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The Spatial Prevalence and Associated Factors of Opioid Overdose Mortality in Milwaukee County, Wisconsin

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THE SPATIAL PREVALENCE AND ASSOCIATED FACTORS OF OPIOID OVERDOSE
MORTALITY IN MILWAUKEE COUNTY, WISCONSIN

by

Andrew Schendl

A Thesis Submitted in
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ABSTRACT

THE SPATIAL PREVALENCE AND ASSOCIATED FACTORS OF OPIOID OVERDOSE MORTALITY IN MILWAUKEE COUNTY, WISCONSIN

by

Andrew Schendl

The University of Wisconsin-Milwaukee, 2021
Under the Supervision of Professor Zengwang Xu

Mortality from opioid overdose has become the leading cause of non-natural death in Milwaukee County, WI in recent years. In order to better understand the opioid epidemic and formulate pro-active responses to the crisis at the local level, this study examines the spatial prevalence and associated factors of opioid overdoses that end in mortality in Milwaukee, WI using the spatial econometrics model. The social determinants of health framework is used to identify the potential related socioeconomic factors associated with opioid abuse. Using principal component analysis, 6 primary components were identified from the chosen social determinants and used as explanatory variables in the econometric analysis. The age-adjusted standardized mortality rate was calculated for each census tract to be used as the dependent variable in the analysis. Socioeconomic status, a prevalence of labor occupations, and the age composition of an area were identified as the variables with a significant contribution to high overdose mortality rates, both directly and indirectly. This study reveals the overall contribution that socioeconomic factors have on the opioid epidemic, indicating the underlying socioeconomic conditions need to be addressed in order to see a reduction in opioid overdose fatalities.

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1. Introduction

The opioid epidemic has quickly become a pervasive public health crisis affecting countless communities across the United States. The number of drug poisoning deaths involving opiates in the United States increased 329% between 2000 and 2014 (Stewart, Cao, Hsu, & Artigiani, 2017). Over 80% of all drug overdoses involve at least one opiate, making opioids the deadliest drug class (CDC Injury Center, 2021).

Opioid abuse is largely driven by the psychological and physiological addiction to the substance. The addictive nature of opioids is largely due to the feelings of pleasure and euphoria that are associated with the drug (Kosten & George, 2002). This addictive nature of opioids is worsened by the development of tolerances, pushing users to consume higher and higher doses of the drugs in order to maintain the same level of high. This tolerance level is dangerous for two reasons. First, as the dosage increases, it becomes increasingly likely that the user will experience an overdose. Without prompt medical attention, an opioid overdose can easily result in death. Second, once a user has developed a tolerance level, stopping use results in the onset of a physical illness known as withdrawal. Withdrawal symptoms can be extreme, leading many users to become dependent on opioids and enter into a perpetual cycle of drug-seeking behavior (Jones et al., 2018, Kosten & George, 2002). However, opioids have been part of the pharmaceutical toolkit for pain relief for centuries. How is it that opioid use disorder has become so prevalent in recent years? In order to better explain the recent developments in opioid abuse, a brief history of how this problem came to exist needs to be examined.

1.1 A Brief History of the Opioid Epidemic

During the mid to late 1800s, a synonymous period of opioid addiction at epidemic levels occurred when the use of opium and morphine was unregulated and used for a variety of ailments from diarrhea to hangovers (Kolodny et. al., 2015). However, by the early 1900s, it was recognized that the amount of addiction occurring was untenable leading to tighter prescription laws and a reluctance from physicians to prescribe opiates (Kolodny et. al., 2015). Since then, opiates were largely avoided as pain management therapy agents until 1986 when the World Health Organization began addressing the undertreatment of pain in cancer patients by encouraging the use of opiates (Jones et. al., 2018).

In 1990 researchers began exploring the idea of using opiates to treat not just cancer patients, but also any patient suffering from chronic pain (Jones et. al., 2018). In 2000, the federation of state medical boards and the Drug Enforcement Agency announced that they would be decreasing the amount of regulatory scrutiny over opioid prescribers, giving the prescribers more freedom to prescribe opiates as a pain management therapy (Jones et. al., 2018). This came while the Joint Commission established new pain management standards, which if not met, worried physicians that federal funding from their hospital would be cut, encouraging more opioid prescriptions (Jones et. al., 2018).

With these more flexible guidelines in place, pharmaceutical companies began pushing opioids as the frontline treatment for pain, labeling their lack of use in pain management as inhumane (Jones et. al., 2018). Simultaneously, they began developing new, more potent formulations, and marketed them as having less potential for abuse, when they actually had high abuse potential (Jones et. al., 2018). One example of this is OxyContin, an extended-release form of oxycodone, which from 1997 to 2002 saw a nationwide increase in prescriptions from 670,000

to 6.2 million (Jones et. al., 2018). A simultaneous marketing campaign lead by opioid manufacturers during this time dissuaded physicians from the idea that opiate use was addictive and rebranded the addiction symptom as a “physical dependence” that held no clinical value (Kolodny et al., 2015).

During the 2000s the overall number of opioids consumed rose from 46,946 kg in 2000, to 165,525 kg in 2012 with the doubling of hydrocodone consumption and a 500% increase in oxycodone consumption (Jones et. al., 2018; Kolodny et. al., 2015). According to the National Vital Statistics System mortality statistics from the Centers for Disease Control and Prevention, between 2003 and 2018 there was a “proportionate quadrupling of prescription opioid sales and mortality in both men and women” (Jones et. al., 2018; Kolodny et. al., 2015). Although the dangers of opioid misuse have been known for decades, the severity of the problem was not recognized until the latter part of the 2010s, with the US Government declaring the opioid epidemic as a public health emergency on October 16, 2017 (Jones et. al., 2018).

1.2 The Opioid Epidemic in Wisconsin and Milwaukee County

In Wisconsin, the opioid epidemic can be classified into three different “waves” occurring at different periods and with different drug classes dominating the crisis (Wisconsin Department of Health Services, 2021). The first wave started in 1999 when opioid overdose deaths began to rise due to the over prescription of opioids crisis (Wisconsin Department of Health Services, 2021). In 2010, a rise in heroin overdose deaths marked the beginning of the second wave. This shift from the first to the second wave is indicated by an 800% increase in the amount of heroin-overdose related hospital admissions in Wisconsin between 2003 and 2012 (Meiman, Tomasallo, & Paulozzi, 2015). This is likely due to the transition of prescription opioid addicts to heroin as a cheaper alternative. During this time, the demographic

characteristics of heroin users shifted towards Whites and people living in rural areas (Meiman, Tomasallo, & Paulozzi, 2015). The second wave began to transition to the third wave in 2014 crisis (Wisconsin Department of Health Services, 2021). This wave is largely attributed to the illegal manufacture of synthetic opioids, such as fentanyl and its analogs, and their inclusion in street heroin (Scholl, 2019). According to the Centers for Disease Control and Prevention, Wisconsin saw an increase of 50% or more visits to the emergency department for opioid overdose treatment between July 2016 and September 2017 (2018). This is largely due to the high potency of fentanyl and other synthetic opioids, driving users to overdose with much less quantity than they are used to.

In Milwaukee County, death from opioid overdose has become the leading cause of non-natural death in recent years, rising from 2.4% of all deaths in 2014 to 3.8% in 2018 (Peterson, Schreiber, Fumo, Lerner, 2019). Between 2003 and 2018 there have been over 2,500 deaths attributed to opioid overdose within Milwaukee County, with over 1,400 occurring between 2013 and 2017. During this period, 22% of deaths were attributed to fentanyl (a synthetic opioid), 30% to heroin, and 17% to oxycodone. As of 2018, opioids made up 84% of the incidences of all drug-related deaths in Milwaukee County (Peterson et. al., 2019). As the most segregated city in the United States with a Segregation Index of 79.8 – indicating that 79.8% of Blacks need to relocate in order to fully integrate with Whites – Milwaukee County provides a unique environment to study the socioeconomic characteristics of opioid overdose behavior (Frey, 2018).

1.3 Research Objectives

Interventions have been developed to mitigate the high overdose mortality rate seen with the recent phase of the epidemic. Naloxone hydrochloride (naloxone), is an opioid antagonist

that temporarily reverses the effects of opioids, giving a potential overdose victim the opportunity to seek further medical treatment (Doe-Simkins et. al., 2009). Currently, in Wisconsin, naloxone is available at various pharmacies without a prescription, and it is also carried by law enforcement and emergency medical personnel. However, this increased availability of naloxone has not affected the increasing overdose mortality rate, signaling that new social interventions are needed.

While naloxone provides a medical intervention against the opioid epidemic, it does not address the underlying issues associated with the crisis. Each community affected has a unique geographic distribution of opioid overdoses. This dissimilarity between communities means that in order to solve the opioid epidemic, a community-based approach must be taken, addressing, and analyzing local geographies as well as local politics. Naloxone should not be viewed as the solution to the opioid epidemic, instead, social interventions need to be developed in order to stop the problem before it starts at the individual and community level. This research takes the first step in discovering the deeper cause for the opioid epidemic in Milwaukee County by investigating the social determinants of health associated with overdose mortality. This data will allow policy makers to target these factors in opioid abuse mitigation. This process begins by analyzing the spatial patterns of opioid overdose while simultaneously identifying the potential sociodemographic social determinants of health.

This research hypothesizes that areas with a concentration of low-quality social determinants of health will have greater incidences of fatal opioid overdoses. In this context, my research question is: “Is the social determinants of health framework consistent with opioid overdose mortality in Milwaukee County?”

2. Literature Review

One key framework for studying the social context of health outcomes is the idea of social determinants of health (SDoH). The SDoH framework was popularized by Michael Marmot, a professor of epidemiology at University College London, and has been applied to study the causative processes of obesity, heart disease, and substance abuse among others (Marmot & Wilkinson, 2005, Dasgupta, Beletsky & Ciccarone, 2017, Kreatsoulas & Anand, 2010, Medvedyuk, Ali & Raphael, 2018). By applying the SDoH framework to the opioid overdose mortality rate, the extent of the sociodemographic factors influence can be determined. This chapter will address the SDoH framework and how it applies to the opioid epidemic, to identify the key factors contributing to opioid overdose mortality rates, as will be discussed in chapter 4.

2.1 Social Determinants of Health Framework

Health is intimately intertwined with the social environment (Marmot & Wilkinson, 2005). Quality of health is not consistent across social, economic, and geographic dimensions. In fact, health inequalities are highly prevalent within modern society, with people of higher socioeconomic status generally receiving a higher quality of care than people of lower socioeconomic status (Marmot & Wilkinson, 2005, Marmot & Wilkinson, 2003, Wilkinson, 2003). This is typically referred to as “The Social Gradient” in which people of poor social and economic status have a higher likelihood of coming down with a serious illness or dying prematurely than those of higher status (Marmot & Wilkinson, 2003). This social gradient is seen globally in countries of all income levels and is a major contributor to health inequalities worldwide (Wilkinson, 2003). The health effects of this social gradient are cumulative, as the longer individuals live with poor social and economic conditions, the more likely they will experience a shorter life-expectancy (Marmot, 2003).

According to the World Health Organization, social determinants of health can be defined as, "...the circumstances in which people are born, grow up, live, work and age, and the systems put in place to deal with illness" (2013). This can include demographic factors such as race/ethnicity, gender, and social class, as well as broader context variables such as education, occupation, the built environment, and health care accessibility (Marmot, 2003, Marmot & Wilkinson, 2005, Short & Mollborn, 2015). These factors are major contributors to overall health quality and longevity in either a direct or indirect way (Marmot, 2003, Braveman, Egerter, & Williams, 2011). These social determinants of health are considered to be nonmedical factors that influence health outcomes in either an 'upstream¹' or a 'downstream²' way (Short & Molborn, 2015, Braveman et al., 2011). That is to say that the social determinants of health are influenced by both direct and indirect effects. For example, an individual's occupation can be considered an upstream determinant (Cloughery, Souza, & Cullen, 2013). People with higher status job titles tend to have better overall health than those with lower-class jobs. This could be due to stress, income inequality, or the exposure of people in lower-wage jobs to physical hazards such as chemicals and manual labor (Marmot, 2003). In this context, the upstream effect would be having a lower education and a low-class job leading to more stress and physical exhaustion, causing a person to smoke cigarettes or abuse drugs (the downstream effect), and ultimately leading to negative health outcomes, such as heart disease or opioid overdose.

While the SDoH framework provides a substantive theoretical background regarding the social context of health, it does not explicitly breakdown the contribution of the various upstream and downstream factors to overall health outcomes. Expanding upon this framework, the County

¹ Upstream social determinants: "Fundamental causes that set-in motion causal pathways leading to (often temporally and spatially distant) health effects through downstream factors" (Braveman et al., 2011).

² Downstream social determinants: "Factors that are temporally and spatially close to health effects (and hence relatively apparent), but are influenced by upstream factors" (Braveman et al., 2011).

Health Rankings (CHR) model groups the SDoH into four different categories (healthy behaviors, clinical care, the physical environment, and social and economic factors) and assigns them a score based on their estimated contribution to health outcomes (Figure 1) (Hood, Gennuso, Swain, & Caitlin, 2016). Healthy behaviors include a variety of downstream factors such as alcohol use, diet/exercise, sexual activity, and tobacco use, collectively making up 30% of the contribution to health outcomes. Clinical care incorporates access and quality of care, both upstream factors, and contributes 20% to health outcomes. The physical environment, an

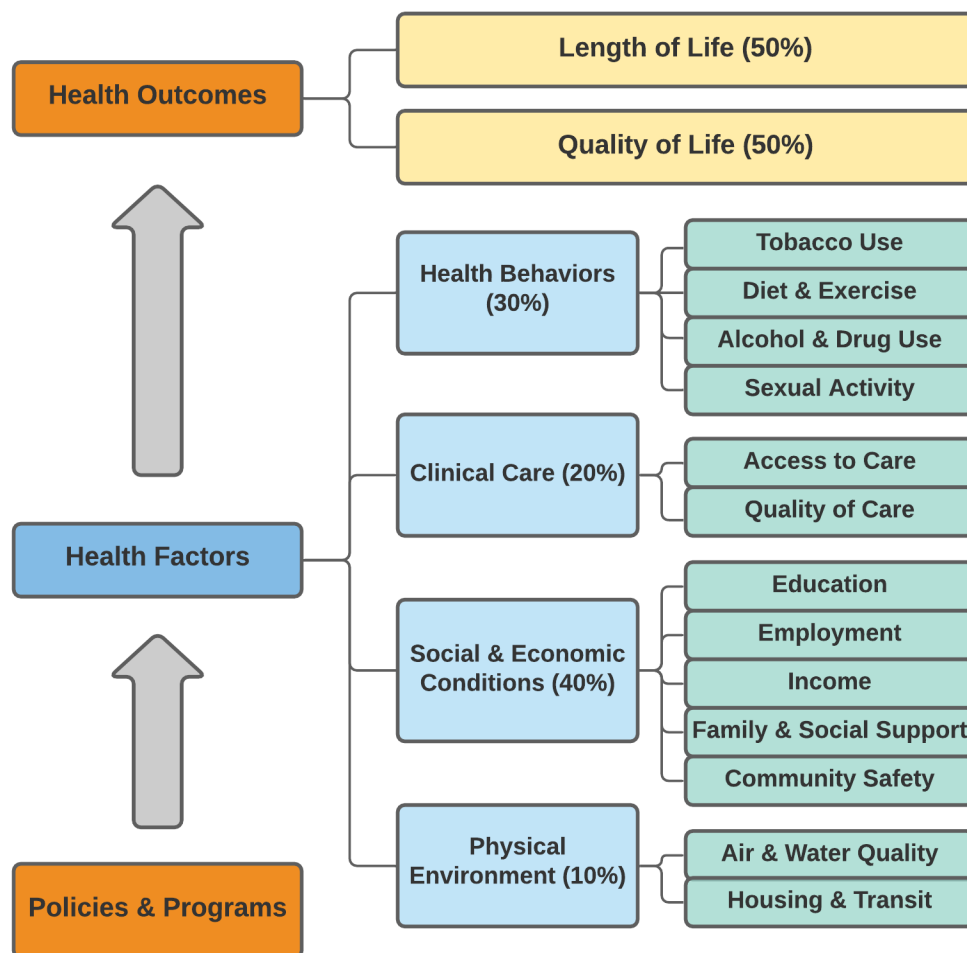


Figure 1. Breakdown of the County Health Rankings Model (Hood et al., 2016), indicating the breakdown of health factors contribution to health outcomes.

upstream factor, contributes 10% and is based on air/water quality and housing/transit factors. Finally, the downstream social and economic factors are considered, including education, employment, income, family structure/social support, and community safety, contributing 40% to overall health outcomes. In this context, health outcomes are considered to be quality of life and length of life (Hood et al., 2016). In chapter 4, this approach will be applied to corroborate the SDoH of the opioid epidemic in Milwaukee County.

2.2 Social Determinants of Opioid Abuse and Overdose

The social context of opioid abuse is not homogenous for all sociodemographic populations. Specific sociodemographic populations are more susceptible to transitioning from opioid users into opioid abusers (Cerdá et al., 2013b, Cerdá et al., 2017, King et al., 2014). Social determinants play a major role in the identification of vulnerable populations to opioid abuse and overdose. Generally, these social determinants include race/ethnicity, gender, age, socioeconomic status, and education level (King et al., 2014, Pear et al., 2019). There is a general consensus that higher concentrations of families in poverty, higher levels of unemployment, and lower levels of educational attainment (high school education or less) are associated with an increase in the rate of opioid overdoses on a national scale (Pear et al., 2019).

However, these vulnerable populations are not identical throughout all geographies. There is significant variation of vulnerable characteristics between urban, suburban, and rural environments. One of the key differences between rural and urban geographies and their associated vulnerability to the opioid epidemic is that the hardest hit groups within urban environments tend to be those that have higher social disadvantage, whereas within rural environments, the abuse of opioids typically extends throughout all social groups, affecting the entire community (Cerdá et al., 2013b, Peters et al., 2019, Wagner et al., 2019). However, while

rural areas may have high levels of opioid abuse, the majority of opioid overdoses that end in death occur in urban metropolitan areas (Scott et al., 2007). For this review, urban environments will be examined for their social determinants of opioid abuse and overdose in order to understand the complex upstream factors associated with opioid overdose mortality.

The urban environment is comprised of many unique neighborhoods, each composed of different sociodemographic groups and income levels. One of the key neighborhood indicators of opioid overdose potential is neighborhood income inequality (Cerdá et al., 2017). This neighborhood inequality fosters distrust in the police for those in the lower income bracket (Bohnert et al., 2010, Cerdá et al., 2017). Residents with lower socioeconomic status are more likely to abuse opioids and less likely to seek help from the authorities when faced with a potentially fatal overdose due to their distrust in the police (Bohnert et al., 2010, Nandi, Galea, Ahern, Bucciarelli, Vlahov, & Tardiff, 2006). This leads to higher overdose rates in neighborhoods suffering from greater inequality.

Another social determinant contributing to opioid abuse and overdose in the urban environment is family fragmentation and household structure. Fragmented families are those in which the nuclear family unit has been fragmented through divorce, separation, or other mechanisms. Single-parent households can also be considered fragmented. According to a 2017 study by Cerdá et al. on opioid-related overdose deaths in New York City, neighborhoods with lower-income and greater amounts of family fragmentation experience higher rates of opioid-related overdoses. One possible explanation for this association is that fragmented families have less parental influence and a fractured familial support system. As members of these families are exposed to opioids, regular usage can quickly develop into abuse as the user does not have a strong family connection to hold them accountable. This can also be felt at the neighborhood

scale as there is less overall social accountability, leading to more drug use in the neighborhood. Similar to neighborhood income inequality, increased family fragmentation also increases distrust in the local authorities, creating a reluctance to call for help in the case of fatal overdose (Cerdá et al., 2017).

2.3 The Differences Between Prescription and Heroin Abuse and Overdose

While the opioid epidemic is typically described as a singular epidemic, it can actually be broken down into four separate epidemic classes: the *heroin* epidemic, the *prescription opioid* epidemic, the *synthetic and prescription opioids* epidemic, and the overlapping *syndemic* (all three epidemic classes combined) (Peters et al., 2019). For the purpose of this section, the heroin epidemic and the prescription opioid epidemic will be examined for their similarities and differences in urban environments.

Between 2000 and 2011, the highest number of heroin involved overdose deaths occurred in Los Angeles County, CA, one of the largest metropolitan areas in the United States (Stewart et al., 2017). Within urban environments, the prescription opioid epidemic and the heroin epidemic demonstrate distinct spatial and social patterns (Cerdá et al., 2017). Similar to the social determinants of all opioids in urban environments, neighborhood income inequality, the level of community trust in the police, and the quality of the urban built environment all contribute to the overall likelihood of fatal overdose occurring due to the usage of heroin (Nandi et al., 2006). Neighborhoods with higher poverty levels also experience greater levels of heroin abuse and overdose (Scott et al., 2007).

However, certain social determinants of the heroin epidemic deviate from the overall social determinants in urban areas. Stewart et al. (2017) conducted a geospatial analysis of heroin overdose mortality in the United States from 2000-2014. This analysis revealed that Whites are

more likely to overdose on heroin than other races. However, there are instances in which Black mortality rates are higher, specifically in cities with larger Black populations. In terms of age and sex, males age 35-54 are the most vulnerable to heroin overdose, however, there is evidence that overdoses among younger age groups are on the rise (Stewart et al., 2017). In terms of mortality, heroin causes more unintentional fatalities in urban environments than prescription opioids (Cordes et al., 2018). This is likely due to the accessibility and affordability of heroin in urban neighborhoods compared to prescription opioids (Cerdá et al., 2017, Scott et al., 2007).

The largest driver of the overall opioid epidemic has been the overprescribing of prescription opioids. While many users of prescription opioids use them as directed, there are increasingly more people that use them for nonmedical purposes (Keyes et al., 2014). This nonmedical use is what comprises the prescription opioid epidemic. While the heroin epidemic in the urban environment has been relatively constant over the last few decades, the prescription opioid epidemic has seen large increases in abuse and overdoses in urban areas (Cerdá et al., 2013a). The prescription opioid epidemic in urban areas has largely affected White and Latino populations with women being the most vulnerable (Cerdá et al., 2013a). Certain neighborhood characteristics are associated with higher incidences of prescription opioid overdoses. Prescription opioid abuse and overdose occurs in different neighborhoods than heroin abuse and overdose. For example, prescription opioid overdoses are more associated with neighborhoods that have greater access to opioids via pharmacies, a population with more people suffering from chronic pain, and higher median neighborhood incomes (Cerdá et al., 2017, Clougherty et al., 2010). Chronic pain is typically more present among people lower on the social gradient working blue-collar manual labor jobs (Marmot & Wilkinson, 2005, Clougherty et al., 2010). Although heroin and prescription opioid use differ in neighborhood and social determinants, one

concerning trend is the transitioning of prescription opioid users towards heroin use (Mars et al., 2014; Ray et al., 2017). This transitioning is largely due to the tightening of restrictions on prescription opioids in recent years (Mars et al., 2014). While this may seem like an appropriate policy decision to mitigate an upstream effect, the results of this decision actually have a more negative impact downstream than originally intended.

2.4 The Connection Between the Built Environment, Health, and Opioid Abuse

The quality of the built environment is correlated with the overall health of the community (Johnson & Shreve, 2020, Renalds et al., 2010). The built environment can be broadly defined as “the human made space in which people, live, work, and recreate on a day-to-day basis” (Roof & Oleru, 2008, p. 24). The urban built environment encapsulates everything from green space, sidewalks, and street cleanliness to population density, parcel zoning, and the social network of the citizens (Renalds et al., 2010, Leyden, 2003). A high-quality urban built environment has greater walkability and is associated with more access to trails and green space, an overall clean environment, greater proximity to grocery stores, and a more mixed variety of land use (Renalds et al., 2010). Within this high-quality environment, residents are more likely to have a higher social capital, increased physical activity, less mental health problems, and fewer incidences of drug overdose than areas with a lower quality environment (Leyden, 2003, Renalds et al., 2010, Johnson & Shreve, 2020). In contrast, a lower-quality built environment is typically associated with urban blight, characterized by dilapidated, abandoned buildings, unclean streets and sidewalks, the presence of graffiti, and less access to green space (Galea, 2005, Hembree et al., 2005, Johnson & Shreve, 2020). This low-quality environment has a negative impact on the overall health of the neighborhood leading to higher rates of depression, an increased rate of

overall mortality, higher rates of crime, and an increased risk of drug abuse (Galea, 2005, Hannon & Cuddy, 2006, Hembree et al., 2005, Johnson & Shreve, 2020).

Some of the most prevalent factors within urban environments contributing to high opioid overdose rates include: the quality of the built environment, overall income inequality, and the prevalence of single parent households in neighborhoods. (Cerdá et al., 2013b). To date, a handful of studies have investigated the association between the built environment and overall drug abuse in urban settings. It has been found that in neighborhoods with more abandoned buildings (a marker for a low-quality built environment) drug-related crimes are more prevalent and overall drug overdose rates are higher (Hannon & Cuddy, 2006). This is likely due to the mere availability of infrequently monitored space for illegal drug-related activity to take place (Hannon & Cuddy, 2006). Neighborhoods with a lower-quality built environment have also been proven to have higher overall mortality rates than areas with fewer negative factors (Hembree, et al., 2005). While this increase in mortality may be partly attributed to the lower walkability score of the area and the subsequent increase in overall morbidity associated with less physical activity; the relationship with the built environment and drug activity also plays a role (Hankey, Marshall, & Brauer, 2012). Although the connection between the built environment, overall physical health, and drug-related activity provides adequate evidence for the association between opioid overdose and a lower-quality built environment, a greater connection can be derived by examining the linkage between the built environment and mental health. In one study, a statistically significant association was found between depression among residents and the presence of copious amounts of graffiti, one indicator of a low-quality built environment (Weich et al., 2002). However, there still remains a paucity of study on the association between the built

environment and opioid abuse and overdose. This study touches on an element of the built environment by including vacant land in the analysis.

3. Data and Methodology

The purpose of this research is to identify how well the SDoH framework applies to the opioid epidemic in Milwaukee County and to quantify the spatial spillover effect present within the mortality rate at the census tract and neighborhood level by applying the spatial econometrics model. The opioid mortality data was sourced from the Milwaukee County medical examiner's office all drug deaths dataset from 2003 to 2018. Records were filtered to only include deaths involving at least one opioid (i.e., heroin, fentanyl, methadone, oxycodone, hydrocodone, morphine, codeine, hydromorphone, meperidine, buprenorphine, tapentadol, oxymorphone, carfentanil, or butorphanol), and deaths that occurred accidentally (excluding suicide, homicide, natural, and undetermined causes). Residence addresses for each decedent inside Milwaukee County were then geocoded. Residence addresses were used as opposed to the death address due to the concentration of deaths occurring at hospitals. These geocoded points were then aggregated to both census tract level and neighborhood level for use in the calculation of the age-standardized death rate.

Explanatory variables to be used in the regression analysis and for the calculation of the mortality rate were sourced from the 2010-2014 American Community Survey (ACS) 5-Year estimates using Social Explorer. 19 variables were extracted (not including total population and the age categories) to be used in the Principal Components Analysis (Table 1). Age categories were aggregated to the following groups: 19 and under (minors), 20 to 34 (young adults), 35 – 54 (middle-aged adults), and 55 and over (older adults). The census tract level data was then interpolated to the neighborhood level using the areal interpolation package 'areal' in R (Prener & Revord, 2019).

3.1 Age-Adjusted Mortality Rate

The mortality rate for each census tract and neighborhood was calculated using the direct standardization method, stratified by age group, creating an age-adjusted mortality rate (ADR). This rate is preferred over count data or an age-specific rate as it creates a comparable standard for each record and takes into account the age-structure of each location, standardizing it to a singular population (Curtin & Klein, 1995). The direct method is applied as each unit of analysis has a known number of occurrences, allowing for the calculation of the age-specific mortality rate (ASpR) (Naing, 2000). The first step in the direct-standardization process is calculating the individual tract/neighborhood age-specific mortality rate per 1,000 people for each age group:

$$ASpR = \frac{\#Deaths\ in\ Age\ Group}{Total\ Population\ in\ Age\ Group} \times 1000$$

The next step is calculating the expected deaths of the standard population. The 2010 Milwaukee County intercensal total population was used as the standard population. This internal standardization allows for a more robust statistical analysis, however, the caveat of using Milwaukee County instead of the total US population as the standard population is that these rates can not be compared to other studies using a different standard population (Curtin & Klein, 1995). The expected deaths were calculated as follows where p is equal to the standard population, and i signifies the ASpR for each of the four age groups:

$$Total\ Expected\ Deaths = \sum \frac{p(ASpR_i)}{1000}$$

The final step in the process is calculating the age-adjusted mortality rate (ADR). The total expected deaths are divided by the standard population and multiplied by 1000 to create a rate

per 1,000 people (given the average population of a census tract/neighborhood this was more appropriate than a larger multiple) (Naing, 2000).

$$ADR = \frac{\text{Total Expected Deaths}}{\text{Standard Population}} \times 1000$$

3.2 Principal Component Analysis

Principal Component Analysis (PCA) is a statistical technique used to reduce the dimensionality of large datasets into more manageable and interpretable forms (Jolliffe & Cadima, 2016, Wold, 1987). PCA takes the original variables and outputs them as a more optimal set of variables (principal components) while still maintaining a large percentage of the variability within the original dataset. The higher the total variance that can be incorporated into the components, the higher the quality of the principal component analysis. When dealing with variables of different measurements, it is necessary to standardize the variables and use the resulting z-scores in the PCA in order to ensure that the PCs are comparable (Jolliffe & Cadima, 2016). In order to properly interpret the variability of the original dataset, it is necessary to perform a rotation of the data to maximize the correlation between the original variables and the PCs (Park & Xu, 2020). Due to the large set of variables chosen for this study, it was necessary to perform a PCA on the ACS variables in order to reduce the dimensionality of the data and mitigate multicollinearity. The variables were standardized, and the resulting z-scores used in the PCA. In order to better understand the result, the PCs were rotated using a varimax rotation. The resulting PCs were then used as explanatory variables in the following regression analyses.

3.3 Multivariate Ordinary Least Squares Regression

Multivariate ordinary least squares regression (OLS) is used to examine how one variable (the dependent variable (y)) relates to a group of explanatory variables (the independent variables (x)) (Rogerson, 2019). A multivariate OLS regression equation can be defined as follows, with p independent variables and where \hat{y} is the predicted dependent variable:

$$\hat{y} = a + b_1x_1 + b_2x_2 + \dots + b_px_p$$

Prior to using a spatial econometrics model, it is necessary to perform an OLS regression in order to test the residuals for spatial autocorrelation using Moran's I statistic (Anselin, 2003, Can, 1990). This study applies the multivariate OLS regression as the first step in examining the relationship between the opioid overdose mortality rate (y) and the PCs (x) resulted in the previous section.

3.4 Spatial Econometrics Model

Spatial econometrics models have been used to study a broad range of topics where spatial autocorrelation or spatial heterogeneity is inherent including crime rates, juvenile delinquency, neighborhood inequality, housing prices, and poverty rates among children (Ceccato, Vania, Haining, Robert, & Signoretta, 2002, Mennis, Harris, Obradovic, Izenman, Grunwald, & Lockwood, 2011, Morenoff, Sampson, Robert, & Raudenbush, 2001, Can, 1990, Voss, Long, Hammer, & Friedman, 2006). Spatial autocorrelation refers to the existence of clusters of "similar or dissimilar values in geographic space" (Can, 1990, p. 258). Spatial autocorrelation denotes that there are spatial trends in the data that cannot be captured by nonspatial models. When spatial autocorrelation is present in the data, it is necessary to use a spatial regression method in order to consider the spatial dependency (Anselin, 2002).

Spatial econometrics is built upon a set of regression equations, each incorporating spatial dynamics in some way (Anselin, 2010). Selecting an appropriate model can be done multiple ways using different approaches. One classical approach is using the Lagrange multiplier tests to identify whether or not the spatial lag or the spatial error model is appropriate based on the significance of their output (Mur & Angulo, 2009). Another method to choosing an appropriate model is by using the spatial Durbin model. The spatial Durbin model contains the foundations of both the spatial lag and spatial error models, nesting them within the equation (Mur & Angulo, 2006). By taking this approach, it is possible to narrow down from the general Durbin model to a more specific econometric model. As with all other econometric models, the Durbin model uses a row-standardized weight matrix to account for the spatial relationship among the data. Considering W as the spatial weight matrix, y as the dimension of the weight matrix and the dependent variable, ε as the error term, and X as the matrix of independent variables, the spatial Durbin model is as follows (Beer & Riedl, 2011):

$$y = \rho Wy + X\beta + wX\gamma + \varepsilon$$

$$\varepsilon \sim N(0, \sigma^2 I)$$

By setting $\gamma = 0$, the spatial lag model is formed. Similarly, the spatial error model is formed by applying $\gamma = -\rho\beta$ (Beer & Riedl, 2011).

The spatial lag model accounts for spatial autocorrelation by incorporating a spatially lagged dependent variable (Wy) into the linear regression equation (Anselin, 2003). This spatial lagged y creates a global spillover effect in which the value of y in one geographic unit affects the value of all other units. In this case, every census tract or neighborhood is influenced by the value of every other census tract. This makes it impossible to interpret the coefficients of the

model in a literal way. Instead, the direct, indirect, and total effects are studied to examine the relationship of the spatial properties within and outside of each census tract. Considering the variables as the same as those described in the spatial Durbin model, the spatial lag model is as follows (Anselin, 2003):

$$y = \rho W y + X\beta + \varepsilon$$

The spatial error model also originates from the spatial Durbin model, however, there are key differences between it and the spatial lag model. Instead of incorporating the spatial dependence into the dependent variable, the spatial error model incorporates spatial autocorrelation into an error term (Can, 1990). This results in the inability to interpret the behavioral reason for the autocorrelation based on the results. The spatial error model is more appropriate when spatial autocorrelation is only relegated to nearby neighbors, not demonstrating a global feedback effect (Anselin & Moreno, 2003). With λ as the spatial autoregressive coefficient and μ as the normal error term, the spatial error model is defined as follows:

$$y = X\beta + \varepsilon$$

$$\varepsilon = \lambda W \varepsilon + \mu$$

In this study, both the Lagrange multiplier test and the spatial Durbin model were used to identify an appropriate model for the data. Based on the diagnostic tests, the spatial lag model was identified as the model of best-fit. For comparison, the spatial error model was also applied, however, the result was not significant enough to be considered. In the following chapter, I will discuss the results of both of these models and explain why the spatial lag model was ultimately chosen to be the most representative.

4. Results and Discussion

Milwaukee County has been heavily impacted by the opioid epidemic, especially in recent years with the introduction of synthetic opioids into the market (Peterson et al., 2019). In 2017, opioids became the leading cause of non-natural death in Milwaukee County, contributing to 3.8% of all deaths. First, this chapter will explore the descriptive statistics of opioid overdose decedents in Milwaukee County. It will then explore the results of the PCA, the regression analysis, and the spatial econometrics model.

4.1 Descriptive Statistics of Opioid Overdose Deaths in Milwaukee County

Of the 3343 drug-related deaths that occurred in Milwaukee County between 2003 and 2018, 2671 were associated with at least one opioid³. The most common mode of death was by accident (n = 2,509), followed by undetermined (n = 78), suicide (n = 72), homicide (n = 5), and natural (n = 1). Just considering the accidental deaths, 70% of the decedents were White, 20% Black, 7.6% were Hispanic/Latino, with the remainder falling into the Other⁴ race category. 1,660 were males, while 849 were female. Between 2003 and 2010, there were only 755 accidental deaths associated with opioid overdose. From 2011 – 2018, the amount of opioid overdose deaths increased nearly 250% to 1,754 incidences. Figure 2 displays the density of accidental opioid overdose deaths in Milwaukee County. Clusters are present on the east side, downtown, the south side, and in West Allis and South Milwaukee. The most prevalent opioids involved in overdose were heroin (n = 819), fentanyl (n = 582), and oxycodone (n = 395). Out of

³ Opioids: heroin, fentanyl, methadone, oxycodone, hydrocodone, morphine, codeine, hydromorphone, meperidine, buprenorphine, tapentadol, oxymorphone, carfentanil, or butorphanol

⁴ The Other racial category includes Asian, American Indian/Alaskan Native, and Native Hawaiian/Pacific Islander.

the 2,509 accidental overdose deaths, over 1,700 involved at least one other substance. Of these mixed drug overdoses, about 600 involved cocaine and about 950 involved a benzodiazepine.

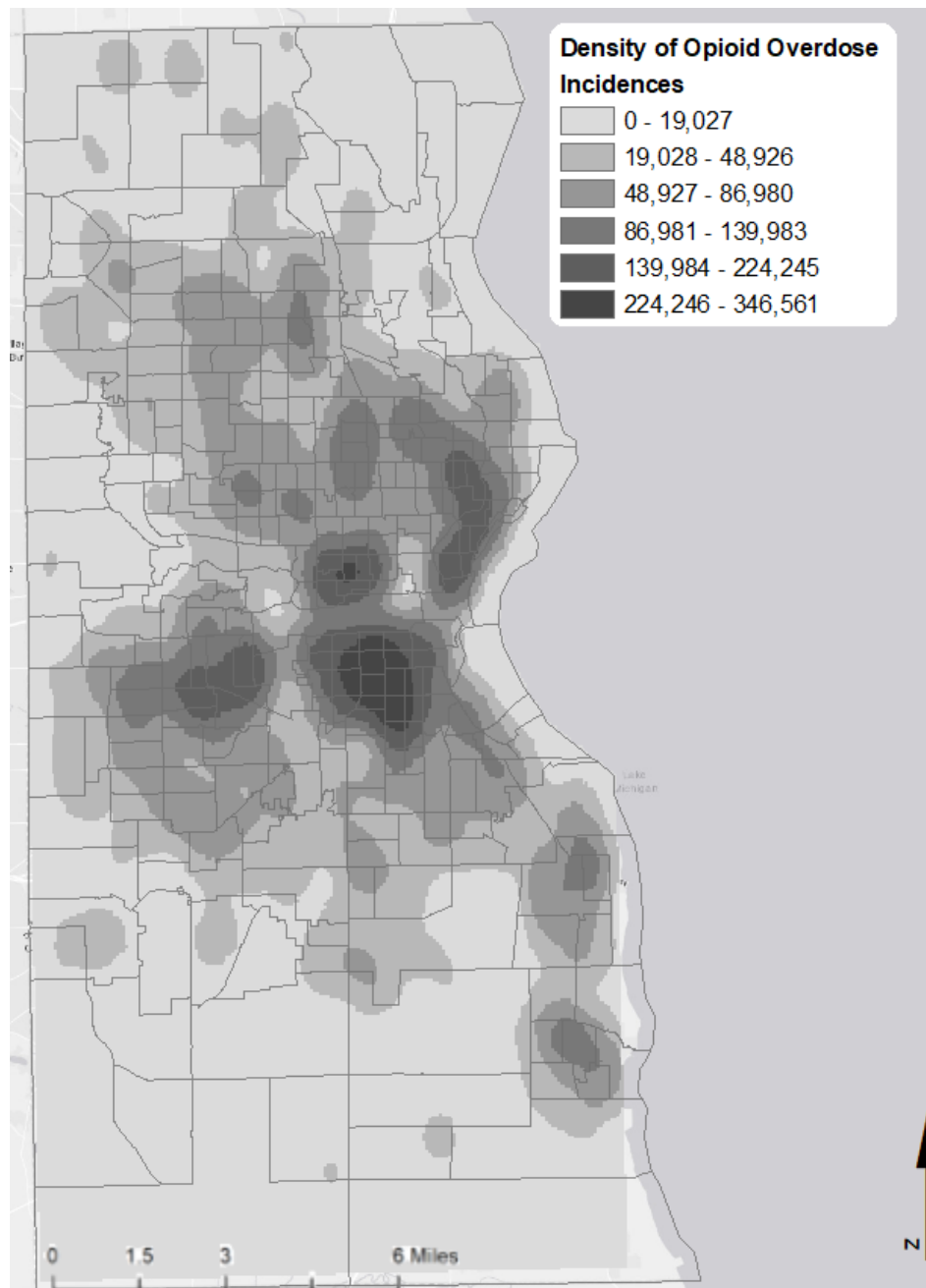


Figure 2. The kernel density of accidental opioid overdoses resulting in death in Milwaukee County. The legend should not be directly interpreted. Instead, a clearer explanation is that darker colored cells have more points around them than lighter color cells. Within these dark clusters, it is more likely that a fatal opioid overdose will occur. Clusters are present on the east side, downtown, the south side, and in West Allis and South Milwaukee.

The average age-adjusted mortality rate (ADR) at the census tract and neighborhood level is 2.9 deaths per 1,000 people and 2.7 deaths per 1,000 people, respectively. Figures 4 and 5 display the ADR at tract and neighborhood level, respectively. The ADR had a positive skew which required a natural log transformation to correct to a normal distribution (Figure 3). The tracts/neighborhoods with no deaths resulted in a value of -Infinity and were replaced with 0s as this resulted in a more significant result than removing the records. This log-transformed value was then used as the dependent variable in the subsequent regression analyses.

4.2 The Distribution of Socioeconomic Factors in Milwaukee County

23 variables representing the built environment, blue-collar occupations, and socioeconomic demographic characteristics were included in the principal component analysis. The PCA resulted in 6 components with eigenvalues greater than one capturing 78% and 80% of the variance at the neighborhood and tract level, respectively. Using the varimax rotated component matrix, the PCs were defined based on a loading value of greater than the absolute value of .5. At the neighborhood level, PC 1 was named “Socioeconomic Disadvantage,” containing variables such as unemployment rate, using public transportation to commute, female-headed households, the poverty rate, and vacant households. PC 2 was named “Hispanic population, labor occupations, and low educational attainment” including total Hispanic population, construction and material moving occupations, and high school educational attainment level. PC 3 was named “Females and Some College Education,” and PC 4 was named “Males and Income Inequality”, containing said variables. PC 5 was named “Age Composition” and negatively correlates with young adults, while positively correlating with middle-aged adults and older adults. PC 6 only contained the Other racial group category and was named “Minority Populations” (Table 1).

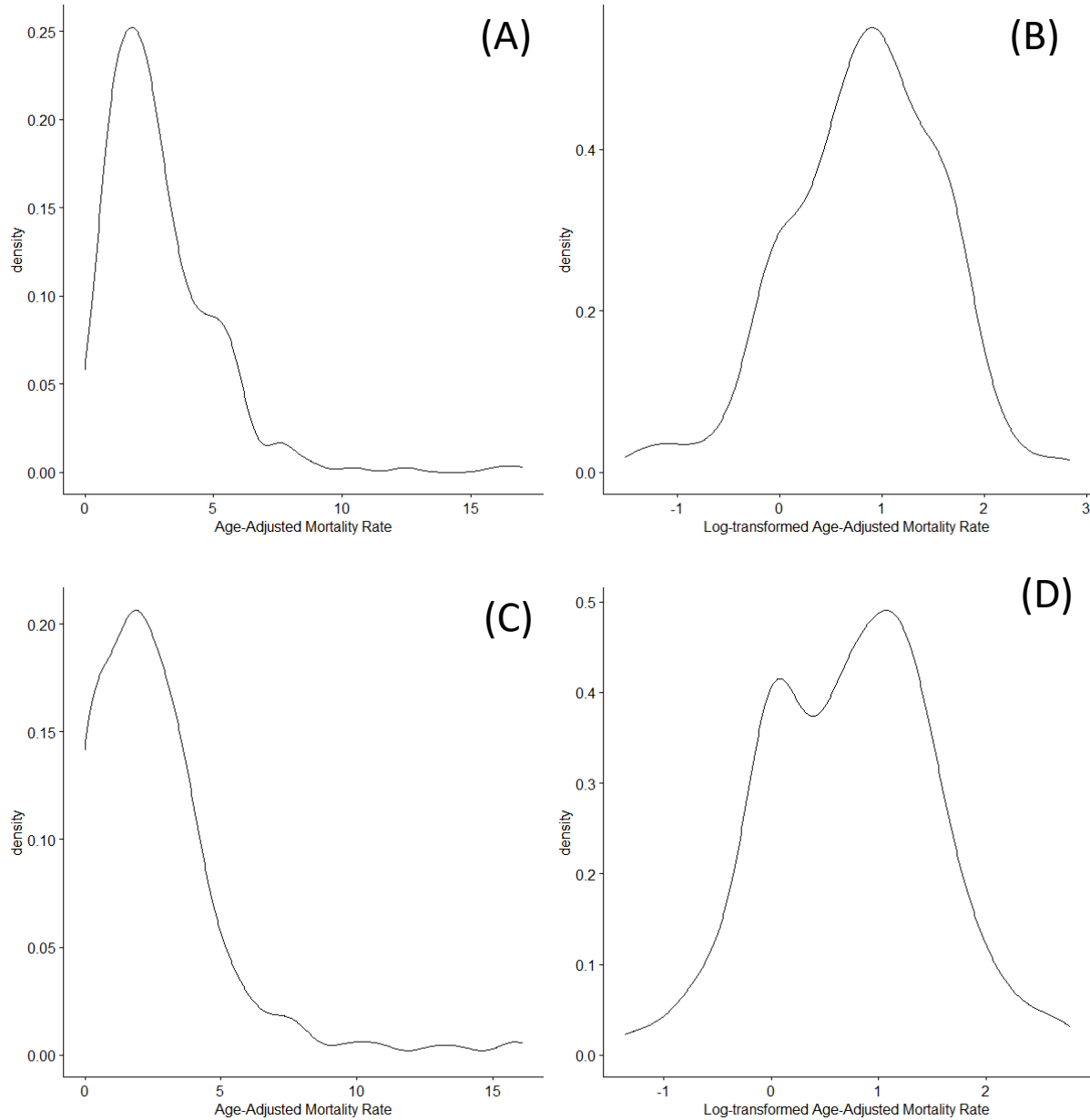


Figure 3. For all plots, the y-axis represents the probability density function, and the x-axis represents the mortality rate. (A) Density plot of the census tract level Age-Adjusted Mortality Rate. (B) Density plot of the log-transformed Age-Adjusted Mortality Rate. (C) Density plot of the neighborhood level Age-Adjusted Mortality Rate. (D) Density plot of the neighborhood level log-transformed Age-Adjusted Mortality Rate.

At the census tract level, the loadings presented slightly different components than the neighborhood level. PC 1 and PC 2 have roughly the same composition as the neighborhood level and retain the same names. PC 3 at the tract level is named “Age Composition and Income Inequality,” positively correlating with young adults, and negatively correlating with middle-

aged adults, while retaining income inequality. PC 4 negatively correlates with males and positively correlates with females, being named “Gender.” PC 5 is named “Some College Education” and PC 6 is named “Minority Population,” each only containing those variables (Table 2).

Figure 6 represents the principal component scores at the census tract level for principal component 1, “Socioeconomic Disadvantage.” Socioeconomic disadvantage appears to be concentrated in the north central area of the county, an area historically known to have high crime rates and a majority Black population. Figure 7 represents principal component 2, “Hispanic Population and Labor Occupations” and is concentrated within the southern half of the county, an area known for lower incomes and a high concentration of Hispanics. Figure 8 represents principal component 3, “Age Composition and Income Inequality.” This PC has higher scores located downtown and along Lake Michigan on the East Side of the county. Figure 9 represents principal component 4, “Gender,” and has a seemingly random distribution across the county. Figure 10 represents principal component 5, “Some College Education,” and has low scores along the northern half of Lake Michigan and south of downtown. Figure 11 represents principal component 6, “Minority Populations,” and has a seemingly random distribution. The resulting PCs will be used as the explanatory variables in the following regression analyses.

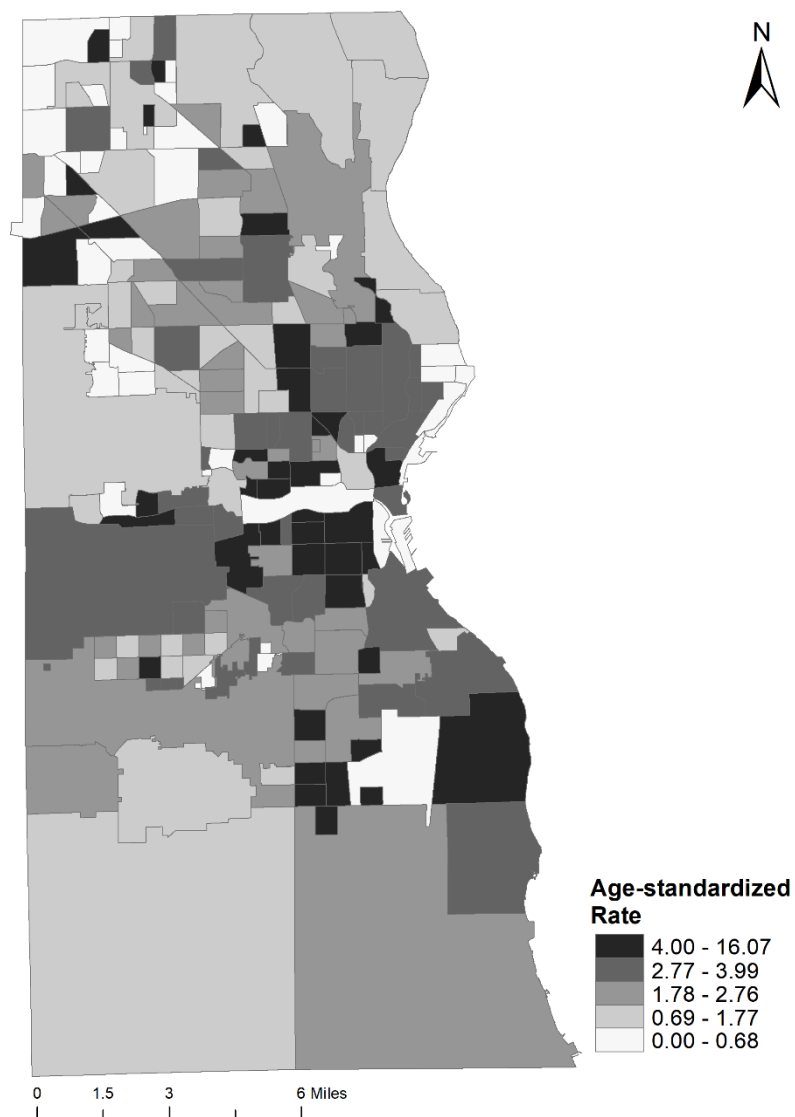


Figure 4. The Age-Adjusted Mortality Rate by Neighborhood in Milwaukee County.

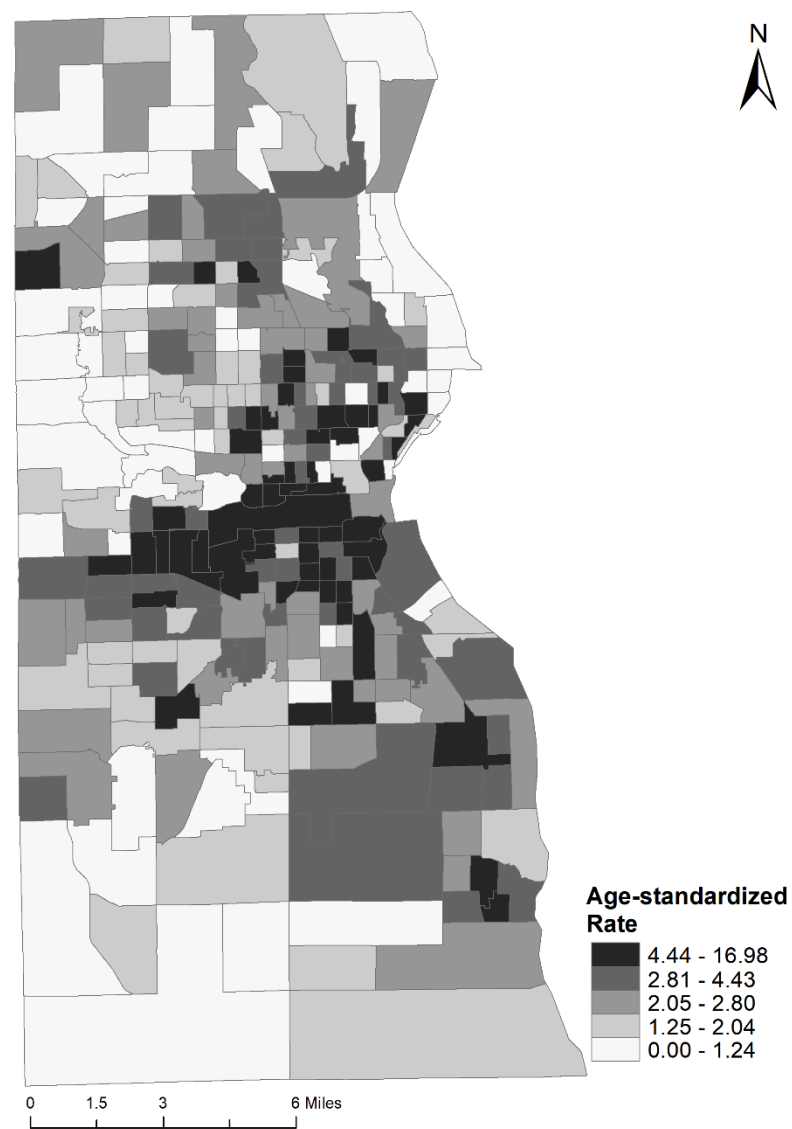


Figure 5. The Age-Adjusted Mortality Rate by Census Tract in Milwaukee County.

Component Number	PC 1	PC 2	PC 3	PC 4	PC 5	PC 6
% of Variance	33.2%	13.3%	9.8%	8.7%	8.4%	5%
PC Name	Socioeconomic Disadvantage	Hispanic Population, Labor Occupations, and Low Education	Females and Some College Education	Males and Income Inequality	Age Composition	Minority Populations
Loaded Variables (as a % excluding median income)	Unemployment (+), White (-), Public Transit (+), Female Headed Household (+), Black (+), Public Assistance Income (+), Poverty (+), Vacant Households (+), Less than HS Edu. (+), Age Under 19 (+), Bachelor's degree (-), Median Income (-)	Total Hispanic Population (+), Construction Occupations (+), Material Moving Occupations (+), High School Education (+)	Some College Education (+), Females (+)	Males (+), Gini Index of income inequality (+)	Age 20 to 34 (-), Age 35 to 54 (+), Age 55 and over (+)	Other racial category (+)

Table 1. This table shows the output for the principal component analysis at the neighborhood level using the varimax rotated sum of squares loadings. The (+) denotes a positive correlation whereas a (-) denotes a negative correlation among the loadings.

Component Number	PC 1	PC 2	PC 3	PC 4	PC 5	PC 6
% of Variance	34.2%	13 %	10.2%	9.6%	7.4%	4.8%
PC Name	Socioeconomic Disadvantage	Hispanic Population, Labor Occupations, and Low Education	Age Composition and Income Inequality	Gender	Some College Education	Minority Populations
Loaded Variables (as a % excluding median income)	Unemployment (+), White (-), Public Transit (+), Female Headed Household (+), Black (+), Public Assistance Income (+), Poverty (+), Vacant Homes (+), Less than HS Edu. (+), Age Under 19 (+), Bachelor's degree (-), Median Income (-), Age 55 and over (-)	Total Hispanic Population (+), Construction Occupations (+), Material Moving Occupations (+), High School Education (+)	Age 20 to 34 (+), Age 35 to 54 (-), Gini Index of income inequality (+)	Males (-), Females (+)	Some College Education (+)	Other racial category (+)

Table 2. This table shows the output for the principal component analysis at the census tract level using the varimax rotated sum of squares loadings. The (+) denotes a positive correlation and the (-) denotes a negative correlation among the loadings.

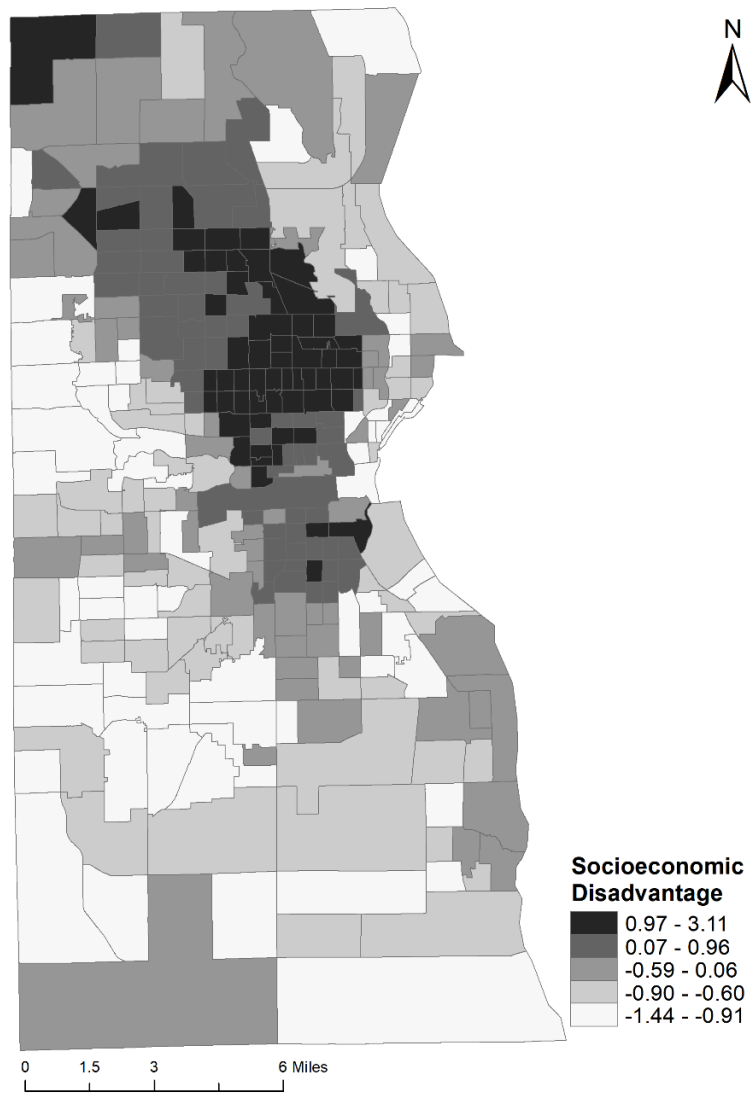


Figure 4. PC Scores for Census Tract Level PC 1 – Socioeconomic Disadvantage

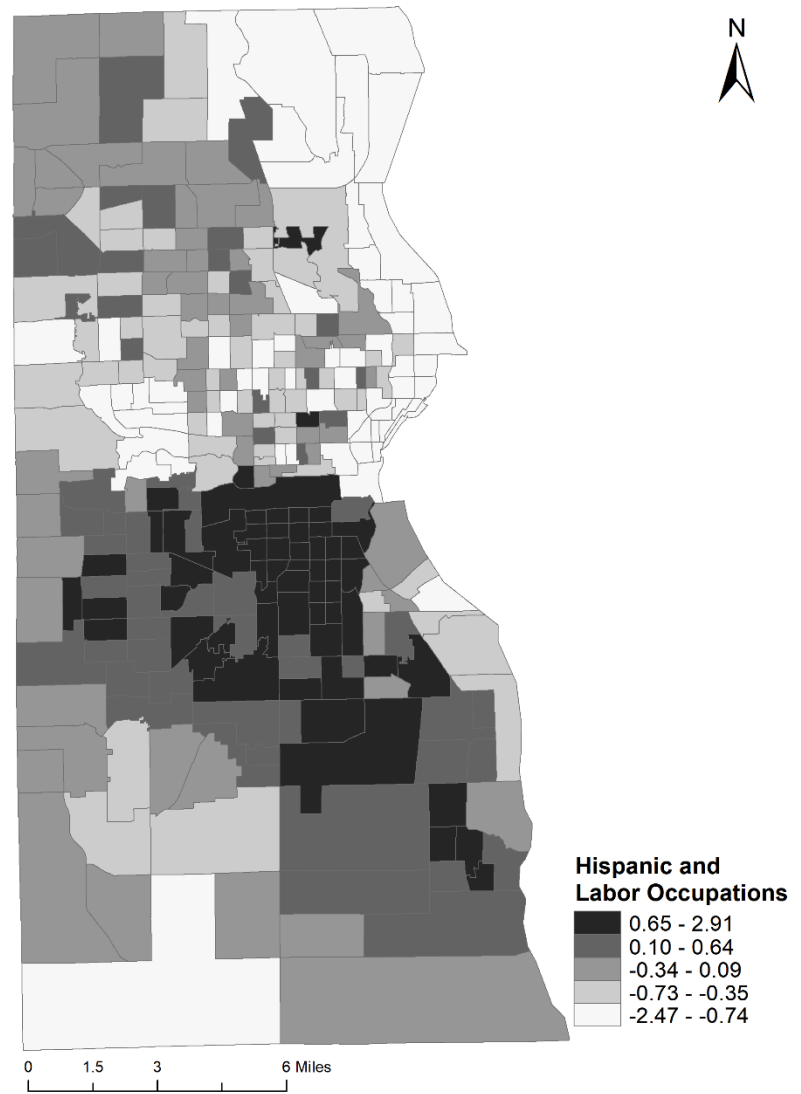


Figure 5. PC Scores for Census Tract Level PC 2 – Hispanic Population and Labor Occupations

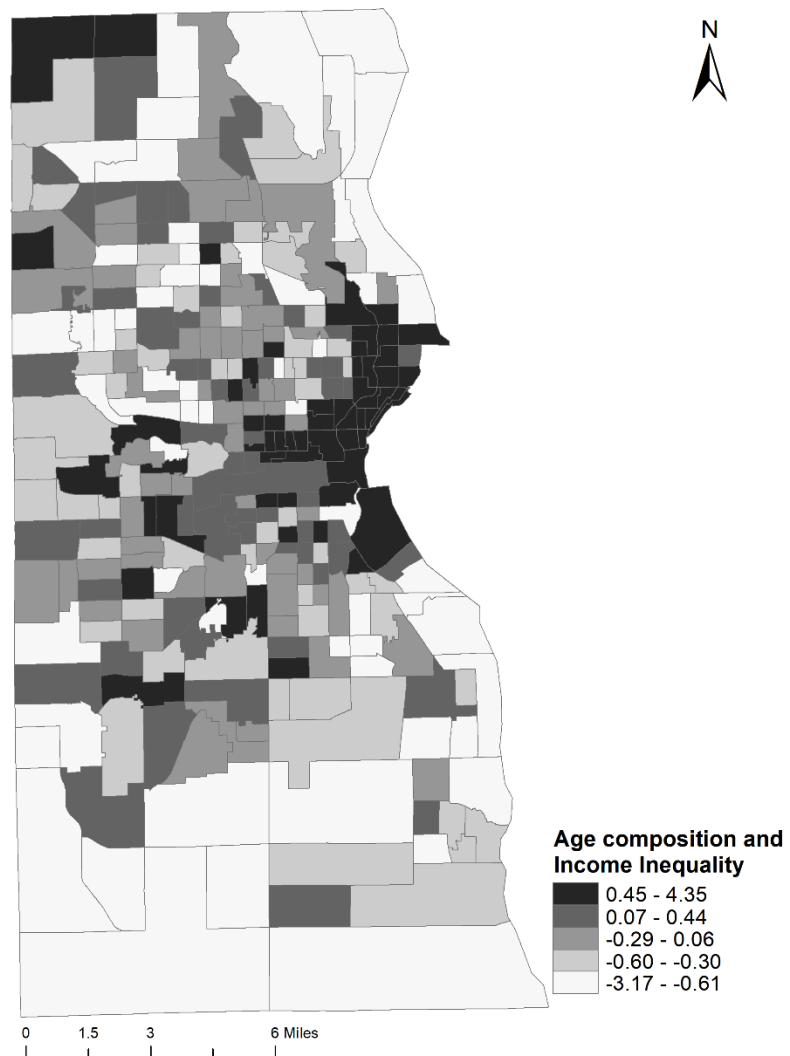


Figure 6. PC Scores for Census Tract Level PC 3 – Age Composition and Income Inequality

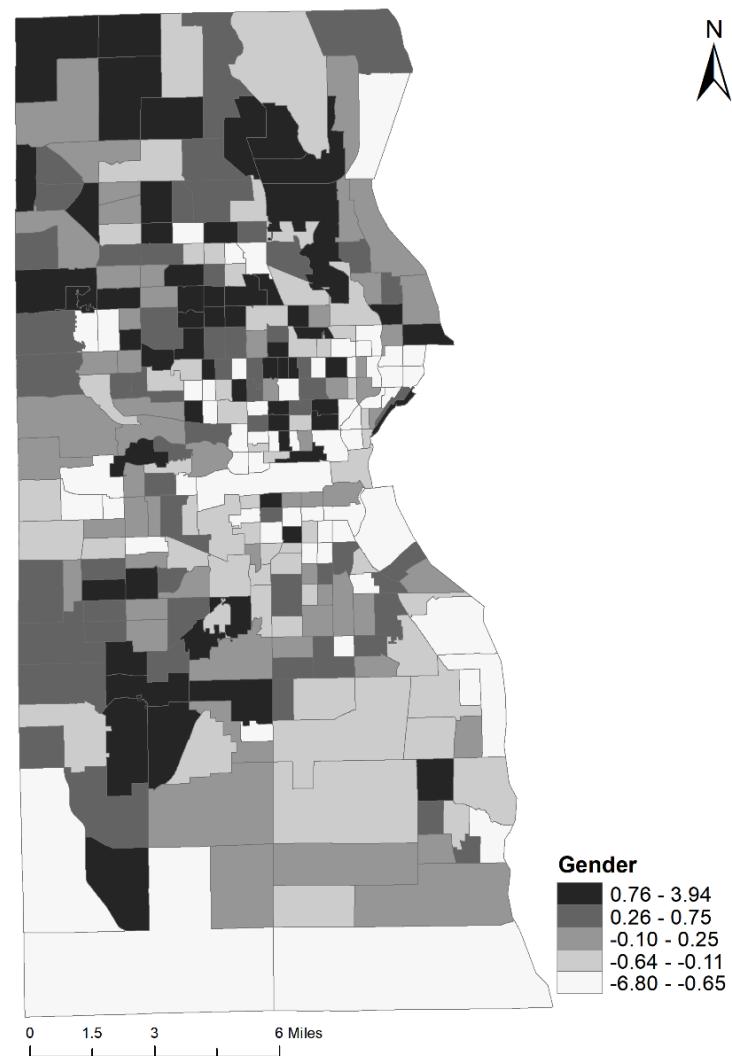


Figure 7. PC Scores for Census Tract Level PC 4 – Gender

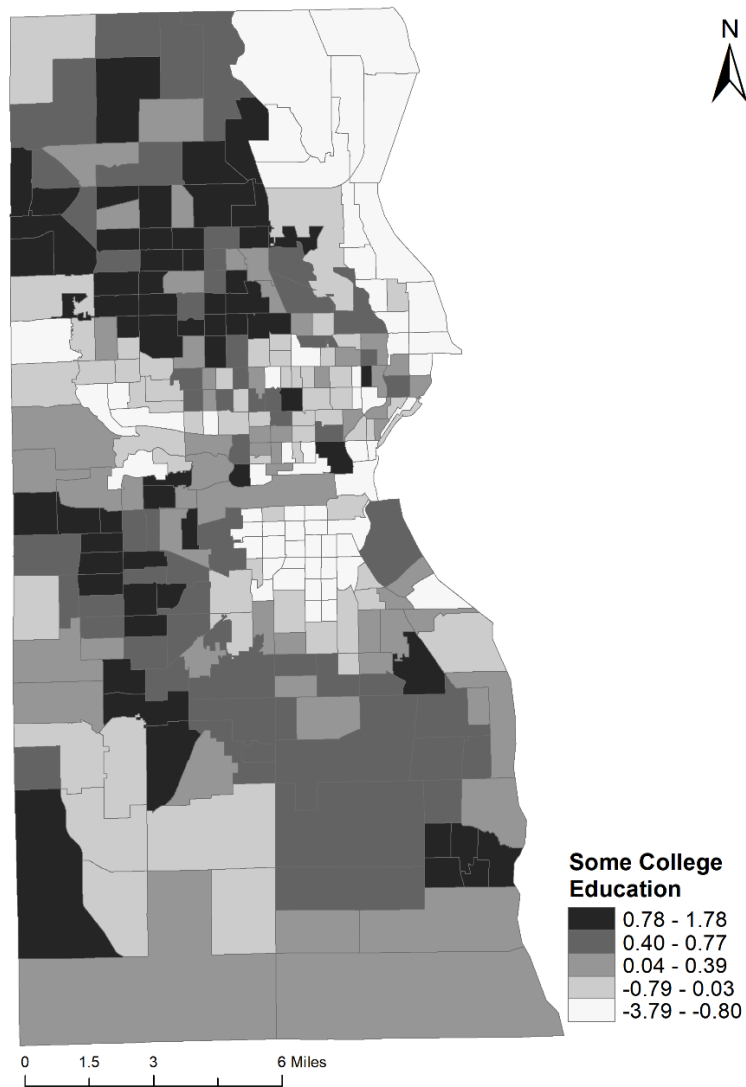


Figure 8. PC Scores for Census Tract Level PC 5 – Some College Education

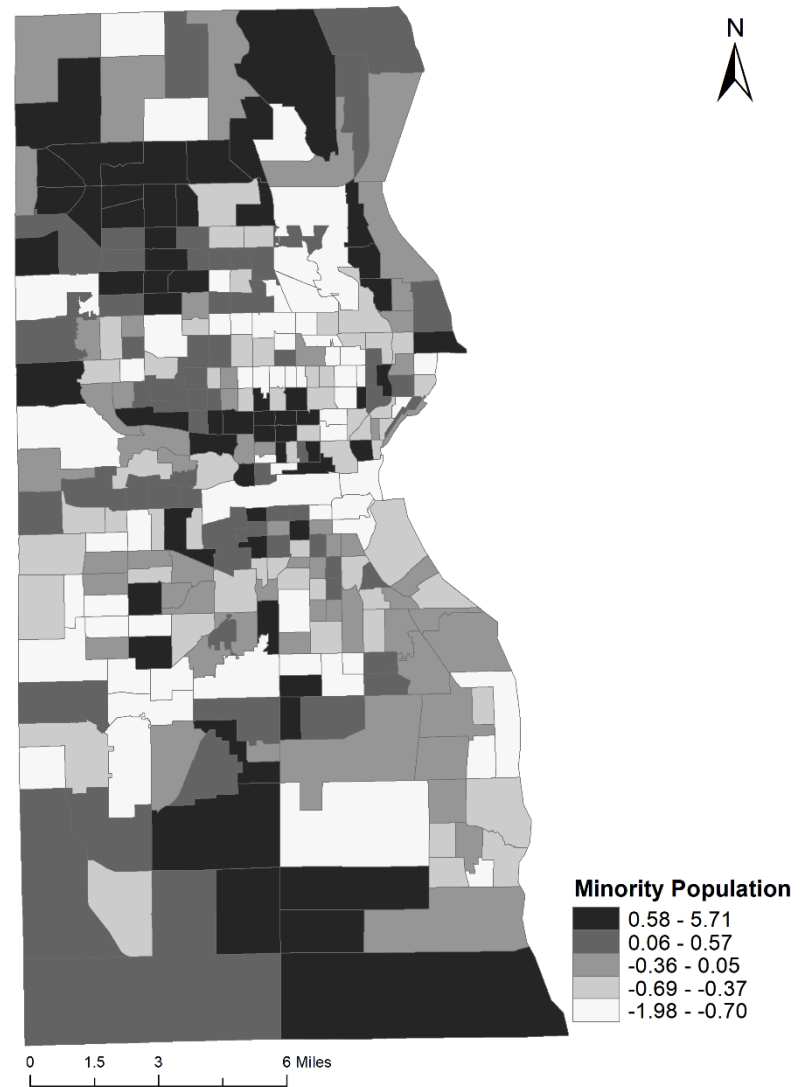


Figure 9. PC Scores for Census Tract Level PC 6 – Minority Population

4.3 The Causal Relationship between Social Determinants and the Opioid Epidemic

Using the PCs as the independent variables and the log-transformed ADR as the dependent variable, multivariate OLS regression was performed at the neighborhood and census tract level in order to detect if there was spatial autocorrelation among the residuals. At the neighborhood level, there was no spatial autocorrelation found among the residuals. This is likely due to the variable size of the neighborhoods and there being more neighborhoods without overdoses. The neighborhood level was removed from the remainder of this study.

At the tract level the multivariate OLS regression results were significant. As the dependent variable was log-transformed to remove the positive skew, the log percent change was calculated by taking the exponential of the coefficient, subtracting 1, and multiplying by 100⁵. This value describes the relationship of the variables with the overdose mortality rate. For every 1 unit increase in PC *X* there is an *x* percent change in the opioid overdose mortality rate. For example, a 1 unit increase for PC 1, socioeconomic disadvantage, will explain a 24% increase in the tract overdose mortality rate (Table 3). Every time there is a one unit increase in PC 1, 2, or 3, the most significant variables, there is an expected increase in the mortality rate by 24%, 30%, or 18%, respectively. Overall, the Adjusted R-squared for this model is 0.29, meaning that these variables can only explain 29% of the variance of the overdose mortality rate in Milwaukee County. However, according to Global Moran's *I*, there is high spatial autocorrelation among the residuals, indicating that it is appropriate to apply a spatial regression model.

⁵ $(\exp(x)-1)*100$ where *x* is the coefficient estimate.

Predictor	<i>b</i>	<i>beta</i>	<i>r</i>	Log %Change
(Intercept)	0.83**			
PC_1	0.22**	0.30	0.30**	24.4%**
PC_2	0.26**	0.36	0.36**	29.7%**
PC_3	0.17**	0.23	0.23**	18.3%**
PC_4	-0.09*	-0.12	-0.12*	-8.2%*
PC_5	0.00	0.01	0.01	0.4%
PC_6	-0.07	-0.09	-0.09	-6.6%
				$R^2 = 0.291$ **

Table 3. Regression results using the log-transformed Age-Adjusted Mortality Rate as the criterion

Note. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. *b* represents unstandardized regression weights. *beta* indicates the standardized regression weights. *r* represents the zero-order correlation.

* indicates $p < .05$. ** indicates $p < .01$.

4.4 The Spatial Influence on the Opioid Epidemic in Milwaukee County

Using the log-transformed age-standardized mortality rate as the dependent variable and the principal components as the explanatory variables the spatial lag autoregressive model was used to identify the relationships between these variables. Rho is the spatial lag parameter that indicates the intensity of the global spillover effect. It measures how much influence each census tract has on all other tracts in the study area. The Rho value of 0.3 indicates that there is a significant positive spatial effect of the opioid mortality rate at the census tract level (Table 4). This could be caused from the tendency of opioid abuse to be concentrated in neighborhoods that extend beyond the boundaries of a census tract. Also, when opioid abuse is present in a community it could be indicative that there are upstream factors at the city or county level that have contributed to this local abuse that may extend across the whole area.

With the spatial lag model, the effect of the log-transformation on the resulting coefficients cannot be translated into a percent change in the same way as the OLS model. However, even without the log-transformation, the coefficients of a spatial lag model cannot be interpreted in the same way as an OLS model because of the global feedback effect. Whenever something in one census tract changes, it effects all other values. Instead, we look at the average direct, indirect, and total effects across all tracts in order to get an understanding of how these variables impact the mortality rate. The average direct effect measures the impact of that variable within the census tract, not considering its neighbors. The average indirect effect measures the spatial effect that each variable has on its neighbors. However, in order to understand the overall impact of these variables, it is necessary to look at the total impact, or the sum of the average direct and indirect impacts.

Across all three categories, PC 1, 2, and 3 are significant. PC 4: Gender, PC 5: Some College Education, and PC 6: Minority Populations are not significant in determining the effects of opioid overdose mortality. PC 2 – Hispanics and Labor Occupations has the highest overall impact at 0.28 indicating that high Hispanic populations and a prevalence of laborious Occupations contribute to higher tract mortality rates. This is possibly due to the increased likelihood of people working in manual labor positions to get injured or experience chronic pain and be prescribed an opiate. Principal Component 1 – Socioeconomic Disadvantage, also has a significant total impact on tract mortality rates. This reinforces the idea of drug abuse and addiction as a disease of despair. People of lower socioeconomic status are also likely to turn to heroin due to it being a cheaper alternative to prescription opioids. However, it is also uncontrolled and is the leading cause of opioid overdose mortality in Milwaukee County. The third principal component, Age Composition and Income Inequality, is also significant, indicating that there is an age structure relating to higher mortality rates and that income inequality plays a role as well. Overall, the estimated R-squared for this model is 0.34, whereas the R-squared for the OLS regression is 0.29 indicating that the Spatial Lag Model is a better fit in explaining this variation. Although the R-Squared seems low, it is still a reasonable result in explaining the opioid mortality rate in terms of the geographic social determinants of health.

Predictor	<i>b</i>	Direct	Indirect	Total
(Intercept)	0.55**			
PC_1	0.17**	0.17**	0.07**	0.25**
PC_2	0.18**	0.18**	0.09**	0.28**
PC_3	0.13**	0.13**	0.06**	0.20**
PC_4	-0.06	-0.06	-0.03	-0.09
PC_5	0.01	0.01	0.00	0.02
PC_6	-0.05	-0.05	-0.02	-0.07
				$R^2 = .341^{**}$
				$Rho = 0.33^{**}$

Table 4. Spatial Lag Model using the log-transformed Age-Adjusted Mortality Rate as the criterion

Note. A significant b-weight indicates the beta-weight and semi-partial correlation are also significant. b represents unstandardized regression weights. Direct indicate the total direct effects. Indirect indicates the total indirect effects. Total indicates the total effects. Rho indicates the spatial lag parameter.

* indicates $p < .05$. ** indicates $p < .01$.

5. Conclusion

This study found that Milwaukee County has significant spatial autocorrelation in opioid overdose mortality rates. It provides an empirical study at the local level of how certain social determinants of health affect fatal opioid overdoses. Overdose mortality demonstrates a positive spatial feedback effect, indicating that the opioid epidemic is not restricted to a geographic boundary, rather it diffuses across the community. Roughly 34% of the total variation was explained by the lag model. Most of the variables used were related to socioeconomic status and demographics, labor occupations and vacant households withstanding. What the results indicate is that the opioid epidemic disproportionately affects communities of lower socioeconomic standing. It is unclear whether this is causative or correlative, given the nature of substance abuse it could be both. This study also found that Hispanic communities and workers engaged in manual labor (which could coincide) have a higher likelihood of fatally overdosing on opioids. In terms of the social determinants of health, the results of the spatial lag model are consistent with the County Health Rankings Model. This study explained 34% of the variation corroborating the County Health Rankings model in which socioeconomic factors only relate back to 40% of the causal factors for health outcomes. Future research should incorporate more of the variables used in the County Health Rankings model to get a better understanding of this behavior. While this study included one variable associated with the built environment (vacant homes), incorporating variables that better explain health behaviors, the built environment, and health care quality and accessibility can further explain the contextual effects of opioid abuse and overdose.

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