22	1.60	(1.33 1.92)	0.73

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.10b Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Ivan and Jeanne ≥74 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by race/ ethnicity

			Hurricane Ivan Exposure			**Hurricane Jeanne Exposure**		
Outcome	**Race/ Ethnicity**		HR	95% CI	p-val	HR	95% CI	p-val
<32 weeks								
	White Non-Hispanic	unexposed	ref			ref		
		exposed	1.09	(0.85 1.41)	n/a	1.16	(0.99 1.35)	n/a
	White Hispanic	unexposed	1.07	(0.99 1.15)		1.08	(1.00 1.17)	
		exposed	1.17	(0.89 1.54)	0.45	1.25	(1.04 1.50)	0.93
	Asian/Pacific Islander	unexposed	1.14	(0.94 1.39)		1.14	(0.93 1.39)	
		exposed	1.25	(0.90 1.73)	0.48	1.31	(1.01 1.70)	0.29
	Other/Multi Racial	unexposed	1.14	(0.94 1.39)		1.13	(0.93 1.38)	
		exposed	1.25	(0.90 1.74)	0.28	1.31	(1.01 1.69)	0.90
	American Indian	unexposed	1.32	(0.81 2.16)		1.62	(1.01 2.62)	
		exposed	1.45	(0.83 2.53)	0.04	1.88	(1.13 3.11)	0.37
	Black Non-Hispanic	unexposed	2.15	(2.00 2.30)		2.14	(2.00 2.30)	
		exposed	2.35	(1.79 3.09)	0.35	2.48	(2.07 2.97)	0.10
	Black Hispanic	unexposed	1.94	(1.72 2.19)		1.93	(1.71 2.19)	
		exposed	2.12	(1.59 2.84)	0.88	2.23	(1.82 2.75)	0.41
<37 weeks								
	White Non-Hispanic	unexposed	ref			ref		
		exposed	1.06	(0.96 1.17)	n/a	1.03	(0.97 1.10)	n/a
	White Hispanic	unexposed	1.16	(1.00 1.36)		1.18	(1.01 1.38)	
		exposed	1.23	(1.02 1.49)	0.68	1.22	(1.03 1.44)	0.71
	Asian/Pacific Islander	unexposed	1.22	(1.13 1.31)		1.21	(1.12 1.30)	
		exposed	1.29	(1.14 1.46)	0.45	1.25	(1.13 1.38)	0.57
	Other/Multi Racial	unexposed	1.21	(1.10 1.32)		1.21	(1.11 1.33)	
		exposed	1.28	(1.12 1.46)	0.70	1.25	(1.12 1.40)	0.38
	American Indian	unexposed	1.39	(1.14 1.70)		1.44	(1.17 1.78)	
		exposed	1.47	(1.18 1.85)	0.12	1.49	(1.19 1.86)	0.68
	Black Non-Hispanic	unexposed	1.62	(1.57 1.67)		1.61	(1.56 1.66)	
		exposed	1.72	(1.55 1.91)	0.67	1.66	(1.55 1.79)	0.36
	Black Hispanic	unexposed	1.50	(1.28 1.77)		1.55	(1.31 1.82)	
		exposed	1.59	(1.31 1.93)	0.50	1.60	(1.34 1.91)	0.55

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.11a Florida 2004 unadjusted and adjusted[1] Hazard Ratio(HR) of Hurricane Charley and Frances ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including Interaction by race

			Hurricane Charley Exposure			**Hurricane Frances Exposure**		
Outcome	**Race**		HR	95% CI	p-val	HR	95% CI	p-val
<32 weeks								
	White	unexposed	ref			ref		
		exposed	1.21	(0.98 1.48)	n/a	1.20	(1.01 1.42)	n/a
	Black	unexposed	1.06	(0.98 1.15)		1.08	(1.00 1.17)	
		exposed	1.28	(1.02 1.61)	0.50	1.29	(1.06 1.58)	0.57
	Other[1]	unexposed	1.11	(0.90 1.37)		1.15	(0.94 1.41)	
		exposed	1.09	(1.00 1.18)	0.48	1.06	(0.99 1.13)	0.68
<37 weeks								
	White	unexposed	ref			ref		
		exposed	1.09	(1.00 1.18)	n/a	1.06	(0.99 1.13)	n/a
	Black	unexposed	1.20	(1.02 1.42)		1.18	(1.00 1.38)	
		exposed	1.31	(1.08 1.57)	0.81	1.24	(1.04 1.48)	0.78
	Other[1]	unexposed	1.20	(1.11 1.30)		1.21	(1.12 1.31)	
		exposed	1.30	(1.16 1.46)	0.99	1.28	(1.15 1.42)	0.96

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.11b Florida 2004 unadjusted and adjusted[1] Hazard Ratio(HR) of Hurricane Ivan and Jeanne ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including Interaction by race

			Hurricane Ivan Exposure			Hurricane Jeanne Exposure		
Outcome	**Race**		HR	95% CI	p-val	HR	95% CI	p-val
<32 weeks								
	White	unexposed	ref			ref		
		exposed	1.09	(0.85 1.41)	n/a	1.16	(0.99 1.35)	n/a
	Black	unexposed	1.07	(0.99 1.15)		1.08	(1.00 1.17)	
		exposed	1.17	(0.89 1.54)	0.45	1.25	(1.04 1.50)	0.93
	Other[1]	unexposed	1.14	(0.94 1.39)		1.14	(0.93 1.39)	
		exposed	1.06	(0.96 1.17)	0.78	1.03	(0.97 1.10)	0.09
<37 weeks								
	White	unexposed	ref			ref		
		exposed	1.06	(0.96 1.17)	n/a	1.03	(0.97 1.10)	n/a
	Black	unexposed	1.16	(1.00 1.36)		1.18	(1.01 1.38)	
		exposed	1.23	(1.02 1.49)	0.68	1.22	(1.03 1.44)	0.71
	Other[1]	unexposed	1.22	(1.13 1.31)		1.21	(1.12 1.30)	
		exposed	1.29	(1.14 1.46)	0.45	1.25	(1.13 1.38)	0.57

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.12a Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Charley and Frances ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by hispanic ethnicity

			Hurricane Charley Exposure				**Hurricane Frances Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.04	(0.96	1.12)	n/a	1.06	(1.00	1.13)	n/a
	Hispanic	unexposed	1.00	(0.93	1.07)		0.97	(0.90	1.05)	
		exposed	1.03	(0.92	1.16)	0.23	1.04	(0.93	1.16)	0.31
<37 weeks										
	Non-Hispanic	unexposed	ref	ref						
		exposed	0.99	(0.96	1.02)	n/a	0.90	(0.88	0.92)	n/a
	Hispanic	unexposed	1.05	(1.02	1.08)		1.02	(0.99	1.06)	
		exposed	1.04	(0.99	1.09)	0.83	0.92	(0.88	0.97)	0.63

Abbreviation: p-val, p-value for interaction; ref, referent

Table S.12b Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Ivan and Jeanne ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by hispanic ethnicity

			Hurricane Ivan Exposure				**Hurricane Jeanne Exposure**			
Outcome	**Race**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.30	(1.12	1.51)	n/a	1.07	(1.00	1.14)	n/a
	Hispanic	unexposed	1.02	(0.95	1.08)		0.98	(0.91	1.06)	
		exposed	1.32	(1.11	1.56)	0.85	1.05	(0.94	1.17)	0.23
<37 weeks										
	Non-Hispanic	unexposed	ref				ref			
		exposed	1.13	(1.06	1.20)	n/a	0.96	(0.93	0.98)	n/a
	Hispanic	unexposed	1.00	(0.97	1.03)		1.05	(1.02	1.08)	
		exposed	1.13	(1.05	1.21)	0.26	1.01	(0.96	1.05)	0.33

Abbreviation: p-val, p-value for interaction; ref, referent

Table S.13a Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Charley and Frances ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by race/ ethnicity

			Hurricane Charley Exposure				**Hurricane Frances Exposure**			
Outcome	**Race/ Ethnicity**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	White Non-Hispanic	unexposed	ref				Ref			
		exposed	1.08	(0.97	1.20)	n/a	1.09	(1.00	1.20)	n/a
	White Hispanic	unexposed	1.07	(0.98	1.17)		1.06	(0.97	1.16)	
		exposed	1.16	(0.99	1.35)	0.52	1.16	(1.00	1.34)	0.23
	Asian/Pacific Islander	unexposed	1.10	(0.87	1.38)		1.16	(0.91	1.49)	
		exposed	1.19	(0.91	1.55)	0.76	1.27	(0.97	1.68)	0.97
	Other/Multi Racial	unexposed	1.14	(0.91	1.42)		1.16	(0.92	1.48)	
		exposed	1.23	(0.95	1.59)	0.82	1.27	(0.98	1.66)	0.75
	American Indian	unexposed	1.56	(0.95	2.55)		1.94	(1.19	3.18)	
		exposed	1.68	(1.01	2.80)	0.37	2.13	(1.28	3.53)	0.18
	Black Non-Hispanic	unexposed	2.18	(2.02	2.36)		2.26	(2.08	2.46)	
		exposed	2.35	(2.02	2.73)	0.35	2.48	(2.15	2.86)	0.41
	Black Hispanic	unexposed	1.85	(1.60	2.13)		1.83	(1.57	2.14)	
		exposed	1.99	(1.64	2.41)	0.05	2.00	(1.65	2.43)	0.13
<37 weeks										
	White Non-Hispanic	unexposed	ref				Ref			
		exposed	1.01	(0.97	1.05)	n/a	0.91	(0.88	0.94)	n/a
	White Hispanic	unexposed	1.16	(1.02	0.99)		1.09	(0.94	1.27)	
		exposed	1.17	(0.99	1.38)	0.25	0.99	(0.85	1.16)	0.97
	Asian/Pacific Islander	unexposed	ref				Ref			
		exposed	1.08	(0.97	1.20)	n/a	1.09	(1.00	1.20)	n/a
	Other/Multi Racial	unexposed	1.07	(0.98	1.17)		1.06	(0.97	1.16)	
		exposed	1.16	(0.99	1.35)	0.52	1.16	(1.00	1.34)	0.23
	American Indian	unexposed	1.10	(0.87	1.38)		1.16	(0.91	1.49)	
		exposed	1.19	(0.91	1.55)	0.76	1.27	(0.97	1.68)	0.97
	Black Non-Hispanic	unexposed	1.14	(0.91	1.42)		1.16	(0.92	1.48)	
		exposed	1.23	(0.95	1.59)	0.82	1.27	(0.98	1.66)	0.75
	Black Hispanic	unexposed	1.56	(0.95	2.55)		1.94	(1.19	3.18)	
		exposed	1.68	(1.01	2.80)	0.37	2.13	(1.28	3.53)	0.18

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.13b Florida 2004 unadjusted and adjusted[1] hazard ratio(HR) of Hurricane Ivan and Jeanne ≥ 39 mph wind speed exposure on extremely preterm (<32 weeks) and overall preterm (<37 weeks) delivery including interaction by race/ ethnicity

			Hurricane Ivan Exposure				**Hurricane Jeanne Exposure**			
Outcome	**Race/ Ethnicity**		HR	95% CI		p-val	HR	95% CI		p-val
<32 weeks										
	White Non-Hispanic	unexposed	ref				ref			
		exposed	1.25	(1.03	1.53)	n/a	1.06	(0.97	1.16)	n/a
	White Hispanic	unexposed	1.07	(1.00	1.15)		1.04	(0.95	1.14)	
		exposed	1.34	(1.08	1.68)	0.77	1.11	(0.96	1.28)	0.10
	Asian/Pacific Islander	unexposed	1.14	(0.93	1.39)		1.13	(0.89	1.42)	
		exposed	1.43	(1.07	1.90)	0.47	1.2	(0.93	1.55)	0.83
	Other/Multi Racial	unexposed	1.15	(0.94	1.40)		1.13	(0.90	1.41)	
		exposed	1.44	(1.08	1.92)	0.68	1.20	(0.93	1.54)	0.92
	American Indian	unexposed	1.34	(0.82	2.19)		1.60	0.96	2.67)	
		exposed	1.68	(0.98	2.86)	0.15	1.70	(1.01	2.87)	0.22
	Black Non-Hispanic	unexposed	2.16	(2.01	2.31)		2.14	(1.98	2.31)	
		exposed	2.71	(2.17	3.37)	0.64	2.28	(1.98	2.61)	0.71
	Black Hispanic	unexposed	1.94	(1.72	2.18)		1.83	(1.58	2.13)	
		exposed	2.43	(1.91	3.09)	0.93	1.95	(1.61	2.35)	0.09
<37 weeks										
	White Non-Hispanic	unexposed	ref				ref			
		exposed	1.16	(1.07	1.25)	n/a	0.96	(0.92	0.99)	n/a
	White Hispanic	unexposed	1.15	(0.99	1.35)		1.25	(1.08	1.46)	
		exposed	1.33	(1.12	1.59)	0.24	1.2	(1.02	1.41)	0.34
	Asian/Pacific Islander	unexposed	1.22	(1.13	1.31)		1.24	(1.14	1.35)	
		exposed	1.41	(1.26	1.57)	0.84	1.19	(1.08	1.31)	0.83
	Other/Multi Racial	unexposed	1.21	(1.10	1.32)		1.19	(1.08	1.32)	
		exposed	1.40	(1.24	1.58)	0.68	1.14	(1.03	1.27)	0.96
	American Indian	unexposed	1.40	(1.15	1.72)		1.40	(1.11	1.75)	
		exposed	1.62	(1.31	2.02)	0.61	1.34	(1.06	1.68)	0.88
	Black Non-Hispanic	unexposed	1.62	(1.57	1.67)		1.61	(1.55	1.66)	
		exposed	1.88	(1.72	2.05)	0.24	1.54	(1.46	1.63)	0.83
	Black Hispanic	unexposed	1.49	(1.26	1.75)		1.65	(1.41	1.95)	
		exposed	1.72	(1.43	2.07)	0.43	1.58	(1.34	1.87)	0.49

Abbreviation: p-val, p-value for interaction; ref, referent

[1]Other/Multiracial Category includes mothers who identified as other, multiracial, Asian/Pacific islander or American Indian

Table S.14 Covariate missingness and availability on birth records and fetal death records for Florida 2004**.**

Covariate	Birth Record.	% Missing in Birth Records	Fetal Death Record
Maternal age	Yes	0.1%	Yes
Maternal race	Yes	0.2%	Yes
Maternal Hispanic ethnicity	Yes	0.9%	Yes
Maternal education	Yes	1.1%	No
Marital status	Yes	0.7%	No
Child sex	Yes	0.01%	Yes
Plurality	Yes	0.5%	No
Prenatal Care	Yes	6.1%	No
Maternal Alcohol use	Yes	1.1%	No
Maternal cigarette smoking	Yes	1.0%	No

WORKS CITED

1. Zotti ME, Williams AM, Robertson M, Horney J, Hsia J. Post-Disaster Reproductive Health Outcomes. Maternal and child health journal. 2012. Epub 2012/07/04. doi: 10.1007/s10995-012-1068-x. PubMed PMID: 22752348.

2. Harville E, Xiong X, Buekens P. Disasters and Perinatal Health: A Systematic Review. Obstet Gynecol Surv. 2010;65(11):713-28. doi: 10.1097/OGX.0b013e31820eddbe. PubMed PMID: WOS:000288002900013.

3. Shultz JM, Russell J, Espinel Z. Epidemiology of tropical cyclones: The dynamics of disaster, disease, and development. Epidemiol Rev. 2005;27:21-35. doi: 10.1093/epirev/mxi011. PubMed PMID: WOS:000230072100005.

4. Blake ES, Landsea CW, Gibney EJ. The Deadliest, Costliest, and Most Intense United States Tropical Cyclones from 1851 to 2010(and Other Frequently Requested Hurricane Facts). In: Service NW, Center NH, editors. Miami, Florida: NOAA; 2011.

5. Malilay J, Henderson A, McGeehin M, Flanders WD. Estimating health risks from natural hazards using risk assessment and epidemiology. Risk analysis : an official publication of the Society for Risk Analysis. 1997;17(3):353-8. Epub 1997/06/01. PubMed PMID: 9232018.

6. Sommer A, Mosley W. East Bengal Cyclone of November, 1970. The Lancet. 1972;299(7759):1030-6.

7. Pelling M, Maskrey A, Ruiz P, Hall L. A Global Report: Reducing Disaster Risk, a Challenge for Dvelopment. In: Recovery UDPBfCPa, editor. One United Nations Plaza, New York, NY 10017, USA: John S. Swift Co.; 2004.

8. Lai BS, La Greca AM, Auslander BA, Short MB. Children's symptoms of posttraumatic stress and depression after a natural disaster: Comorbidity and risk factors. Journal of affective disorders. 2012. Epub 2012/09/15. doi: 10.1016/j.jad.2012.08.041. PubMed PMID: 22974469.

9. Xiong X, Harville EW, Mattison DR, Elkind-Hirsch K, Pridjian G, Buekens P. Hurricane Katrina experience and the risk of post-traumatic stress disorder and depression among pregnant women. American journal of disaster medicine. 2010;5(3):181-7. Epub 2010/08/13. PubMed PMID: 20701175; PubMed Central PMCID: PMCPMC3501144.

10. Fullerton CS, Ursano RJ. Posttraumatic stress disorder: Acute and long-term responses to trauma and disaster: American Psychiatric Publishing, Incorporated; 2009.

11. Tschoegl L, Below R, Guha-Sapir D. An analytical review of selected data sets on natural disasters and impacts. Centre for Research on the Epidemiology of Disasters. 2006.

12. Bertrand M, Duflo E, Mullainathan S. How much should we trust differences-in-differences estimates? National Bureau of Economic Research, 2002.

13. Allison PD. Fixed effects regression models: Sage Los Angeles; 2009.

14. Kaufman JS. Commentary: Why are we biased against bias? International journal of epidemiology. 2008;37(3):624-6.

15. Nelder JA, Baker R. Generalized linear models: Wiley Online Library; 1972.

16. Rockville M. Mental health: A report of the Surgeon General. US Department of Health and Human Services, National Institute of Mental Health, US Publication Service. 1999.

17. Guill C, Shandera WX. The effects of Hurricane Mitch on a community in northern Honduras. Prehospital and Disaster Medicine. 2001;16(03):166-71.

18. Kirschenbaum A. Chaos organization and disaster management: CRC; 2003.

19. Dash N, Hearn Morrow B. Return delays and evacuation order compliance:: the case of Hurricane Georges and the Florida Keys. Global Environmental Change Part B: Environmental Hazards. 2000;2(3):119-28.

20. Baker EJ. Hurricane evacuation behavior. International Journal of Mass Emergencies and Disasters. 1991;9(2):287-310.

21. Health UDo, Services H. Report of the Surgeon General's Conference on Children's Mental Health: A national action agenda2000.

22. O'Connell ME, Boat T, Warner KE. Preventing Mental, Emotional, and Behavioral Disorders Among Young People: Progress and Possibilities: National Academies Press; 2009.

23. Perou R, Bitsko RH, Blumberg SJ, Pastor P, Ghandour RM, Gfroerer JC, et al. Mental health surveillance among children-United States, 2005-2011. MMWR Surveill Summ. 2013;62(Suppl 2):1-35.

24. Harville EW, Xiong X, Buekens P, Pridjian G, Elkind-Hirsch K. Resilience after hurricane Katrina among pregnant and postpartum women. Women's health issues : official publication of the Jacobs Institute of Women's Health. 2010;20(1):20-7. Epub 2010/02/04. doi: 10.1016/j.whi.2009.10.002. PubMed PMID: 20123173; PubMed Central PMCID: PMCPMC2822707.

25. Abadie A. Semiparametric difference-in-differences estimators. The Review of Economic Studies. 2005;72(1):1-19.

26. Athey S, Imbens GW. Identification and inference in nonlinear difference-in-differences models. Econometrica. 2006;74(2):431-97.
27. Lavigne JV, Faier-Routman J. Psychological adjustment to pediatric physical disorders: A meta-analytic review. Journal of Pediatric Psychology. 1992;17(2):133-57.

28. Siddique S, Banerjee M, Ray MR, Lahiri T. Attention-deficit hyperactivity disorder in children chronically exposed to high level of vehicular pollution. European journal of pediatrics. 2011;170(7):923-9.

29. Fernández-Somoano A, Lertxundi A, Lertxundi N, Mendez MA, Tardón A. Research| Children's Health. Environmental health perspectives. 2012;120(1):145.

30. Kayentao K, Garner P, van Eijk AM, Naidoo I, Roper C, Mulokozi A, et al. Intermittent preventive therapy for malaria during pregnancy using 2 vs 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review and meta-analysis. JAMA : the journal of the American Medical Association. 2013;309(6):594-604. Epub 2013/02/14. doi: 10.1001/jama.2012.216231. PubMed PMID: 23403684.

31. Brabin BJ. An analysis of malaria in pregnancy in Africa. Bulletin of the World Health Organization. 1983;61(6):1005-16. Epub 1983/01/01. PubMed PMID: 6370484.

32. Eisele TP, Larsen DA, Anglewicz PA, Keating J, Yukich J, Bennett A, et al. Malaria prevention in pregnancy, birthweight, and neonatal mortality: a meta-analysis of 32 national cross-sectional datasets in Africa. The Lancet infectious diseases. 2012;12(12):942-9. Epub 2012/09/22. doi: 10.1016/s1473-3099(12)70222-0. PubMed PMID: 22995852.

33. Mulder EJH, de Medina PGR, Huizink AC, Van den Bergh BRH, Buitelaar JK, Visser GHA. Prenatal maternal stress: effects on pregnancy and the (unborn) child. Early human development. 2002;70(1-2):3-14. doi: 10.1016/s0378-3782(02)00075-0. PubMed PMID: WOS:000179684300002.

34. Bates DV. The effects of air pollution on children. Environmental health perspectives. 1995;103(Suppl 6):49.

35. Pielke Jr RA, Gratz J, Landsea CW, Collins D, Saunders MA, Musulin R. Normalized hurricane damage in the United States: 1900–2005. Natural Hazards Review. 2008;9(1):29-42.

36. Twenge JM, Nolen-Hoeksema S. Age, gender, race, socioeconomic status, and birth cohort difference on the children's depression inventory: A meta-analysis. Journal of abnormal psychology. 2002;111(4):578.

37. Doocy S, Daniels A, Dick A, Kirsch TD. The human impact of tsunamis: a historical review of events 1900-2009 and systematic literature review. PLoS currents. 2013;5.

Epub 2013/07/17. doi: 10.1371/currents.dis.40f3c5cf61110a0fef2f9a25908cd795. PubMed PMID: 23857277; PubMed Central PMCID: PMCPMC3644289.

38. Nicolescu R, Petcu C, Cordeanu A, Fabritius K, Schlumpf M, Krebs R, et al. Environmental exposure to lead, but not other neurotoxic metals, relates to core elements of ADHD in Romanian children: performance and questionnaire data. Environmental research. 2010;110(5):476-83.

39. Sanchez P, Vazquez F, Serrano L. Autism and the built environment. Autism spectrum disorders—from genes to environment InTech, Croatia. 2011.

40. Allen AT, Flinn AM, Moore WF. The 81st Medical Group obstetrics and gynecology flight's role during Hurricane Katrina. Military medicine. 2007;172(2):199-201. Epub 2007/03/16. PubMed PMID: 17357777.

41. Hamilton DR, Gavagan T, Smart K, Weller N, Upton LA, Havron DA, et al. Houston's medical disaster response to Hurricane Katrina: part 2: transitioning from emergency evacuee care to community health care. Annals of emergency medicine. 2009;53(4):515-27. Epub 2009/01/13. doi: 10.1016/j.annemergmed.2008.10.024. PubMed PMID: 19135759.

42. Hoxsey RJ, Smith M, Miller JM, Jr., Nolan TE. Surviving disaster: assessment of obstetrics and gynecology training at Louisiana State University-New Orleans before and after Hurricane Katrina. The American journal of the medical sciences. 2008;336(2):151-5. Epub 2008/08/16. doi: 10.1097/MAJ.0b013e318180f635. PubMed PMID: 18703912.

43. Badakhsh R, Harville E, Banerjee B. The childbearing experience during a natural disaster. Journal of obstetric, gynecologic, and neonatal nursing: JOGNN / NAACOG. 2010;39(4):489-97. Epub 2010/07/16. doi: 10.1111/j.1552-6909.2010.01160.x. PubMed PMID: 20629936; PubMed Central PMCID: PMCPMC2906827.

44. Organization (WHO) WH. Physocological consequenses of disasters; prevention and management. Geneva Switzerland: Health DoM; 1992 Contract No.: WHO/MNH/PSF/91.3.

45. Norris FH. Psychosocial consequences of natural disasters in developing countries: what does past research tell us about the potential effects of the 2004 tsunami? [Washington, D.C.]: Dept. of Veterans Affairs; 2005.

46. Ursano RJ, Fullerton CS, Norwood AE. Terrorism and disaster: Individual and community mental health interventions: Cambridge University Press; 2003.

47. Doocy S, Daniels A, Murray S, Kirsch TD. The human impact of floods: a historical review of events 1980-2009 and systematic literature review. PLoS currents. 2013;5. Epub 2013/07/17. doi: 10.1371/currents.dis.f4deb457904936b07c09daa98ee8171a. PubMed PMID: 23857425; PubMed Central PMCID: PMCPMC3644291.

48. Steinglass P, Gerrity E. Natural Disasters and Post-traumatic Stress Disorder Short-Term versus Long-Term Recovery in Two Disaster-Affected Communities1. Journal of applied social psychology. 1990;20(21):1746-65.

49. McFarlane AC, Papay P. Multiple diagnoses in posttraumatic stress disorder in the victims of a natural disaster. The Journal of nervous and mental disease. 1992;180(8):498-504.

50. Neria Y, Nandi A, Galea S. Post-traumatic stress disorder following disasters: a systematic review. Psychological medicine. 2008;38(4):467-80.

51. Hamilton BE, Sutton PD, Mathews TJ, Martin JA, Ventura SJ. The effect of Hurricane Katrina: births in the U.S. Gulf Coast region, before and after the storm. National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2009;58(2):1-28, 32. Epub 2009/09/17. PubMed PMID: 19754006.

52. Gibbons E, Garfield R. The impact of economic sanctions on health and human rights in Haiti, 1991-1994. American Journal of Public Health. 1999;89(10):1499-504.

53. Hamilton DR, Gavagan TF, Smart KT, Upton LA, Havron DA, Weller NF, et al. Houston's medical disaster response to Hurricane Katrina: part 1: the initial medical response from Trauma Service Area Q. Annals of emergency medicine. 2009;53(4):505-14. Epub 2009/01/13. doi: 10.1016/j.annemergmed.2008.10.014. PubMed PMID: 19135760.

54. Christian LM. Psychoneuroimmunology in pregnancy: immune pathways linking stress with maternal health, adverse birth outcomes, and fetal development. Neuroscience and biobehavioral reviews. 2012;36(1):350-61. Epub 2011/07/27. doi: 10.1016/j.neubiorev.2011.07.005. PubMed PMID: 21787802; PubMed Central PMCID: PMCPMC3203997.

55. Federenko IS, Wadhwa PD. Women's mental health during pregnancy influences fetal and infant developmental and health outcomes. CNS spectrums. 2004;9(3):198-206. Epub 2004/03/05. PubMed PMID: 14999160.

56. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. Early human development. 2002;70(1-2):3-14. Epub 2002/11/21. PubMed PMID: 12441200.

57. Wadhwa PD, Culhane JF, Rauh V, Barve SS, Hogan V, Sandman CA, et al. Stress, infection and preterm birth: a biobehavioural perspective. Paediatric and Perinatal Epidemiology. 2001;15(s2):17-29.

58. Sandman CA, Glynn L, Schetter CD, Wadhwa P, Garite T, Chicz-DeMet A, et al. Elevated maternal cortisol early in pregnancy predicts third trimester levels of placental

corticotropin releasing hormone (CRH): priming the placental clock. Peptides. 2006;27(6):1457-63.

59. Hobel C, Culhane J. Role of psychosocial and nutritional stress on poor pregnancy outcome. The Journal of nutrition. 2003;133(5):1709S-17S.

60. Hobel CJ, Dunkel-Schetter C, Roesch SC, Castro LC, Arora CP. Maternal plasma corticotropin-releasing hormone associated with stress at 20 weeks' gestation in pregnancies ending in preterm delivery. American journal of obstetrics and gynecology. 1999;180(1):S257-S63.

61. Mancuso RA, Schetter CD, Rini CM, Roesch SC, Hobel CJ. Maternal prenatal anxiety and corticotropin-releasing hormone associated with timing of delivery. Psychosomatic Medicine. 2004;66(5):762-9.

62. Hobel CJ, Dunkel-Schetter C, Roesch SC, Castro LC, Arora CP. Maternal plasma corticotropin-releasing hormone associated with stress at 20 weeks' gestation in pregnancies ending in preterm delivery. American journal of obstetrics and gynecology. 1999;180(1 Pt 3):S257-63. Epub 1999/01/23. PubMed PMID: 9914629.

63. Alder J, Fink N, Bitzer J, Hosli I, Holzgreve W. Depression and anxiety during pregnancy: a risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2007;20(3):189-209. Epub 2007/04/18. doi: 10.1080/14767050701209560. PubMed PMID: 17437220.

64. Blaikie P, Cannon TD, Davis I. I. and Wisner, B. 1994. At Risk: Natural Hazards, People's Vulnerability and Disasters. London: Routledge; 1994.

65. Aday LA. At risk in America: The health and health care needs of vulnerable populations in the United States: Wiley. com; 2002.

66. Fothergill A, Maestas EG, Darlington JD. Race, ethnicity and disasters in the United States: A review of the literature. Disasters. 1999;23(2):156-73.

67. Tees MT, Harville EW, Xiong X, Buekens P, Pridjian G, Elkind-Hirsch K. Hurricane Katrina-related maternal stress, maternal mental health, and early infant temperament. Maternal and child health journal. 2010;14(4):511-8. Epub 2009/06/26. doi: 10.1007/s10995-009-0486-x. PubMed PMID: 19554438; PubMed Central PMCID: PMCPMC3472436.

68. Xiong X, Harville EW, Mattison DR, Elkind-Hirsch K, Pridjian G, Buekens P. Exposure to Hurricane Katrina, post-traumatic stress disorder and birth outcomes. The American journal of the medical sciences. 2008;336(2):111-5. Epub 2008/08/16. doi:

10.1097/MAJ.0b013e318180f21c. PubMed PMID: 18703903; PubMed Central PMCID: PMCPMC2635112.

69. Vesga-Lopez O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Archives of General Psychiatry. 2008;65(7):805.

70. Collazo CR. Psychological interventions for people exposed to disasters. Disasters and mental health. 2005:81-97.

71. Harville EW, Xiong X, Smith BW, Pridjian G, Elkind-Hirsch K, Buekens P. Combined effects of Hurricane Katrina and Hurricane Gustav on the mental health of mothers of small children. Journal of psychiatric and mental health nursing. 2011;18(4):288-96. Epub 2011/03/23. doi: 10.1111/j.1365-2850.2010.01658.x. PubMed PMID: 21418428; PubMed Central PMCID: PMCPMC3472438.

72. Cohan CL, Cole SW. Life course transitions and natural disaster: marriage, birth, and divorce following Hurricane Hugo. Journal of family psychology: JFP: Journal of the Division of Family Psychology of the American Psychological Association (Division 43). 2002;16(1):14-25. Epub 2002/03/28. PubMed PMID: 11915406.

73. Janerich DT, Stark AD, Greenwald P, Burnett WS, Jacobson HI, McCusker J. Increased leukemia, lymphoma, and spontaneous abortion in Western New York following a flood disaster. Public health reports (Washington, DC : 1974). 1981;96(4):350-6. Epub 1981/07/01. PubMed PMID: 7255659; PubMed Central PMCID: PMCPMC1424239.

74. Harville EW, Tran T, Xiong X, Buekens P. Population changes, racial/ethnic disparities, and birth outcomes in Louisiana after Hurricane Katrina. Disaster medicine and public health preparedness. 2010;4 Suppl 1:S39-45. Epub 2010/09/01. doi: 10.1001/dmp.2010.15. PubMed PMID: 23105034.

75. Savage J, Giarratano G, Bustamante-Forest R, Pollock C, Robichaux A, Pitre S. Post-Katrina perinatal mood and the use of alternative therapies. Journal of holistic nursing : official journal of the American Holistic Nurses' Association. 2010;28(2):123-32; quiz 33-5. Epub 2010/06/05. doi: 10.1177/0898010109348388. PubMed PMID: 20522707.

76. Zahran S, Snodgrass JG, Peek L, Weiler S. Maternal Hurricane Exposure and Fetal Distress Risk. Risk Analysis. 2010;30(10):1590-601. doi: 10.1111/j.1539-6924.2010.01453.x. PubMed PMID: WOS:000282696900016.

77. Duff EM, Cooper ES. Neural tube defects in Jamaica following Hurricane Gilbert. Am J Public Health. 1994;84(3):473-6. Epub 1994/03/01. PubMed PMID: 8129070; PubMed Central PMCID: PMCPMC1614825.

78. Glynn LM, Wadhwa PD, Dunkel-Schetter C, Chicz-DeMet A, Sandman CA. When stress happens matters: effects of earthquake timing on stress responsivity in pregnancy. American journal of obstetrics and gynecology. 2001;184(4):637-42.

79. Torche F. The effect of maternal stress on birth outcomes: exploiting a natural experiment. Demography. 2011;48(4):1473-91.

80. Oyarzo C, Bertoglia P, Avendaño R, Bacigalupo F, Escudero A, Acurio J, et al. Adverse perinatal outcomes after the February 27th 2010 Chilean earthquake. Journal of Maternal-Fetal and Neonatal Medicine. 2012;25(10):1868-73.

81. Tan CE, Li HJ, Zhang XG, Zhang H, Han PY, An Q, et al. The impact of the Wenchuan earthquake on birth outcomes. PloS one. 2009;4(12):e8200. Epub 2009/12/10. doi: 10.1371/journal.pone.0008200. PubMed PMID: 19997649; PubMed Central PMCID: PMCPMC2781160.

82. Weissman A, Siegler E, Neiger R, Jakobi P, Zimmer EZ. The influence of increased seismic activity on pregnancy outcome. European Journal of Obstetrics & Gynecology and Reproductive Biology. 1989;31(3):233-6. doi: http://dx.doi.org/10.1016/0028-2243(89)90158-5.

83. Hibino Y, Takaki J, Kambayashi Y, Hitomi Y, Sakai A, Sekizuka N, et al. Health impact of disaster-related stress on pregnant women living in the affected area of the Noto Peninsula earthquake in Japan. Psychiatry and clinical neurosciences. 2009;63(1):107-15.

84. Neuberg M, Pawlosek W, Lopuszanski M, Neuberg J. [The analysis of the course of pregnancy, delivery and postpartum among women touched by flood disaster in Kotlin Klodzki in July 1997]. Ginekologia polska. 1998;69(12):866-70. Epub 1999/05/04. PubMed PMID: 10224743.

85. Neuberg M, Jakubowska-Szwed B, Neuberg J. [Reproductive behavior after the flood disaster in Klodzko region--July 1997]. Ginekologia polska. 2001;72(12):1037-41.

86. Dancause KN, Laplante DP, Oremus C, Fraser S, Brunet A, King S. Disaster-related prenatal maternal stress influences birth outcomes: Project Ice Storm. Early human development. 2011;87(12):813-20.

87. Simeonova E. Out of sight, out of mind?: the impact of natural disasters on pregnancy outcomes: CESifo, Center for Economic Studies & Ifo Institute for economic research; 2009.

88. Martin JA, Hamilton BE, Ventura SJ, Osterman M, Kirmeyer S, Mathews T, et al. Births: final data for 2009. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2011;60(1):1.

89. MacDorman MF, Munson ML, Kirmeyer S. Fetal and perinatal mortality, United States, 2004. National vital statistics reports. 2007;56(3).

90. Martin JA, Hoyert DL, editors. The national fetal death file. Seminars in Perinatology; 2002: Elsevier.

91. Wilcox A. Fertility and Pregnancy: An Epidemiological Perspective. New York, New York: Oxford University Press; 2010.

92. Roth J. NCHS's Vital Statistics Birth Cohort Linked Birth/Infant Death Data In: (2003-2005) NCfHS, editor. http://www.nber.org/data/linked-birth-infant-death-data-vital-statistics-data.html: National Center for Health Statistics (2003-2005).

93. Damus K. Prevention of preterm birth: a renewed national priority. Current Opinion in Obstetrics and Gynecology. 2008;20(6):590-6.

94. Martius JA, Steck T, Oehler MK, Wulf KH. Risk factors associated with preterm (< 37+ 0 weeks) and early preterm birth (< 32+ 0 weeks): univariate and multivariate analysis of 106 345 singleton births from the 1994 statewide perinatal survey of Bavaria. European journal of obstetrics, gynecology, and reproductive biology. 1998;80(2):183.

95. Preterm Birth: Causes, Consequences, and Prevention. Behrman RE, Butler AS, editors. Washington DC: National Academy of Sciences; 2007.

96. Behrman RE, Butler AS. Preterm Birth: Causes, Consequences, and Prevention. Behrman RE, Butler AS, editors. Washington DC: National Academy of Sciences; 2007.

97. Medicine Io. Preterm Birth: Causes, Consequences, and Prevention. Behrman RE, Butler AS, editors. Washington DC: National Academy of Sciences; 2007.

98. Copper RL, Goldenberg RL, Das A, Elder N, Swain M, Norman G, et al. The preterm prediction study: Maternal stress is associated with spontaneous preterm birth at less than thirty-five weeks' gestation. American journal of obstetrics and gynecology. 1996;175(5):1286-92.

99. Goldenberg RL, Rouse DJ. Prevention of premature birth. New England Journal of Medicine. 1998;339(5):313-20.

100. Carballo M, Hernandez M, Schneider K, Welle E. Impact of the Tsunami on reproductive health. JRSM. 2005;98(9):400-3.

101. Gasseer NA, Dresden E, Keeney GB, Warren N. Status of women and infants in complex humanitarian emergencies. Journal of Midwifery & Women’s Health. 2004;49(S1):7-13.

102. Goldenberg RL, Cliver SP, Mulvihill FX, Hickey CA, Hoffman HJ, Klerman LV, et al. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for

low birth weight among black women. American journal of obstetrics and gynecology. 1996;175(5):1317-24.

103. Fiscella K. Race, perinatal outcome, and amniotic infection. Obstet Gynecol Surv. 1996;51(1):60-6.

104. Martin JA. United States vital statistics and the measurement of gestational age. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:13-21. Epub 2007/09/22. doi: 10.1111/j.1365-3016.2007.00857.x. PubMed PMID: 17803614.

105. Collins Jr JW, Hawkes EK. Racial differences in post-neonatal mortality in Chicago: What risk factors explain the black infant's disadvantage? Ethnicity & Health. 1997;2(1-2):117-25.

106. Florida CHARTS Birth and Fetal Death County Data. In: Health FDoP, editor. http://www.floridacharts.com/charts/: Florida Department of Public Health; 2013.

107. Lu MC, Chen B. Racial and ethnic disparities in preterm birth: the role of stressful life events. American journal of obstetrics and gynecology. 2004;191(3):691-9.

108. Huber DG, Gulledge J. Extreme weather and climate change: Understanding the link, managing the risk: Pew Center on Global Climate Change; 2011.

109. Van Aalst MK. The impacts of climate change on the risk of natural disasters. Disasters. 2006;30(1):5-18.

110. Emanuel KA. THE DEPENDENCE OF HURRICANE INTENSITY ON CLIMATE. Nature. 1987;326(6112):483-5. doi: 10.1038/326483a0. PubMed PMID: WOS:A1987G673300056.

111. Haines A, Patz JA. Health effects of climate change. JAMA: the journal of the American Medical Association. 2004;291(1):99-103.

112. Ahern M, Kovats RS, Wilkinson P, Few R, Matthies F. Global health impacts of floods: epidemiologic evidence. Epidemiol Rev. 2005;27(1):36-46.

113. Langner J, Bergström R, Foltescu V. Impact of climate change on surface ozone and deposition of sulphur and nitrogen in Europe. Atmospheric Environment. 2005;39(6):1129-41.

114. Kunreuther H, Michel-Kerjan E. At War with the Weather. Massachusetts Institute of Technology. 2009.

115. Kunreuther H, Michel-Kerjan EO. At war with the weather: Managing large-scale risks in a new era of catastrophes: The MIT Press; 2009.

116. Ohl CA, Tapsell S. Flooding and human health: the dangers posed are not always obvious. BMJ: British Medical Journal. 2000;321(7270):1167.

117. Webster PJ, Holland GJ, Curry JA, Chang HR. Changes in tropical cyclone number, duration, and intensity in a warming environment. Science. 2005;309(5742):1844-6. doi: 10.1126/science.1116448. PubMed PMID: WOS:000231989500046.

118. Agency FEM. Hurricanes. In: Security USDoH, editor. FEMA.gov2012.

119. Smith JB, Schneider SH, Oppenheimer M, Yohe GW, Hare W, Mastrandrea MD, et al. Assessing dangerous climate change through an update of the Intergovernmental Panel on Climate Change (IPCC)"reasons for concern". Proceedings of the National Academy of Sciences. 2009;106(11):4133-7.

120. Gray WM, Landsea CW, Mielke PW, Berry KJ. PREDICTING ATLANTIC BASIN SEASONAL TROPICAL CYCLONE ACTIVITY BY 1-AUGUST. Weather and Forecasting. 1993;8(1):73-86. doi: 10.1175/1520-0434(1993)008<0073:pabstc>2.0.co;2. PubMed PMID: WOS:A1993LL62600005.

121. Landsea CW, Nicholls N, Gray WM, Avila LA. Downward trends in the frequency of intense Atlantic hurricanes during the past five decades. Geophysical Research Letters. 1996;23(13):1697-700. doi: 10.1029/96gl01029. PubMed PMID: WOS:A1996UT00900038.

122. Landsea CW. A CLIMATOLOGY OF INTENSE (OR MAJOR) ATLANTIC HURRICANES. Monthly Weather Review. 1993;121(6):1703-13. doi: 10.1175/1520-0493(1993)121<1703:acoima>2.0.co;2. PubMed PMID: WOS:A1993LE00900008.

123. Meehl GA, Arblaster JM, Tebaldi C. Understanding future patterns of increased precipitation intensity in climate model simulations. Geophysical Research Letters. 2005;32(18):L18719.

124. Culliton TJ. Population: Distribution, Density and Growth. In: Administration(NOAA) NOaA, editor. Silver Spring, MD1998.

125. Census. Bot. Population of states and counties of the United States: 1790-1990, from the 21 decennial censuses. US Department of Commerce. 1996;226 pp.

126. Campbell MM. Tsunami and the silent tide: the invisible challenge of women's health. Journal of Family Planning and Reproductive Health Care. 2005;31(2):95-7.

127. Redwood-Campbell LJ, Riddez L. Post-tsunami medical care: health problems encountered in the International Committee of the Red Cross Hospital in Banda Aceh, Indonesia. Prehospital and disaster medicine. 2006;21(S1):S1-S7.

128. Ewing B, Buchholtz S, Rotanz R. Assisting pregnant women to prepare for disaster. MCN: The American Journal of Maternal/Child Nursing. 2008;33(2):98.

129. Tong VT, Zotti ME, Hsia J. Impact of the Red River catastrophic flood on women giving birth in North Dakota, 1994–2000. Maternal and child health journal. 2011;15(3):281-8.

130. Allen V, O'Connell C, Liston R, Baskett T. Maternal morbidity associated with cesarean delivery without labor compared with spontaneous onset of labor at term. Obstetrics & Gynecology. 2003;102(3):477-82.

131. Declercq E, Menacker F, MacDorman M. Maternal risk profiles and the primary cesarean rate in the United States, 1991-2002. American Journal of Public Health. 2006;96(5):867-72. doi: 10.2105/ajph.2004.052381. PubMed PMID: WOS:000237154400030.

132. MacDorman M, Declercq E, Menacker F. Recent Trends and Patterns in Cesarean and Vaginal Birth After Cesarean (VBAC) Deliveries in the United States. Clinics in Perinatology. 2011;38(2):179-+. doi: 10.1016/j.clp.2011.03.007. PubMed PMID: WOS:000292169700003.

133. Abrams B, Newman V. Small-for-gestational-age birth: maternal predictors and comparison with risk factors of spontaneous preterm delivery in the same cohort. American journal of obstetrics and gynecology. 1991;164(3):785.

134. Astolfi P, Zonta L. Risks of preterm delivery and association with maternal age, birth order, and fetal gender. Human Reproduction. 1999;14(11):2891-4.

135. Cleary-Goldman J, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Impact of maternal age on obstetric outcome. Obstetrics & Gynecology. 2005;105(5, Part 1):983-90.

136. Ecker JL, Chen KT, Cohen AP, Riley LE, Lieberman ES. Increased risk of cesarean delivery with advancing maternal age: indications and associated factors in nulliparous women. American journal of obstetrics and gynecology. 2001;185(4):883.

137. Fraser AM, Brockert JE, Ward RH. Association of young maternal age with adverse reproductive outcomes. New England Journal of Medicine. 1995;332(17):1113-8.

138. Peipert JF, Bracken MB. Maternal age: an independent risk factor for cesarean delivery. Obstetrics and gynecology. 1993;81(2):200.

139. Health FDo. FLORIDA VITAL STATISTICS ANNUAL REPORT. In: Health FDo, editor. http://www.flpublichealth.com/VSBOOK/pdf/2005/Births.pdf2005.

140. Norwitz ER, Lockwood CJ, Barss VA. Postterm pregnancy. Up to date on line version.18.

141. Kruk MC, Gibney EJ, Levinson DH, Squires M. A climatology of inland winds from tropical cyclones for the eastern united states. Journal of Applied Meteorology and Climatology. 2010;49(7):1538-47.

142. Brettschneider B. Climatological hurricane landfall probability for the United States. Journal of Applied Meteorology and Climatology. 2008;47(2):704-16.

143. Health FDo. FLORIDA VITAL STATISTICS ANNUAL REPORT. In: Health FDo, editor. http://www.flpublichealth.com/VSBOOK/pdf/2004/Births.pdf2004.

144. Harter L, Starzyk P, Frost F. A comparative study of hospital fetal death records and Washington State fetal death certificates. American Journal of Public Health. 1986;76(11):1333-4.

145. Greb A, Pauli R, Kirby R. Accuracy of fetal death reports: comparison with data from an independent stillbirth assessment program. American journal of public health. 1987;77(9):1202-6.

146. Northam S, Knapp TR. The reliability and validity of birth certificates. Journal of Obstetric, Gynecologic, & Neonatal Nursing. 2006;35(1):3-12.

147. Vinikoor LC, Messer LC, Laraia BA, Kaufman JS. Reliability of variables on the North Carolina birth certificate: a comparison with directly queried values from a cohort study. Paediatric and perinatal epidemiology. 2009;24(1):102-12.

148. Kowaleski J. State definitions and reporting requirements for live births, fetal deaths, and induced terminations of pregnancy (1997 revision). Hyattsville, Maryland: National Center for Health Statistics. 1997.

149. Wier ML, Pearl M, Kharrazi M. Gestational age estimation on United States livebirth certificates: a historical overview. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:4-12. Epub 2007/09/22. doi: 10.1111/j.1365-3016.2007.00856.x. PubMed PMID: 17803613.

150. Steer P. The epidemiology of preterm labour. BJOG: An International Journal of Obstetrics & Gynaecology. 2005;112(s1):1-3.

151. Engle WA, editor. A recommendation for the definition of “late preterm”(near-term) and the birth weight–gestational age classification system. Seminars in perinatology; 2006: Elsevier.

152. Henriksen TB, Wilcox AJ, Hedegaard M, Secher NJ. Bias in studies of preterm and postterm delivery due to ultrasound assessment of gestational age. Epidemiology. 1995:533-7.

153. Callaghan WM, Dietz PM. Differences in birth weight for gestational age distributions according to the measures used to assign gestational age. American journal of epidemiology. 2010;171(7):826-36.

154. Oken E, Kleinman KP, Rich-Edwards J, Gillman MW. A nearly continuous measure of birth weight for gestational age using a United States national reference. BMC pediatrics. 2003;3(1):6.

155. Ananth CV. Menstrual versus clinical estimate of gestational age dating in the United States: temporal trends and variability in indices of perinatal outcomes. Paediatric and Perinatal Epidemiology. 2007;21(s2):22-30.

156. Hausman J, Kuersteiner G. Difference in difference meets generalized least squares: Higher order properties of hypotheses tests. Journal of Econometrics. 2008;144(2):371-91.

157. Puhani PA. The treatment effect, the cross difference, and the interaction term in nonlinear "difference-in-differences" models. Economics Letters. 2012;115(1):85-7.

158. Ai C, Norton EC. Interaction terms in logit and probit models. Economics letters. 2003;80(1):123-9.

159. Polańska K, Jurewicz J, Hanke W. Review of current evidence on the impact of pesticides, polychlorinated biphenyls and selected metals on attention deficit/hyperactivity disorder in children. International journal of occupational medicine and environmental health. 2013;26(1):16-38.

160. Platt RW, Joseph K, Ananth CV, Grondines J, Abrahamowicz M, Kramer MS. A proportional hazards model with time-dependent covariates and time-varying effects for analysis of fetal and infant death. American journal of epidemiology. 2004;160(3):199-206.

161. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology. 1999:37-48.

162. Selvin S. Statistical analysis of epidemiologic data: Oxford University Press; 2004.

163. Park IV, Corson MS. Directed Acyclic Graph.

164. Smith SK, McCarty C. Fleeing the storm (s): An examination of evacuation behavior during Florida's 2004 hurricane season. Demography. 2009;46(1):127-45.

165. Van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Statistical methods in medical research. 2007;16(3):219-42.

166. Pennell CE, Jacobsson B, Williams SM, Buus RM, Muglia LJ, Dolan SM, et al. Genetic epidemiologic studies of preterm birth: guidelines for research. American journal of obstetrics and gynecology. 2007;196(2):107-18.

167. Hansen CA, Barnett AG, Jalaludin BB, Morgan GG. Ambient air pollution and birth defects in Brisbane, Australia. PloS one. 2009;4(4):e5408.

168. Lee SJ, Hajat S, Steer PJ, Filippi V. A time-series analysis of any short-term effects of meteorological and air pollution factors on preterm births in London, UK. Environmental research. 2008;106(2):185-94.

169. Grabich SC, Horney J, Konrad CE, Lobdell DT. Measuring the Storm: Methods of Quantifying Hurricane Exposure in Public Health. Natural Hazard Review. Under Review.

170. Zandbergen PA. Exposure of US counties to Atlantic tropical storms and hurricanes, 1851–2003. Natural Hazards. 2009;48(1):83-99.

171. Currie J, Rossin-Slater M. Weathering the storm: hurricanes and birth outcomes. Journal of health economics. 2013;32(3):487-503. Epub 2013/03/19. doi: 10.1016/j.jhealeco.2013.01.004. PubMed PMID: 23500506; PubMed Central PMCID: PMCPMC3649867.

172. Cutter SL, Smith MM. Fleeing from the hurricane's wrath: Evacuation and the two Americas. Environment: Science and Policy for Sustainable Development. 2009;51(2):26-36.

173. Lechner M. The estimation of causal effects by difference-in-difference methods: Now; 2011.

174. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The Lancet. 2008;371(9606):75-84.

175. York TP, Strauss III JF, Neale MC, Eaves LJ. Racial differences in genetic and environmental risk to preterm birth. PloS one. 2010;5(8):e12391.

176. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bulletin of the World Health Organization. 2010;88(1):31-8.

177. Henriksen TB, Baird DD, Olsen J, Hedegaard M, Secher NJ, Wilcox AJ. Time to pregnancy and preterm delivery. Obstetrics & Gynecology. 1997;89(4):594-9.

178. Perry RW, Lindell MK. The psychological consequences of natural disaster: A review of research on American communities. Mass Emergencies. 1978;3(2-3):105-15.

179. Cutter SL, Boruff BJ, Shirley WL. Social vulnerability to environmental hazards*. Social science quarterly. 2003;84(2):242-61.

180. PLATT RW, LOUIS GMB. Unique Methodologic Challenges in Reproductive and Perinatal Epidemiology. Reproductive and Perinatal Epidemiology. 2011:298.

181. Klein J, Moeschberger M. Survival analysis: statistical methods for censored and truncated data. Springer-Verlag, New York, NY. 2003.

182. Kim J, Oh SS. The virtuous circle in disaster recovery: who returns and stays in town after disaster evacuation? Journal of Risk Research. 2014;17(5):665-82.

183. Adamo SB, de Sherbinin A. The impact of climate change on the spatial distribution of populations and migration. Population Distribution, Urbanization, Internal Migration and Development: An International Perspective. 2011;161.

184. Doocy S, Dick A, Daniels A, Kirsch TD. The human impact of tropical cyclones: a historical review of events 1980-2009 and systematic literature review. PLoS currents. 2013;5. Epub 2013/07/17. doi: 10.1371/currents.dis.2664354a5571512063ed29d25ffbce74. PubMed PMID: 23857074; PubMed Central PMCID: PMCPMC3644287.

185. McCarthy FX. FEMA's Disaster Declaration Process: A Primer. In: Service CR, editor. http://www.fas.org/sgp/crs/homesec/RL34146.pdf: CRS Report for Congress; 2011.

186. Demuth JL, DeMaria M, Knaff JA. Improvement of advanced microwave sounding unit tropical cyclone intensity and size estimation algorithms. Journal of applied meteorology and climatology. 2006;45(11):1573-81.

187. Demuth JL, DeMaria M, Knaff JA, Vonder Haar TH. Evaluation of Advanced Microwave Sounding Unit tropical-cyclone intensity and size estimation algorithms. Journal of Applied Meteorology. 2004;43(2):282-96.

188. State FDo. Florida Facts http://www.stateofflorida.com/Portal/DesktopDefault.aspx?tabid=95: U.S. Census Bureau; State of Florida.com Research; 2013 [cited 2013 09/2013].