Characterizing the geographic variability and socioeconomic factors of opioid mortality in North Carolina, 2014-2016

By

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December, 2019

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The opioid crisis has proven to be one of the most devastating drug epidemics experienced in the United States. While many studies have associated the rise in opioid mortality rates to overprescribing of opioid painkillers, few have attempted to explore socioeconomic factors that may be drivers in the ongoing crisis. A need exists to ascertain the relationship between socio-economic factors and opioid mortality trends. Here, a multiple regression analysis aids in the exploration of the relationship between opioid mortality in North Carolina and socioeconomic and geographic measures.

Several studies have offered key socio-economic measures that may be indicative of higher rates of opioid mortality such as low income, low educational attainment, disability, and recently occupational patterns. While some studies have analyzed the geographic variability of opioid mortality trends, few have attempted to analyze these factors simultaneously. Two

multiple regression models are generated for two separate outcomes: total age-adjusted opioid mortality rate and white age-adjusted opioid mortality rate. All models control for age, region, and metropolitan status.

County-level mapping of age-adjusted opioid mortality rates reveals regional disparity across three outcomes; total, white, and non-white age-adjusted opioid mortality. Regions that exhibit extremely high percentages of opioid mortality in the state include the western region for the total opioid mortality, eastern region for white opioid mortality, and central region for non-white opioid mortality. Regression models for total age-adjusted produced an R^2 value of .460 and an adjusted R^2 value of .371. Regression models for white age-adjusted produced an R^2 value of .460 and an adjusted R^2 of .386. Total and white-age-adjusted opioid mortality was found to be positively correlated with eastern and western region designation, percent of those with income and benefits of $10,000-$14000, percent of those with a high school diploma or less, and disability. This study demonstrates the necessity to examine regional and socioeconomic factors concerning opioid mortality to generate more effective countermeasures to the ongoing drug crisis.

Characterizing the geographic variability of opioid mortality trends in North Carolina, 2014-2016

A Thesis

Presented to the Faculty of the Department of Geography, Planning, and Environment

East Carolina University

In Partial Fulfillment of the Requirements for the Degree

M.S. Geography

by

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DEDICATION

I dedicate this thesis to my loving family, who has been my pillar of support during the entirety of my time enrolled at East Carolina University. During the most difficult times in graduate school, you all have been one of the few sources of support that I have. I can honestly say that I am truly blessed to have you all in my life. Thank you for everything.

ACKNOWLEDGEMENTS

I am very fortunate that I have had the privilege of attending East Carolina University. I would like first to thank my committee members Katherine Jones and Karen Mulcahy for their support and contribution to this research. I would also like to thank the faculty and staff in the East Carolina University Department of Geography, planning, and environment, which allowed me to attend this graduate program as well as provided me with help and support. I want to thank my fellow undergraduate and graduate peers who have helped me cope with the common stress that comes with pursuing a college degree.

Last, and most importantly, I would like to thank my advisor Dr. Thad Wasklewicz who encouraged me to pursue this research as well, providing me with guidance and knowledge during my time in graduate school. I will never forget the times we spent together, and I wish everyone the best of luck in all of your life endeavors.

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Framing the Drug Epidemic

The United States is currently experiencing one of the worst drug epidemics in our nation's history (Paulozzi, 2010; Kolodny et al., 2015). According to the United States Department of Health and Human Services, there were 70,237 drug overdose deaths in the United States in 2017 (Hedegard et al., 2017). Consumption of opioid pain relievers, such as OxyContin, has increased by nearly 500% while hydrocodone consumption doubled from 1999-2011 (Jones, 2013; Kolodny et al. 2015). Drug deaths that involve synthetic opioids have increased from 0.3 per 100,000 in 1999 to 9.0 per 100,000 in 2017 (Hedegarrd et al., 2017). The global supply of opioid pain killers is enough to treat pain relief across the globe, but only 20% of the world population has access to these pharmaceutical products (Seya et al., 2011; Buitrago, 2013; Kunnumpurath et al., 2018). The misuse of opioid prescription pain killers and its illicit variants is now a serious public health issue that has elicited the health care community, government organizations, and community stakeholders to generate practical solutions to mitigate the crisis.

The "opioid crisis" is not a new phenomenon, and to better understand the current drug epidemic, it is essential to understand the history of opioid use in the USA. There have been multiple opioid epidemics in our nation's history, starting with the first recorded epidemic occurring around the mid-1800s (Kolodny et al., 2015). The primary driver of this initial crisis was iatrogenic morphine in conjunction with the development of hypodermic medication (Kolodny et al., 2015). Opioid consumption from the mid-19th century to the turn of the 20th century increased by 538% (Kolodny et al., 2015). Different demographics used opium and

morphine for a variety of purposes. Soldiers treated injuries and diarrheal infections with opium (Kolodny et al., 2015). Mothers would administer opioid solutions and patented medicines on themselves and their children (Kolodny et al., 2015). The development of pain reliever analgesics such as aspirin, improvements in physician training, and forewarnings from literature informing the medical community of the risks of using morphine for medical treatment led to declining addiction rates in the early 1920s (Kolodny et al., 2015).

The second opioid epidemic was associated with non-medical heroin use in urban areas starting in the 1960s and lasted through the 1970s (Kolodny et al., 2015; James & Jordan., 2018). Minority populations living in urban areas were disproportionately affected by heroin use and addiction at the end of the decade (Kolodny et al., 2015). The response to this crisis was the passing of laws that criminalized drug use and possession in the United States (James & Jordan., 2018). One example was the notorious Rockefeller Drug laws passed in 1973 in the state of New York, which called for mandatory life sentencing for selling, possession, and use of an ounce of morphine, cocaine, opium, and heroin (James & Jordan., 2018). While the laws were aimed at drug kingpins, they resulted in the conviction of non-violent, first-time offenders, and the inordinately affected blacks with a heroin use disorder (James & Jordan., 2018). The passing of drug penalization laws and increased enforcement led to the beginning of the "War on Drugs" in the USA (Malea., 2014).

The origins of the current crisis were first highlighted in published research on chronic pain treatment in the 1980s (Porteney, 1986; Kolodny et al., 2015). Opioid use had gradually increased in the 1980s, and by the mid-1990s, opioid use had accelerated with the introduction of OxyContin, a variant of oxycodone manufactured by Purdue Pharma (Kolodny et al., 2015). Purdue Pharma funded educational programs through financial grants, direct sponsorships, and

launched a multifaceted campaign to encourage long-term use of opioid pain relievers (Kolodny et al., 2015).

The American Pain Society started a campaign entitled "Pain is the Fifth Vital sign" at their annual conference in 1996. Health care professionals were encouraged to assess pain with the same urgency as vital signs and implored vigorous use of opioids for chronic pain (Kolodny et al., 2015). Many government entities and health care organizations embraced the fifth vital sign to increase the identification and treatment of pain, especially with OPR's (Kolodny et al. 2015).

While opioid prescriptions became ubiquitous with pain treatment for much of the late 20th and early 21st centuries, another source of the epidemic was emerging in the form of a purer strain of street heroin called Mexican black tar heroin (Lockwood, 2018). This narcotic found its way into the United States and has been distributed from the west coast to the eastern parts of the United States (Stewart et al., 2017; Lockwood, 2018). The consumer of this variant of heroin was usually younger people residing in predominantly white neighborhoods (Lockwood, 2018). Those who were already addicted to OxyContin and other opioid pain relievers were transitioning to black tar heroin, which is cheaper and easier to access (Lockwood, 2018).

Previous studies highlighted the disproportionate distribution of opioid misuse and poisoning deaths in the United States (Paulozzi and Ryan 2006; Hedegaard et al., 2018). In states such as Multiple states (including New Mexico, North Carolina, Tennessee, Florida, Louisiana, Kentucky, Missouri, Indiana, Ohio, Michigan, Pennsylvania, Florida. Maine, New Hampshire, Connecticut, New Jersey, Delaware, and the District of Columbia) have drug overdose rates higher than the national average (Hedgegaard et al., 2018). Some studies noted variations in opioid mortality rates in rural areas (Cicero et al., 2007; Le laid et al., 2014; Mack

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et al., 2017) and urban areas (Riggs et al., 2015; Monnat et al., 2015). Furthermore, while some studies have suggested that Non-Hispanic white males are experiencing high opioid mortality rates (Stewart et al. 2017; Corda et al. 2013; Song et al., 2017), other researchers show variation among various demographic groups in terms of sex, age, and ethnicity/race (Shah et al, 2007; Green et al, 2013; Seth et al, 2018).

North Carolina is also experiencing a similar epidemic of opioid addiction and death. The state is ranked among the 20 states in the U.S. with a drug overdose rate higher than the national rate (Hedgegaard et al., 2018). Unintentional opioid overdose deaths have increased from >100 deaths in 1999 to >1300 deaths in 2016 (Kansagra & Cohen, 2018).   Opioid prescription sales in the past 20 years have increased dramatically with the number of opioid products sold from 1997 to 2010 increasing 183% for morphine, 224% for oxycodone, 291% for fentanyl, 607% for methadone, and 839% for oxycodone (Modarai et al., 2013; Cordes, 2018). Significant clusters of the highest prescribing sources of these products were found in the western part of the state (Modaraiet al., 2013; Cordes, 2018). In 2007, Whitmire and Adams (2010) conducted a study of Medicare beneficiaries and found that unintentional overdose deaths were overwhelming associated with age groups ranging from 25 to 44 years of age, rural areas, and among Whites in contrast to a control sample (Whitmire and Adams, 2010).

While previous studies indicated that the root cause of the epidemic is the sale of prescription opioids, few studies have explored examining the socioeconomic factors that may also be influencing the spatial pattern of opioid-related mortality rates. Given that there is demographic and geographic variation in the opioid-related fatalities, geographic spatial analysis of the current crisis is warranted. By identifying local hotspots of high opioid mortality rates and

the factors that influence the variation across space, an opportunity may present itself to allow for the development of more intense targeted interventions.

The results of this style of research will reveal unique associations of opioid mortality rates concerning other contextual factors. This would provide a nuanced view of the current drug epidemic in North Carolina instead of viewing the crisis as being mostly driven by the supply of these prescription pain killers and their illicit counterparts. This style of study can also be used to inform policymakers and health care professionals who may be interested in generating practical countermeasures and solutions to the ongoing health crisis in North Carolina and beyond.

Literature Review

Epidemiological studies have already taken the initiative in analyzing the opioid crisis for various regions around the country. Rollheiser et al. (2018) examined prescription rates by congressional district in the United States using prescription rate data from the CDC QuintilesIMS Transactional Data Warehouse. Their results revealed disproportionate geographic patterning of prescribing rates with the highest prescription rates per congressional district in southeastern states such as Alabama, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Virginia, and Oklahoma (Rollheiser et al., 2018). Congressional districts in New York, California, and Virginia were reported to have lower prescribing rates compared to the prescribing rates throughout the country. Piper and his colleagues (2018) conducted a study on the medical use of opioids in the United States from 2006-2016. Using national dispensed data collected from the U.S. Drug Enforcement Administration, they analyzed dispensing patterns across the country (Piper et al., 2018). Their results suggested variation in distributing rates across the country with the highest dispensing rates occurring in Rhode Island and the lowest in North Dakota (Piper et al., 2018). Christos and Grigoras (2018) examined opioid mortality

trends and prescription rate patterns in the United States using the Medicare Part D prescription

rate data and opioid mortality data from the CDC WONDER database. Their results revealed

that county-level prescription rates were correlated with county-level opioid mortality rates

(Grigoras et al., 2018).

While national trends show geographic variation in opioid use and prescription patterns,

other studies have been examining the opioid epidemic in each state. For example, Piercefield et

al. (2010) conducted a study examining mortality trends of unintentional drug-related deaths in

Oklahoma from 1994-2006 and prescription over the counter medication from 1994-2006. Their

results revealed that the leading drug type used in fatalities was opioid analgesics and anxiolytics

(Piercefield et al., 2010). They also discovered that from 1997-2006, the sale of opioid

prescription medication had increased exponentially around the same time when the opioid-

related drug fatalities took place (Piercefield et al., 2010). In Connecticut, Green et al. (2011)

examined geographic patterns of opioid overdose deaths in Connecticut using mortality data

from 1997-2007. They conducted a regression analysis to ascertain the risk factors that are

contributing to the mortality trends they observed during the period. Their results revealed that

the most frequently cited drugs associated with opioid-related fatalities were opioid prescription

products such as hydrocodone, methadone, and fentanyl (Green et al., 2011). Geographic

analysis patterns of opioid mortality rates revealed that prescription opioid deaths occurred more

frequently in suburban and small-town areas while heroin deaths were likely to happen in large

metropolitan areas (Green et al., 2011).

Research studies examining opioid mortality trends have also found variability in the

demographic composition of decedents who suffered an opioid overdose and death in terms of

age, sex, and race. Several studies indicated Non-Hispanic white males between the ages of 25-

54 years of age are the demographic group that has been mostly impacted by the opioid epidemic in terms of mortality (Shah et al, 2007; CDC 2009; Piercefield et al, 2010; Rudd et al, 2016; Slavova et al, 2017; Nechuta et al, 2018). While this demographic group appears to be grossly affected by the current opioid drug crisis, other studies have indicated variation in mortality rates in terms of sex, age, and race/ethnicity. For example, Seth et al. (2018) conducted a state-level analysis in drug overdose deaths involving opioids, psychostimulants, and cocaine in the United States from 2015-2016. There were notable increased opioid-related deaths in age groups higher than 15 years of age as well as among Hispanics, whites, blacks, and Asian/Pacific Islanders (Seth et al., 2018). In another national study, Alexander et al. (2018) examined opioid mortality trends among blacks and white residents from 1979- 2015 and discovered different patterns in white and black opioid mortality deaths based upon three consecutive waves that occurred during the study period. The first wave took place between 1979 to the mid-1990s, which was driven mostly by heroin deaths in both racial/ethnic groups. The second wave took place between the mid-1990s to 2010 which was driven by natural and synthetic opioid deaths among whites with no significant increases in opioid mortality for blacks, however from 2010 to current, heroin and synthetic opioid driven deaths increased in both demographics (Alexander et al., 2018).

Social demographic characteristics of opioid mortality deaths have also been found to vary across U.S. states. The CDC (2009) conducted a study examining prescription opioid overdose death trends from 2004 to 2007 in Washington state, which identified over 50% of the cohort consisted of males between the ages of 45-54 years of age and enrolled in Medicaid (CDC, 2009). In New Mexico, a study examining drug mortality trends from 1990 to 2005 discovered that the demographic composition also varied among sex and race strata (Shah et al., 2007). The highest overdose rates in New Mexico were among Hispanic males, followed by

white males, Hispanic females, American Indian males, and American Indian females (Shah et al., 2007). A study examining drug overdose death trends from 1994 to 2006 in Oklahoma revealed that the highest fatalities were among men and people between the ages of 35 to 54 years of age, with an increase in mortality rates for both sexes (Piercefield et al., 2006).

While previous studies have associated mortality rates with the availability of opioid pain medication and heroin, other studies have suggested socioeconomic factors may be related to misappropriation of opioids and opioid-related deaths. Several studies conclude there is an association between rising opioid misuse and mortality in rural areas in the United States (Cicero et al., 2007; Le Lait et al., 2014; Mack et al., 2017). Mack et al. (2017) examined drug misuse and overdose patterns in metropolitan and non-metropolitan areas in the United States. Their study combined the National Survey of Drug Use and Health (NSDUH) to analyze illicit drug use patterns with mortality data provided by the National Vital Statistics System-Mortality (NVSS-M) on drug disorders during 2003-2014 to analyze mortality patterns from 1999-2015. They found that from 1999-2003, metropolitan areas had higher drug overdose rates that nonmetropolitan regions, however in 2004, the drug overdose rates in metropolitan and nonmetropolitan areas began to converge (Mack et al., 2017). The drug overdose death rate in nonmetropolitan areas was reported to be slightly higher than in metropolitan areas by 2015 (Mack et al., 2017). Rigg and Monnat (2015) examined urban and rural patterns of opioid misuse among adults in the United States using NSDUH survey data from 2011-2012 and found adults who likely engaged in abuse of opioid pain medication were respondents from urban areas as opposed to respondents from rural areas (Rigg & Monnat, 2015). Lelait et al. (2014) examined exposure rates of prescription opioids in rural and urban areas in the United States. Their results revealed that when adjusting for population, exposure cases increased with

increases in population in rural areas, but when adjusting for unique recipients dispensed drug rates (URDD), exposure rates decreased with the growing population in rural areas (Le Lait et al., 2014). These studies hypothesize opioid misuse and mortality trends also seem to differ between urban and rural status.

Income has also be identified as a likely factor in opioid fatalities (Hester et al., 2012; Cerda et al., 2013). Cerda et al. (2013) examined analgesic drug overdose-related deaths and income level patterns in New York City and found fatalities involving analgesic opioids were less likely to occur in less fragmented neighborhoods with high income (Cerda et al., 2013). In New Hampshire, Hester et al. (2012) examined prescription opioid fatalities and their associated risk factors using mortality data from 2003-2007 at the zip code level. They observed prescription opioid mortality rates varied with median household income. Lower rates of prescription opioid mortality were reported for zip codes with higher median household income (Hester et al., 2012).

Richardson et al. (2015) examined educational disparities in the United States regarding drug mortality rates from 1994-2011. They found drug overdose death rates were higher among demographic groups with the educational attainment of a high school diploma or less (Richardson et al., 2015). Pear et al. (2019) examined prescription opioid overdose patterns in association with several socioeconomic variables such as educational attainment and found an association with significant increases in prescription opioid overdose and areas with lower educational attainment (Pear et al., 2019). However, Hester and colleagues (2012), when examining socioeconomic factors related to opioid fatalities in New Hampshire, did not find an association between populations with educational attainment with less than a high school diploma and opioid mortality rates.

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The role of occupational patterns and opioid mortality has been another major area of research, with some claiming that a high number of individuals with workplace injuries are prescribed opiate pain killers (Franklin et al., 2008). Moraro et al. (2018) examined opioid mortality rates in 26 occupational groups in the United States and found occupation groups in construction or energy extraction, as well as health care practitioners, had the highest rates of prescription opioid mortalities. Monnat (2018) discovered that USA counties dependent on mining and service occupations were associated with significantly higher rates of drug mortality.

Current research has shown opioid mortality appears to be correlated to demographic factors such as age, sex, and race, but are also potentially related to socioeconomic factors (income, educational attainment, workplace disability, and occupation) and geographic factors (rurality and urbanicity). In this proposed study, it will be imperative that these compounding factors be further analyzed in the context of North Carolina to investigate if and how they affect the distribution of opioid poisoning deaths across the state.

Chapter 2

Recent news reporting has been inundated with stories related to the role of corporate pharmaceutical companies who pushed the sale and use of opioid pain killers in locations across United States where death rates soared ("The Washington Post, 2019; Davies, 2019; Associated Press & McLaughlin, 2019; Richer, 2019; Gusovsky 2015;). North Carolina has been an area exposed to these practices and has also seen other non-medical forms of opioids proliferate within the state. From 1999 to 2017, opioid driven deaths in North Carolina has reached over 13,000 (North Carolina Department of Health and Human Services, 2018). Opioid-related EMS visits have more than doubled in North Carolina, with visits increasing from 2,967 in 2010 to 5,777 in 2017 (NCDHHS, 2018). The cost of opioid poisoning deaths in NC has reached 2.5 billion in 2017 (NCDHHS, 2018). While we have characterized how these drugs have entered North Carolina, more information is required to examine factors driving people to use these drugs and the spatial patterns associated with these driving factors.

The aim here is to use statistical and GIS mapping techniques to study the patterns of opioid mortality rates and the factors that influence them in North Carolina. The following questions will be explored:

Q1. How do county-level opioid mortality rates vary across North Carolina?

Q2. Which racial populations are most prone to opioid mortality between 2014 and 2016 in North Carolina?

Q3. Are factors such as income, educational attainment, job occupation, and work disability correlated with opioid mortality across North Carolina, as has been identified in the previous studies?

The origin of the current crisis began with research published on opioid use for chronic pain treatment in the 1980s (Porteney, 1986; Kolodny et al., 2015). A study examined 11,000 patients receiving opioids concluded that the addiction was rare among patients in medical patients who did not have a history of addiction (Jones et al., 2019; Porter and Jick, 1980). Opioid use in chronic pain treatment increased moderately in the 1980s. However, it was in the mid-'90s where opioid use accelerated (Kolodny et al., 2015). Johnson and Johnson, Purdue Pharma, Endo Pharmaceuticals and other large drug manufacturers took initiative by providing funding to nonprofit organizations such as the American Pain Society whose leadership campaigned for the use of opioids in chronic pain treatment by recognizing pain as the "fifth vital sign" (Kolodny et al., 2015; Catan & Perez., 2018). Many government entities and health care organizations embraced the fifth vital sign to increase the identification and treatment of pain, especially with opioid pain relievers (Kolodny et al. 2015). More recently, news reports detailing communications between representatives of pharmaceutical companies and suppliers revealed a coordinated effort to purposely distribute large quantities of opioid pain killers to increase corporate profits while deaths soared in communities across the United States (Davies, 2019; The Washington Post, 2019). Even more distressing is that from 2006 to 2012, 76 billion oxycodone and hydrocodone pain pills were distributed across the United States by America's largest drug companies with distributors such as McKesson Corp, Walgreens, Cardinal Health, AmerisourceBergen, CVS, and Walmart contributing to 75% of the distribution of these pain killers during the time period (Higham et al, 2019).

While opioid prescriptions became ubiquitous with pain treatment for much of the late 20th and early 21st centuries, another source of the epidemic was emerging with the rise of heroin

use and overdose deaths (Jones., 2013; SAMSHA, 2010). The National Survey on Drug Use and Health in 2010 reported an estimate of 400,000 respondents who indicated past year use in 2002 and an increase of an estimated 600,000 respondents who revealed past use of heroin in 2010 (SAMSHA, 2010). Several studies have indicated individuals who are already addicted to opioid pain killers are transitioning to heroin (Lankenau., 2012; Peavy et al., 2012; Jones., 2013).

Opioid misuse and overdose-related deaths are disproportionate across the United States (Paulozzi and Ryan, 2006; Hedegaard et al., 2018). Multiple states (including New Mexico, North Carolina, Tennessee, Florida, Louisiana, Kentucky, Missouri, Indiana, Ohio, Michigan, Pennsylvania, Florida. Maine, New Hampshire, Connecticut, New Jersey, Delaware, and the District of Columbia) have drug overdose rates higher than the national average (Hedgegaard et al., 2018). Within these states, there are noted variations in opioid mortality rates in rural areas (Cicero et al., 2007; Le laid et al., 2014; Mack et al., 2017) and urban areas (Riggs et al., 2015; Monnat et al., 2015). Lastly, it has been noted that Non-Hispanic white males are experiencing high opioid mortality rates (Stewart et al. 2017; Corda et al. 2013; Song et al., 2017), but there are findings that highlight variation among different demographic groups in terms of ethnicity/race, sex, and age (Shah et al., 2007; Green et al., 2013; Seth et al., 2018).

North Carolina is also experiencing a similar epidemic of opioid addiction (Figure 1). The state is one of the 20 states in the U.S. with a drug overdose rate higher than the national rate (Hedgegaard et al., 2018). Unintentional opioid overdose deaths increased from over 100 deaths in 1999 to over 1300 deaths in 2016 (Kansagra & Cohen, 2018). Sales for prescription opioids in the past 20 years have increased dramatically. Opioid products sold in North Carolina from 1997 to 2010 rose 183% for morphine, 224% for oxycodone, 291% for fentanyl, 607% percent for methadone, and 839% for oxycodone (Modarai et al., 2013; Cordes, 2018). The western part

of the state has been noted to possess significantly high prescribing rates for opioid pain killers (Modaraiet al., 2013; Cordes, 2018). Whitmire and Adams (2010) conducted a study of Medicare beneficiaries and found that unintentional overdose deaths were overwhelmingly associated with age groups ranging from 25 to 44 years of age, rural areas, and among Whites in contrast to a control sample (Whitmire and Adams, 2010).

While previous studies indicated the root cause of the epidemic is the sale of prescription opioids, few studies have explored the socioeconomic factors influencing the spatial pattern of opioid-related mortality rates. A spatial analysis of the current crisis is warranted, given the demographic and geographic variation in the opioid-related fatalities. The identification of local hotspots of high opioid mortality rates and the factors that influence the variation across space will lead to the development of more intense targeted interventions.

Research results from these types of research should lend themselves to uncovering unique associations of opioid mortality rates in light of other contextual factors and their spatial patterns. The findings could also provide a nuanced view of the current drug epidemic instead of viewing the crisis as being mostly driven by the supply of these prescription pain killers and their illicit counterparts. This study can also be used to inform policymakers and health care professionals who may be interested in generating effective countermeasures and solutions to the ongoing health crisis in North Carolina and beyond.

Literature Review: The geographic variability of the opioid crisis is well documented across several epidemiological studies examining prescription rate patterns at various geographical scales. Piper et al. (2018) conducted a study examining state-level dispensing patterns of prescription opioids from 2006-2016. Their results revealed variations in distribution and dispensing rates in opioid analgesics across the country. Rhode Island exhibited the highest

dispensing rate, while North Dakota had the lowest during the study period. A study vetting prescription rate patterns for opioids by congressional district in the United States using data extracted from the CDC Quintiles IMS Transactional Data Warehouse found inordinate prescription rate patterns across the United States by congressional district in 2016 with congressional districts in Alabama, Kentucky, Tennessee, Mississippi, Arkansas, Virginia, and Oklahoma exhibiting highest prescribing rates (Rollheiser et al., 2018). Congressional districts in New York, California, and Virginia were reported to have lower prescribing rates compared to the prescribing rates throughout the country.

While national studies found differential patterns in prescribing and opioid use behavior, many other studies have tended to focus efforts on the state-level to assess trends on a finer scale. Green et al. (2011) examined geographic patterns and potential risk factors of opioid overdose in the state of Connecticut using mortality data from 1997-2007. They discovered that suburban areas and small towns experienced opioid deaths regularly, while heroin driven deaths occurred in large metropolitan areas (Green et al., 2011). They also discovered that prescription opioid products such as methadone, hydrocodone, and fentanyl were the most frequently cited drugs associated with opioid deaths in Connecticut during the study period (Green et al., 2011). In Oklahoma, Emily Piercefield and Colleagues (2010) examined unintentional drug-related deaths and over the counter medication from 1994-2006. They found sales for opioid prescription medication increased exponentially during the same time when opioid fatalities took place from 1997-2007 (Piercefield et al., 2010). Grigoras et al. (2018) analyzed county-level opioid mortality trends and prescription rate patterns in the United States using the Medicare Part D prescription rate data and opioid mortality data from the CDC WONDER database for years

2013 and 2014. Their results revealed that county-level opioid mortality rates were correlated with county-level prescription rates (Grigoras et al., 2018).

The demographic composition of decedents who suffered an opioid overdose death has also been found to vary in terms of sex, age, and race. The demographic group that has been grossly impacted by the opioid epidemic in terms of mortality are Non-Hispanic white males between the ages of 25-54 years of age (Shah et al, 2007; CDC 2009; Piercefield et al, 2010; Rudd et al, 2016; Slavova et al, 2017; Nechuta et al, 2018). While this demographic group appears to be grossly affected by the current opioid drug crisis, other studies have indicated variation in mortality rates in terms of sex, age, and race/ethnicity (Alexander et al., 2018; Seth et al., 2018; Unick, et al., 2017;Cerdá et al., 2013; Green et al., 2011). For example, a national study examining opioid mortality trends among black and whites from 1979 to 2018 in the United States revealed different patterns of opioid mortality deaths based upon three consecutive waves that occurred during the study period (Alexander et al., 2018). The initial wave took place between 1979 to the mid-1990s, with heroin being the most significant driver of deaths in both racial/ethnic groups (Alexander et al., 2018). The next wave took place between the mid-1990s to 2010 which synthetic and natural opioids primarily drove opioid deaths with both racial/ethnic groups exhibiting no significant changes in for rates for blacks, however from 2010 to current, both demographics experienced significant increases in heroin and synthetic opioid deaths (Alexander et al., 2018). A state-level analysis identified notable increases in opioid (including psychostimulants and cocaine) related deaths among Hispanics, whites, blacks, and Asian/Pacific islanders with age groups higher than 15 exhibiting increases in opioid-related deaths from 2015-2016 (Seth et al., 2018).

Several studies have also indicated variation in opioid mortality deaths across U.S. states. An examination of drug mortality trends in New Mexico from 1990 to 2005 found variation among race and sex strata with the highest overdose rates in New Mexico among Hispanic males, followed by white males, Hispanic females, American Indian males and American Indian females (Shah et al., 2007). In Oklahoma, Piercefield et al. (2006) discovered both sexes exhibited increases in opioid mortality from 1994 to 2006, whereby the highest fatalities were among men and people between the ages of 35 to 54 years of age. The CDC conducted a study examining opioid overdose deaths in Washington state from 2004 to 2007 and revealed that over 50% of the cohort consisted of males between the ages of 45-54 years of age and enrolled in Medicaid (CDC, 2009).

While previous studies have found associations between opioid mortality trends and the availability of opioid pain medication and its illicit variants, other studies have been examining the association between socioeconomic factors and opioid mortality trends. Several studies have suggested an association between rising opioid misuse and mortality in rural areas in the United States (Cicero et al., 2007; Le Lait et al., 2014; Mack et al., 2017). Rigg and Monnat (2015) examined rural and urban patterns of opioid misuse among adults in the United States using the National Survey of Drug Use and Health (NSDUH) survey data from 2011-2012. They discovered that respondents who reported the abuse of opioid pain medication were adults living in urban areas as opposed to respondents from rural areas (Rigg & Monnat, 2015). Mack et al. (2014) conducted a study examining drug misuse and overdose trends in metropolitan and nonmetropolitan areas using NSDUH from 2003-2014 and mortality data from the National Vital Statistics System-Mortality (NVSSM) from 1999-2015. Their results revealed that the 1999 metropolitan areas had higher drug overdose rates than nonmetropolitan regions. However, in

2004, the drug overdose rates in metropolitan and nonmetropolitan areas began to converge (Mack et al., 2017). By 2015, nonmetropolitan areas had drug overdose rates slightly higher than metropolitan areas (Mack et al., 2017). Lelait et al. (2014) examined exposure rates of prescription opioids in rural and urban areas in the United States and found when adjusting for population, exposure cases increased with increases in population in rural areas, but when adjusting for unique recipients dispensed drug rates (URDD), exposure rates decreased with the growing population in rural areas (Le Lait et al., 2014).

Studies examining drug overdose deaths have also noted an association between income and opioid fatalities (Hester et al., 2012; Cerda et al., 2013). Hester et al. (2012) examined prescription opioid fatalities in New Hampshire and their associated risk factors using mortality data from 2003-2007 at the zip code level. One notable finding was the heterogeneity of zipping code level opioid mortality rates in association with median household income and zip codes with reported higher median household income had lower rates of prescription opioid mortality rates (Hester et al., 2012). In New York City, Magdalena et al. (2013) conducted a study examining analgesic drug overdose deaths and income level patterns from 1990 to 2006. Their results indicated that opioid analgesic deaths were less likely to occur in less fragmented neighborhoods with high income (Cereda et al., 2013).

An association between opioid mortality and disability has also been corroborated between in several independent studies (Franklin et al., 2008; Hester et al., 2012; Song, 2017; Cordes, 2018). Song (2017) conducted a study examining opioid driven hospitalizations and mortality in the United States from 1993-2014 using data gathered from the National Inpatient Sample of the Healthcare Cost and Utilization Project. Patients who were hospitalized for opioid poisonings were more likely to be white and Medicare beneficiaries with disabilities between the

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ages of 50-64 years of age. Cordes (2018) conducted a study examining county-level opioid mortality trends in North Carolina from 1999-2015 using mortality data from the North Carolina State Center for Health Statistics Injury-Free NC database. One major finding from the study was an association between prescription opioid mortality and the percentage of people with a disability (Cordes., 2018). Hester et al. (2012), in their study examining opioid fatalities in New Hampshire from 2003-2007, also found an association between zip-code level opioid mortality rates and the percentage of people with a disability.

A growing body of literature has suggested an association between educational attainment and drug poisoning deaths. Pear et al. (2019) examined zip code level prescription opioid overdose patterns in the United States across seventeen states from 2002-2014 in association with various socioeconomic variables, including educational attainment. Their results revealed that areas with significant increases in opioid overdose were associated with areas with lower educational attainment. Richardson et al. (2015) conducted a study examining educational disparities and drug mortality rates from 1994-2011 in the United States. They discovered that demographic groups with the educational attainment of a high school diploma or less exhibited higher drug overdose rates (Richardson et al., 2015). Hester et al. (2012), when examining socioeconomic factors and opioid fatalities in New Hampshire, revealed an association between populations with educational attainment less than a high school diploma and opioid mortality rates.

A final variable commonly explored in the literature is occupational patterns and opioid mortality. A high number of individuals with workplace injuries are prescribed opiate pain killers treat them, and this has been identified as a leading cause of addiction (Franklin et al., 2008). Hawkins et al. (2019) conducted a study examining differences in opioid overdose deaths

by occupation and industry in Massachusetts using mortality data gathered from the Massachusetts Registry of Vital Records. Individuals working in industries such as agriculture, construction, forestry, fishing and hunting, transportation and warehousing, administrative and support and waste management services, accommodation and food services and other services except public administration had significantly higher rates of opioid-related overdose deaths than all other workers (Hawkins et al., 2019).   Additionally, they discovered that workers in occupations of farming, fishing, and forestry, installation, maintenance and repair, production, transportation, material moving, food preparation and serving related, healthcare and support and building and grounds cleaning and maintenance also had significantly higher rates of opioid overdose deaths during the study period (Hawkins et al., 2019). Moraro et al. (2018) examined opioid mortality rates in 26 occupational groups in the United States from 2007-2012. Their results indicated occupation groups in agriculture, construction, forestry, fishing and hunting, transportation, as well as health care practitioners had the highest rates of prescription opioid mortality (Morano et al., 2018). Monnat (2018) conducted a study examining opioid supply and socioeconomic factors related to drug mortality rates in the United States and discovered counties dependent on mining and service occupations were associated with significantly higher rates of drug mortality.

The review of the current research literature provides clear evidence of links between opioid mortality and demographic factors such as age, sex, and race. There are also strong indications of relations to socioeconomic factors (income, educational attainment, workplace disability, and occupation) and geographic factors (rurality and urbanicity). There has not been a comprehensive study to date investigating these types of relations in North Carolina. Here, the

aforementioned factors are examined in an attempt to provide a deeper understanding of the complex relationships surrounding opioid poisoning deaths across the state.

Methods

Data Sources: County-level mortality were gathered from the Health Systems Research and Development unit in the ECU Department of Health. Mortality data include all unintentional opioid deaths from the years 2014-2016. Deaths to be included in the study will be all unintentional deaths in which the underlying cause is listed as drug poisoning (ICD10 codes X40-44, X60-64, X85, Y10-14) and any of the contributing cause of death codes that were opium, heroin, methadone, or synthetic opioids (T40.4, T40.1, T40.2, T40.3, Y40.4, T40.6).

Regional variability in county-level opioid mortality rates is measured geographically by classifying North Carolina into Western, Eastern, and Central regions (Figure 1).

Metropolitan status for counties in North Carolina is taken from the USDA nine-category Rural-Urban Continuum Codes (RUCC) for 2013 (USDA ERS, 2013) (Figure 2). RUCC are recategorized into three categories: Large metropolitan counties with populations of 1,000,000 or more (RUCC1: RUCCs 1, 2, and 3), small metropolitan counties adjacent to large metropolitan counties with populations between 25,000 to less than 2500 (RUCC2: RUCCs 4, 6, and 8), and small metropolitan counties not adjacent to metropolitan counties with populations between 25,000 to less than 2500 (RUCC 3: RUCCs, 5, 7, and 9).
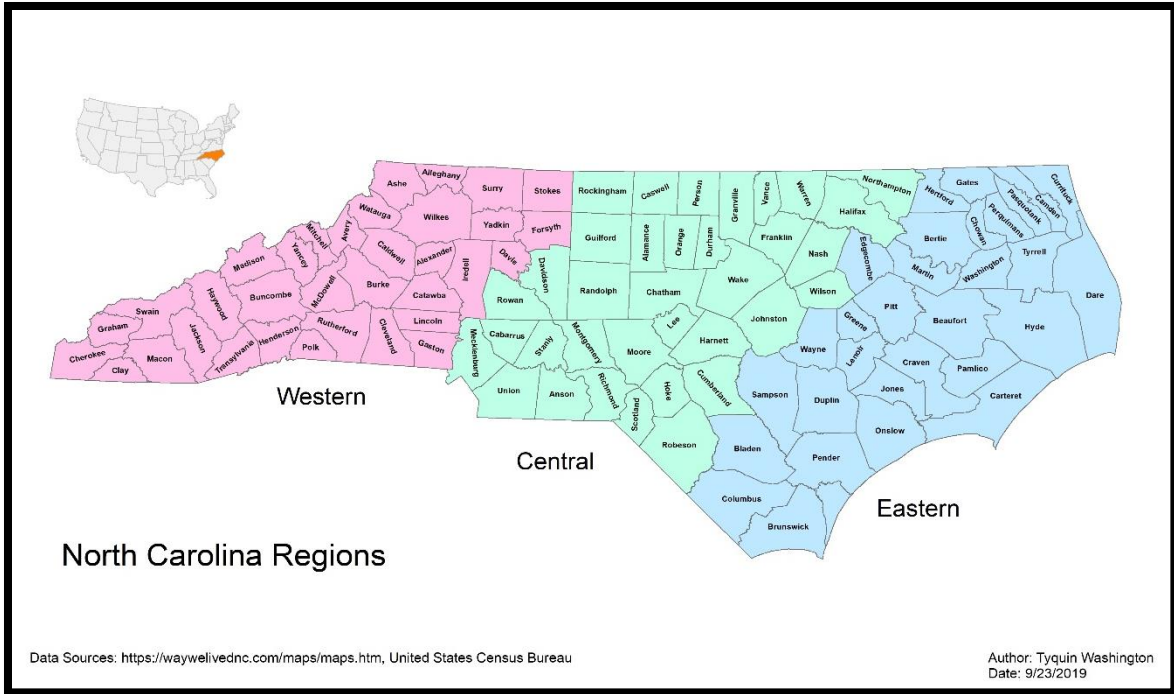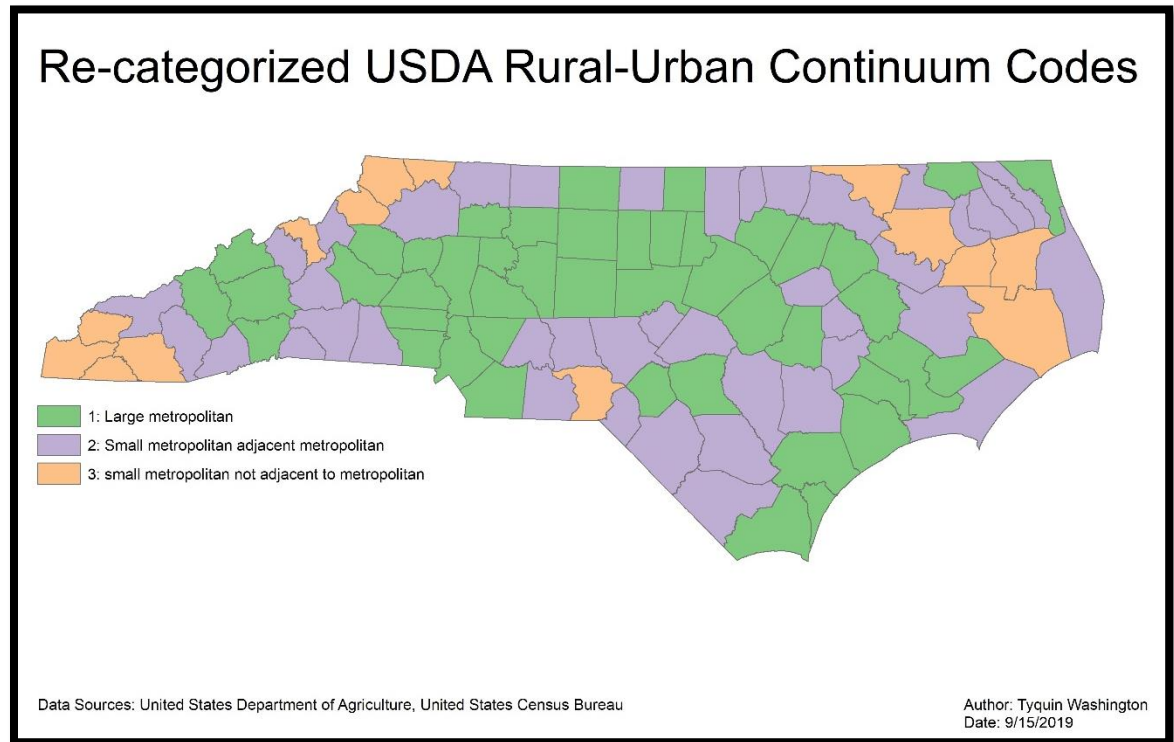
Figure 1: Regional Map of North Carolina

Figure 2: Recategorized Urban-Rural Continuum Status with the following categories. Notes: Large metropolitan counties with populations of 1,000,000 or more (RUCC1: RUCCs 1, 2, and 3), small metropolitan counties adjacent to large metropolitan counties with populations between 25,000 to less than 2500 (RUCC2: RUCCs 4, 6, and 8), and small metropolitan counties not adjacent to metropolitan counties with populations between 25,000 to less than 2500 (RUCC 3: RUCCs, 5, 7, and 9).

County-level socioeconomic measures were extracted from the American Community Survey 2013-2017 DP03, which was downloaded from the United States Census Bureau factfinder website (https://factfinder.census.gov).

Occupational data were taken from the American Community Survey 2013-2017 S2401, which consists of occupation estimates for all civilians over the age of 16 and separated by sex (https://factfinder.census.gov). Occupation rates for each county are calculated using the following equation:

$$\frac{Total\ number\ of\ civilians\ employed\ in\ an\ occupation}{total\ number\ of\ civilians\ employed} * 100$$

Demographic Analysis and disease mapping: A statistical analysis and disease mapping of the unintentional opioid deaths will be employed to answer research question Q1. The demographic and socioeconomic characteristics of the decedents will be analyzed to gauge the mortality population distribution. Age-adjusted mortality rate maps for opioid-related deaths for the total opioid-related deaths and the stratified white and non-white deaths in North Carolina. An age-adjusted rate allows for comparisons between population groups in different geographical areas.

For this study, an age-adjusted rate is calculated for all age groups. The direct method is the most commonly used for obtaining an age-adjusted rate which can be defined as follows (Breuscher, 1998):

$$Age\ adjusted\ death\ rate = \frac{\#\ of\ Deaths}{total\ standard\ population}\ X\ 100,000$$

The standard population, in this case, will be the 2000 U.S. population or a "standard million" as the denominator. The proportion by age must be maintained when using the 2000 U.S. standard population. An alternative to using the direct method involves using a weighted formula method defined as follows (Breuscher, 1998):

$$Directly\ age-adjusted\ rate = \sum_{i=1}^{10}(w_i, p_i)$$

Where p, is the age-specific mortality rate for age group i and w_i is the proportion of the standard population in age group i.

When calculating age-adjusted rates, there is the possibility of encountering random errors, especially when the number of events is small, a confidence interval will need to be figured to get more precise estimations of age-adjusted rates. The standard error for the age-adjusted rate is defined as follows (Breuscher, 1998):

$$\sqrt{\sum_{i=1}^{10}w_i^2\left(\frac{p_i}{n_i}\right)}$$

Smaller confidence intervals indicate more precise estimates for age-adjusted rates. Rates were calculated using a statistical software package and spatially joined to a North Carolina county shapefile in ESRI ArcMap 10.6 using county centroids (ESRI, 2016).

Analyzing the relationship between spatially varying factors and opioid deaths: To ascertain whether there is an association between the opioid poisoning deaths and the potential socioeconomic, demographic, and geographic characteristics and series of statistical analyses will be performed to check if the association currently exists using the county-level data. An ordinary least square regression (OLS) is a global model for assessing spatial relationships between two or more variables. This regression method was used to assess the strength of the relationship between the dependent variable (opioid mortality rates) and the independent variables of interest (socioeconomic, demographic, and geographic characteristics). According to Charlton and Fotheringham (2009), a multiple linear regression model can be defined using the following equation:

$$Y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_j x_j + \epsilon$$

Where Y is the response variable, and the parameters are represented by β_0 and β_1 that are estimated in the model. The explanatory variable x_j followed by the error term ϵ (Charton & Fotheringham, 2009).

Regression analysis identified key variables that measured low income, low educational attainment, disability, and occupation in North Carolina. Variables selection involved removing any variables from the model with a significance above 0.05. Socio-economic variables included in the regression analysis consist of percent of those with the educational attainment of high school diploma or equivalent only, percent of families with income and benefits with less than $10,000, percent of families with income and benefits between $10,000-$14,000, and percent of those with a disability.

When initially testing for variables measuring poverty, I considered indicators of poverty frequently cited in the literature such as median household income, median income, per capita income, Gini inequality index, and the poverty rate, but I found them to be not significant in the regression model, so they were subsequently removed from the analysis. However, there is some indication in the literature that suggests that income/poverty matters concerning opioid use and overdose mortality trends, so alternative variables measuring income were tested for significance in the model using the percentage of families with income and benefits, which is broken down into specific income ranges. The ranges that produced the best results are the percentage of families with income and benefits with less than 10,000 and the percentage of families with income and benefits 10,000-14,000.

Variables for the regression analysis are based on those frequently cited in the literature and are often cited for having impacted opioid misuse and overdose deaths. Occupational variables such as construction and extraction, farming, fishing, and forestry, health practitioners, and service occupations such as food preparation occupations were tested before running the final analyses, and some of them were not included in the analysis because they were not significant. Occupational variables selected for analysis include farming, fishing, and forestry (percent), community and social services, business and financial occupations, and production occupations (percent). Regression models were compared by using the adjusted R square with the final models chosen to be those with the highest adjusted R square value. Once models were finalized, residuals were examined for normal distribution. The OLS regression analysis was performed using SAS Institute's JMP software (v. 14).
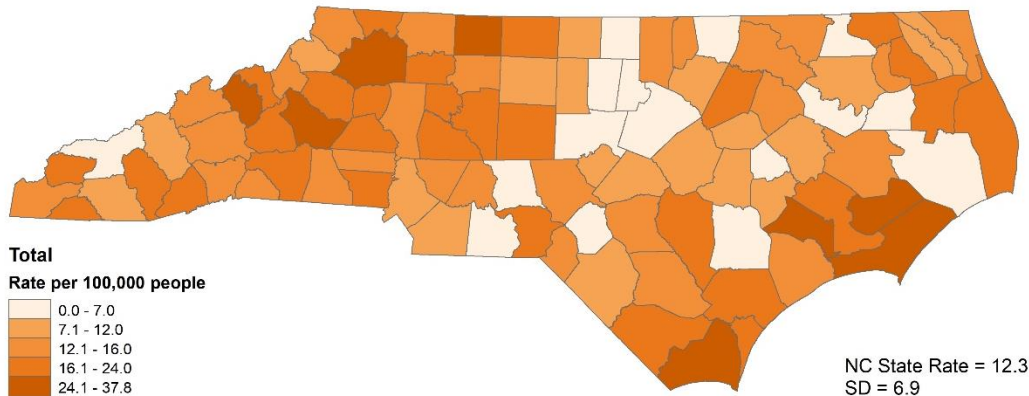
Results

Descriptive Statistics & Disease Mapping: Total, white, and non-white age-adjusted opioid mortality rates exhibit substantial variation in opioid drug-related deaths in North Carolina (Figures 3, 4, and 5). The state age-adjusted rate for North Carolina is 12.33 per 100,000 persons for the total age-adjusted opioid mortality rate with a standard deviation of 6.9. (Figure 3). Regional differences in county-level mortality rates are also present in North Carolina (Figure 6). Percentage of counties with rates higher than the state rate includes 73% in the western region, 48% in the central region, and 46% in the eastern region for total opioid mortality rates.

The state age-adjusted rate in North Carolina for white age-adjusted opioid mortality is 18.95 per 100,000 persons with a standard deviation of 7.8 (Figure 4). The percentage of counties with rates higher than the state rate for white opioid mortality includes 38% of counties in the western region, 28% in the central region, and 48% of counties in the eastern region (Figure 6).

The state age-adjusted rate in North Carolina for the non-white age-adjusted opioid mortality is 4.97 per 100,000 persons with a standard deviation of 12.7. The percentage of counties with rates higher than the state rate for Non-white opioid mortality includes 41% of counties in the western region, 48% in the central region, and 41% in the eastern region (Figure 6).

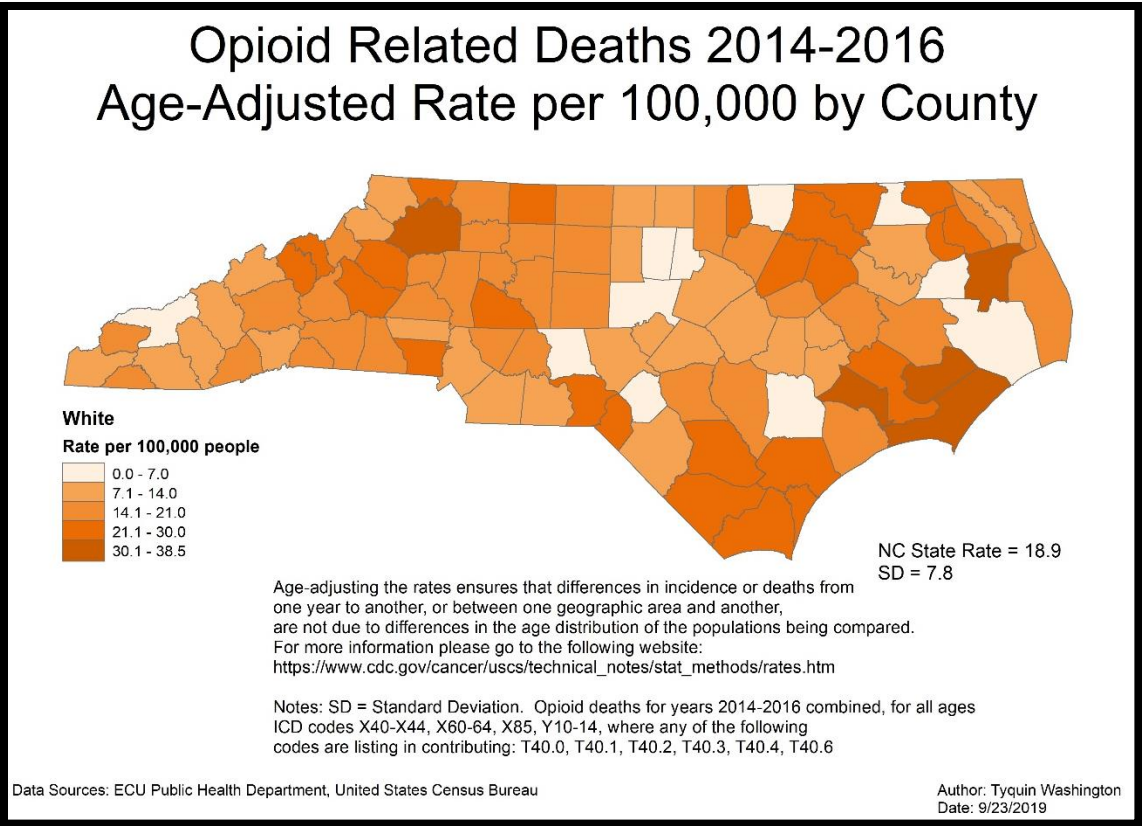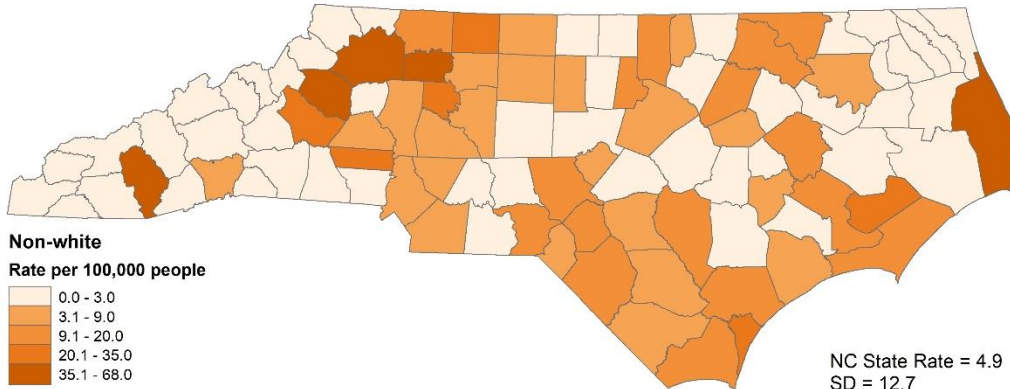Figure 3: Total Age-Adjusted Rate Map for all Opioid-Related Deaths 2014-2016

Figure 4: White Age-Adjusted Rate Map for all Opioid-Related Deaths 2014-2016

Opioid Related Deaths 2014-2016
Age-Adjusted Rate per 100,000 by County

Non-white
Rate per 100,000 people

- 0.0 - 3.0
- 3.1 - 9.0
- 9.1 - 20.0
- 20.1 - 35.0
- 35.1 - 68.0

NC State Rate = 4.9
SD = 12.7

Age-adjusting the rates ensures that differences in incidence or deaths from
one year to another, or between one geographic area and another,
are not due to differences in the age distribution of the populations being compared.
For more information please go to the following website:
https://www.cdc.gov/cancer/uscs/technical_notes/stat_methods/rates.htm

Notes: SD = Standard Deviation. Opioid deaths for years 2014-2016 combined, for all ages
ICD codes X40-X44, X60-64, X85, Y10-14, where any of the following
codes are listing in contributing: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6

Data Sources: ECU Public Health Department, United States Census Bureau

Author: Tyquin Washington
Date: 9/23/2019

Figure 5: Non-white Age-Adjusted Rate Map for all Opioid-Related Deaths 2014-2016
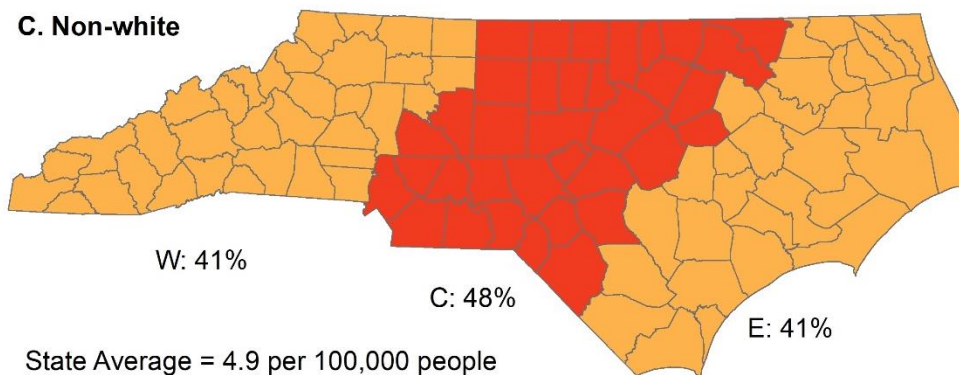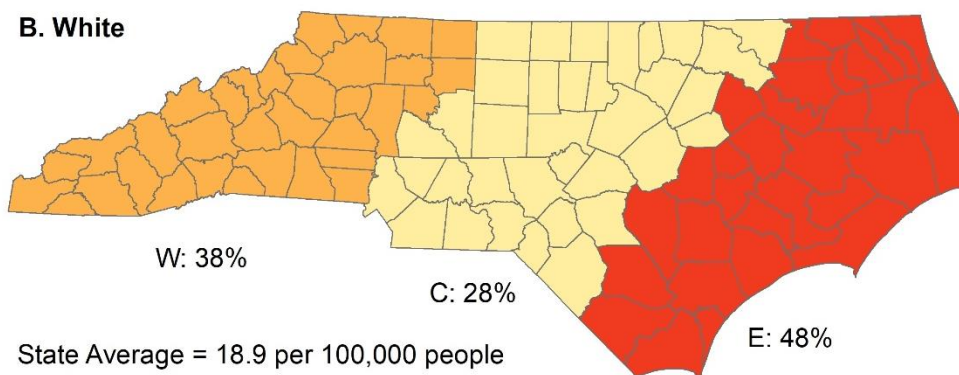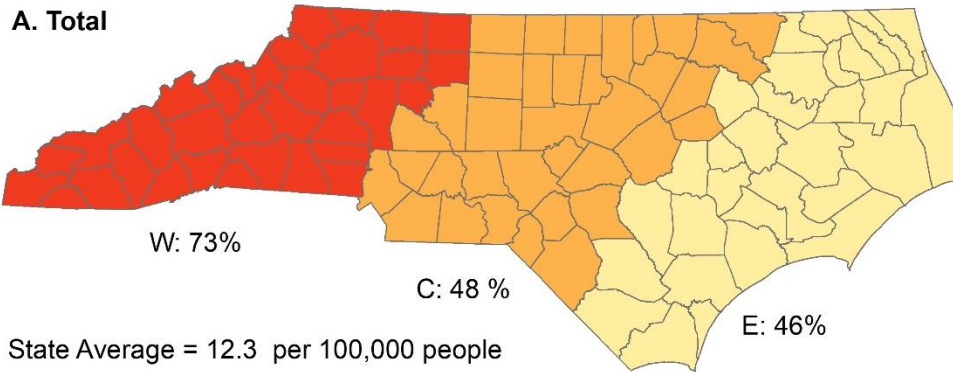
Figure 6: Percentage of Counties with Mortality Rates higher than the State Rate for Opioid-Related Deaths 2014-2016 total (A), white (B), and non-white (C).

Total age-adjusted mortality rate: A multiple linear regression identified the relationship

between opioid mortality and geographic, economic, and occupational measures. A significant

regression model ($F(12, 87) = 5.8669$, $p < .0001$) was developed, with an R^2 of .447 and an

adjusted R^2 of .371. The geographic variables showed significant regional scale relationships,

but more localized measures targeted at examining urban vs. rural populations were not

statistically significant. Geographic variables such Eastern Region (B = 4.20, p = .01) and

Western Region (B 6.02, p = .007) both have a statistically significant positive relationship with

the total opioid mortality rate (Table 2). Urban-Rural Continuum variables such as small

metropolitan adjacent (B = -1.27, p.35) and small metropolitan not adjacent (B = -3.52, p = .11)

did not have a significant relationship with the white age-adjusted opioid mortality rate.

Socio-economic measures also displayed significant relationships with opioid mortality.

Percent of those with a high school diploma or equivalent (B = .356, p = 0.04) and percent of

those with a disability (B = .88, p = .001) also had significant positive relationships with the total

opioid mortality rate. Percent family income and benefits with less than $10,000 (B = -.70, p =

.03) had a significant negative relationship with the total opioid mortality rate while percent

family income and benefits ranging from $10,000-$14,000 (B = 1.10, p = .02) did have a

significant positive relationship with the total mortality rate.

Several occupation measures displayed significant relationships with opioid mortality.

Percentage of people employed in farming, fishing and hunting occupations (B = -1.31, p = .007)

as well as community and social service occupations (B = -3.64, p = .000) had a significant

negative relationship with opioid mortality. The percentage of those employed in business and

financial operations occupations (B = 1.74, p = .01) had a significant positive relationship with

opioid mortality. Percent of those employed in production occupations did not have a significant

relationship with the total opioid mortality rate (B = -.38, p = .06).

Table 2. Multiple regression results on county-level total age-adjusted opioid mortality rates, 2014-2016

Variable	B	$S.E.\ B$	β	t	p
Intercept	-7.79	(6.52)	0	-1.19	.23
Western Region	6.02	(1.49)	-.41	4.03	.000***
Eastern Region	4.20	(1.74)	.28	2.41	.018*
Small Metro Adjacent	-1.27	(1.36)	-.09	-0.93	.35
Small Metro Not Adjacent	-3.52	(2.20)	-.17	-1.60	.11
high school (%)	.356	(.17)	.27	2.03	.045*
Disability (%)	.88	(.26)	.44	3.31	.001**
family income: < \$10,000 (%)	-.70	(.33)	-.22	-2.12	.03*
family income: \$10-\$14,000 (%)	1.10	(.48)	.24	2.27	.02*
farming, fishing, & forestry (%)	-1.31	(.47)	-.30	-2.74	.007**
Community Service & Social Service (%)	-3.64	(1.02)	-.30	-3.55	.000***
Business & Financial (%)	1.74	(.67)	.31	-2.58	.011*
Production (%)	-.38	(.20)	-.22	-1.90	.06
R^2	0.447				
$Adj.R^2$	0.371				
F	5.86***				

County N = 100

Note: S.E. = standard error, ***p < .001; **p < .01; p* < .05; two tailed tests

White age-adjusted opioid mortality rate: The results from the multiple linear regression

analyses indicated a significant regression model (F(12, 87) = 6.18, p < .0001), with an R^2 of

.460 and an adjusted R^2 of .386. Similar to the total age-adjusted rate, geographic variables also

revealed significant regional scale relationships for both Eastern Region (B = 6.16, p = .002) and

Western Region (B = 3.70, p = .03) both having a significant positive relationship with the total

opioid mortality rate (Table 3). The localized measures for assessing the urban and rural

continuum such as small metropolitan adjacent (B = -1.81, p = 0.24) and small metropolitan not

adjacent (B = -3.70, p = .06) did not have significant relationship with the white age-adjusted opioid mortality rate.

Socioeconomic measures also revealed significant relationships concerning opioid mortality for the white age-adjusted rate. Percent of those with a high school diploma or equivalent (B = .64, p = .001) and percent of those with a disability (B = .93, p = .002) also had a significant positive relationship with the total opioid mortality rate. Percent family income and benefits ranging from $10,000-$14,000 (B = 1.99, p = .02) also has a significant positive relationship with the total mortality rate, however percent family income & benefits with less than $10,000 (B = -.52, p = .16) did not have a significant relationship with the white age-adjusted opioid mortality rate.

Occupations measures also revealed significant relationships between opioid mortality such as percentage of people employed in farming, fishing & hunting occupations (B = -1.97, p = .000) as well as community and social service occupations (B = -3.17, p = .007) and percent production occupations (B = -.47, p = .04) have a significant negative relationship with opioid mortality. Percentage of those employed in business and financial operations occupations (B = 2.36, p = .011) had a significant positive relationship with opioid mortality. Percent to those employed in production occupations did not have a significant relationship with the total opioid mortality rate (B = -.38, p = .06).

Table 3. Multiple regression results from county-level white age-adjusted opioid mortality rates, 2014-2016

Variable	B	S.E. B	β	t	p
Intercept	-19.42	(7.34)	0	-2.65	.009**
Western Region	3.70	(1.68)	.22	2.20	.03*
Eastern Region	6.16	(1.96)	.36	3.14	.002**
Small Metro Adjacent	-1.81	(1.53)	-.11	-1.18	.24
Small Metro Not Adjacent	-3.70	(2.47)	-.20	-1.89	.06

high school (%)	.64	(.19)	.43	3.29	.001**
Disability (%)	.93	(.30)	.41	3.09	.002**
family income: < $10,000 (%)	-.52	(.37)	-.14	-1.41	.16
family income: $10-$14,000 (%)	1.99	(.55)	.38	3.62	.000***
farming, fishing, & forestry (%)	-1.97	(.47)	-.39	-3.66	.000***
Community Service & Social Service (%)	-3.17	(1.15)	-.22	-2.75	.007**
Business & Financial (%)	2.36	(.76)	.37	3.10	.011*
Production (%)	-.47	(.22)	-.24	-2.08	.04*

R^2	.460
Adj. R^2	.386
F	6.18***

County N = 100

Note: S.E. = standard error, ***$p < .001$; **$p < .01$; p* < .05; two tailed tests

Non-white age-adjusted opioid mortality rate: Regression results for Non-white age-adjusted

opioid mortality are notably absent in this study, but a regression analysis was attempted to

explore the relationship between it and the covariates used in this research. Initial results

revealed an uneven distribution of residuals, which violates the assumption of homoscedasticity.

This violation is likely due to skewness in the distribution of age-adjusted opioid mortality rates

for non-whites due to small numbers in the sample. Many counties in North Carolina have no

deaths recorded for non-white opioid mortality, and while attempts are made to reduce skewness

by use of transformations to approximate a normal distribution to conduct the analysis,

ultimately, the analysis proved to be unfeasible. I acknowledge that the lack of regression results

for non-white is a critical limitation in this study, and future efforts will be made to ensure that

adequate sample size that approximates a normal distribution is acquired to carry out such an

analysis in the foreseeable future.

Discussion & Conclusions

The results of this study confirm what many previous studies have identified regarding the opioid epidemic in the United States and some of the demographic and socioeconomic factors that may be related to opioid mortality. However, novel insights are provided about opioid mortality trends in North Carolina by indicating regional differences in county mortality rates as well as unique insights of the role of occupational factors concerning the current drug crisis in the state.

Disease mapping and descriptive statistics confirm that county-level opioid mortality rates differ in North Carolina from 2014-2016. County-level opioid mortality rates exhibit variation across the state, with several counties exhibiting opioid mortality rates that are higher than the state average rate for the total, white, and non-white opioid mortality. Opioid mortality rates also appear to differ across race/ethnicity from 2014-2016, with whites exhibiting state average rate that is higher than non-whites during this period. This finding suggests that whites were more prone to opioid mortality in North Carolina than non-whites during the study period. This phenomenon has also been noted in several studies that have indicated this disproportion in opioid mortality trends among whites with respect to other ethnic groups (Shah et al, 2007; CDC 2009; Piercefield et al, 2010; Rudd et al, 2016; Slavova et al, 2017; Nechuta et al, 2018). This variation is further highlighted by regional differences in counties with high rates of opioid mortality with the western region exhibiting the highest percentage of counties with rates higher than the state average for the total opioid mortality, followed by the eastern region for white opioid mortality, and finally the central region for non-white opioid mortality. One potential explanation is the rise in heroin and other synthetic opioid narcotics that are becoming more

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commonplace in the last several years (NCDHHS, 2018). As lawmakers and health officials have become increasingly aware of the dangers of misusing opioid painkillers, prescribing them to patients has come with additional oversight and regulations to deter misuse. That has unfortunately likely pushed current addicts from prescription opioid pain killers to more illicit opioid drugs such as fentanyl and heroin. Another potential explanation regarding regional differences for whites and non-whites across the state could be related to differential access to prescription opioids, with whites having more access to opioid pain killers than non-whites. (James & Jordan., 2017; National Public Radio, 2017). This pattern of preference may be rooted in institutionalized racism in the medical system towards people of color, with some studies indicating some minorities receiving less treatment for pain than whites (Green et al., 2003; Bernabei et al., 1998). Other factors that may be driving differential patterns of opioid mortality include the price of opioid pain killers, cultural differences, and drug preference (James & Jordan., 2017). A qualitative assessment in drug use and mortality among ethnic-racial groups would likely be necessary to further evaluate this phenomenon in North Carolina with particular focus on pain management practices and patterns of opioid distribution in white and nonwhite communities.

The regression analysis results suggest several key conclusions about the role of income, educational attainment, job occupation, rural-urban status, region, and work disability concerning opioid mortality in North Carolina that need to be addressed. The regional variables for eastern and western regions of North Carolina having a positive relationship with the opioid mortality rate for the total and white opioid age-adjusted mortality rates suggest that death rates in these regions are higher in comparison to the referenced Central Region. This observation has been previously documented by James Cordes (2018), who also discovered differential patterns of

opioid mortality in western and eastern counties in North Carolina from 1999-2015. Future research will focus on examining regional disparity in opioid-related deaths for North Carolina by reviewing current allocated resources and methods in counties that appear to be struggling in mitigating opioid abuse and overdose deaths. Further monitoring of hospitalizations and EMS records related to opioid overdose, increase in health treatment and support programs for current addicts as well as interviews with current and past opioid abusers may shed more light on this phenomenon.

While assessing the relationship between the indicator variables small metro counties adjacent to metropolitan areas and small metro counties not adjacent to rural counties, there were found to be not statistically significant in the regression analysis for total and white opioid mortality. This observation runs counter to what several national studies and some state-level studies have indicated that there are disproportionate opioid mortality deaths in rural counties in contrast to urban counties in the United States. However, that does not mean that disparity between urban-rural communities and health outcomes does not exist in North Carolina. Recently the North Carolina Health and Human Statistics announced that six rural counties would share $1.2 million in grant funding to facilitate the development of programs and services to mitigate opioid abuse in these communities (NCDHHS.gov, 2019). People living in rural areas in North Carolina may struggle with opioid drug abuse because of the lack of resources such as health insurance, health care facilities, and shortage of health professionals that are necessary to not only mitigate opioid abuse but also improve overall health in these communities (North Carolina Institute of Medicine, 2014).

Next, is the relationship between income and opioid mortality, while families with income and benefits with $10,000-$14,000 show a significant positive relationship for both the

total and white age-adjusted opioid mortality rates, families with income and benefits with less than $10,000 did show a significant negative relationship for the total age-adjusted rate, but not for the white age-adjusted rate. These results suggest that while low income may be a factor related to opioid mortality, families in extreme poverty may be unable to acquire the prescription opioids or their illicit counterparts because of the burdensome expense of supporting a drug abuse disorder. Likewise, families with reported incomes from $10-$14,000 may be able to afford opioid pain relievers or illicit counterparts. This finding is in agreement with other studies that have suggested a relationship between areas with high rates of opioid mortality and low income (Hester et al., 2012; Cerda et al., 2013). One potential explanation is the cuts to social safety net programs such as food stamps and Medicaid, which are a crucial aid for low-income families.

Furthermore, as income inequality increases, health outcomes tend to be worse (Lynch et al., 2004; Kondo et al., 2012; Krisberg, 2016; Macinko et al., 2004; Pickett and Wilkins, 2015). More research will be necessary to further examine the role of income and health disparity in North Carolina, especially concerning opioid overdose mortality in North Carolina. Decreasing income disparity will likely become a major task for policymakers and health care professionals going forward. Some recommendations to alleviate this issue would increase the minimum wage, invest in education programs, and provide greater access to resources that facilitate wealth growth for working in middle-class families.

A positive relationship was found between disability and opioid mortality for both the total and white age-adjusted opioid mortality rates suggest that those with an employment-based disability may be at risk of experiencing an opioid-related overdose death. This finding is in agreement with other studies that have found similar observations (Cordes, 2019; Hester et al.,

2012).   One explanation for this phenomenon is the increased prescribing of opioid pain killers to treat chronic pain conditions related to workplace injuries (Franklin et al., 2015; Hester et al., 2012; Franklin et al., 2008). Opioids may be contributing to disablement and perpetuating physical dependence for individuals who suffer from chronic workplace pain (Franklin et al., 2015; Juurlink and Dhalla, 2012). One potential recommendation is improving oversight in a prescription written for opioid pain killers to treat chronic pain as well as encouraging health care practitioners to offer alternative pain management methods besides prescription opioid pain killers.

Educational attainment of a high school diploma only shows a significant positive relationship implies that populations with the educational attainment of only a high school diploma or equivalent are at risk of experiencing an opioid-related death. This finding is supported by other studies that have found similar relationships between drug mortality and individuals with lower educational attainment (Richardson et al., 2015; Pear et al., 2019). One explanation is the most recent economic downturn which led to an increase in substance abuse and the use of prescription pain killers in the last decade (Carpenter et al., 2017). Furthermore, this phenomenon is likely related to overall health where people with higher education tend to have higher life expectancy than those with less education (North Carolina Institute of Medicine, 2014; Meara et al., 2008; Cutler & Lleras-Muney, 2006). Policymakers and health care professionals will need to take note of this phenomenon and develop resources to aid people with low educational attainment and provide them with employment opportunities that offer benefits and pay.

Finally, is the relationship between occupation participation rates and opioid mortality, suggesting that some occupations may offer a buffer against opioid addiction while others appear

to increase the risk of opioid abuse. Individuals working in farming, fishing, and forestry occupations may not have health insurance to offset the cost of prescription opioid pain killers, which would make it difficult to acquire them. Community and social services occupations were also found to have a negative relationship with opioid mortality. These occupations include counselors, clergy, social workers, lawyers, judges, and teachers. This occupation group may have firsthand awareness of the negative consequences of opioid use. Production occupation groups also had a negative relationship with opioid mortality. One potential explanation is the presence of routine drug testing in some of these occupations which may discourage substance abuse. Business and financial operations occupations revealed a positive relationship with opioid mortality suggesting that populations participating in these occupations are at risk of experiencing an opioid overdose. Future research will be necessary to assess these relationships between occupation and opioid mortality thoroughly. Monitoring current opioid use behavior in various occupations including business and financial occupations in North Carolina will likely be necessary to illuminate opioid-related misuse in occupations across the state further.

This study identified spatial trends in opioid mortality in North Carolina by examining opioid-related fatalities from 2014-2016. Disease mapping results revealed variability across counties in North Carolina for total, white, and non-white opioid mortality. Regional maps further highlight the severity and complexity of opioid fatalities across the state during the period. Regions with the highest rates for opioid mortality include the western region for the total opioid mortality, eastern region for white opioid mortality, and central region for Non-white opioid mortality. Regression results revealed that the western region, eastern region, disability, educational attainment of high school diplomas, and families with income and benefits of $10-$14,000, and percent of those employed in business and financial occupations are positive

correlates with the total and white age-adjusted opioid mortality rates. It also revealed that families with less than $10,000, percent of those working in farming, fishing, and forestry, production, and community and social services occupation have a negative relationship with the total and white age-adjusted opioid mortality. Health care professionals and policymakers who are interested in generating intervention programs will need to continue to examine the spatial and socio-economic dynamics of opioid addiction and mortality for the foreseeable future.

Chapter 3

Summary Statement: The study addressed key questions related to county-level opioid mortality rates in North Carolina. Mortality rates vary spatially across the three regions in North Carolina for the total, white, and non-white adjusted opioid mortality rates. Several socioeconomic measures are associated with higher opioid rates of opioid mortality such as income, educational attainment of a high school diploma, disability status, and business and financial operations occupations. While socioeconomic measures such as low income, low educational attainment, and disability may be potential drivers to the ongoing drug epidemic, certain occupations such as agriculture, community service, and production may offer a protective effect and/or deterrence against opioid mortality, while other occupations such as business and financial occupations may increase the risk of exposure and misuse of opioids. The findings in this study provide an important contribution to current epidemiological and geographical studies examining factors related to opioid mortality. Furthermore, the results also provide a unique insight on the crisis concerning North Carolina, however, there is more work that needs to be done to fully grasp the complexity of the opioid epidemic in North Carolina and beyond.

Limitations: Findings are to be taken into consideration in light of some limitations. The current study was limited by the reporting and scale of the data provided to study opioid mortality in North Carolina. The mortality deaths reported in this study are assumed to have been reported by the North Carolina State Medical Examiner; however, I acknowledge that there is a possibility that some fatal opioid-related deaths may not have been reported due to misclassification. Furthermore, given the data and methods employed, it was not possible to

ascertain individual-level demographic data such as age, sex, prescription history, employment status, marital status, and other unique identifiers that could potentially provide further information about the deceased population due to lack of access to death certificate data. Further research will be directed to acquiring granular mortality data as well as assessing the reliability and accuracy of using mortality data in epidemiological research.

The methods and data classification conducted in this study was unable to find a statistical relationship between opioid-related fatalities and the urban-rural continuum, which may be due to the coarseness of the county-level measures being unable to assess this relationship fully. There is potential that such a relationship exists in North Carolina, but to fully analyze it would require finer resolution spatial data. Furthermore, the urban-rural continuum is malleable, which shifts across time, and geographical area as populations grow and recede. Attempt to compare them by sorting them into distinct categories may be a futile effort. Future research will need to be done to explore this relationship thoroughly as well as to assess the reliability of recategorizing geographic categories for analytical purposes.

Methodological issues of this analysis will also be addressed. I initially conducted the analysis of this study with the intent to provide a multiple regression model for the total, white, and non-white age-adjusted opioid mortality rates, however due to the lack of data in several counties for the non-white age-adjusted rate, I was unable to fully assess the relationship between it and the covariates used in this study. Future research should assess these relationships for all mortality outcomes to avoid potential biases and to address potential factors related to opioid mortality fully.

Finally, data aggregated at the county level may skew or mask important local patterns of opioid mortality, which may further difficult measuring factors that may be driving the current

drug epidemic. The mortality data currently available in North Carolina is at the county level, it

is certainly possible that mortality rates may be driven by factors that are undetectable at the

county level and may be further illuminated by measuring opioid mortality trends at more finer

resolution spatial units such as zip code level, census tract, or census block group level.

Furthermore, it is difficult to explain such a human-driven phenomenon such as opioid mortality

trends, given that there are other factors at play that may not be possible to measure using a

quantitative approach in this study. Future research would likely receive enhancement by

combining a quantitative and qualitative analysis to understand the complexity of the current

drug epidemic. This study may also have suffered issues such as ecological bias (Hester et al.,

2012; Jacques, 2004).

     In 2017 the North Carolina Opioid Action Plan was announced with the goal of creating

and implementing strategies to combat the current epidemic by reducing supply of opioid

prescription pain killers and illicit opioids, increase the awareness by educating youth about drug

misuse, increase the availability of naloxone and connect overdose survivors to care, expand

recovery and treatment care systems, and measure results and revise strategies as needed

(NCDHHS, 2017) Two years after the announcement and implementation of the plan, EMS

department visits for opioid overdoses have decreased for the first time over a decade ago,

opioid use treatment has increased by 20 % for uninsured and Medicaid beneficiaries, opioid

pain killer, dispensing have decreased by 24 % and buprenorphine dispensing has increased by

15% (NCDHHS, 2019). This study provides unique insight into the relationship between opioid

mortality in North Carolina for income, occupation, educational attainment, and region. The

findings in this study can be used by policymakers, public health practitioners, and community

stakeholders who are interested in devising and executing effective countermeasures to the

ongoing drug epidemic in this state. There is further potential to focus efforts in examining opioid abuse behavior in certain occupational groups and give incentives towards higher education or alternative educational programs to facilitate upward economic mobility and job security. State-level or federal level social safety net programs need to be widely available especially for families who are struggling below or barely above the poverty line in terms of income. North Carolina still has a long way to go to address the current drug epidemic, but with teamwork, time, and dedication, there is room to hope that one day we will overcome this. Recognizing factors contributing to higher rates of opioid abuse and fatality will be crucial in confronting the drug epidemic in the United States.

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