ABSTRACT

Title of dissertation: MULTI-DIMENSIONAL MEASURES OF GEOGRAPHY AND THE OPIOID EPIDEMIC: PLACE, TIME AND CONTEXT

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The opioid crisis has hit the United States hard in recent years. Behavioral patterns and social environments associated with opioid use and misuse vary significantly across communities. It is important to understand the geospatial prevalence of opioid overdoses and other impacts related to the crisis in order to provide a targeted response at different locations. This dissertation contributes a framework for understanding spatial and temporal patterns of drug prevalence, treatment services access and associated socio-environmental factors for opioid use and misuse. This dissertation addresses three main questions related to geography and the opioid epidemic: 1) How did drug poisoning deaths involving heroin evolve over space and time in the U.S. between 2000-2016; 2) How did access to opioid use disorder treatment facilities and emergency medical services vary spatially in New Hampshire during 2015-2016; and 3) What were the relations between socio-environmental factors and numbers of emergency department patients with drug-related health problems over space and time in Maryland during 2016-

2018. For the first study, this dissertation developed a spatial and temporal data model to investigate trends of heroin mortality over a 17-year period (2000-2016). The research presented in this dissertation also involved developing a composite index to analyze spatial accessibility to both opioid use disorder treatment facilities and emergency medical services and compared these locations with the locations of deaths involving fentanyl to identify possible gaps in services. In the third study for this dissertation, I utilized socially-sensed data to identify neighborhood characteristics and investigated spatial and temporal relationships with emergency department patients with drug-related health problems admitted to the four hospitals in the western Baltimore area in Maryland during 2016 to 2018, in order to identify the dynamic patterns of the associations in terms of various socio-environmental factors.

MULTI-DIMENSIONAL MEASURES OF GEOGRAPHY AND THE OPIOID EPIDEMIC:

PLACE, TIME AND CONTEXT

by

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Dedication

To my parents

Lin Zhao (赵琳) *and Bingru Cao* (曹炳汝)

For their unconditional support and encouragement

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List of Abbreviations

E2SFCA: Enhanced two-step floating catchment area

ED: Emergency Department

EMS: Emergency Medical Services

GIS: Geographic Information System

GTWR: Geographically Temporally Weighted Regression

NDEWS: National Drug Early Warning System

NLP: Natural Language Processing

OSM: OpenStreetMap

VGI: Volunteered Geographic Information

Chapter 1 An overview of current trend of opioid epidemic

1.1 Motivation

Opioid use and misuse has been growing as public health emergency in the United States over the past decade. In 2017, approximately 30.5 million people over the age of 12 in the U.S. were reported to have used an illicit drug at some time in the past 30 days, according to the 2018 National Survey on Drug Use and Health (NSDUH) administered by the Substance Abuse and Mental Health Services Administration (SAMHSA) (Center for Behavioral Health Statistics and Quality, 2018). This is an increase of approximately 200% over the past decade, and has raised public concern. The increasing numbers in substance use and misuse have contributed to a significant increase in the number of mortality from drug overdose, which has been a leading cause of deaths across the country. Over 3 million individuals suffered an overdose involving an opioid, and 0.5 million were estimated to have a heroin use disorder till 2017 (Center for Behavioral Health Statistics and Quality, 2018). This harmful pattern has captured the attention of public health researchers as well as health geographers, and raised questions how, why, and where people become addicted to illicit substances, and what can be done to treat or prevent substance use disorders.

Geographers contribute a framework that involves building connections among people and places, cultures and activities. The contributions from geography for drug addiction are potentially a better understanding of the spatial patterns of opioid use and misuse, its diffusion over space and time, its interaction with geographical and social environments, and the barriers and strategies for treatment and prevention of opioid epidemic. Considered as a public health issue, opioid use and misuse can be explored by modifying and utilizing current geographic theories and methodologies from health and medical geography. These tools and methods are centered on geospatial computing with wider applications for spatial and social analyses. These would include exploring spatial and temporal patterns of health disparities, spatial and temporal data mining for health information, modeling spatial access to health care services, and understanding the dynamic associations between geographic locations and health outcomes. These fundamental themes in health geography are applicable to research on opioid-related health problems. In addition, high volumes of geocoded data for different substance use and social environment factors (e.g., different drug types and demographic variables) are becoming available, along with new high-speed computing platforms for data processing. Meanwhile, the sources of geospatial data for investigating substance use and misuse have been rapidly expanding, from survey data and medical examiner data, medical research institutions and government agencies, to socially sensed data (e.g., Twitter and OpenStreetMap), and from GPS-embedded devices (e.g., cell phones), providing volunteered geographic information (VGI) (Goodchild, 2007) and spatial behavior patterns. The richness in these different data types, and innovative geospatial techniques for modeling such data, are improving the foundation for geography and opioid use-related research from both quantitative and qualitative perspectives at personal and global scales.

This dissertation consists of three studies to examine spatial and spatiotemporal patterns of opioid use and misuse especially involving heroin, fentanyl and other opioids from the perspectives of the evolving patterns of mortalities from different drugs, disparities of access to treatment services, and the association between neighborhood characteristics and drug-related health problems. These geospatial measurements from GIScientists described the trends of opioid epidemic from multiple dimensions. The unique insights from the discovered spatial and temporal patterns and associations are important to local health officials and policy-makers for creating timely solutions in response to the opioid crisis and to offer strategies that result in a meaningful reduction to the burden of the tremendous loss of lives and social welfare.

1.2 Research on opioid epidemic: past and present

Although the opioid crisis started impacting the US approximately twenty years ago, research on opioids and overdoses due to illicit substances can be traced back to the 1970s when poly-drug toxicity was noted and mortalities caused by injecting illicit substances by older age groups were witnessed worldwide (Brecher, 1972; Manning & Ingraham, 1983; Stephen J, 1983). With the development of data collecting approaches, studies in metropolitan locations in the US (e.g., New York City and San Francisco) in 1990s used illicit substance overdose data collected from surveys and from medical examiners based on blood and urine samples (H. Cooper, Friedman, Tempalski, Friedman, & Keem, 2005; Davidson et al., 2003; Galea et al., 2003; Hahn, Evans, Ochoa, Davidson, & Moss, 2003; Seal et al., 2001). Using detailed personal information, these studies were able to reveal disparities of illicit drug use in terms of different demographic groups (e.g., race, ethnicity, gender, and age). In New York City, higher prevalence of opioids and other illicit substances (e.g., cocaine and methadone) were found among Latinos and African Americans, males, and middle-aged individuals (i.e., 35-44 years old) (Galea et al., 2003). In San Francisco, however, higher risk groups associated with recent fatal or non-fatal heroin overdoses were younger (< 30 years old), or had experienced an overdose, had been arrested for illicit drug use in the past year, or lived in low-income communities alone (Davidson et al., 2003; Seal et al., 2001). These studies based on event-level overdose data contributed to overdose prevention efforts with medical assistance, which were not applicable to the earlier 1970-1980 studies using witness data.

Since 2010, the rise in mortality due to opioid (e.g., heroin) use and misuse has been mostly associated with misuse of prescription opioids (e.g., oxycodone and hydrocodone), as well as long history of usage of recreational opioids and other substances (e.g., cannabis and cocaine) (M. Ford & Dulaney, 2014; Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2014). Earlier studies largely focused on opioid overdoses in large metropolitan locations including New York City and San Francisco (Galea et al., 2003; Hahn et al., 2003). Since 2010, however, the numbers of drug poisoning deaths involving heroin and other opioids has been increasing in rural locations in the US (Cicero, Ellis, Surratt, & Kurtz, 2014; Meiman, Tomasallo, & Paulozzi, 2015). The major drivers for this change include the lower street price of heroin and rising access to this substance. Drug poisoning deaths involving heroin increased seven folds from 2000 to 2014 in the US. While heroin was a major cause of death, since 2013, mortality involving fentanyl overdoses has increased sharply and since 2015 has been a more severe threat to public health compared to heroin, as fentanyl is embedded with more potent chemicals (30-50 times more powerful than heroin) and can easily be mixed with heroin or other drugs (e.g., cocaine) (Baldwin et al., 2018; Ciccarone, Ondocsin, & Mars, 2017).

In addition, studies have found that illicit drug use is significantly associated with neighborhood disadvantage and perceived stress (Brenner, Zimmerman, Bauermeister, & Caldwell, 2013) as well as residential instability (Molina, Alegría, & Chen, 2012). Neighborhoods with lower socioeconomic status (i.e., lower median household income and higher percent of disabled workers) are clustered with respect to fatal and non-fatal overdoses from prescription opioids and other illicit drugs (Hester, Shi, & Morden, 2012; Mennis & Mason, 2011).

The harmful health outcomes from opioid epidemic raised discussions of whether there are insufficient treatment services (i.e., buprenorphine or methadone maintenance programs, naloxone administration from emergency medical services, and also psychosocial services) in certain locations. The increasing pattern of drug poisoning deaths in, for example, rural locations, may be exacerbated by lower numbers of physicians (e.g., physicians to administer buprenorphine to treat opioid use) and longer distances to travel associated with lower frequencies of visits to treatment centers (Rosenblatt, Andrilla, Catlin, & Larson, 2015; Young, Rudolph, Quillen, & Havens, 2014). Locations with lower socioeconomic status were also found to lack substance use disorder treatment services (Cook & Alegria, 2011). In terms of demographic disparities, Black and Hispanic population groups were found to be less likely to complete a treatment episode than Whites, and that these disparities vary among users of different substances (Mennis & Stahler, 2016). Regarding disparities among gender groups, females have better recovery resources from heroin use than males due to their better family and social relationships, and more access to informal support (Neale, Nettleton, & Pickering, 2014).

These studies form a critical reminder that research on the topic of illicit drug use has come a long way since 1970s, and in the past decade especially, has started drawing deeper attention on understanding the trends and prevention pathways (Coffin & Rich, 2019). The current challenges stemming from the substantial increase in opioid use and mortality, but limited access to treatment services, as well as neighborhood disadvantages require more scientists to conduct quantitative and qualitative studies to investigate this epidemic. More efforts on new insights and innovative approaches to explore current trends and implications are essential to reduce further substantial losses to the opioid crisis.

1.3 Geography and the opioid crisis

Since behavioral patterns and social environments related to opioid use and misuse vary significantly among different communities across the country an important way to evaluate and understand the prevalence of opioid overdoses and its associated factors is to investigate the geospatial aspects of the crisis. As geographers, we aim to contribute to research in this area by connecting location, environment and drug use. Geographic patterns of opioid use and misuse have been investigated across the country since early 2000s. Spatial patterns vary significantly in terms of different topics (e.g., opioid mortality and illicit drug use) and have revealed high-risk locations. In 2002 (early in the emerging opioid crisis), Maine had the highest sale rate of opioid analgesics in the U.S., while New Mexico held the highest mortality rate involving drug poisoning (Paulozzi & Ryan, 2006). During the ten-year period of 1999-2009, there was more than a 300% increase in drug poisoning deaths, with the highest age-adjusted rates in Pacific, Mountain and East South Central regions (e.g., Utah and Tennessee), and the lowest age-adjusted rates in West North Central region by 2009 (Rossen, Khan, & Warner, 2013). During 2007-2009, significant geographic clusters of drug poisoning deaths were reported along the north Pacific coast, the southwest, Gulf Coast and Appalachia (Rossen, Khan, & Warner, 2014). More recent studies on illicit drug use disorder found hot spots in West Virginia and Kentucky in 2014 (Dwyer-Lindgren et al., 2018). With respect to the pattern of drug poisoning deaths involving heroin, high rates of mortality in the US in 2014 moved from the West coast in early 2000 to the Great Lakes region in 2010, reaching Ohio Valley, New England and the Mid-Atlantic states by 2016 (Stewart, Cao, Hsu, Artigiani, & Wish, 2017). Fentanyl mortality became a high risk in Appalachian and Northeast region in 2016 (Jalal et al., 2018).

As mentioned in Section 1, geospatial techniques used to investigate spatial and spatial-temporal patterns of public health issues have also been applied in geography and drug addiction research. Geographic determinants (e.g., street network and neighborhood characteristics) have been considered as important elements in previous drug use and misuse studies. Spatial Bayes' estimation to solve small area and small number limitations of studies on illicit drug use have been performed in a number of studies in the literature (Dwyer-Lindgren et al., 2018; Rossen et al., 2013, 2014; Stewart et al., 2017). Spatial scan statistics were applied in a study in Boston to identify spatial clusters of youth use of marijuana in certain neighborhoods in the city (Duncan et al., 2016). Spatial regression analysis was applied in a study that used a simultaneous autoregressive spatial error model to investigate associations between fatal prescription opioid poisonings and socioeconomic factors in New Hampshire with results showing that fatal poisonings are more likely to occur in areas with lower median household income or greater percentage of disabled workers (Hester et al., 2012). Distance based analysis has been conducted in investigating availability and access to substance use disorder treatment services. For example, buffer analysis based on a 10-min driving distance of drug treatment facilities in Houston, TX was applied to measure spatial accessibility to drug use treatment centers in 2013 (Kao, Torres, Guerrero, Mauldin, & Bordnick, 2014). Using a P-median model for location-allocation analysis has been utilized to identify locations based on data from 2017 to discern where pharmacies stocking naloxone are needed most in Pittsburg, PA (Dodson, Yoo, Martin-Gill, & Roth, 2018). Different thresholds for variable driving time catchment sizes are accounted for different locations (i.e., urban and rural) in terms of measuring access to opioid use disorder treatment facilities and emergency medical services (Cao, Stewart, Wish, Artigiani, & Sorg, 2019). Additionally, geo-located socially sensed data have become popular in investigating social behaviors, including physical activities and food choices (X. Chen & Yang, 2014; Macdonald, 2019). In the context of opioid epidemic research, a web platform has been used to retrieve data for illicit drug use, including conducting surveys on Facebook and harvesting geotagged tweets using key words filtering for substance use (e.g., smoking, alcohol and illicit drugs) (Borodovsky, Marsch, & Budney, 2018; Meng, Kath, Li, & Nguyen, 2017). These approaches to accessing and analyzing data from social media provide efficient way to understand the geospatial pattern of opioid crisis and alleviate risky behaviors.

1.4 Dissertation Outline

This dissertation aims at developing an in-depth understanding of geography in the context of the opioid epidemic in the U.S. The overall objective of this dissertation is to model spatial and temporal patterns of the prevalence, treatment access and associated social environmental factors for opioid use and misuse. In order to achieve this goal, this research set three specific objectives described in Chapters 2, 3, and 4 respectively: 1) To investigate the spatial and temporal patterns of drug poisoning deaths involving heroin in the US between 2000-2016 in order to identify how the trend evolved over space and time; 2) To model spatial access to opioid use disorder treatment facilities and emergency medical services (EMS) in New Hampshire in order to identify where gaps may exist; and 3) To model the spatial and temporal patterns of patients admitted to four emergency departments (ED) in Maryland with a chief complaint and/or diagnosis of overdose or drug-related health problem, in relation to neighborhood characteristics in order to identify dynamic socio-environmental factors. To achieve these three objectives, the corresponding research questions are as follows:

1) How do drug poisoning deaths involving heroin impact different population groups (age, gender, race and ethnicity) and relate to urbanization across the US during 2000-2016?
2) How does access to opioid use disorder treatment facilities and EMS services vary spatially in New Hampshire during 2015-2016?
3) How are socio-environmental factors associated with ED patients over space and time in Maryland during 2016-2018?

This dissertation consists of 5 chapters. Chapter 1 describes the motivation and background for the research topics that comprise this dissertation. I discuss the importance as a geographer in investigating the prevalence of opioid crisis and how the cutting edge techniques in the geospatial field can contribute to an understanding and to the response to opioid crisis. In addition, I conducted a comprehensive review of literature on substance use disorder and how this crisis impact various population groups and different locations. This trend has been reviewed from early 1970s to current literature in a more consistent way. Based on the current issues found in literature, I described research questions in this dissertation to provide a better understanding of geography and substance use disorder from the perspectives of space and time.

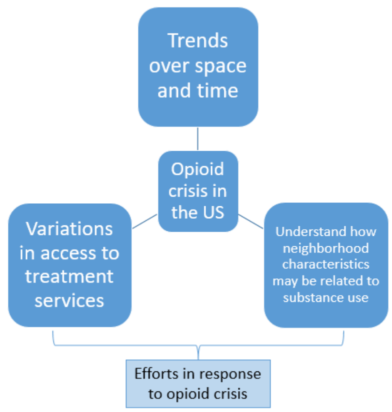


Figure 1-1 Dissertation structure

Chapter 2 describes the spatial and temporal patterns of drug poisoning deaths involving heroin across the country. This reflects the degree to which death rates from heroin overdoses evolved across the U.S. and over time. Chapters 3 examines access to opioid use treatment services in the context of a rapid rise in the number of deaths involving fentanyl in New Hampshire, a state hard hit by the ongoing opioid crisis. Chapter 4 investigates the degree to which ED patients are spatially and temporally associated and socio-environmental factors (Figure 1-1).

The research described in Chapter 2 discusses three key topics: 1) How are small area and small number techniques used to represent the spatial patterns of drug poisoning deaths involving heroin across the U.S. for the period from 2000 to 2016? 2) How have the spatial-temporal patterns of drug poisoning deaths involving heroin changed over time in the U.S. and what techniques can be applied to reveal their evolution? 3) How have the changing patterns of heroin death rates affected population groups (e.g., race, age and gender)? This Chapter investigates the degree to which spatial patterns changed for various population groups, as well as in terms of different locations (e.g., urban *vs.* rural). As heroin mortality is still relatively speaking a rare incident, there is a need to overcome small area and small number problems when doing spatial analysis. This Chapter describes research that applied spatial empirical Bayes' estimation to alleviate this issue. The results indicated an expansion of mortality in rural counties in recent years, and an increasing pattern among African American populations, as well as younger age groups, and females. To investigate spatial and temporal evolution of drug poisoning deaths involving heroin, the concept of "core clusters" (J. Chen, Roth, Naito, Lengerich, & Maceachren, 2008) is used when performing SaTScan analysis, in order to identify location of high risk from heroin mortality across the country during this study period. Part of the results of this Chapter was published as "Geospatial Analysis of Drug Poisoning Deaths Involving Heroin in the USA, 2000–2014" in the *Journal of Urban Health* in 2017 (Stewart et al., 2017). The analysis, results, and discussion have been updated to 2016 for this dissertation.

As the opioid crisis was beginning to experience a new threat, that of fentanyl, Chapter 3 focuses on the topic of spatial access to treatment with two key questions: 1) What are the determinants of a spatial model of impact for opioid users in New Hampshire, a New England state that was experiencing a high rate of deaths involving fentanyl? 2) How to design a composite index of spatial access that included two key aspects relating to opioid use disorder, treatment facilities and EMS services in the cases of an overdose? Fentanyl is a more powerful drug than heroin and had already caused double the number of deaths compared to heroin since 2015. The National Drug Early Warning System (NDEWS) undertook a Hotspot Study in 2017 in New Hampshire to examine the cause and manner of death for fentanyl overdoses. This Chapter adopted a popular model for computing spatial accessibility – the enhanced two-step floating catchment area (E2SFCA) model–and integrated it with the Huff model, to investigate spatial access to opioid use disorder treatment facilities and EMS services. To be more applicable to New Hampshire and access to opioid use and misuse, I adjusted model parameters regarding the driving times and impedance functions, as well as modified the E2SFCA for assessing access to EMS. A composite index was designed to evaluate the overall degree of spatial access to *both* treatment facilities and EMS services across the state of New Hampshire. The variation in access to treatment services was compared with data on fentanyl deaths (01/2015-09/2016) and identify where the gaps were during the study time period. Part of this dissertation Chapter has been published as "Determining spatial access to opioid use disorder treatment and emergency medical services in New Hampshire" in the *Journal of Substance Abuse Treatment* (Cao et al., 2019).

Chapter 4 focuses on Question 3, where three detailed method questions are addressed: 1) How does the geographic pattern of emergency department (ED) patients with chief complaint and/or diagnosis of overdose or drug-related health problems change over time? 2) How do socially sensed data identify neighborhood characteristics? 3) How are ED patients in relation to neighborhood over space and time in Maryland? Continued from chapter 3, this chapter utilized data from treatment admissions for drug overdoses.

In addition, in chapter 3, analysis for access to treatment services for opioid use only includes treatment with medication (e.g., methadone and buprenorphine). Another important treatment patients with drug addiction is psychosocial services on mental health. In chapter 4, neighborhood characteristics are described using both census data with socioeconomic variables and also geo-located socially sensed data (e.g., Twitter data) on depression, crime and drug use. This chapter designed a model using machine learning and natural language processing (NLP) approaches to accurately filter the text on these three topics in Twitter text. As both socio-environmental factor data and ED patient data are at month-zip level, spatial and temporal regression is applied to build association between these two elements. To identify the actual place and time where ED patients are significantly associated with different variables, geographically temporally weighted regression (GTWR) is applied to estimate the correlation. The results revealed time and location in Maryland that psychosocial services are potentially needed in order to alleviate the stress of drug overdose.

Chapter 5 summarizes the major findings of Chapters 2-4, and concludes the significance of each chapter. The contribution of this dissertation builds unique insights for the understanding of spatial and temporal heterogeneity of opioid epidemic and indicates new information that is useful for policy makers to intervene opioid use and misuse in high-risk regions. At the end, chapter 5 reveals the limitation of this dissertation and provides future directions to contribute in geography and opioid epidemic research.

Chapter 2 Geospatial Analysis of Drug Poisoning Deaths involving Heroin in the United States, 2000-2016

Abstract

We investigate the geographic patterns of drug poisoning deaths involving heroin by county for the United States from 2000 to 2016. The county-level patterns of mortality are examined with respect to age-adjusted rates of death for different classes of urbanization and racial and ethnic groups, while rates based on raw counts of drug poisoning deaths involving heroin are estimated for different age groups and by gender. To account for possible underestimations in these rates due to small areas or small numbers, spatial empirical Bayes' estimation techniques have been used to smooth the rates of death and alleviate underestimation when analyzing spatial patterns for these different groups. The geographic pattern of poisoning deaths involving heroin has shifted from the west coast of the US in the year 2000, to New England, the Mid-Atlantic region, and the Great Lakes and central Ohio Valley by 2016. The evolution over space and time of clusters of drug poisoning deaths involving heroin is confirmed through SaTScan analysis. For this period, White males were found to be the most impacted population group overall, however, Blacks and Hispanic are suffering high impacts in counties where significant populations of these two groups reside. Our results show that while 35-54 year olds were the most highly impacted age group by county from 2000 to 2010, by 2016 the trend had changed with an increasing number of counties experiencing higher death rates for individuals 25-34 years. The percentage of counties across the US classified as large metro with deaths involving heroin is estimated to have decreased from approximately 73% in 2010 to just fewer than 50% in 2016, with a shift to small-metro

and non-metro counties. Understanding the geographic variations in impact on different population groups in the US has become particularly necessary in light of the extreme increase in the use and misuse of street drugs including heroin, and the subsequent rise in opioid-related deaths in the US.

2.1 Introduction

According to the US National Center for Health Statistics at the Centers for Disease Control and Prevention[1], the number of deaths from prescription drugs increased over 300% between 2000 and 2017. For the same period, heroin initiation rose from 108,000 in the US in 2005, to 178,000 in 2011, to 472,000 in 2017 (Center for Behavioral Health Statistics and Quality, 2015, 2018). Drug poisoning deaths involving heroin increased seven folds from 2000 (1,842 reported deaths) to 2017 (15,409 reported deaths). The recent spike in the number of overdose deaths involving the misuse of opioid analgesics has been reported widely and linked to the expanded use of prescription opioids (M. Ford & Dulaney, 2014; Mars et al., 2014) and the pattern of shifting from prescription opioid use to heroin use has been a topic of investigation as researchers are seeking to understand the reasons underlying this shift. In one study, an increase in heroin overdoses was found to be linked to therapeutic errors (e.g., incorrect doses or the administration of an incorrect substance) that resulted in exposure to oxycodone (Coplan, Kale, Sandstrom, Landau, & Chilcoat, 2013). And additional reporting found that increases in non-medical uses of pharmaceutical opioids (e.g., oxycodone) was occurring even as pharmaceutical

[1] https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

companies were making formulations of some drugs that were more difficult to inject, where opioid users were resorting to different formulations that included intravenous use (Dertadian & Maher, 2014). The increasing trend of non-medical uses, misuses, and fatal poisonings involving prescription opioids have led to an over 300% increase in mortality in the US from 2000 to 2017[2].

Prior research has used for example, Multiple Cause of Death data from National Vital Statistics reporting to track trends in drug poisoning deaths in the US, however, it is understood that localities may differ widely on the percentage of deaths reported (Rossen et al., 2013, 2014). Keeping this potential reporting limitation in mind, this research differs from prior research by tracking deaths involving heroin at the county level. In this study, we use CDC WONDER Multiple Cause of Death data to investigate the geographic patterns of drug poisoning deaths involving heroin by county for the US from 2000 to 2014. The patterns are examined with respect to a set of key factors including urbanization, race and ethnicity, age, and gender in order to understand the impact from the rise in heroin use and related deaths on different population groups at county level. As part of this research, we investigate the geospatial patterns of overdose deaths involving heroin, and the location and extent to which clusters of overdose deaths are identified. Through this study, we show the burden of heroin overdose deaths on US counties as well as on different population groups at key intervals during this fifteen-year period. This geographic-based research provides a perspective on how the rate of deaths varies over space and time, and gives insights that can be useful for interventions and improved

[2] https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

planning in relation to heroin misuse in the US and to alleviate the burden of mortality in certain counties and states.

2.2 Background

A rise in overdoses involving heroin has been noted globally. A survey conducted in Australia between 2012 and 2013 among heroin users from either methadone maintenance treatments, drug-free residential rehabilitation or detoxification programs, noted that 67.5% of participants with heroin initiation had overdose records (Darke et al., 2014). A growing risk from overdoses involving heroin was also found in a recent UK study by Strang (2015) that reported life-threatening overdoses were experienced by half of heroin or opiate misusers in Scotland and England during 1993 and 2008. In Columbia, a 2010 study found a mean rate of 3.2 times of injections per day among heroin injectors, with this high rate of injection putting these users at greater risk of HIV infections (Mateu-Gelabert et al., 2016).

Research on heroin use includes evidence that in certain locations there has been an increase in heroin use by younger persons in recent years, where younger drug users have been more likely to use syringes multiple times for heroin injection (Cedarbaum & Banta-green, 2016). In Seattle's metropolitan area, for example, heroin has been a primary cause of death among younger individuals (age under 26) as a result of opioid overdoses and prescription opioid misuse (Jenkins et al., 2011; Peavy et al., 2012). In a study investigating heroin use in North Carolina between 2007 and 2013, found overdose deaths have shifted from opioid analgesics to heroin, and researchers found that there was a decrease in the average age of deceased individuals from 38.7 years in 2007, to 35.5 years in 2013(Dasgupta et al., 2014).

Studies have also examined the impact of drug poisoning deaths on racial and ethnic groups. Research based on nationwide survey during 2002 to 2011 shows non-Hispanic Whites were at high risk of heroin use during this period and there was an increasing trend among Hispanics in mid 2000s(Martins, Santaella-Tenorio, Marshall, Maldonado, & Cerda, 2015). A more recent study in San Francisco reported that the opioid overdose mortality between 2010 and 2012 mostly occurred among middle-aged non-Hispanic White males (and over 9% of these deaths involved heroin)(Visconti, Santos, Lemos, Burke, & Coffin, 2015).

The distribution of drug poisoning deaths between urban and rural locations has also been a topic of study. Research has revealed that overdoses involving opioid use have severely impacted adults living in urban places compared to rural adults due to a higher usage of substances including prescription drugs (Day, Conroy, Lowe, Page, & Dolan, 2006; Rigg & Monnat, 2015). A case study in urban San Francisco found a consistently high injection frequency by heroin users since the late 2000s (Wenger, Lopez, Comfort, & Kral, 2014). However, a rapid increase in prescription opioid use and drug poisoning deaths involving heroin among residents living in rural areas in the US have also been reported to be on the rise due to the lower costs of heroin as well as increased accessibility to this drug (Cicero et al., 2014; Cicero, Surratt, Inciardi, & Munoz, 2007; Meiman et al., 2015). Our study will investigate urban-rural spatial patterns of drug deaths involving heroin.

Geospatial analysis methods have been applied in substance use research (Rossen et al., 2013, 2014; Rudd, Seth, David, & Scholl, 2016). As drug poisoning deaths at county level across the US are not a common event, small-area estimation technique (e.g., mixed effect model) has been applied by Rossen (Rossen et al., 2013, 2014) to alleviate unstable results. In their research, major hot spots of deaths from drug poisoning were identified in North Pacific coast, Southwest, Gulf coast and Appalachia during 2007-2009. Spatial accessibility to substance use treatment facilities has been analyzed using buffer analysis based on a 10-min driving distance in order to investigate whether the availability of these facilities possibly plays a negative role with respect to heroin injections due to decreasing concerns about access to injections in the future (Beardsley, Wish, Fitzelle, O'Grady, & Arria, 2003; Kao et al., 2014). Research into the associations between fatal prescription opioid poisonings and socioeconomic factors in New Hampshire used spatial regression analysis with a simultaneous autoregressive spatial error model to show that fatal poisonings were more likely to occur in areas with lower median household income or greater percentages of disabled workers (Hester et al., 2012). In our research, we apply spatial methods including spatial and spatiotemporal cluster analysis and spatial smoothing techniques to investigate the impact of drug poisoning deaths involving heroin at county-level across the US in order to identify how the impact on different population groups has changed over space and time, and locations in the US where this impact is highest.

2.3 Methods

2.3.1 Data

The annual numbers of drug poisoning deaths involving heroin for each US county for the period 2000-2016 were collected from Centers for Disease Control and Prevention—Wide-ranging Online Data for Epidemiologic Research[3] (CDC WONDER). The data

[3] http://wonder.cdc.gov/

collected are for cases corresponding to poisoning codes representing categories for Underlying Cause of Deaths (UCD) that are classified using the International Classification of Disease, Tenth Revision (UCD-ICD-10). This category includes: X40-X44 (accidental poisoning); X60-X64 (intentional poisoning); X85 (assault); Y10-Y14 (poisoning undetermined intent); and the type of drug involved indicated by the classifications under Multiple Cause of Deaths (MCD) MCD-ICD-10, for this study, T40.1 (heroin). These codes were selected based on previous literature (Rossen et al., 2014). Raw number of deaths by county and year were collected for the 48 contiguous states in the United States. In the CDC WONDER dataset, when the number of deaths in a county is lower than 10, the data are suppressed and values are not presented for use. In fact, the data (age-adjusted rates for total population and racial and ethnic groups, and raw counts for the remaining groups) are suppressed for most US counties for each population category. The number of counties where data is available is summarized in Table 2-1. Our study area covers the 48 contiguous states in the US with 3,109 counties.

In order to understand the impact and geographic patterns of poisoning deaths involving heroin in the U.S, we also acquired the data by age, gender, racial group and ethnicity. We categorized age groups as following: ages 18-24 years, 25-34, 35-54, and 55 years and above. In the CDC WONDER database, reportable data existed for two racial groups during the time we collected data, African American and White, and for Hispanic and non-Hispanic counts. These variables (categories in age and racial groups) were selected under the guidance of Center for Substance Abuse Research (CESAR) in University of Maryland. As poisoning deaths involving heroin are relatively rare and involve small numbers, GeoDa's tools (GeoDa 1.6.7, Anselin, Luc, Illinois, 2018) for spatial empirical

Bayes' estimation have been used to smooth the rate of deaths and alleviate small area problems across the country when analyzing spatial patterns in terms of total population and these sociodemographic variables. For this estimation, we used raw counts (for age and gender patterns) and age-adjusted drug poisoning death rates (for spatial, racial, and urbanization pattern analyses) as event data, and county population as base data, and spatial weights were defined based on queen contiguity (i.e., counties that share at least one boundary are considered as neighbors). The smoothed rates were estimated for the entire study time period. The rates that are mapped, including rates for 2000, 2005, 2010 and 2016, are presented using a natural breaks classification method.

Each county was assigned an urban-rural classification that follows the scheme used by the National Center for Health Statistics[4]. In this research, we aggregated counties into four categories: large metro (population ≥1 million); medium metro (population 250,000-999,999); small metro (population<250,000); and non-metro (including micropolitan and non-core counties). The urban-rural classification for 2006 is used for analysis of the period 2000-2009, while the classification for 2013 is applied for the period 2010-2016.

[4] http://www.cdc.gov/nchs/data_access/urban_rural.htm

Table 2-1 Number of counties with data (raw counts or age-adjusted rates) on the number of deaths by drug poisoning involving heroin

	2000	2005	2010	2016
Total population*	21	21	31	181
White*	14	16	27	164
Black*	3	1	0	16
Hispanic*	1	2	2	20
Female	4	5	10	101
Male	37	39	63	259
18-24yrs	1	1	8	26
25-34yrs	6	4	19	145
35-54yrs	26	26	31	154
55yrs and above	1	1	4	47

*Age-adjusted rates

2.3.2 Geostatistical analysis

Spatial autocorrelation

To investigate the geographic pattern of drug poisoning deaths involving heroin in the US, a global Moran's I test (Moran, 1948) was performed using ArcGIS 10.5 (ESRI, Redlands, CA, 2018) to examine whether there is a possibility that the spatial pattern of poisoning deaths is clustered. This test was applied on the spatial empirical Bayes' estimated rates of deaths involving heroin in the US for 2000 to 2016. In addition, to better explore the spatial pattern of deaths involving heroin among neighboring counties, Local Indicators of Spatial Association (LISA statistic) (Anselin, 1995) was performed to measure the local spatial autocorrelation and clustering tendency of these deaths. From this analysis, counties with higher rates of drug deaths involving heroin can be identified.

As a counterpart of global Moran's I, local Moran's I index for each county was also generated using ArcGIS. This statistic indicates whether each county has a positive or negative spatial autocorrelation based on the pattern of deaths. A clustered or dispersed spatial pattern is illustrated by a positive or negative Moran's I value along with a z-score falling between -1.96 and 1.96. This test was applied to the spatial empirical Bayes' estimated rates of deaths from 2000 to 2016.

Space-time scan statistics

To understand how geographic patterns of clustering have emerged and evolved between 2000 and 2016, a scan statistic was applied using SaTScan software (SaTScan 9.4, Kulldorff, Martin, 2018). For this evaluation, SaTScan analysis was undertaken for raw counts of deaths based on a Poisson probability model, scanning for areas with high numbers of deaths involving heroin, and using a null hypothesis that the expected number of drug poisoning deaths involving heroin in each county is proportional to the population size of the county (Kulldorff, 1997). This analysis is performed using a likelihood ratio test, and the function is equal to the following:

$$L = \left(\frac{c}{E[c]}\right)^{c} \left(\frac{C - c}{C - E[c]}\right)^{C-c} I()$$

Where C denotes the total number of deaths, c is the observed number of deaths within the scanning window and $E[c]$ refers to the covariate adjusted expected number of deaths within the test window. $I()$ is an indicator function equal to 1 since this test is set to scan only for clusters with high numbers of deaths, i.e., more deaths within the window than expected (Kulldorff, Heffernan, Hartman, Assuncao, & Mostashari, 2005). The maximum size of the scanning window is defined as 5% of the population at risk since deaths involving heroin typically comprise a low percentage of the causes of deaths in a population (e.g., about 0.3% of the population died from heroin poisoning in 2016)[5]. However, this size of window could hide small clusters of deaths. In order to detect stable counties within core clusters, we applied a sensitivity analysis (Barro et al., 2015; J. Chen et al., 2008) and investigated a range of eight maximum-sized scanning windows: 0.2% of population at risk, 0.4%, 0.6%, 0.8%, 1%, 2%, 4% and 5%. The maximum temporal cluster size is always defined as one year since the dataset we are working with are annual counts of drug poisoning deaths involving heroin. The criteria for reporting hierarchical clusters is that no cluster centers are in less likely clusters, which indicates there could be clusters that overlap each other. In this sensitivity analysis, we defined a core cluster as a cluster that has a low percentage of counties with a low relative risk. In this test, the relative risk index in each county indicates how much more common poisoning deaths involving heroin are in a county compared to other counties, following the equation below:

$$RR = \frac{c/E[c]}{(C-c)/(E[C]-E[c])}$$

Where RR>1 reveals a high risk of death. In this sensitivity analysis, low risk refers to counties where RR<1. Based on the results, a threshold of 33% is used to represent what is considered a low percentage of counties with low risk. To qualify as a statistically significant cluster, p-values of each core cluster have to be lower than 0.01, where the significance of these clusters was determined by Monte Carlo simulation with 999

[5] http://www.cdc.gov/drugoverdose/data/overdose.html

random replications. To detect the stability of a county belonging to a core cluster, we applied the reliability index computation as follows(J. Chen et al., 2008):

$$R_i = \frac{C_i}{\mathrm{S}}$$

Where $\mathrm{R_i}$ denotes the stability value for county i, S is the total number of scans (in this case, 8 scans), and C_i refers to the number of scans when county i falls in a core cluster. Since there is the possibility that clusters overlap, this reliability index could be larger than 1. The reliability index reveals stable core clusters but also reveals possible heterogeneous patterns within core clusters.

2.4 Results

2.4.1 Spatial and temporal pattern of drug poisoning deaths involving heroin

In terms of raw counts of deaths involving heroin, a total of 82,470 deaths are reported for the period 2000 and 2016. Between 2000 and 2011, the highest number of deaths in the US occurred in Los Angeles County, CA (169 deaths in 2000 with a peak number in 2002 of 182). In 2012, the highest number had shifted to Cuyahoga County, OH (135 deaths). In 2014 and 2016, the highest number of drug poisoning deaths involving heroin occurred in Cook County, IL (323 and 535 deaths respectively).

Spatial empirical Bayes' estimation techniques were applied to spatially smooth age-adjusted death rates for four different time points including 2000, 2005, 2010 and 2016. This analysis returns a spatial pattern that started in 2000 with counties on both the east and west coasts of the US, expanding into the central US (e.g., Missouri and Ohio) by 2010, and then spreading rapidly from 2010 to 2016 throughout New England, the mid-Atlantic, and Great Lakes and Ohio Valley regions (Figure 2-1). In 2000, 103 counties in the US had spatially smoothed age-adjusted rates, with the highest rate being estimated for Passaic County, NJ, and the second and third highest rates in Valencia County, NM and Kern County, CA, respectively. In 2005, the highest spatially smoothed rate had shifted to Baltimore City, MD, followed by Miami County, OH. Since 2005, the spatially smoothed age adjusted rates have remained high in the Ohio Valley region. By 2010, 160 counties were impacted in the US, an approximately 55% increase from 2000, with the highest age-adjusted death rates estimated for Jefferson County, MO, followed by Clermont County, OH, and Bracken County, KY. Six years later, in 2016, 657 counties have spatially smoothed age-adjusted deaths. The highest rate is estimated for Rio Arriba County, NM. Four counties in the Ohio Valley region comprise the highest two categories of death rates including Berkeley and Cabell Counties, WV, Campbell County, KY, and Marion County, OH. Note that no spatially smoothed rate based on age-adjusted deaths involving heroin was estimated for Rio Arriba County, NM prior to 2014.

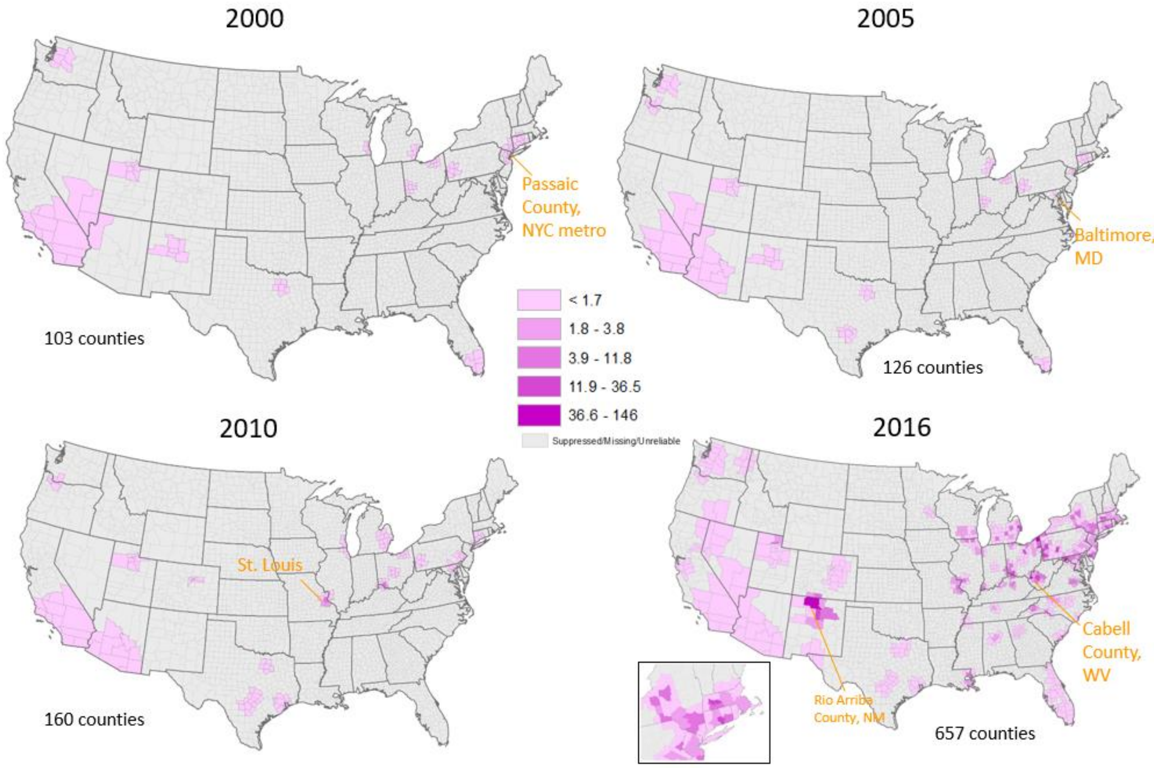


Figure 2-1 Spatial empirical Bayes' estimation of rate of age-adjusted deaths involving heroin for 2000, 2005, 2010, and 2016

2.4.2 Racial and ethnic patterns of deaths involving heroin

There were 71,847 deaths (approximately 87.1% of total deaths) from drug poisoning overdoses involving heroin among Whites during the period 2000 to 2016, compared to 9,375 (11.4%) deaths for Blacks, and 9,691 (about 11.8%) for Hispanic individuals. In 2000, after spatial smoothing using age-adjusted rates, Whites comprised 56.9% of the total rates (based on White and Black deaths). This percentage increased to 88% in 2005, approached 100% of the estimated rates in 2010, and then decreased to 85.03% in 2016. Black spatially smoothed and age-adjusted death rates decreased from 43.1% in 2000 to 12% in 2005, and further declined to less than 1% in 2010, and then increased to 14.97%

in 2016. For Hispanics, the percentage of spatially smoothed age-adjusted rates increased from 0.8% in 2000 to 15.6% in 2005, and then declined to 4.9% in 2010 and 30.6% in 2016.

In 2000, Kern County, CA appeared to have the highest spatially smoothed age-adjusted rate for Whites (rate of 1.1 per 100,000). The high rates shifted to counties around Bernalillo County, NM and into the Great Lakes region (e.g., northern Pennsylvania and eastern Michigan) in 2005. In 2010, four counties in Ohio and Missouri had spatially smoothed age-adjusted death rates for Whites that exceeded 60 per 100,000. By 2016, the upward trend increased even more sharply for Whites, with most of these deaths occurring in counties in the northeast, mid-Atlantic, and Great Lakes regions of the US (a total of 617 counties) (Figure 2-2). Together, these 617 counties represent approximately 60% of the total US White population. The highest spatially smoothed age-adjusted rate of 377.5 per 100,000 in 2016 was found in Rio Arriba County, NM followed by a rate of 72.3 per 100,000 in Cabell County, WV (Figure 2-2).

In 2000, the spatially smoothed age-adjusted rate was as high as 3.9 per 100,000 for Blacks in Essex County, NJ, with no spatially smoothed White age-adjusted death rates being estimated for this county. In 2005, Macomb County, MI (north of Detroit) had the highest spatially smoothed age-adjusted rate for Blacks, with a rate of 0.7 per 100,000, which is higher than the rate for Whites in this county. In 2010, due to small numbers and corresponding data suppression in CDC WONDER, no spatially smoothed age-adjusted rates were estimated for Blacks for any counties. Eight counties in the US did have deaths including Wayne County, MI with a raw count of 18 deaths in this year. In 2016, however, the rates had increased and 72 counties that together represent approximately

23.1% of the US Black population and 15% of total deaths involving heroin, had spatially smoothed age-adjusted death rates for Blacks. The highest rate of 42 per 100,000 occurred in St. Louis, MO (an independent city administered as a county). Thirty-eight out of these 72 counties had spatially smoothed rates that exceeded the rates found for Whites, including counties in Wisconsin, Missouri, Illinois (the smoothed rate for Black deaths in Cook County was over four times that of White deaths), Michigan, Maryland (Baltimore City and Montgomery County, MD), Ohio, Virginia, and the District of Columbia (Figure 2-2).

For Hispanics, a significant increase in percentage of spatially smoothed age-adjusted rate from 2000 to 2005 (0.8% to 15.6%) which was found in 3 counties surrounding Los Angeles, CA with a total rate as low as 0.3 per 100,000 in 2000, shifting to 8 counties surrounding San Antonio in Texas, total rate of 4.3 per 100,000 in 2005. A similar pattern existed in 2010 for Hispanics. In 2016, 93 counties in the Southwest, Great Lakes and New England regions that together represent approximately 36% of the US Hispanic population had smoothed age-adjusted death rates per 100,000. These counties include Rio Arriba County, NM with spatially smoothed age-adjusted death rate of 443 per 100,000, and Hampden County, MA with a rate of 29.5 per 100,000. Fifty-two of these counties had spatially smoothed age-adjusted death rates for Hispanics that exceeded the rates for both Black and White populations. Among these, 3 counties were in Connecticut, 13 in New Mexico, 17 in Texas, 9 in Arizona, 5 in Wisconsin, and 5 in Florida.

To verify the trend, we conducted a chi-squared test for death rates among racial and ethnic group following the time periods. The result shows p=0.031 which means a significant association between spatially smoothed age-adjusted death rates among racial groups and time period.

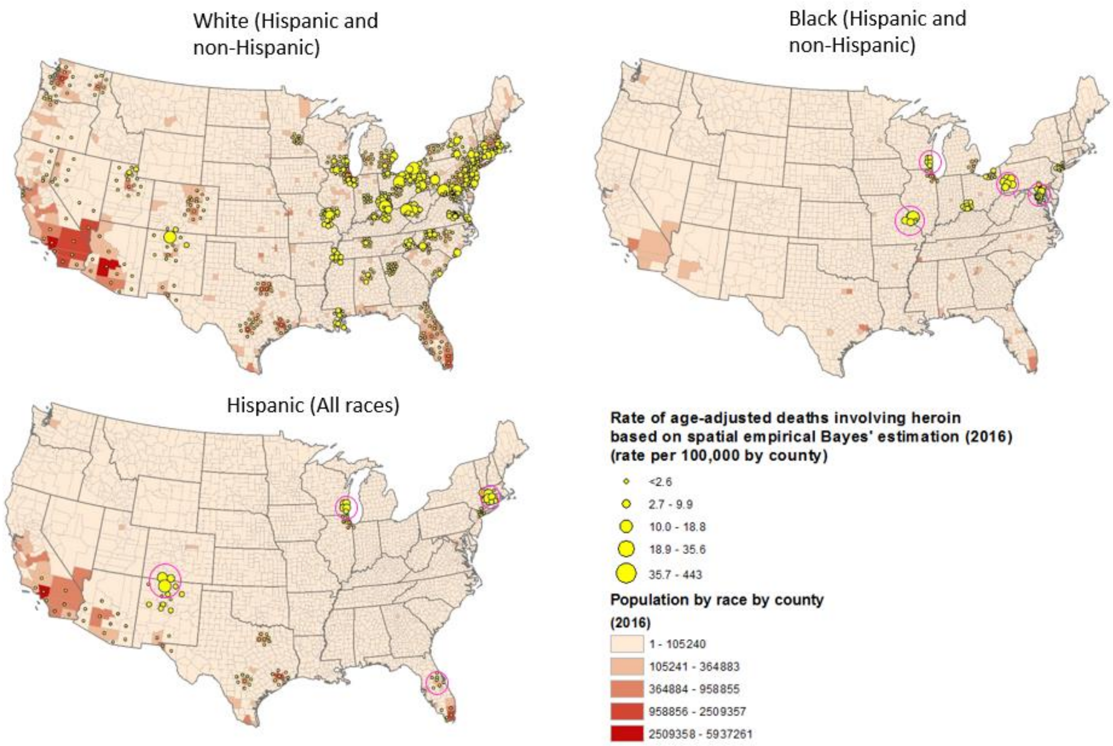


Figure 2-2 Spatial empirical Bayes' estimation of age-adjusted rate of deaths involving heroin per 100,000 for 2016 by race and ethnicity. Each map depicts the population data for the corresponding racial and ethnic group (i.e., White, Black, and Hispanic).

2.4.3 Urban-rural patterns of drug poisoning deaths involving heroin

We investigated whether drug poisoning deaths involving heroin have impacted urban or rural counties more frequently for the period 2000-2016, and found that approximately 68% of the raw counts of deaths (56,089 deaths) occurred in counties that are categorized as large metro (i.e., population > 1 million), significantly exceeding the number of deaths in small-metro counties (population 50,000-249,999) (4622 deaths). The percentage of counties that are classified as large-metro with a spatially smoothed death rate increased from 56.3% in 2000, to 62.4% in 2005, and to 73.1% in 2010, and then decreased to approximately 49.9% in 2016 (328 out of 657 counties found to have a spatially smoothed age-adjusted death rate per 100,000 are classified as large-metro in 2016) (Figure 2-3). Based on the spatial empirical Bayes' estimated age-adjusted rates, the mean spatially smoothed rates for deaths involving heroin are actually lower in large-metro counties than small-metro or non-metro counties in each year from 2000 to 2016. While only 12 small-metro counties had spatially smoothed age-adjusted death rates before 2011, in 2016, spatially smoothed age-adjusted death rates were found for 59 small-metro counties (approximately 6% of total deaths involving heroin). A similar, increasing pattern was found to exist for counties classified as non-metro, representing more rural locations. In 2016, there were 142 non-metro counties with a spatially smoothed age-adjusted rate of deaths involving heroin, while before 2012, only 25 were non-metro counties (12 non-metro counties in 2000, 14 in 2005, and 17 in 2010. Note that some of these counties had rates in each of these years). To verify this trend, a correlation statistical test was conducted. The result shows a stronger correlation between death rates and urbanization in 2005 ($r=0.2$, $p<0.001$) while a weaker correlation in 2016 ($r=0.09$, $p<0.001$).

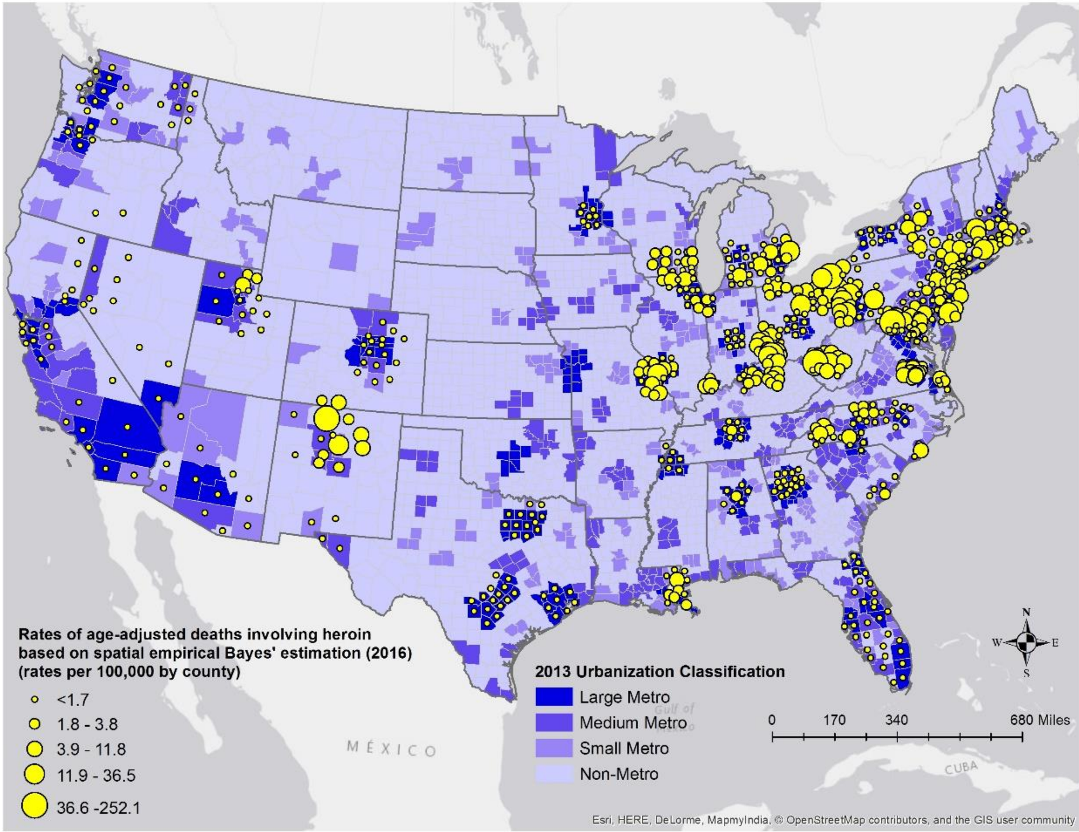


Figure 2-3 Spatial empirical Bayes' estimated rate of deaths involving heroin per 100,000 by county (2016) and urbanization classification (2013)

2.4.4 Patterns of drug poisoning deaths involving heroin by age and gender

For an analysis of the trends in deaths involving heroin by age and gender, we examined four age categories: 18-24 years, 25-34 years, 35-54 years, and over 55 years and used spatial empirical Bayes' estimation of the rate of deaths involving heroin poisoning per 100,000. Due to data suppression in the CDC Wonder dataset when raw counts are lower than 10, many counties had suppressed counts pertaining to either age or gender groups. We found that in 2000, 72.3% of the spatially smoothed death rates (applied to raw counts) occurred among 35-54 year olds while 21.7% were 25-34 year olds, and were located in the Mountain region (e.g., Salt Lake City, UT) and in New England respectively. In 2005, the percentage for 35-54 year olds increased to approximately 78%, involving 35 counties in the Mountain, Great Lakes, New England, and Mid-Atlantic regions. While these spatially smoothed rates remain high for this age group in the following 10 years until 2016, the percentage of deaths for this group decreases to around 40% in 2010, and 35% in 2016. Meanwhile, the age groups of impacted individuals shift towards younger ages. In 2005, about 14% of spatially smoothed death rates applied to 25-34 year olds in 10 counties near Pittsburgh, PA and Detroit, MI. In 2010, the percentage increased sharply to 41% for this age group (108 counties mainly in the Great Lakes region), and in 2016, the 25-34 year old group accounted for almost 55% of the spatially smoothed death rates (564 counties impacted). Of these impacted counties, 41 counties in New England, Mid-Atlantic and the Ohio Valley region had spatially smoothed death rates over 35 per 100,000 (which ranks in the highest 5% of rates for this group). For the youngest age group, 18-24 years, there was also an increase in spatially smoothed rates from 6.8% and 7 counties in 2005 (around Dallas, TX), to 11.4% and 43 counties in 2010 (impacting counties near Los Angeles, Phoenix, New York City, Cleveland, Chicago, Dallas, and San Antonio), and to 12% and 135 counties in 2014 (impacting the Southwest, the Great Lakes region, Ohio Valley, and New England) but decreased to 5% in 2016 (impacting counties around Cleveland, OH, and Mid-Atlantic region). The temporal trend in disparities of spatially smoothed age-adjusted death rates among age groups has be verified with chi-squared test with p value equal to 0.0178.

An examination of gender using spatial empirical Bayes' estimation found that males were impacted more than females from overdose deaths involving heroin during 2000-

2016, but the estimated rates of male deaths show a decrease over time. In 2000, 96.3% of the estimated poisoning deaths involving heroin occurred among males in 160 counties across the US. In 2005, this had decreased to 94.6% but expanded to 181 counties. Before 2010, Allegheny County, PA was the most impacted county for male deaths, with Baltimore City, MD and Passaic County, NJ also belonging to the category with the highest spatially smoothed male death rates. In 2010, the spatially smoothed rates for male deaths decreased to 91.3% while expanding to 277 counties, with the highest rates estimated for Clermont County, OH and St. Louis City, MO. In 2016, male deaths decreased further to 81.4% while expanding to 537 counties. The highest spatially smoothed rate in 2016 occurred in Cabell County, WV, while counties in New England, the Ohio Valley and the Great Lakes regions were also impacted by high rates of male deaths.

In contrast, while remaining low, the spatially smoothed rate of deaths for females gradually increased from 5% in 2005, to 8.7% in 2010 and reached 18.6% in 2016. The spatial pattern of deaths among females shifted from 22 counties in southern California and Great Lakes region in 2000, to 60 counties in the Midwest in 2010, and to 167 counties in 2016, including counties in the Mountain region, New England, and mid-Atlantic areas. In 2016, the estimated rates suggest that while females were impacted in less than one percent of counties, 11 counties in Ohio Valley had estimated death rates that exceeded the rates for males. The spatially smoothed rate for Kenton County, KY was estimated at 2.5 per 100,000 (over four times the rates for males), and Beaver County, PA where the spatially smoothed rate for female deaths is estimated to be 1.4 per 100,000 (exceeding the rate for males by almost 50%). The temporal trend in disparities of spatially smoothed age-adjusted death rates among gender groups has be verified with chi-squared test with p value equal to 0.0178.

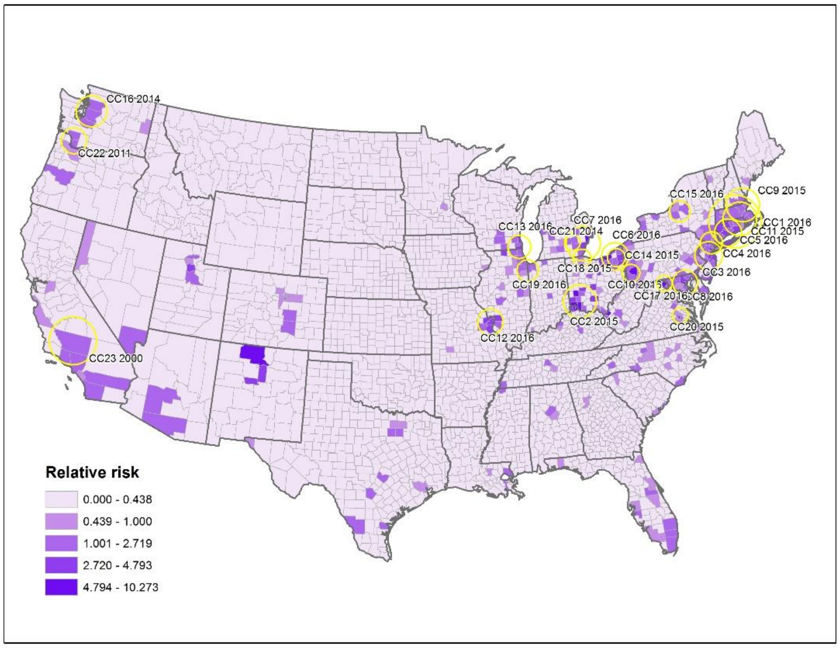
2.5 Spatiotemporal patterns of drug poisoning deaths involving heroin

To learn more about the evolution and patterns of deaths involving heroin in the US, and to identify locations where concentrations of deaths may exist, spatial cluster analysis was undertaken using global Moran's I and LISA statistics. Cluster analysis of summed age-adjusted death rates using spatial empirical Bayes smoothing during 2000 to 2016 shows it is unlikely that the spatial pattern is random as illustrated by a positive Moran's I of 0.287. In addition, a p-value smaller than 0.01 indicates the result is statistically significant. The result of local Moran's I for the summed spatially smoothed deaths rate during the study period found 402 counties belong to high-high clusters (i.e., counties with high spatially smoothed rates of drug poisoning deaths involving heroin that are adjacent to counties with similarly high counts) are located in New England, the mid-Atlantic and central Ohio Valley regions, as well as in the Mountain region and on the west coast, for example, counties around Seattle, WA. The analysis also returned high-low outliers (where counties with high spatially smoothed rates adjacent to counties with low counts) including Costilla County, CO, near Rio Arriba County, NM, and Toledo, OH, as well as Greene County, IL near St. Louis, MO.

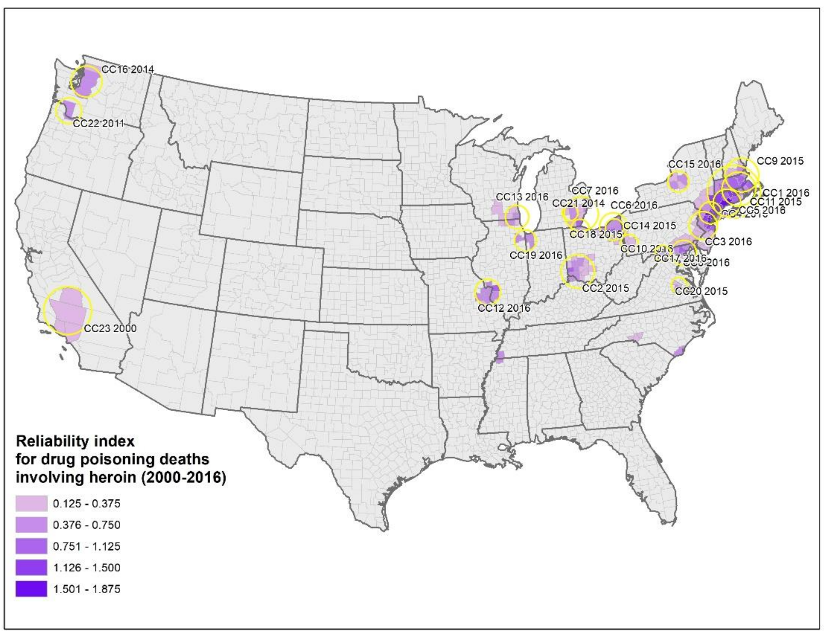
Cluster analysis using spatial and temporal scan statistics (SaTScan) was performed to understand more clearly the evolution of hotspots or clusters of drug poisoning deaths involving heroin over space and time. Based on raw counts of deaths, the SaTScan statistical algorithm returns a relative risk index for each county (Figure 2-4a). This analysis revealed 23 spatiotemporal core clusters ordered by likelihood ratio. As SaTScan has a tendency to generate clusters that are broad in spatial extent and include a large number of low-risk counties, a set of core clusters are defined as low percentage of counties with low risk (below 33% in this research) and where the likelihood ratio of a cluster is higher than 80 (J. Chen et al., 2008) (Figure 2-4a). As indicated by p-values < 0.01, all the core clusters are statistically significant. The high-risk counties (relative risk index > 2.7) are in New England and central Ohio Valley. Approximately 59% of counties with high risk indices are found in core clusters 1 to 10. The highest risk index is associated with St. Louis City, MO in 2016, corresponding to core cluster 12.

Based on the complete dataset for 2000-2016, 23 core clusters are identified and ranked by the value of likelihood ratio. In Figure 2-4a, relative risk indexes are classified using natural breaks, but with breaking value 1 to separate high and low risky counties. The first of these, core cluster 1, contains 34 counties in Massachusetts, New Hampshire, Connecticut, Rhode Island and New York, where approximately 70% of the counties have relative risk index over 1 (highest index value of 4.6 in Hartford County, CT). Core cluster 2 occurred in 2015 and contains 15 counties at the intersection of Ohio, Kentucky and Indiana. Both these core clusters have high likelihood ratios (1756.5 and 1617.4 respectively). Core cluster 3-4 are located in Mid-Atlantic in 2016, including 21 and 14 counties (respectively) in east Pennsylvania, New Jersey and lower New York. In addition to core clusters for 2015 and 2016 in New England, Mid-Atlantic and Great Lakes region, earlier core clusters appeared in southern California for 2000, counties around Portland, OR for 2011, Seattle, WA for 2014 and Michigan for 2014. Among these core clusters, however, it can be noted that Los Angeles County did not maintain an association with a core cluster after 2000.

A sensitivity analysis using SaTScan shows the reliability of a county belonging to one of the core clusters, where while adjusting the maximum size of risk population (based on 0.2% of the county population at risk, 0.4%, 0.6%, 0.8%, 1%, 2%, 4% and 5%), the likelihood ratio remains higher than 80 through the eight sensitivity runs (Figure 2-4b). This analysis identifies which counties continue to be detected as clusters using these different percentages of population at risk, and based on the numbers of drug poisoning deaths involving heroin across the US for 2000-2016. The highest reliability index is higher than 1 and corresponds to Essex County, NJ (reliability index 1.875). Throughout the different runs of the sensitivity analysis, it was found that this county appears in two of the identified core clusters (clusters 3 and 4). Twenty-seven counties in the New England and Mid-Atlantic states (8 counties in Connecticut, 7 in New York, 7 in New Jersey, 3 in Massachusetts, and also Baltimore, MD and St. Louis, MO) have scores higher than 1 (i.e., counties in multiple core clusters). The core clusters for these counties appeared in 2015 and 2016. The results show that while many counties in the US have experienced an impact from drug poisoning involving heroin, few counties are part of a core cluster for multiple years until 2014, when counties in New England, the mid-Atlantic and Great Lakes regions form core clusters that continue through 2016.



(a)



(b)

Figure 2-4 (a) Relative risk of drug poisoning deaths involving heroin by county and core clusters (2000-2016) (b) Reliability index by county and core clusters (2000-2016)

2.6 Discussion

Analyzing the spatial and spatiotemporal pattern of drug poisoning deaths involving heroin in the US during 2000-2016 shows the pattern of an increasing impact of overdose deaths involving heroin in the US with varying impacts among different population groups by urbanization, age, gender, race and ethnicity. Research on prescription opioid misuse in 2011 and 2012 found that urban residents were more likely to misuse prescription opioids than individuals living in rural locations. In our study, we found that while higher spatially smoothed age-adjusted rates for drug poisoning deaths involving heroin were estimated for counties classified as large-metro, data from more recent years shows a growing number of small-metro and non-metro counties to be impacted by drug poisoning overdoses involving heroin. This finding coincides with previous research that heroin use extends to Whites living outside urban areas, where heroin may be more available and less costly and used by individuals who misuse opioids (Cicero et al., 2014; Meiman et al., 2015; Peavy et al., 2012).Our research finds that the spatially smoothed estimated rate of deaths among Whites is significantly higher than for other racial groups. However, we found that the spatially smoothed Black death rates are estimated to be high in certain urban locations (exceeding the rate of other population groups) with a corresponding high Black population (e.g., Baltimore, MD and St Louis, MO). Previous research for 1990-2005 found that heroin overdoses particularly impacted Hispanic males in New Mexico (Shah, Lathrop, Reichard, & Landen, 2008). We also found a high rate of deaths for Hispanics in 2005, which corresponds to an increasing trend of heroin use among Hispanics during mid 2000s (Martins et al., 2015). In 2016, thirteen counties in New Mexico were estimated to be impacted by a high age-adjusted spatially smoothed rates among Hispanics, higher than the spatially smoothed rates estimated for Whites and Blacks in those counties.

Males aged 35-54 years are the gender-age group most impacted overall, while spatially smoothed death rates for younger age groups showed an increase since 2005. These results correspond with the findings from studies on heroin use in Seattle where it was found that younger heroin and opioid injectors were more at risk than older heroin injectors (Banta-Green et al., 2015) and that 39% of heroin users in a study using data collected for 2010-2014 were ages 18-29 years (Cedarbaum & Banta-green, 2016). The major causes of this upward trend of overdoses among younger users include recent increased access to prescription opioids, injection behaviors and networks, HIV risk perceptions and sharing of syringes (Jenkins et al., 2011; Peavy et al., 2012; Pollini et al., 2011). In addition, our study revealed an increase in the estimated rate of deaths of males aged over 55 years in New England, the Ohio Valley, California and New Mexico in 2016. Smoothed age-adjusted death rates for females were significantly lower than for males overall. However, in 2016, hotspots for females based on spatially smoothed estimated rates were found in New Mexico and Ohio, where smoothed death rates were estimated to exceed the rates for males. Similar findings also appeared in research using data from 1990-2005 on overdoses involving heroin, white females in New Mexico were found to be a highly impacted group (Shah et al., 2008).

The spatiotemporal cluster analysis of drug poisoning deaths involving heroin using SaTScan indicates the counties that comprise core clusters in New England, Mid-Atlantic and Great Lakes region corresponded to the two highest categories of spatially smoothed rates of deaths in 2016. The counties in these regions also correspond to the highest two categories of spatially smoothed rates of deaths among males aged 25-54 in 2016. According to our analysis, the 23 core clusters in Figure 2-4 contain 65% of counties that fall in the three highest classes of spatially smoothed rate of deaths for Whites, and 84% of counties that fall in this same group of classes for Blacks. Approximately 59% of counties in the core clusters are categorized as large-metro areas while 8.3% are small-metro. Our analysis revealed a significant hotspot using both Moran's I and SaTScan in the Seattle region in 2014 that is also discussed in studies on drug use in Seattle (Banta-Green et al., 2015; Cedarbaum & Banta-green, 2016). Although the risk index is high (> 2.7) in three counties in New Mexico, these counties do not belong to any of the core clusters mapped in Figure 2-4a. These counties do show up in the results of local Moran's I test as statistically significant high-low outliers that contribute to a spatially variable impact from deaths involving heroin for these areas.

2.7. Limitations

Previous studies have pointed out that drug poisoning deaths data may be underestimated as classifying drug poisoning deaths relies heavily on the professional judgment of medical examiners and coroners and that methods and expertise may vary widely across jurisdictions and this could have a substantial impact when analyzing county-level drug deaths data (Rossen et al., 2013, 2014). This limitation should be acknowledged regarding the data on drug overdose (poisoning deaths) involving heroin used for this research as well, and could mean that although we have used spatial empirical Bayes estimation techniques, our results may still be underrepresenting the possible number of deaths. Also, due to the small number of counties with reportable data (raw counts or age-adjusted rates) for certain population groups before 2010, the spatially smoothed estimates for these years may benefit from further sensitivity analysis. In addition, regarding the use of drug-specific (e.g., heroin) drug-involved poisoning deaths there may be variability in attributing drug type to drug poisoning deaths. For example, one research study noted that 25% of drug poisoning deaths did not have drug type available (Rossen et al., 2014). Therefore, the deaths may have included multiple drug types in this study. Finally, since county size is so variable, the calculation of weights based on neighboring counties used in the geostatistical analyses, for example, Moran's I, may be overestimated for some counties. Some studies have examined this in more detail (Rossen et al., 2014) and alternative weighting approaches using K-nearest neighbors have been proposed.

2.8 Conclusions

The analysis of the geographic distribution and spatiotemporal clustering of drug poisoning deaths involving heroin in the US during 2000-2016 provides a comprehensive view of the variations in the patterns of mortality rate from these overdoses involving heroin based on race and ethnicity, urbanization, age, and gender. Our research reveals significant clusters of deaths existed in southern California in 2000, emerging again in 2013 in counties in New England, the mid-Atlantic, and Great Lakes region, and persisting in these counties through 2016. In general, while White populations are impacted the most overall by drug poisoning deaths involving heroin, both Black and Hispanic population groups are estimated to also be significantly impacted in counties where these populations are higher. With respect to urbanization, our study shows a significant decrease in the spatially smoothed rate of deaths per 100,000 by county in large-metro areas from 2010 to 2016, and a shift to small-metro and non-metro counties.

From the perspective of age and gender, our study revealed an increasing trend over time of drug poisoning deaths involving heroin among younger ages (18-24 and 25-34 years), as well as female populations in the northeast and central states of the US, especially in 2014 based on spatially smoothed rates. This study provides understanding of the evolving pattern of deaths from overdoses involving heroin across the country for this time period. The variation of impacts and burden on different population groups is important for developing strategies and policies regarding substance use and misuse interventions for a range of different urbanization classes (e.g., small metro and non-metro) and population groups (e.g., Blacks, Hispanics, younger individuals, and females). A better understanding of these dynamics is critical to intervention and reductions in mortality in high-risk counties. Solutions could include planning for nasal naloxone distribution that is considered worldwide as a highly effective antidote for intervening deaths from heroin overdoses (Strang, 2015; Walley et al., 2013). The mortality data in this Chapter, however, had limitation that deaths could be caused by drug types other than heroin (e.g., fentanyl). This potential introduced research topic, to examine geographic patterns associated with the use and misuse of other opioids including fentanyl in Chapter 3.

Chapter 3 Determining spatial access to opioid use disorder treatment and emergency medical services in New Hampshire

Abstract

This research presents an analysis of spatial access to both opioid use disorder treatment facilities and emergency medical services in New Hampshire during 2015-2016, a period during which there was a steep increase in unintentional overdoses involving fentanyl. For this research, spatial access was computed using the enhanced two-step floating catchment area model combined with the Huff model to assess access across New Hampshire and give attention to supply-side parameters that can impact spatial access. The model is designed to measure access to healthcare services for opioid use disorder patients offered at treatment centers or from buprenorphine treatment practitioners, as well as from emergency medical services across New Hampshire. A composite index of accessibility is proposed to represent overall access to these different treatment services for opioid use disorder patients. Geospatial determinants of spatial access included street network distances, driving times and distance decay relationships, while other key factors were services availability and population demand. Among the towns with the highest composite access scores, approximately 40% were metropolitan locations while 16% were rural towns. The insights from this research showed that for this period, while the opioid crisis was impacting many towns in New Hampshire, high levels of access to treatment services were not uniform across the state. When comparing the access results with data on the towns of residence for individuals who died from unintentional overdoses involving fentanyl during 2015 and 2016, estimates found that approximately 40% of the towns were not estimated to be in the highest class of access to treatment

services at the time. This research provides information for local public health officials to support planning strategies to address opioid use disorder treatment access in high-risk regions.

3.1 Introduction

There has been a steep rise in opioid-related deaths in the US since 2010, with numbers of opioid overdose deaths reaching over 47,000 in 2017[6]. The spatial pattern of these overdose deaths shifted from the US west coast in the early 2000s to New England, Appalachia, and the Ohio Valley by 2016 (Jalal et al., 2018; Rossen et al., 2014; Ruhm, 2017; Stewart et al., 2017). In New England, specifically in Connecticut, Massachusetts and New Hampshire, opioid-related overdoses tripled between 2011 and 2016 (Rudd et al., 2016), and in New Hampshire, opioid-related emergency department visits increased by 70% between 2011 and 2015 (Daly et al., 2017). Since 2013, the number of overdoses and deaths involving fentanyl have increased significantly to the point where fentanyl is now a major threat to public health, impacting states such as Ohio, West Virginia, New Hampshire, and Rhode Island among others (Ciccarone, 2010; Gladden, Martinez, & Seth, 2016; Marshall et al., 2017; Peterson et al., 2016). Overdoses involving fentanyl have become much more widespread due to the fact that fentanyl contains more powerful chemical analogues than heroin and is cheaper, easier to manufacture, and is difficult to distinguish from other illicit substances (Baldwin et al., 2018; Ciccarone et al., 2017; Green & Gilbert, 2016; Somerville et al., 2017).

[6] https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

In 2015, increases in fentanyl-related overdose deaths were occurring at a very high rate in New Hampshire, and this spurred a National Drug Early Warning System (NDEWS) HotSpot study in 2016 on unintentional overdoses involving fentanyl. The mission of NIDA-supported NDEWS is to monitor indicators of emerging drugs in the United States. To achieve this mission, NDEWS staff monitor available opioid use indicators and sponsor HotSpot studies to investigate local drug outbreaks. According to NDEWS, while the number of New Hampshire deaths caused by fentanyl was less than 20 per year up to 2013, the number had increased to over 280 in 2015 (Sorg, Wren, Stewart, & Cao, 2017). The New Hampshire study assessed among other factors, the geospatial relationships between the location of drug use, place of residence, and place of death for decedents from drug overdoses in New Hampshire between 01/2015 and 09/2016. The analysis demonstrated that most of the fatal drug overdoses occurred in metropolitan areas (NDEWS, 2017; Sorg et al., 2017).

The rise of use disorders and mortality from opioids including fentanyl, has raised attention on whether these patients are receiving adequate treatment services. The 2016 National Survey on Drug Use and Health (NSDUH) administered by the Substance Abuse and Mental Health Services Administration (SAMHSA) reported that although approximately 21 million people aged 12 or older needed treatment for substance use in 2016, almost 90% of these patients reported that they did not receive professional treatment in the previous 12 months (Substance Abuse and Mental Health Services Administration, 2017). Previous research investigated the risks associated with not receiving timely treatments (e.g., buprenorphine-naloxone, access to methadone clinics and emergency medical services) among individuals with opioid use disorders both in the

US and globally (Dodson et al., 2018; Dunlop et al., 2017; Lo et al., 2018; Yarborough et al., 2016). For example, in the U.S., a study based on outpatient treatment centers in Baltimore found patients traveling more than 4 miles were significantly associated with a shorter length of stay for treatment completion (Beardsley et al., 2003). In New York City, a one-mile travel distance was utilized as threshold for analyzing spatial access to syringe exchange programs among drug injectors and a median of 10% of district surface area were within this distance in 2005 (H. L. F. Cooper et al., 2011). A study in Houston, TX found that heroin injectors tended to live closer to treatment facilities, in order to get assistance and reduce injecting (Kao et al., 2014). Other factors that influence behaviors among opioid users include lower socioeconomic levels (and higher crime rates) for neighborhoods (Kwan et al., 2018a) and that impede access to opioid treatment programs and impact treatment continuity among drug users (Mennis et al., 2012).

In New Hampshire, there has been a significant increase in treatment demand for patients with opioid use disorders. The number of opioid-related emergency department visits in July 2016 were double the number from February 2016, and treatment admissions associated with heroin and fentanyl significantly exceeded that for prescription opioids (NDEWS Coordinating Center, 2016). In addition to the services from opioid use disorder treatment facilities, receiving treatment from emergency medical service (EMS) providers, especially naloxone administration at the scene is also critically important when an opioid drug overdose occurs (Faul et al., 2015, 2017). In New Hampshire, a low likelihood of receiving interventions from EMS was found in rural locations (Sorg et al., 2017). Enhancing access to both treatment facilities and EMS services including administering naloxone is important for state and local health planning officials and related stakeholders in reducing the impacts associated with opioid use disorder, especially in a state where a significantly high number of deaths from fentanyl poisoning have been identified. However, very few studies have investigated spatial access to more than one type of resource, e.g., treatment facilities and EMS.

Spatial access refers to the geographic barriers that might exist between service suppliers and population demand (Joseph & Phillips, 1984). A standard approach to measure spatial access uses a gravity-based model that considers the spatial interactions between population locations and service locations based on how far patients are willing to travel (Guagliardo, 2004; Kim & Kwan, 2003; Kwan & Hong, 1998). This framework has been widely used in health care studies and is often used to explain impedances in patients' travel to health care services given the availability of facilities (Cao, Stewart, & Kalil, 2016; Gharani, Stewart, & Ryan, 2015; Ye & Kim, 2014). In this research, we investigate the key factors or determinants of accessibility that include street network distance, driving time, and distance decay, as well as services availability and population demand to provide a measure of access to key treatment resources for New Hampshire. This work involves an analysis of spatial access to opioid use disorder treatment centers and programs, locations of buprenorphine treatment practitioners, and EMS services by town for 2015 – 2016, a key period during the opioid crisis in New Hampshire. We combine accessibility indices to produce a composite index of spatial access that provides an overall pattern of accessibility to key treatments including emergency response services across the state, and compare this result with known locations (towns) of fatal overdoses that involved fentanyl during this period. The findings provide support for local state stakeholders for allocating scarce treatment resources during the national opioid epidemic.

3.2 Methods

3.2.1 Data

New Hampshire has 10 counties and 259 county subdivisions, including 222 towns, 13 incorporated places, and 24 other spatial entities (including grants, locations, purchases and townships). This state is composed of 120 rural and small towns (population < 10,000), with an overall population in 2015 of 1.3 million (Figure 3-1). For this research, spatial analyses were undertaken at the granularity of county subdivision (town level), to be consistent with the NDEWS HotSpot study, where the number of overdoses involving fentanyl and possibly other drugs was reported at the same spatial granularity. Details of towns and corresponding demographic data for 2015 obtained from the American Community Survey are listed in Appendix A. The analysis also uses the number of heroin and prescription opioid treatment admissions for New Hampshire during 2015-2016 as reported by the New Hampshire Department of Health and Human Services[7]. The number of treatment admissions for each town were estimated based on the proportion of town population in each county. In order to investigate spatial access from towns to opioid use disorder treatment centers, this research analyzed locations of 49 treatment centers in the state of New Hampshire from SAMHSA[8], released in February 2017. The full list of service settings and treatment types for the centers are listed in Appendix B. In addition, the locations of 125 buprenorphine treatment practitioners were also collected from

[7] https://www.dhhs.nh.gov/dcbcs/bdas/documents/dmi-2016-overview.pdf
[8] https://findtreatment.samhsa.gov/locator?

SAMHSA. In New Hampshire, the cities of Manchester and Nashua designated 16 fire stations as *Safe Stations* to help fast track patients seeking treatment for opioid use disorders[9]. The analysis of spatial access to emergency medical services (EMS) was based on data for 172 EMS stations, collected from the State Department of Safety, Division of Fire Standards & Training & Emergency Medical Services[10] for fire stations with transport licenses and Yellow pages[11] for private EMS services (e.g., American Medical Response in Manchester). These data were accessed in 2017.

Another dataset in this research included data on 492 decedents in New Hampshire whose deaths occurred between 01/2015 and 09/2016, and were reported to be from drug poisoning due to fentanyl alone or in combination with other drugs and/or alcohol. Most victims were white, male, and between 20-39 years old (Sorg et al., 2017). Data about these deaths were collected as part of the collaboration between NDEWS New Hampshire HotSpot study researchers and the Office of the Chief Medical Examiner in New Hampshire.

The spatial data for this research included boundaries for 259 county subdivisions (e.g., towns) from TIGER/Line Shapefiles, street network data from OpenStreetMap, population totals for each town, as well as socioeconomic variables from the US Census Bureau's American Community Survey (ACS)[12] for 2015. The urban-rural classification is from USDA's Rural-Urban Commuting Area (RUCA) Codes[13], and were aggregated into 4 categories: metropolitan (urbanized areas of 50,000 and more population),

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[9] https://www.manchesternh.gov/Departments/Fire/Safe-Station
[10] https://www.nh.gov/safety/divisions/fstems/ems/documents/unitdirectory.pdf
[11] https://www.yellowpages.com/search?search_terms=ambulance+services&geo_location_terms=NH
[12] https://www.census.gov/programs-surveys/acs
[13] https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx

micropolitan (large urban clusters of 10,000 to 49,999 population), small town (small urban clusters of 2,500 to 9,999 population), and rural areas (outside urban areas or urban clusters) (Figure 3-1).

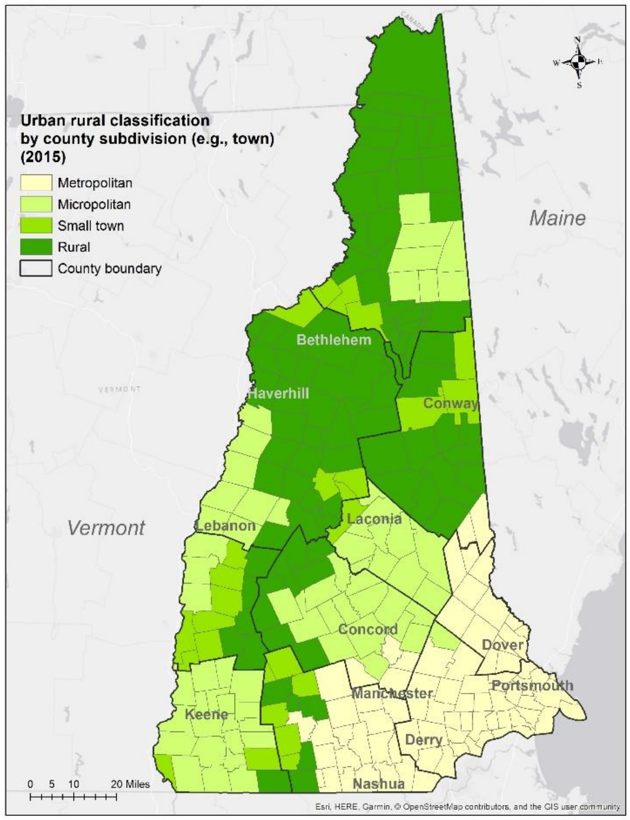


Figure 3-1 Urban-rural classification for New Hampshire by county subdivision (towns) (n = 259) for 2015

3.2.2 Geospatial determinants for calculating access to substance use disorder treatment facilities

The analysis of spatial access to substance use disorder treatment facilities includes access to treatment centers, buprenorphine physicians, and Safe Stations. To model spatial access from town centroids to these locations, the enhanced two-step floating catchment area (E2SFCA) model (W. Luo & Qi, 2009) and the Huff model were used

(Huff, 1963). E2SFCA was built based on the original two-step floating catchment area (2SFCA) developed by (W. Luo & Wang, 2003) and overcomes the limitation in the original 2SFCA model where driving time is the same from an origin to all destinations falling into the catchment area (i.e., a defined driving time threshold) of this origin. Instead, the E2SFCA model captures variable catchment sizes (i.e., variable driving times) using an impedance function between each origin (e.g., centroid of town) and destination (treatment service location) pair and measures distance and time-based accessibility for local populations with respect to receiving health care.

The Huff model (Huff, 1963) has also been applied in human mobility research to investigate place-based accessibility espcially in the context of urban services (B. Y. Chen et al., 2017; Lu, Shaw, Fang, Zhang, & Yin, 2017). The use of the Huff model with E2SFCA was reported by Luo (2014), where the Huff model was applied to quantify the probability of selecting a health care service site among available services sites, based on the capacity or suitability of each facility. In this study, we accounted for the total number of treatment types that each center, doctor's office, or fire station (Safe Station) is able to provide.

The advantage of using both models together is that supply side properties are represented based on the different service settings and treatment services available at the treatment locations. The supply parameter of the model refers to the number of service settings (e.g., inpatient treatment) in each substance use disorder treatment center, Safe Station Program, or buprenorphine physician office. The demand parameter denotes the population of heroin and prescription opioid treatment admissions in each town that falls into the catchment area of each treatment center. In this study, the number of treatment admissions are used as a proxy for the population that is at-risk for opioid use disorder and needing these services. The access score of each town is computed based on the sum of treatment service-treatment admission ratios for each service site that falls into the catchment area of each town centroid. The catchment area is defined based on an impedance function. A Gaussian function is used to model the impedance function capturing the smoothing that fits best with the distance decay effects assumed for this analysis. The travel times for driving between each town centroid and substance use disorder treatment center were calculated using an Origin-Destination matrix based on Open Street Map (Package osrm in R 3.2.5). However, the following time adjustments were made for the impedance function:

$$t_{ij} = m * t_{ij} + n \qquad (1)$$

where t_{ij} represents the travel time for driving between each town centroid i and substance use disorder treatment facility j. Parameters m and n represent the indices of time adjustments and weights applied due to different travel scenarios.

To account for differences between actual and estimated driving times in different locations across the State, we undertook tests using Google Maps at different times of the day. Based on the fact that rural roads in New Hampshire have fewer vehicles and lower populations we multiplied 1.1, 1.3, 1.3, 1.4 to the estimated travel times to represent travel in rural, small town, micropolitan and metropolitan towns respectively (Carr, Branas, Metlay, Sullivan, & Camargo, 2009). However, accounting for a longer travel time for patients residing in rural locations compared with patients living in urban places, we also set different driving time thresholds for rural, small town, micropolitan, and metropolitan. To identify the impedance coefficient for each urban-rural category, we tested driving times for these categories using Google maps. For travel to treatment locations, 45 min was set as an accessible driving time threshold for rural locations, 35 minutes for small town, 30 minutes for micropolitan, and 25 minutes for metropolitan towns (Table 3-1). The values of impedence coefficients are determined when the Gaussian function approaches 0 (e.g., 0.01 as threshold for this study) at 45, 35, 30 and 25 of each subzone (Cao et al., 2016; Wan, Zhan, Zou, & Chow, 2012). This impedance function was applied in both the E2SFCA and Huff models in this analysis.

Spatial access to buprenorphine physicians was computed using E2SFCA since these locations offered only a single type of service. In this analysis, all the service sites are weighted equally, with one physician at each location. The remaining computation follows the approach for computing spatial accessibility to treatment centers, adopting Gaussian weights for the impedance function and distinguishing rural, small town, micropolitan and metropolitan using 45 min, 35 min, 30 min and 25 minutes as driving time thresholds for each population center respectively.

3.2.3 Access to emergency medical services (EMS)

To compute spatial access from town centroids to EMS service locations, we made some modifications to the E2SFCA. According to a national study on EMS administration of naloxone, the proportion of 911 calls requiring EMS associated with drug overdoses is less than that for other incidents (e.g., stroke and heart attack) (Faul et al., 2015, 2017). Therefore, to estimate access to EMS specifically for opioid use disorder, we subtracted the demand ratio for non-opioid EMS sevices (e.g., cardiac or trauma services) from the demand ratio for substance use-related EMS services for the first step of E2SFCA:

$$R_u = \frac{E_u}{\sum_{k \in d_r} P_{k(opioid)} g(t_{ku})} - \frac{E_u}{\sum_{k \in d_r} P_{k(non-opioid)} g(t_{ku})} \quad (2)$$

$$A_{Ei} = \sum_{u \in d_r} R_u g(t_{iu}) \quad (3)$$

where E_u refers to the number of emergency transport vehicles (i.e., ambulances) for each EMS station u. $P_{k(non-opioid)}$ denotes population that town total population subtracting heroin and prescription opioid treatment admissions in each town. This represents the population for other, non-opioid patients who utilized EMS services. In equation (2), the original ratio $\frac{E_u}{\sum_{k \in d_r} P_{k(opioid)} g(t_{ku})}$ possibly overestimates the number of opioid use disorder patients accessing EMS services and therefore, the current R_u represented an effective ratio of EMS-opioid use disorder patients. The final A_{Ei} measures spatial accessibility to EMS specifically for opioid use disorder patients. The impedance function $g(t_{iu})$ for this analysis applied an inverse power function to represent the distance decay effects for emergency service scenarios.

Previous research has reported that the national average emergency response time in the U.S. is 15 min 19 sec[14]. In this analysis, 20 min was set as an access threshold for emergency transport vehicles' driving time responding to rural calls, and this threshold is gradually reduced for small towns and micropolitan towns, and to 13 min for metropolitan towns. These times may vary of course for different locations and response times in certain urban locations may be considerably faster than 13 minutes. The values of the impedance coefficient were determined when the inverse power function reaches

[14] https://www.autoinsurancecenter.com/emergency-response-times.htm

0.01 for each category. For EMS services, there may also be differences in activation times (the time between receiving a 911 call and ambulance dispatch) between urban and rural locations, as well as between volunteer and non-volunteer fire stations, where volunteers may be paged to respond to an emergency and require additional minutes for travel. Therefore, in addition to different values for index m for urban and rural towns, we applied 3, 2, 2 and 1.5 minutes as activation times for rural, small towns, micropolitan and metropolitan towns respectively (Carr et al., 2009) and for volunteer fire stations, we added an additional 3 minutes in travel time due to volunteer and off-site personnel response.

Table 3-1 Summary of distance decay function parameters and driving time adjustments

	Driving time threshold for Gaussian function (min)	**Impedance coefficient in Gaussian function**	**Driving time threshold for Inverse Power function (min)**	**Impedance coefficient in Inverse Power function**	$\boldsymbol{m}$ **(Eq.1) for** $\boldsymbol{t_{ij}}$ **and** $\boldsymbol{t_{iu}}$	$\boldsymbol{n}$ **(Eq.1) for** $\boldsymbol{t_{iu}}$ **(min)**
Urban-rural classification						
Rural	45	440	20	1.54	1.1	3
Small town	35	270	18	1.6	1.3	2
Micropolitan	30	200	15	1.7	1.3	2
Metropolitan	25	135	13	1.8	1.4	1.5
EMS station type						
Volunteer	--	--	--	--	--	3
Non-volunteer	--	--	--	--	--	0

3.2.4 Deriving a composite index for spatial accessibility

In order to achieve an overall understanding of spatial accessibility across the state of New Hampshire during this time period for the different types of treatment services, we have combined the accessibility indices together to create a single composite index that reflects all aspects of treatment–non-emergency and emergency–that opioid use disorder patients may require.

To create the composite index, the first step involved normalizing the two indices for treatment centers and buprenorphine physicians (A_{Ti} and A_{Bi}) to a range between 0 and 1, considering the direct proportion of each access index (A_i) using equation (4) (Abuzied, Yuan, Ibrahim, Kaiser, & Saleem, 2016). The normalized indices A_{Ti} and A_{Bi} were summed to compute composite index A_{TBi}. Through this normalization approach, the original distribution of access scores of each type of treatment can be maintained. The second step, to include EMS services as part of the final index , we normalized both A_{TBi} and A_{Ei} to the range of 0 and 1 following equation (4), and summed up the two normalized indices to get an overall accessibility score for opioid use treatment services for each town in New Hampshire (Eq. 5).

$$A_{norm} = (A - A_{min})/(A_{max} - A_{min}) \tag{4}$$

$$A_{comp} = (A_{Ti(norm)} + A_{Bi(norm)})_{norm} + A_{Ei(norm)} \tag{5}$$

3.3 Results

3.1 How spatial access to key treatment services varies across New Hampshire

We conducted both separate and combined analyses of spatial accessibility investigating access to treatment centers, buprenorphine treatment practitioner locations, and EMS services in New Hampshire. While the spatial variations across the state meant that no strong relationship held everywhere, when the association between access to treatment centers and access to EMS services was examined using a Pearson’s correlation test, a slightly positive relationship was found with a coefficient of 0.147, p-value 0.017, and t-value 2.402 (CI 95%) (Figure 3-2). This suggests that in general, where access to treatment centers was higher, access to EMS services also tended to be higher.

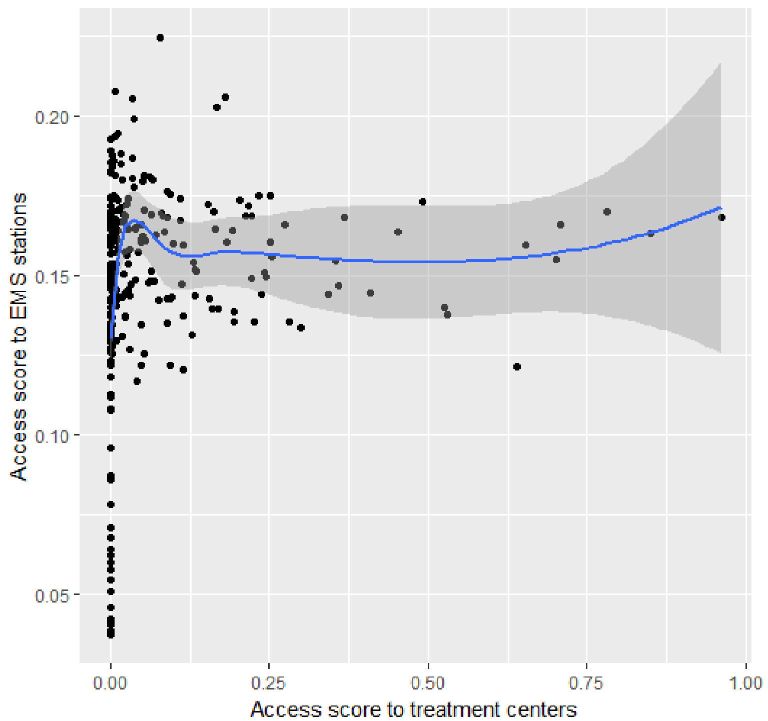
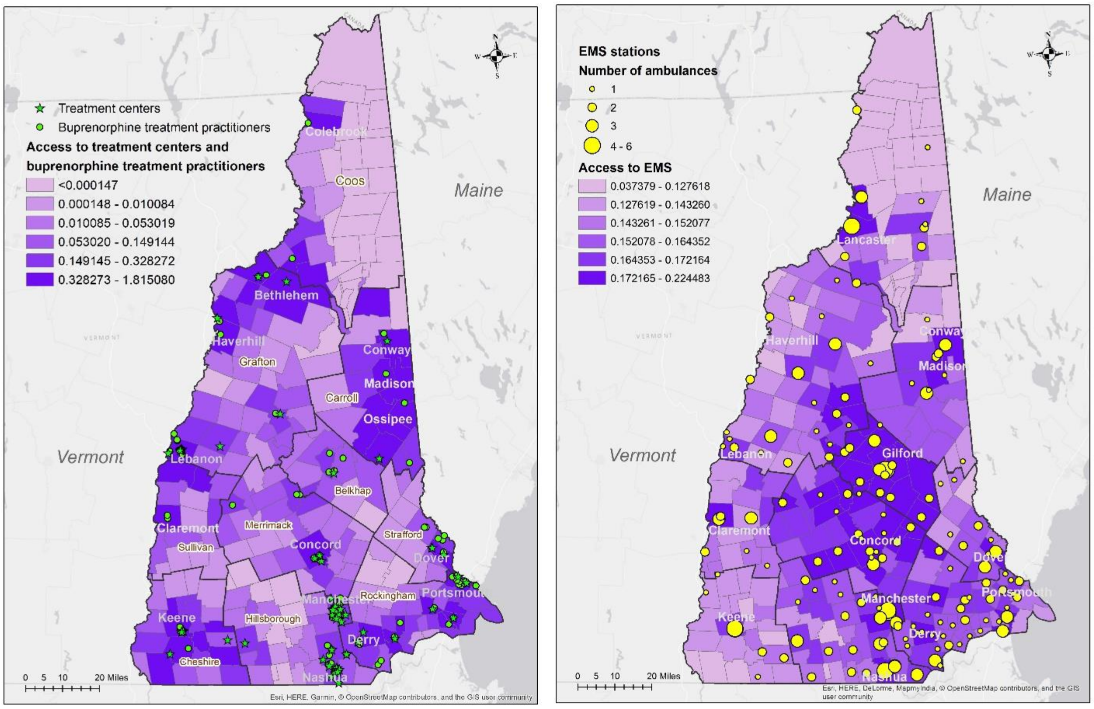


Figure 3-2 Association between access to opioid use disorder treatment centers and access to EMS services (New Hampshire, 2015 – 2016, n = 259 towns)

A combined analysis of spatial access to opioid use disorder treatment centers and buprenorphine treatment practitioner locations (referred together as *treatment facilities*) is shown in Figure 3-3a. For mapping, a quantile classification was used where each class contains approximately 15% of towns (approximately 45 towns). We found that for access to treatment facilities, towns along the borders of New Hampshire with Vermont, Massachusetts, and Maine including Conway, Portsmouth, Keene, Lebanon and Bethlehem were in the highest class of access scores. The cities of Manchester and Nashua fall into the second highest class of access. In the northern part of the state, certain towns, e.g., Colebrook and Ossipee were examples of rural towns that were also in the highest group of access to treatment facilities. With respect to EMS services, access was found to be high especially in mid-to-southern New Hampshire (e.g., Gilford, Concord, and Manchester) (Figure 3-3b). Lancaster in Coos County and Conway in Carroll County were other examples of towns that had the highest estimates of access to EMS services.

Our results found that access to both service types together (i.e., treatment facilities *and* EMS services) for this period was estimated to be higher in southern, more populous locations than in northern, remote and less populated areas of the state (Figure 3-4). The top 5 locations with the highest composite access scores were Hampstead, Keene, Conway, Portsmouth, and Lebanon. For northern rural locations Haverhill and Bethlehem in northern Grafton County, and Whitefield and Carroll in Coos County were found to be in the top class of composite access. Lower composite scores for spatial access during this period were returned for towns in northern Coos County, and towns in Sullivan and Grafton Counties in western New Hampshire, as well as towns in Hillsborough County.



(a) (b)

Figure 3-3 Spatial access for New Hampshire, 2015-2016, n=259 towns for (a) treatment facilities (composite access index for treatment centers and buprenorphine treatment practitioners, E2SFCA and Huff model) and (b) EMS (modified E2SFCA model).

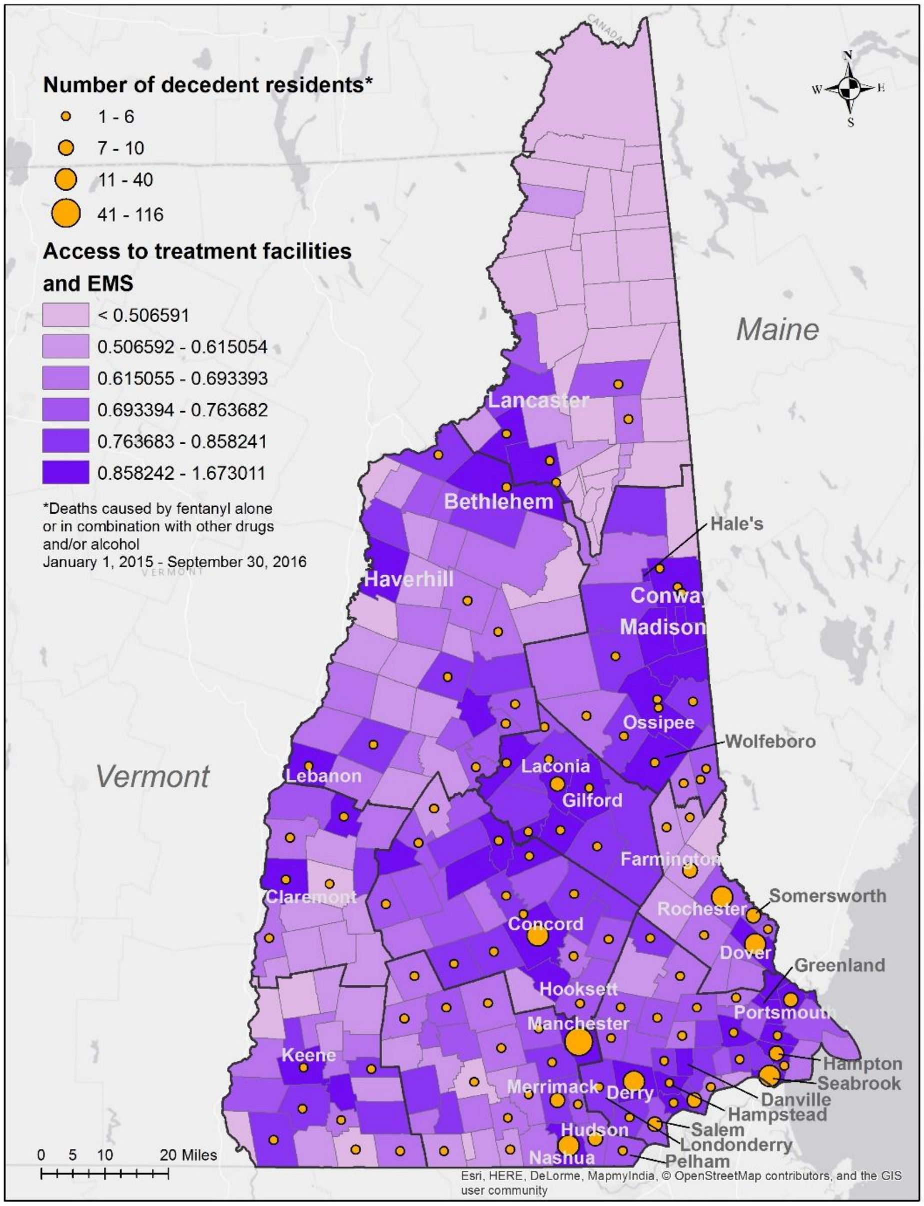


Figure 3-4 Composite index of spatial accessibility to treatment facilities and EMS, with towns of residence of decedents from fentanyl overdoses (New Hampshire, 2015-2016, n=259 towns)

3.2 Spatial accessibility and drug poisoning deaths caused by fentanyl or other drugs

The spatial pattern of individual drug poisoning deaths caused by fentanyl alone or in combination with other drugs and/or alcohol between 01/2015 and 09/2016 based on town of residence for 492 decedents (a total of 105 towns) was examined (Figure 3-4). Natural breaks was applied for categorizing the number of decedent residents in Figure 3-4. These individuals resided in 112 county subdivisions and villages, with 7 towns (Seabrook, Concord, Dover, Rochester, Derry, Nashua and Manchester) having more than 10 decedent residents each during the period of study. Analysis of the correlation between the estimated number of opioid treatment admissions by town and the number of decedent residents by town returned a strong positive correlation (coeff. 0.894, CI 99.9%).

In general, the correlation between composite access scores and decedent residents is positive, but weak, with coefficient 0.151 and p-value 0.0005. This indicates a general good access situation across the state, but still lack access in certain locations. Approximately 27% of the towns with decedent residents (29 out of 105 towns) were found to have composite index scores in the highest class (i.e., access to treatment facilities *and* EMS services) based on our model (Figure 3-4). These towns accounted for a total of 289 decedents (approximately 60% of the total). Among the 17 towns with highest estimates of opioid treatment admissions, Merrimack, Nashua, Seabrook, Dover, Derry, Laconia, Manchester, Hampton, Concord and Portsmouth had the highest composite access scores. However, seven towns that were associated with higher numbers of opioid treatment admissions (>5) for this period and also higher numbers of decedent residents (>7) had low composite access scores (lowest three classes). These towns include Farmington, Somersworth, Rochester, Salem, Pelham, Hudson, and Hooksett. Towns with fewer than 5 decedent residents (and towns with no decedent residents for this period) were likely to be associated with smaller populations in general.

Among this group, while about 15% of these towns were estimated to have high access (e.g., Conway and Bethlehem), approximately 35% were in the lowest two classes of access to both types of treatment services. Towns with lower access were mostly northern and western rural towns.

3.3 Spatial accessibility and urbanization

We also investigated the association between spatial access and towns classified based on urbanization: metropolitan (29.2%), micropolitan (24.6%), small town (10.4%), and rural (35.8%) as per 2015. Among the towns in the highest class of access to treatment facilities, approximately 32.5% were rural towns (Table 3-2). These towns included Madison and Wolfeboro in Carroll County, and Bethlehem and Haverhill in Grafton County. Seven towns were classified as small towns including Conway and Hale's (Figure 3-3a). Thirty-five percent of towns in the highest class of access to EMS were metropolitan while 14% were rural towns. Metropolitan and micropolitan locations represented approximately 70% of the towns with the highest composite index scores (Figure 3-4). Higher access indices are returned for Manchester, Nashua, Seabrook, and Greenland, as well as for some rural towns such as Haverhill and Bethlehem. This trend between access and urbanization was verified through a Chi-squared test with $p<0.01$.

Table 3-2 Counts and percentage of NH towns estimated to be in the highest class of composite access (treatment facilities, EMS, and both services) by urbanization category

	Metropolitan	Micropolitan	Small town	Rural
Access to treatment facilities	13 (30.2%)	9 (20.9%)	7 (16.3%)	14 (32.5%)
Access to EMS	15 (34.9%)	18 (41.9%)	4 (9.1%)	6 (13.6%)
Access to both services	17 (39.5%)	12 (27.9%)	7 (16.3%)	7 (16.3%)

Chi-squared test $p < 0.01$

3.4 Spatial accessibility and socioeconomic factors

In addition to urbanization, we also investigated whether there were any associations between the spatial access results and certain socioeconomic variables including median household income, the percentage of residents with employment, and the percentage of residents with a bachelor's or higher degree (Table 3-3). The results showed locations with larger populations that were full-time employed, higher median household income and college-educated, were found to have higher access to treatment. Education showed a stronger positive correlation with access to treatment facilities in locations including Portsmouth (close to the University of New Hampshire), Merrimack, Hampton and Lebanon (close to Dartmouth College). Employment was found to have a higher positive association with access to EMS, as well as with composite access scores. Locations with both high values of employment and median household income were mostly in Rockingham and Strafford Counties (including Portsmouth, Hampstead and Derry) and these locations also corresponded with high access to both types of treatment services.

Table 3-3 Correlation coefficient between spatial accessibility and median household income (MHI), % of residents with employment (EMP), and % of residents with bachelor's or higher degree (EDU)

	MHI (p-value)	**EMP (p-value)**	**EDU (p-value)**
Access to treatment facilities	0.109 (0.075)	0.122 (0.047)*	0.207 (0.001)*
Access to EMS	0.570 (<0.001)*	0.640 (<0.001)*	0.436 (<0.001)*
Composite access	0.461 (<0.001)*	0.520 (<0.001)*	0.430 (<0.001)*

*Statistically significant with $p<0.05$

3.4 Discussion

In this research, we investigated the characteristics of spatial access to opioid use disorder treatment services, to both treatment facilities (including buprenorphine treatment practitioner locations), and emergency medical services. We undertook a comprehensive analysis of spatial access using an integration of the E2SFCA model and Huff model for modeling access to treatment facilities, as well as a modified E2SFCA for modeling access to EMS services. The integration of the two models plus the adjustment to the E2SFCA model make this approach for determining spatial accessibility more realistic and provide a better fit for modeling access to opioid use disorder services. Instead of using simple buffer zones to analyze access to treatment services, our models reflect the different patterns of locations of different types of services as well as the role of several key determinants, including street network distance, driving time, distance decay, treatment services availability and population demand.

The results show a marked variation in access to opioid use disorder treatment services across the state with higher access mainly located in the southern part of the State following the trend of where the larger population centers exist. The patterns varied for the different treatment service types. For example, towns along the western border with Vermont and the eastern border with Maine had higher access to opioid use disorder treatment facilities, while central and southern towns had generally higher access to EMS. Certain rural towns, for example, at the border of Merrimack County and Grafton County, with higher access scores for EMS services, may benefit from EMS stations located in nearby larger centers. However, certain locations did not show high access to all treatment resources. For example, for locations with high estimates of opioid treatment admissions, even where the set of services including outpatient, residential, and inpatient services may be available, access may be insufficient.

In general, good spatial access to treatment centers, buprenorphine treatment practitioners, fire stations with Safe Station programs, and EMS stations with multiple service vehicles, plus an optimal road network were the characteristics of locations with high composite spatial access scores. These locations were also associated with higher socioeconomic status. This corresponds to relationships found in previous research by Stahler et al. (2016) and Stein et al. (2015) who both reported higher opioid use associated with groups with lower socioeconomic status. The analysis of urban-rural differences indicated that only approximately 33% of rural towns were in the highest category of access to treatment facilities. This percentage went down to 16% for the highest class of composite access (both treatment facilities and EMS together). For rural towns, there was an overall lower number of treatment centers and buprenorphine treatment practitioners, as well as EMS stations. This finding corresponds to previous research on rural patients and the degree to which they experience lower opportunities for receiving opioid use disorder treatment due to e.g., lack of physicians, current technology, and longer travel distances (Browne et al., 2016; Rosenblatt et al., 2015; Sigmon, 2015).

The analyses also showed that certain towns (e.g., Rochester) that were impacted by high numbers of fentanyl deaths between 01/2015 and 09/2016, did not necessarily have high access to *all* types of treatment services. We found that approximately 40% of decedent individuals during the study period resided in towns that were not estimated to have the highest composite access. This suggests a possible gap in the location of treatment services for patient populations in certain towns during this time. While in some locations (e.g., Manchester), there was estimated to be good access to treatment services, the numbers of treatment admissions and fentanyl deaths were still high. Further investigation is needed to get a clearer understanding of whether other factors may be contributing to impeding access for these individuals. The locations where higher numbers of fentanyl decedents resided, however, varied with respect to access to different treatment services. This indicates that while many of the towns with generally larger estimates of opioid treatment admissions and larger numbers of decedent residents scored high with respect to spatial in access for EMS, they did not also score highly for spatial access to treatment facilities (or *vice versa*), i.e., they did not have high access to both types of services. These low access zones highlight locations that could be looked at in more detail by local health officials to determine whether additional resources should be planned for these locations.

3.5 Limitations

In this research, data on the number of beds and physicians were unavailable. Psychosocial therapies and counseling services were not part of this analysis, and so are not included as service settings that represent the varying capacities of opioid use disorder treatment centers. This could result in underestimations relating to treatment centers and less variation among centers in general. Potential overestimation of access to buprenorphine treatment practitioners may exist due to over-counting of possibly waivered physicians from the SAMHSA dataset (Huhn & Dunn, 2017). When analyzing access to EMS, we retrieved the number of emergency transport vehicles based on publicly accessible data sources. However, the numbers were estimated for most private ambulance stations based on spot checking across the state and therefore could be underestimated. And while the spatial extent of this research is the state of New Hampshire, and the treatment centers, buprenorphine treatment physicians, and EMS stations are within the state boundary, there could be a potential underestimation of access for towns near the state's boundary due to possible access for these residents receiving treatment outside the state.

The treatment admission data this research used were reported by county, and were estimated to town level based on the proportion of population in each town. There could be underestimation in low populated locations and overestimation in more highly populated places. The opioid treatment admissions data do not include Medicaid and private-insured individuals. These limitations could be possibly improved by further sensitivity analysis.

3.6 Conclusions

Enhancing access to treatment services is an important step for local public health officials as they work to reduce the risks and impacts from high numbers of individuals suffering with opioid use disorders. The contribution of this research is that we have designed an approach to measure spatial access to opioid use disorder treatment services in relation to *both* treatment facilities and emergency medical services in New Hampshire, a state hit particularly hard by the opioid crisis. This study provides a detailed investigation of the degree to which access to treatment for opioid use disorder patients varied across the state during 2015-2016. The results from this research identified locations where there is gap between access to treatment services and impacts from fentanyl overdoses.

The unique insights from investigating spatial access for both treatment facilities and EMS together provides information that local health stakeholders (e.g., opioid use disorder treatment service planners and healthcare professionals) can use for decision support and could provide further strategies to improve treatment access in at-risk regions, for example, for locating additional treatment services. This analysis could be beneficial to other states currently being impacted by the opioid crisis where geographical insights could identify gaps in services that may impact different population groups.

For future research, insurance providers and waiting time for patients to access treatment, as well as the locations of police stations that are reported to possibly serve as deterrents to treatment access are additional factors that could contribute to impeding access and could be future determinants in the model. In this Chapter, however, we did not include the types of facilities, for example, psychosocial and counseling facilities. The socio-environmental factors that are related to psychosocial services used by patients with opioid use and misuse will be introduced in Chapter 4.

Chapter 4 Modeling space-time association between patients with drug-related health problems and socially-sensed neighborhood characteristics in Maryland

Abstract

This paper investigated spatial and temporal patterns of emergency department patients with chief complaint and/or diagnosis of overdose or drug-related health problems for the four hospitals in western Baltimore during 2016-2018. The ZIP code-level patterns of overdose patients were also examined for different population groups include race, age and gender. Dynamic neighborhood characteristics were identified using socially-sensed data (i.e., geo-tagged Twitter data) at ZIP code level by 3-month. Three major variables – crime, drug use and depression, were extracted from Twitter content using natural language processing and machine learning technologies including topic modeling and sentiment analysis. Socioeconomic data were also applied as part of estimation of neighborhood characteristics. Spatial and temporal association between socio-environmental variables and the adjusted rates of overdose patients was assessed at both global level using spatial lag regression with fixed time effect and local level using geographically and temporally weighted regression. The results showed statistically significant change in adjusted rates of overdose patients from June to November 2017 in Maryland. High rates occurred in western downtown Baltimore City and also northeastern part of Anne Arundel County. The correlations with socio-environmental variables revealed that factors that are highly correlated do not appear at the same location all the time. Statistically positive association was identified between crime related tweets and adjusted rates of patients in ZIP codes in Baltimore City in mid-2017

and in northern Anne Arundel County in 2018. The variables changed however to unemployment in mid and late 2018 among ZIP codes in Baltimore City. Understanding the dynamic spatial associations between socio-environmental variables and adjusted rates of overdose patients is necessary for local health officials to address corresponding solutions to improve psychosocial services and relieve the burden of opioid crisis.

4.1 Introduction

Illicit drug overdose and related health problems have become leading public health issues among Americans. The recent opioid crisis has raised topics among public health researchers to develop effective pathways to reduce risks from opioids. Previous research shows this epidemic has impacted many regions in the US including recent spikes in mortality in many states including Ohio, West Virginia, Maryland and Massachusetts (Dwyer-Lindgren et al., 2018; Rossen et al., 2013, 2014; Stewart et al., 2017). Demographic groups impacted by the adverse health outcomes (i.e., death) from opioid use disorder have shifted from being mostly male, middle-aged and White, to larger numbers of females, younger age groups, and African American and Hispanic (Cicero et al., 2014; Kiang, Basu, Chen, & Alexander, 2019).

Socio-environmental factors have been found to have significant associations with disparities in health behaviors or outcomes (Palmer, Ismond, Rodriquez, & Kaufman, 2019). Previous research discussed the degree to which built environment including socioeconomic status is associated with dietary habits (Lagström et al., 2019), cardiovascular disease (Cebrecos et al., 2019), and substance use disorder (Kwan et al., 2018b). Studies also found that increasing rates in drug overdose and mortality may be associated with behavioral health problems (e.g., excessive alcohol drinking and crime), psychological distress and economic impact (e.g., health care cost) (Insel, 2008; Sacks, Gonzales, Bouchery, & Brewer, 2015; Wagner et al., 2018; White, Birnbaum, Mareva, & Katz, 2005). A recent national survey study found prescription drug misuse was more likely in neighborhoods that were socially disorganized and with lower levels of social capital (J. A. Ford, Sacra, & Yohros, 2017; Molina et al., 2012). A study in a midsized city in Ohio found that hotspots of violent crimes were also identified as being linked to drug use (Curtis, Curtis, Porter, Jefferis, & Shook, 2016). In addition to socioeconomic factors, the level of psychological distress in neighborhoods was also found to be associated with illicit drug use (Boardman, Finch, Ellison, Williams, & Jackson, 2001). A recent study in Philadelphia reported that an increasing pattern of substance use disorder among adolescents was associated with high-risk characteristics in certain places (Mennis & Mason, 2011). Individuals who were highly exposed to life concerns (e.g., unemployed and low income) and experiencing adverse mental health were found to be significantly associated with opioid use disorder (Sellström, O'Campo, Muntaner, Arnoldsson, & Hjern, 2011; Stein et al., 2015). The relationship between substance use disorder and neighborhood characteristics has addressed demand of local psychosocial treatment services, beyond traditional treatment involving only medication (Mennis et al., 2012). Therefore, this research aims to investigate spatial and temporal association between patients with drug-related health problems and socio-environmental factors.

To identify neighborhood characteristics, this research used socially sensed data (e.g., Twitter data) from the perspectives of both space and time, to explore the dynamic association with patients who had drug-related health problems in Maryland. In recent years, socially sensed data have become a valuable source for studying public health and social behaviors. Geo-tagged social media data have been widely used in geography and public health research. These topics include understanding spatial heterogeneity of healthy food access (X. Chen & Yang, 2014; Widener & Li, 2014), revealing transmission patterns and geographical footprint of infectious diseases such as influenza and Zika virus (Allen, Tsou, Aslam, Nagel, & Gawron, 2016; Gomide et al., 2011; Stefanidis et al., 2017), and exploring the spatial pattern of obesity nationwide in the U.S. (Ghosh & Guha, 2013). A national study during 2015-2016 utilized geo-tagged tweets to estimate prevalence of substance use and identify hotspots of substance use activities at state level (Meng et al., 2017). To examine neighborhood characteristics associated with obesity and diabetes in Utah, geo-tagged tweets were adopted to extract content of caloric density of food, physical activities, and positive mood for each ZIP code (Nguyen et al., 2017, 2016). The high efficiency of using geo-tagged social media data brings significant potential in geospatial and public health studies. Researchers are able to retrieve large quantity of dataset using automatic programming approach, which saves time and labor and augments conventional survey data (Goodchild & Glennon, 2010). The large amount of data at accurate spatial and temporal scale provides richness in various topics discussed among citizens (Goodchild, 2007). However, it should be noted that geo-tagged Twitter data only represent 1% of total tweets, and 15% of Internet users who post tweets, with a majority of young adults aging 15-30 years being most active on Twitter (Filho, Almeida, & Pappa, 2015; Jiang, Li, & Ye, 2018; Lansley & Longley, 2016; Longley, Adnan, & Lansley, 2015).

This research presents an innovative framework to investigate socio-environmental factors in relation to emergency department (ED) patients with drug-related health problems. Given the efficiency and potency of geo-tagged social media data, we extracted three social factors: depression, crime and drug use. Using both geo-tagged Twitter data and socioeconomic variables, we construct novel indicators at ZIP code level for three years (2016-2018) by month for the state of Maryland. To investigate associations between these characteristics and ED patients, we applied a geographically and temporally weighted regression model to identify times and locations that socio-environmental factors were significantly correlated. Implications for strategies to add psychosocial services in specific neighborhoods could be addressed based on the results of this research.

4.2 Methods

4.2.1 Data

Maryland has 24 counties and 469 ZIP code regions, with an overall population of 6 million in 2018. For this research, spatial and temporal analyses were undertaken at the granularity of ZIP codes, to be consistent with emergency department admission data, where the individual records were reported at the same spatial granularity. The electronic records for the patients were collected with drug toxicology test results in order to track the types of drugs detected in patients presenting to the emergency department (ED) with a chief complaint and/or diagnosis of overdose or drug-related health problems. Toxicology screens were typically ordered for suspected drug users, persons with psychiatric illnesses, or persons with an altered mental state. These data were retrieved from Epic electronic health record (EHR) software to track patient information[15] for four west Baltimore hospitals and included 6607 records for the period January 2016 –

[15] https://www.epic.com/

December 2018. These patients' records were for: The University of Maryland Baltimore Washington Medical Center (BWMC), University of Maryland Medical Center Midtown Campus (MTC), University of Maryland Medical Center (UMH), and University of Maryland St. Joseph Medical Center (SJMC). These records contained patient information including ZIP codes or residence, race, age, gender, emergency department, month and year of admissions, and drug toxicology test results for eight different drugs: opiates, cocaine, benzodiazepines, marijuana, methadone, amphetamine, barbiturates, and phencyclidine (PCP). For this research paper, analysis was based on 6290 records whose residential ZIP codes were in Maryland. This was approximately 95% of entire dataset. The data description of these 6290 cases are described in Table 4-1.

To investigate socio-environmental factors that are spatially and temporally associated with ED patients, we utilized both socially sensed data (e.g., Twitter data) and socioeconomic variables from the US Census Bureau's American Community Survey[16]. In this research, we retrieved 30,022,075 geo-tagged tweets in Maryland from January 2016 to December 2018. Twitter data were collected using Amazon Web Service, where original geo-tagged tweets for the United States were retrieved through Twitter streaming API (application programming interface, a protocol for building software applications) and stored by the Center for Substance Abuse Research, University of Maryland. In general for this streaming API, 1% of all tweets contain geolocation information (Kevin Makice, 2009). This geolocation information can be at two granularities: in a descriptive form (e.g., list of town names or place names) or with accurate GPS coordinates. The Twitter data we collected were with GPS coordinates. For the tweets that did not have

[16] https://www.census.gov/programs-surveys/acs

geo coordinates, we calculated the centroid point coordinates using four boundary points' coordinates. The original format of tweets returned from API are JavaScript Object Notation (JSON) objects with needed information: created time, place, latitude, longitude, user id, Twitter content. Socioeconomic variables from U.S. Census include percentage of population with no high school degree, unemployment rate, poverty rate, median house value. These data were collected for the year 2017 at ZIP code level for the state of Maryland and are static data for the entire study period.

The spatial data for this research included boundaries for 469 ZIP code regions and 24 counties from TIGER/Line Shapefiles. In terms of geography, ZIP code boundaries do not line up with county boundaries in Maryland. For the spatial analysis and mapping in this research, we adopted administrative boundaries for ZIP code and county, and thus assigned ZIP code regions to the county that administers them according to information publicly available from the State of Maryland [17].

[17] https://data.imap.maryland.gov

Table 4-1 Data description of four EDs with demographic information (N= 6290, 2016-2018)

	BWMC (N=2414, 38%)	MTC (N=1956, 31%)	UMH (N=1318, 21%)	UMSJMC (N=602, 10%)
Sex				
Male	1481 (61%)	1380 (71%)	936 (71%)	314 (52%)
Female	933 (39%)	576 (29%)	382 (29%)	288 (48%)
Age				
<30	844 (35%)	199 (10%)	211 (16%)	215 (36%)
31-40	674 (28%)	284 (15%)	252 (19%)	117 (19%)
41-50	372 (15%)	422 (22%)	264 (20%)	98 (16%)
51-60	334 (14%)	714 (36%)	405 (31%)	79 (13%)
60+	190 (8%)	337 (17%)	186 (14%)	93 (15%)
Mean Age (SD)	34 (13.79)	50 (12.39)	48 (13.45)	36 (16.97)
Race				
White	1922 (80%)	329 (17%)	395 (30%)	433 (72%)
Black or African American	402 (17)	1573 (80%)	887 (67%)	142 (24%)
American Indian or Alaskan Native	2 (0.08%)	0 (0%)	0 (0%)	1 (0.2%)
Asian	16 (0.7%)	4 (0.2%)	5 (0.4%)	8 (1%)
Other	51 (2%)	18 (0.9%)	13 (1%)	17 (3%)
Travel distance (network)				
Mean Time (min)	11.9	7.23	8.4	15.14

4.2.2 Spatial and temporal patterns of ED patients

To investigate spatial and temporal patterns of ED patients with a chief complaint and/or diagnosis of overdose or drug-related health problems in Maryland, we adjusted the number of patients by 10,000 population in each ZIP code in 2017 and the total number of admissions for each month. When exploring the spatial patterns of demographic characteristics, age groups were classified as 18-29 years old, 30-39, 40-49, 50-59 and 60 and above; racial groups were classified as White, Black and Asian; and male and female for gender groups. Each sub group was normalized by the corresponding population of each demographic group in each ZIP code region in 2017. To further test for statistically significant changes in the adjusted rates of ED patients, a prospective statistical test –

cumulative sum (CUSUM), was applied for the time period 01/2016-12/2018. This approach has been used to identify significant changes in the mean values of a series of variables in the domain of public health studies (Cao, Renschler, & Jacquez, 2014; Rogerson & Yamaha, 2008). The approach is expressed as follows:

$$S_t = max(0, S_{t-1} + z_t - k) \qquad (1)$$

Where $S_0 = 0$ and S_{t-1} refers to the CUSUM value of ED admissions in the previous month. The threshold value h is defined as:

$$h \approx \left(\frac{ARL_0+4}{ARL_0+2}\right) \ln\left(\frac{ARL_0}{2}+1\right) - 1.166 \quad (2)$$

ARL is referred to average run of length and is computed to capture the length of sequence between signal occurrences (i.e., change in the adjusted rates of ED patients). We selected a threshold of 4, based on the critical value of ARL_0 set to 500. Under this circumstance, the value of k in Eq.1 is equal to 0.5 as a critical value, according to Table C1 in Appendix C. In this research, when CUSUM value is over 4, the model triggers a signal that a statistically significant change of ED admission for SUD occurred in a certain month. This computation was implemented using qcc package in R 3.5.1.

4.2.3 Twitter processing

To build space-time associations between neighborhood characteristics and ED patients, we generated indicators for socio-environmental variables based on both Census data and Twitter data. For this study, we collected 30,022,075 geo-tagged tweets in Maryland from January 2016 to December 2018. The workflow for Twitter processing is described in Figure 4-1.

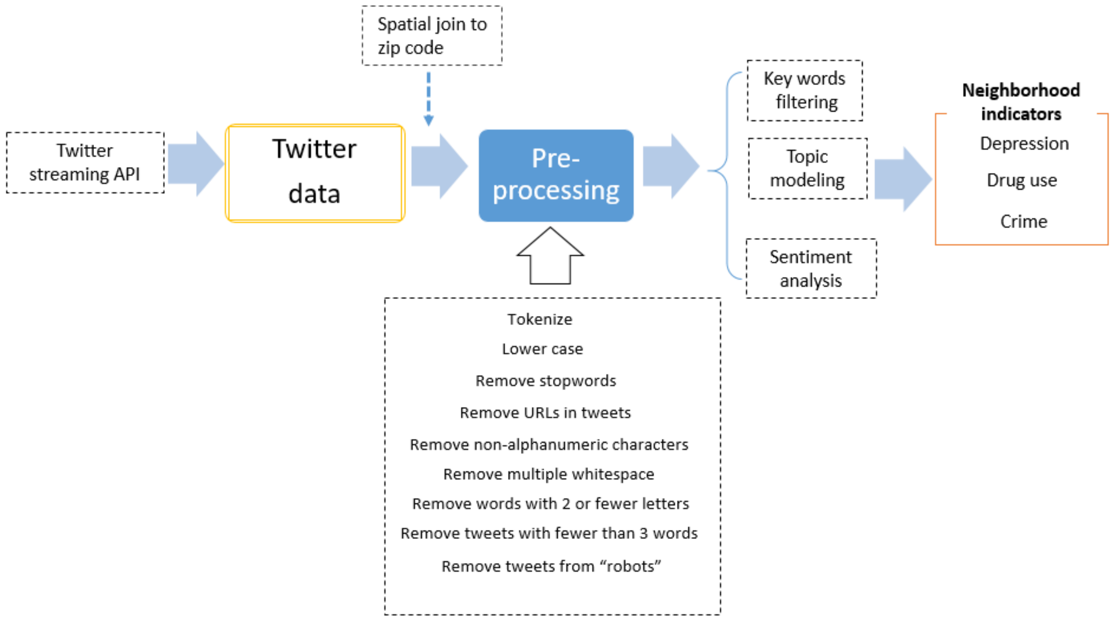


Figure 4-1 Work flow for Twitter processing

Spatial join

All tweets including state name abbreviation "MD" under "place" attribute were collected. However, in this case, place names with "MD" are also included that could potentially refer to organizations or places that are outside of Maryland (i.e., MD Anderson Cancer Center, TX). A spatial join was performed to link 99% of tweets (29,733,149) to their corresponding ZIP code locations. As introduced in section 2.1, when tweets have GPS coordinates, we used their latitude and longitude directly. However, when tweets have only place information (e.g., "College Park, MD"), we computed the centroid coordinates of the bounding box under the "geo" attribute, using the two pairs of latitude and longitude in the northeast and southwest corners. To conduct the spatial join, we used an algorithm for building an R-Tree index using the rtree package in Python 2.7, along with two additional GIS libraries, Shapely and Fiona, to implement spatial joins, creating a spatial index using the ZIP code polygon data (Guttman, 1984). The R-Tree algorithm is a classic algorithm that performs fast spatial searches by grouping spatial data (i.e., points and polygons) into rectangles, narrowing the search space, and that is optimized for tackling large spatial datasets (Alborzi & Samet, 2007; Beckmann, Kriegel, Schneider, & Seeger, 1990). In this way, each tweet was assigned a ZIP code.

Data cleaning

In order to retrieve socio-environmental factors from tweets, we performed natural language processing and data mining steps to process the Twitter content. The pre-processing of Twitter text first tokenized words and made each word in each tweet lowercase. The next step removed the following text: stop words (selected from Python English *stopwords* library) (i.e., commonly used words such as “the” and “a”), stickers (i.e., emoji), hyperlinks (URLs), hashtags, punctuations, non-alphanumeric characters, words with 2 or fewer letters, and finally multiple white spaces. After removing this content, tweets from “robots” defined as the number of daily tweets over 15 from the same account, were also removed (Lansley & Longley, 2016). These represented a total of 16,000 tweets for the entire study period. Finally, tweets with fewer than 3 words were also removed from the database. These steps were implemented using the nltk package in Python 2.7.

Retrieve socio-environmental variables

For this research, three factors were selected that were related to ED admissions for substance use disorder based on previous studies: drug use, violent crime and depression

(Mennis & Mason, 2011; Molina et al., 2012; Stein et al., 2015). We applied three steps of filtering to the pre-processed tweets: key words filtering, topic modeling and sentiment analysis.

Key words filtering. A selected list of key words for each topic is presented in Table 4-2. These terms were collected from the Urban Thesaurus[18] and slang/street names in the commonly misused drugs chart from the National Institute on Drug Abuse[19]. Words with an asterisk indicate possible spellings with other tenses or forms. For the topic of "drug use", we did not specify recreational use or medical use so both uses may be captured in these analyses. Not all terms are listed in Table 4-2. In total, there were 65 key words for depression, 43 for crime, and 71 for drug use. Target tweets were retrieved when one of the terms occurred in the tweets.

Table 4-2 Selected list of key words for each Twitter variable

Variable	Key words
Depression	never, emotion*, anxious, hate, complain, disappoint*, sad, ruin, struggle, afraid, selfish, unhappy, gloomy, depress*, upset, fail, disconsolate, miserable, stress, overwhelm, horrible*, dislike*, morose, goofer, grumpy, feel* down, dizzurped, feel* like crap, heartbreak, drowsy, sigh, mcsad, blue period, drowsy, emolarious, eeyorish, mopey
Crime	Murder, attack, cop, rape, police*, violence, victim, crime, kill, gun, shoot*, brutal, armed, robbery, assault, felon, suspect, kidnap, in custody, kingpin, gta, burglary, burgerly, thief*, dead on arrival*, break in*, crimbot
Drug use	Heroin, black tar, china white, weed, benzo, smoke* pot, cocaine, fentanyl, painkiller*, Adderall, oxycontin, Xanax, giggle smoke, jolly green, crack head, nose candy, on crack, white stuff, road dope, jelly beans, snow coke, Barbie, gold dust, aunt hazel, disco biscuits

*indicates stemming, including words formatted with "ed", "s", "ing", "ly", "ves", "ing"
Note: This is a selected list of keywords. Not all words are listed.

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[18] https://urbanthesaurus.org/synonyms
[19] https://www.drugabuse.gov/sites/default/files/cadchart.pdf

Topic modeling. The results from key words filtering included many tweets that were false positives. For example, discussions on politics relating to the opioid crisis were retrieved, which was not considered as a “drug use” activity. In order to filter these tweets, topic modeling was applied to classify each tweet into a certain topic, using single-topic Latent Dirichlet Allocation (st-LDA) in Java (Hong, Yang, Resnik, & Frias-Martinez, 2016). LDA is an unsupervised word-based statistical model, first introduced in 2003 (Blei, Ng, & Jordan, 2003), a support vector machine classifier based approach to mine topics in text documents in a given corpus based on the distribution of words frequency. In this model, each word is identified with a probability of being assigned to each of the latent topics. Each topic is also assumed to have a unique distribution of words. LDA has been widely applied in place-based research for various topics such as wildfire and land use classification (Adams, McKenzie, & Gahegan, 2015; Fan & Stewart, 2015; Fu, McKenzie, Frias-Martinez, & Stewart, 2018). For this study, we used st-LDA, a model designed specifically for classifying Twitter content, assuming only one topic was assigned to each tweet given the 280 characters limitation. We set 10 topics for each variable in this research, to filter non-related topics, for example, photo shooting or health care and politics discussions. True positive tweets were filtered for each topic and used for subsequent analysis.

Sentiment analysis. For the variable “depression", we performed sentiment analysis after topic modeling. This was due to the analysis of tweets discussing depression indicating that false positives were present, for example, some tweets mentioned being “stress free”. Sentiment analysis is a computational process that classifies opinions expressed in text (Pang & Lee, 2008). This approach has been widely used in identifying public opinions on different life events including disaster resilience and traffic experiences (Xu, Li, & Wen, 2018; Zou, Lam, Cai, & Qiang, 2018). We applied sentiment analysis to retrieve tweets that referred to depression in general, or being depressed. We utilized the VADER (Valence Aware Dictionary for sEntiment Reasoning) package in Python 2.7 (Hutto & Gilbert, 2014), that is a sentiment lexicon and rule-based model especially attuned to social media context, sensitive to both the polarity (i.e., whether positive or negative) and intensity (i.e., the degree of positive or negative) of sentiments. Each tweet returned a score for positive, neutral, negative and compound sentiments. The compound score was normalized to the range (-1, 1), while negative scores ranged from (-1, -0.05), neutral scores (-0.05, 0.05), and positive scores (0.05, 1). Positive compound scores represented upbeat emotions in tweet content while negative compound scores indicate more pessimistic emotions. In this research, we classified and retrieved "depression" tweets based on compound negative scores.

After the steps described above, we extracted a set of tweets that were more closely associated with the three socio-environmental factors being studied. In total, we retrieved 328,660 (1.1%) tweets associated with crime, 759,234 (2.6%) with depression, and 27,056 (0.1%) for drug use.

4.2.4 Modeling spatial and temporal associations

An important contribution of this research is to investigate the spatial and temporal associations between the adjusted rates of ED patients with drug-related health problems and socio-environmental factors from both Twitter data and U.S. Census Bureau. To implement spatio-temporal association computation, we did the following data pre-processing: 1) ZIP codes with no census data (e.g., ZIP code for an airport region with no associated census data) or no ED admissions were excluded in this analysis; 2) We normalized tweets for each topic by total tweets for the corresponding topic by ZIP code and did this also for the monthly ratio of total tweets by corresponding ZIP code; 3) we aggregated the data to periods of 3-months due to the small number of ED admissions by month; 4) To model spatial and temporal associations, all data, including the normalized ED admissions data, normalized tweets for each variable, and census variables are standardized to normal distribution with mean 0, standard deviation 1; 5) To avoid multicollinearity among independent variables, a linear correlation test was conducted among these variables; and 6) All ZIP code polygons were converted to centroid points whose latitude and longitude are used in the computation.

To investigate the spatial and temporal association between ED patients and socio-environmental factors, we first conducted a global statistical test, spatial lag regression with fixed time effect implemented using splm package in R 3.5.1, supported with spdep, maptools and rgdal packages. The model is expressed as follows:

$$R_{it} = \rho \sum w_{ij} R_{it} + \beta_0 + \sum_n \beta_n X_{nit} + a_i + u_{it} \qquad (3)$$

The spatial weight matrix w_{ij} was built using an estimated 10-mile Euclidean distance between ZIP code centroids. The computation was based on the projection of UTM-18N Zone (Universal Transverse Mercator) using the North American 1983 datum for the state of Maryland. We set 10-mile distance thresholds based on tests for our study area, i.e., a value that is close to the maximum distance between two ZIP code centroids. We applied spatial lag regression for this study because it contains a spatially lagged dependent variable to incorporate spatial dependency and captures a potential diffusion process across spatial units (i.e., ZIP codes) (Lacombe & Shaughnessy, 2007; Sun, Hong, & Li, 2010). A fixed effect model fits the study in terms of using the same set of areas during the different time periods (Baltagi, 2001; Millo, 2014). For this research, the adjusted rates of ED patients were considered as the dependent variable, while all the socio-environmental factors were the independent variables. However, local variations (i.e., in each 3-month period and in each ZIP code) of associations between the adjusted rates of ED patients and socio-environmental factors may not be fully captured with this model. For example, the percentage of poverty is not positively associated (with or without statistical significance) with ED patients for all locations during the entire time period.

In order to explore local variations of association across space and time, we applied geographically and temporally weighted regression (GTWR) (Fotheringham, Crespo, & Yao, 2015; Huang, Wu, & Barry, 2010; Wu, Li, & Huang, 2014). The model is expressed as follows:

$$y_i = \beta_0(\mu_i, v_i, t_i) + \sum_k \beta_k(\mu_i, v_i, t_i)X_{ik} + \varepsilon_i \quad (4)$$

Spatial and temporal nonstationary was constructed in the weight matrix based on spatial-temporal distances determined from (μ, v, t) between observation i and all the other observations. The same projection described above was applied. This model returned a correlation coefficient for each ZIP code region for every 3-month period, with the corresponding statistical significances. The same variables used in spatial lag regression with fixed time effects were used in GTWR performance. The adaptive Gaussian kernel was adopted to assign spatial weights for each ZIP code observation, where bandwidth is searched using an Akaike Information Criteria (AIC). Space-time distances were determined through a linear combination: $d^{ST} = \lambda d^{S} + \mu d^{T}$. This was implemented using the GWModel package in R 3.5.1.

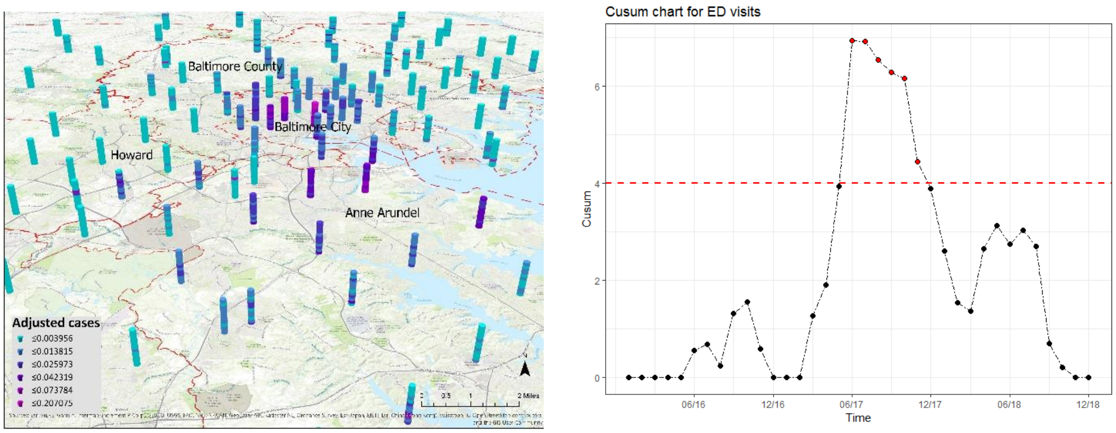
4.3 Results

4.3.1 Spatial and temporal patterns of ED patients

The adjusted rates of ED patients with drug-related health problems by ZIP shows a general pattern of high rates across the study area during late 2017 (Figure 4-2a). In Figure 4-2, the bottom (lowest) layers of each hexagon represented earlier time periods (e.g., January 2016) while the upper layers represented more recent dates (e.g., December 2018). The rates were consistently high in west downtown Baltimore for the entire study period. In this region, higher rates were returned for late 2017 and 2018, compared to other time periods. Outside Baltimore City, continuous hotspots were also found in neighboring, northern Anne Arundel County. Higher rates occurred in 2016 and early 2017 in this region compared to other time periods. In addition, a few locations in Baltimore County (e.g., Gwyn Oak, MD in July 2018) and Howard County (e.g., Jessup, MD and Savage, MD in July 2017) were estimated with high adjusted rates of ED patients with drug-related health problems.

To further investigate spatial and temporal patterns, a CUSUM test was conducted and the results are displayed in Figure 4-2b. The result showed that between June and November 2017, the adjusted rates exceeded the threshold value of CUSUM and indicated a statistically significant change during this time period. A local CUSUM test found that locations with statistically significant change during this period included western Baltimore City, as well as northeastern Anne Arundel County (locations around Pasadena, MD and Glen Burnie, MD).

In terms of urine tests for the eight types of drugs (note that the opiate screen used by the hospitals could not detect fentanyl and therefore likely underestimated the number of users), adjusted rates of patients appeared high for opiates, cocaine and benzodiazepine compared to other drugs (Figure 4-3). Overall, admissions with opiates showed a decreasing trend throughout the study period. Hotspots were also identified for cocaine and benzodiazepine in early 2016. High rates remained for admissions involving cocaine through mid-2017 and mid-2018.



(a) (b)

Figure 4-2 Spatial and temporal patterns of adjusted cases of ED patients

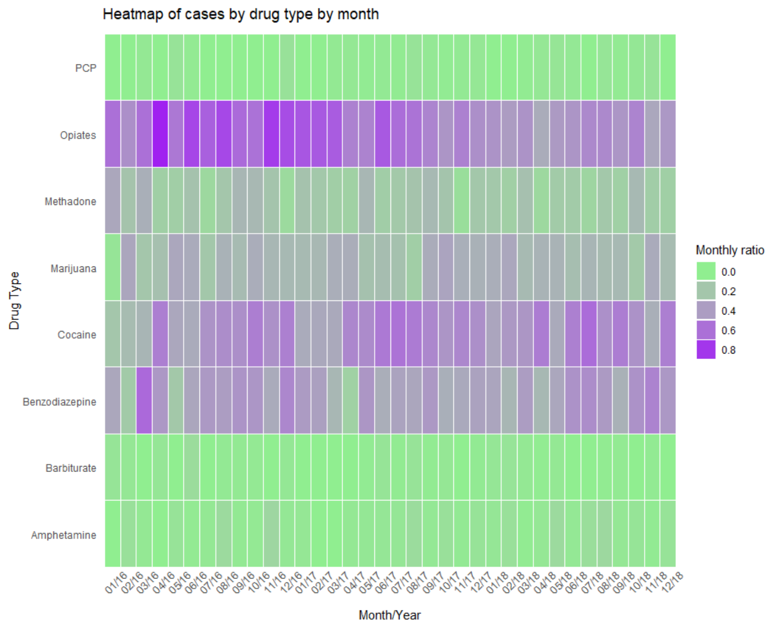


Figure 4-3 Hotspots of adjusted cases for 8 drug types in each month

4.3.2 Spatial patterns of demographic groups

Due to the relatively small numbers of ED patients with drug-related health problems across the region when breaking down to both spatial and temporal level, a purely spatial distribution of adjusted rates (normalized raw counts by 10,000 population of each corresponding demographic group) was displayed in Table 4-3 at county level. The proportion of adjusted rates for each demographic group in each of the eight counties (94% of ED patients) were listed. The results showed that in Baltimore City, there was a high proportion of ED patients aged over 50. In Anne Arundel County, Carroll County, Montgomery County, and Prince George's County, a higher proportion of admissions were of age under 40. In terms of racial groups, Blacks residing in Baltimore City and places surrounding Baltimore City comprised the higher proportion of admissions. For more distant residential locations, for example in north Baltimore County, Carroll County and Anne Arundel County, Whites were the largest group of admissions. In addition to older age groups and Blacks, patients from Baltimore City were comprised of mostly of male patients. Female patients resided in Harford County, Anne Arundel County and Carroll County.

Table 4-3 Proportion of each demographic group of ED patients in 8 counties in Maryland (values in %)

	Gender		Race			Age				
County	**Male**	**Female**	**White**	**Black**	**Asian**	**18-29**	**30-39**	**40-49**	**50-59**	**over 60**
Anne Arundel	61.61	38.39	**49.16**	42.33	8.51	**34.81**	29.26	16.32	13.53	6.08
Baltimore	67.49	32.51	42.35	51.86	5.79	23.89	22.11	22.76	21.09	10.15
Baltimore City	71.35	28.65	28.66	**66.36**	4.97	8.67	14.31	26.38	**37.87**	12.77
Carroll	56.04	43.96	100.00	0.00	0.00	**40.63**	19.85	18.31	18.93	2.29
Harford	59.77	40.23	**52.41**	47.59	0.00	31.91	**38.76**	13.31	12.89	3.13
Howard	74.94	25.06	23.14	72.89	3.97	27.10	29.44	18.18	16.98	8.31
Montgomery	62.39	37.61	31.95	68.05	0.00	**68.43**	14.37	11.12	3.58	2.51
Prince Georges	68.40	31.60	84.87	15.13	0.00	39.79	**39.49**	8.50	6.74	5.48

Note: Chi-squared test p=0.0295

4.3.3 Spatial and temporal associations

To make our results using socially-sensed data for identifying discussion on crime, drug use and depression more solid, we did correlation test between ZIP locations of crime-related tweets and crime incidents with geo-coordinates in Baltimore City[20] during 2016-2018. A coefficient of 0.565 was returned with p-value 0.0009. We also did a correlation test between county locations of drug-related tweets and mortality rates involving drug poisoning for the 8 counties (listed in Table 4-3) in Maryland during 2016-2018. A coefficient of 0.748 was returned with p-value 0.00001.

[20] https://www.baltimorepolice.org/crime-stats/crime-map-data-stats

We applied spatial lag regression with fixed time effect to explore spatial and temporal correlation between the adjusted rates of ED patients with drug-related health problems and the seven socio-environmental variables. A pre-analysis on multi-collinearity indicated significant correlations among poverty, median house value, percentage of unemployment and population percentage with no high school degree (Table 4-4).

Table 4-4 Correlation matrix for socio-environmental variables

	Crime	**Depression**	**Drug use**	**Unemploy ment**	**Poverty**	**Median house value**	**No high school degree**
Crime	1	-0.3	0.23	0.15	0.11	-0.04	0.08
Depression		1	-0.35	-0.04	-0.05	-0.08	-0.03
Drug use			1	0.2	0.33	-0.2	0.14
Unemployment				1	0.77***	-0.78***	0.38***
Poverty					1	-0.72***	0.5***
Median house value						1	-0.38***
No high school degree							1

Significant codes: '***' 0.001

Therefore, we performed four separate analyses (models) to control these four variables for the three tweet-derived variables, crime, depression and drug use and the four census-derived variables population percentage of unemployment, under poverty level, with no high school degree, and median house value (e.g., model 1 controlled population percentage under poverty level, percentage with no high school degree and median house value). Table 4-5 summarizes the results of correlation coefficients with significance level for all seven of the socio-environmental variables. This global model returns statistically significance for all variables within at least $p<0.1$. Therefore, we kept all variables for further local statistical testing. The R-squared result from this model is 0.319, indicating that the global regression model explains less than half of the variation

(Table 4-5a). The R-squared increased to 0.4023 for Baltimore City (Table 4-5b), while for Baltimore County (Table 4-5c) and Anne Arundel County (Table 4-5d), the R-squared values returned 0.0654 and 0.1472 respectively. The spatial lag coefficient (i.e., lambda) showed statistical significance for $p<0.001$, suggesting that spatial dependence (i.e., distance between ZIP codes) played a significant role when modeling associations and generating more reliable estimates of coefficients via specifying spatial interaction types. The statewide results (Table 4-5a) show the strongest positive relationship between the population percentages below poverty level with adjusted rates of ED patients, followed by the population with no high school degree. This global test returned a positive trend between adjusted rates of ED patients and these 2 socio-environmental factors. Crime-related tweets, unemployment, and median house values, however, were found to have a negative association with the adjusted rates of ED patients. To further investigate the local correlations (i.e., for different locations and time periods), we conducted a geographically and temporally weighted regression (GTWR), to consider the variables with neighboring ZIP codes and time periods.

Table 4-5 Summary of spatial lag regression with fixed time effect

a. Results for statewide analysis

	Coefficients			
Variable	**Model 1**	**Model 2**	**Model 3**	**Model 4**
Depression	0.034773*	0.034766*	0.034102*	0.034741*
Drug use	0.053642 .	0.053875 .	0.053649 .	0.053663 .
Crime	-0.024318 .	-0.024533 .	-0.024301 .	-0.024329 .
Unemployment%	-0.041293 .			
Poverty%		0.51453 ***		
No High school degree			0.2451 **	
Median House Value				-0.25047 **
Lambda	0.210537 **	0.210537 **	0.210537 **	0.210537 **
R square	0.319	0.322	0.318	0.319
Adjusted R	0.314	0.315	0.310	0.314
p-value	<2.2E-16	<2.2E-16	<2.2E-16	<2.2E-16

Significant codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1

b. Results for Baltimore City

	Coefficients			
Variable	**Model 1**	**Model 2**	**Model 3**	**Model 4**
Depression	0.01423*	0.01418*	0.01426*	0.01423*
Drug use	0.03265 .	0.03259 .	0.03262 .	0.03296 .
Crime	0.13265 .	0.13193 .	0.13201 .	0.13233 .
Unemployment%	0.16321 *			
Poverty%		0.53214 ***		
No High school degree			0.10236 **	
Median House Value				0.36241 ***
Lambda	0.376651**	0.376651**	0.376651**	0.376651**
R square	0.4023	0.4011	0.4023	0.4026
Adjusted R	0.453	0.451	0.453	0.459
p-value	<2.2E-16	<2.2E-16	<2.2E-16	<2.2E-16

Significant codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1

c. Results for Baltimore County

Variable	Coefficients			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Depression	0.023156*	0.023152*	0.023064*	0.023134*
Drug use	0.008542 .	0.008536 .	0.008544 .	0.008531 .
Crime	-0.01228 .	-0.01234 .	-0.01265 .	-0.01222 .
Unemployment%	-0.01243 .			
Poverty%		0.43621 ***		
No High school degree			0.0736 **	
Median House Value				-0.27963 **
Lambda	0.134056 **	0.134056 **	0.134056 **	0.134056 **
R square	0.0654	0.0652	0.0654	0.0651
Adjusted R	0.184	0.183	0.184	0.180
p-value	<2.2E-16	<2.2E-16	<2.2E-16	<2.2E-16

Significant codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1

d. Results for Anne Arundel County

Variable	Coefficients			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Depression	0.004216*	0.004214*	0.004208*	0.004215*
Drug use	0.011423 .	0.011412 .	0.011433 .	0.011405 .
Crime	0.08347 .	0.08351 .	0.08366 .	0.08353 .
Unemployment%	0.13542 *			
Poverty%		0.46324 ***		
No High school degree			0.19235 ***	
Median House Value				-0.02361 **
Lambda	0.264327 **	0.264327 **	0.264327**	0.264327 **
R square	0.1472	0.1471	0.1472	0.1476
Adjusted R	0.096	0.095	0.096	0.098
p-value	<2.2E-16	<2.2E-16	<2.2E-16	<2.2E-16

Significant codes: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1

The GTWR results produced a set of local coefficients by ZIP code and 3-month period between the adjusted rates of ED patients and the seven socio-environmental factors, with statistically significant values. Table 4-6 summarized the descriptive statistics for the coefficients of each of the seven variables from the GTWR analyses including model diagnostics. The model diagnostics returned 0.8175 for R-squared, indicating that the

GTWR model explained approximately 82% of the variance in the dataset. This was significantly improved from the global spatial temporal regression test described above. The standard deviation of residuals was as low as 0.006, suggesting a good model fit. These values showed the distributions of coefficient for each socio-environmental factor for all the locations across the entire time period. All coefficients ranged from negative values to positive values. Among all the variables, unemployment rate and population with no high school degree had larger ranges compared to the other variables. Although the median coefficient of *crime* was negative, indicating half of the observations were negatively correlated, the maximum coefficient was 0.035. This high correlation was located in Brooklyn (in the southern part of Baltimore City) during April-June 2017.

Table 4-6 Summary of statistical description of coefficients

	Crime	**Depression**	**Drug use**	**Unemploy ment**	**Poverty**	**Median house value**	**No high school degree**
Min	-0.053800	-0.031468	-0.032003	-0.061329	-0.036527	-0.060080	-0.075618
Max	0.034624	0.046268	0.023880	0.095294	0.013113	0.034418	0.097732
Range	0.088424	0.077736	0.055882	0.156623	0.049640	0.094497	0.173350
Median	-0.000708	0.000483	-0.001355	0.001254	0.001409	0.002339	-0.002608
Mean	-0.000462	-0.000578	-0.002098	0.000819	0.001259	0.005832	-0.004709
Var	0.000136	0.000112	0.000048	0.000426	0.000022	0.000130	0.000792
Std.Dev	0.011656	0.010570	0.006906	0.020645	0.004647	0.011419	0.028144

AIC = -7310.98

R^2 = 0.8175

S.D. for residuals: 0.006

In order to identify the places and times, and explain the associations between socio-environmental factors and the adjusted rates of ED admissions for the four studied hospitals, we selected cases with positive coefficients where p-values < 0.01 for each of the seven socio-economic variables. We mapped four time periods, April-June 2016, April-June 2017, April-June 2018, and Oct-Dec 2018 to compare coefficients of these seven factors for the majority of the ZIP codes of the admitted patients (Figure 4-4). Sizes of circles represent values of coefficients and colors represent the different variables. Significant variation is identified across space and time for these seven factors. In general, a strong correlation between adjusted rates of ED patients with drug-related health problems with all the variables was found in early 2016 in Baltimore County (region 1 in Figure 4-4a). This shifted to Baltimore City by mid-2017 and by late 2018, included locations in Anne Arundel County (region 10 in Figure 4-4d). In mid-2017, tweets related to crime were found to be strongly associated ($r > 0.03$) with residential locations in downtown Baltimore City. During this period and later in 2017, tweets related to drug use were also found to be highly correlated with the adjusted rates of ED patients ($r > 0.012$) in neighborhoods in the southern part of Baltimore City and northern Anne Arundel County (region 7 in Figure 4-4b,. In mid-2016, tweets related to depression appeared to be strongly associated with the adjusted rates of ED patients who were residing in Baltimore County (region 1 in Figure 4-4a), Howard County (region 3 in Figure 4-4a). This also was the case in Baltimore City in mid-2017, and in northern Anne Arundel County (region 10 in Figure 4-4d) in 2018 ($r > 0.025$). In the City of Baltimore, rates of ED patients were found to be positively correlated with median house values in downtown area during the study period ($r > 0.03$). This also held true in Anne Arundel County in early 2016 (region 5 in Figure 4a) and again in mid-2018 (region 8 in Figure 4-4c). There was a strong relation between the adjusted rates of ED patients and the percentage of population with no high school degree, in both early 2016 in northern

Baltimore County and Anne Arundel (regions 1 and 4 in Figure 4-4a), and again in late 2018 in Anne Arundel (r >0.05). A high correlation was found between adjusted rates of ED patients and percentage of population with income below poverty level in western Baltimore in early 2016 (region 2 in Figure 4-4a) and again in late 2018 (region 9 in Figure 4-4d). Strong associations were also found between unemployment and the ZIP codes with adjusted rates of ED patients in mid-2017 in Baltimore County (region 6 in Figure 4-4b) (r > 0.01) and again in 2018 in the City of Baltimore.

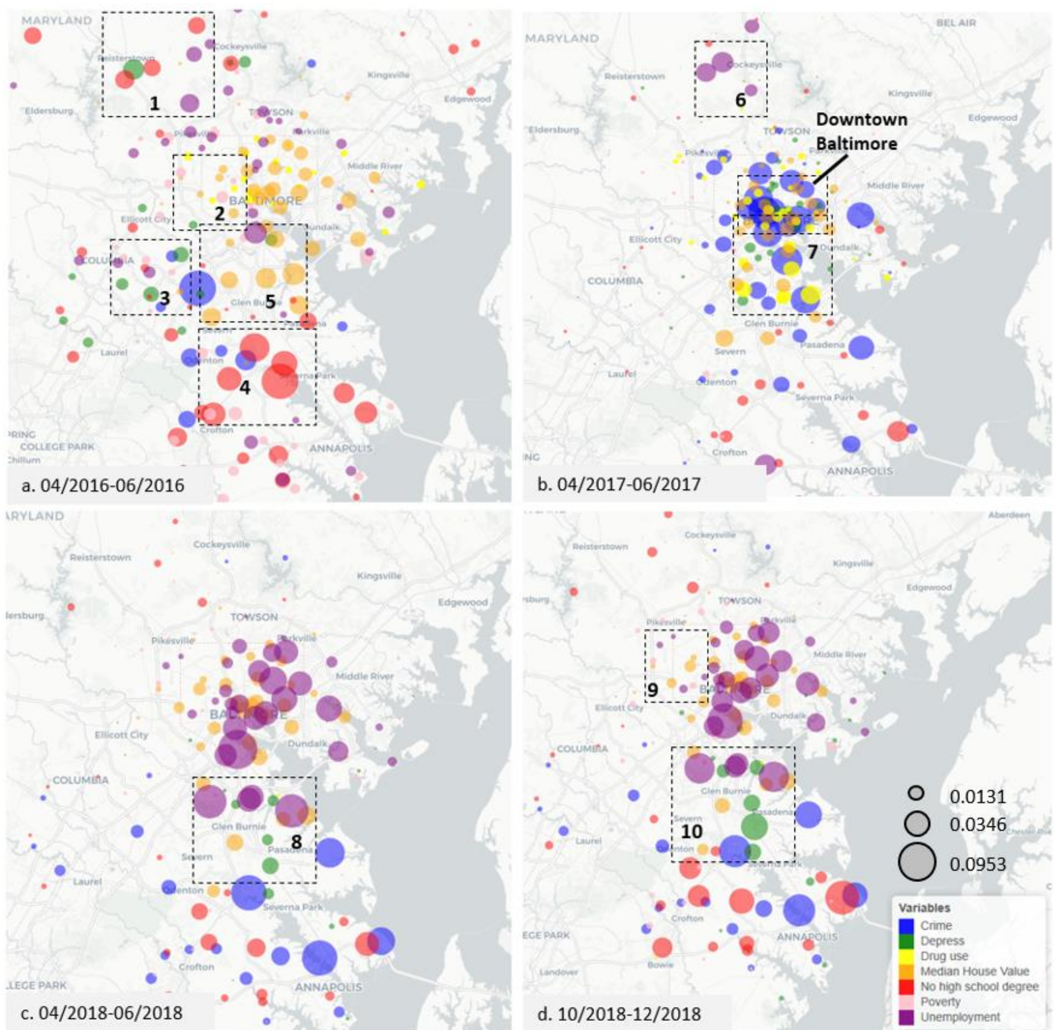


Figure 4-4 GTWR coefficients between adjusted rates of ED patients and seven socio-environmental factors for each ZIP code for different time periods

4.4 Discussion

In this research, we investigated spatial and temporal patterns of adjusted rates of ED patients with drug-related health problems in Maryland during 2016-2018. Spatial patterns of demographic disparities were also explored as part of this research. We conducted a comprehensive analysis to investigate socio-environmental factors across space and time and their relationship with adjusted rates of ED patients. Instead of using traditional survey data, we automatically retrieved Twitter data that contains geo-locations and time, to identify changing neighborhood characteristics. Larger datasets were provided in a more efficient way (i.e., saving time and labor) to achieve our research goal. In addition to using a global regression model, we applied GTWR, a local regression model to build spatial and temporal associations between the adjusted rates of ED patients with drug-related health problems and socio-environmental variables. We adjusted distance thresholds between neighboring ZIP codes for the spatial weight matrix to make our model more suitable for our study area. A local indicator of coefficient was returned for each ZIP region at 3-month level with significance. In this way, the space-time variations of associations among the set of variables can be identified.

The demographic variations in the ED patient data showed a cluster of older aged individuals who were Black in Baltimore City. However outside Baltimore City, younger aged individuals also appeared to cluster, for example, in Howard County and Baltimore County. This demographic pattern supports previous research that Baltimore City has long history of injection drug users (e.g., heroin) that are mostly male, African American, and an average of 25-30 years old during early 1990s, and a mean age of 38 in early 2000s (Carneiro, Fuller, Doherty, & Vlahov, 1999; Gandhi, Kavanagh, & Jaffe, 2006;

Sherman et al., 2005; Williams & Latkin, 2007). And the increasing rate in intoxication deaths has been reported as the most rapid group for the individuals of 55 and above during 2010-2016 (Hogan, Rutherford, & Schrader, 2017).

The results show variations in the adjusted rates of ED patients across the State during the three-year period. Statistically significant change occurred during June to November 2017. During this period, the number of adjusted cases was high in west downtown Baltimore (region 1 in Figure 4-5) and also in the northeastern part of Anne Arundel County (region 2 in Figure 4-5). During this period, tweets related to crime, depression and drug use, were highly correlated with the adjusted rates of ED patients for drug-related health problems in these two regions. In addition, median house values and the percentage of population with no high school degree were found to be associated. This result corresponds to previous literature that life concerns from different aspects (e.g., stressful work and expensive living cost) are positively related to illicit drug use and misuse (Sellström et al., 2011; Stein et al., 2015). In these regions, increasing access to psychosocial services as well as improvements in education could be considered in order to alleviate the burden of substance use disorder. In addition, previous research (e.g., involving drug use in Philadelphia, PA) also noted lower socioeconomic status was related to substance use disorder (J. A. Ford et al., 2017; Mennis & Mason, 2011). In this research, the high number of adjusted rates of ED patients also appeared to be high in downtown Baltimore in mid-2018. Our GTWR results indicated that during this period in downtown Baltimore, unemployment was one factor that appeared to share a strong association with the adjusted rates of ED patients (Figure 4-4c). This corresponds to previous research that an increasing risk of illicit drug use in the neighborhood with disadvantages, where unemployment is a significant factor (Karriker-Jaffe, 2013; Williams & Latkin, 2007). Specifically, one study in Baltimore indicated low percentage (<20%) of employment among individuals who injected heroin or cocaine and kept living in the same neighborhood with disorders for over 10 years (Davey-Rothwell, Siconolfi, Tobin, & Latkin, 2015).

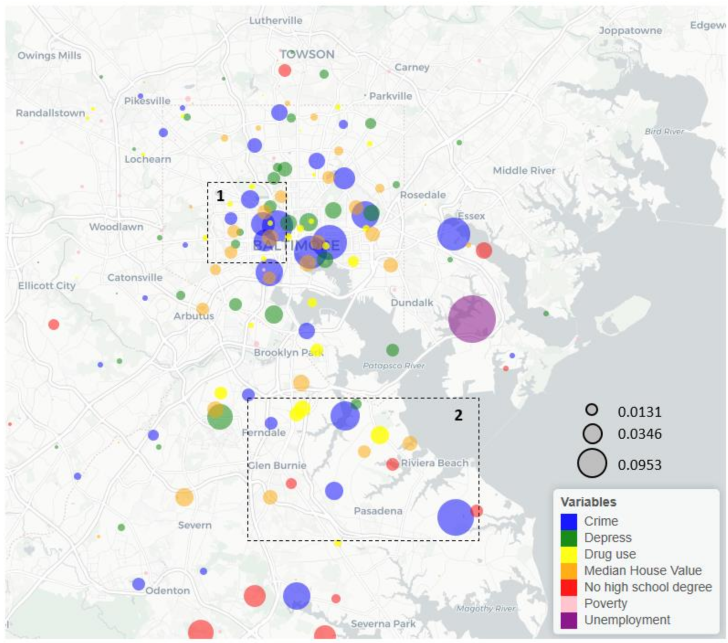


Figure 4-5 GTWR coefficients between adjusted rates of ED patients and seven social environmental factors during the time period 07/2017-09/2017

4.5 Limitations

In this research, we acknowledge several limitations regarding the dataset and analysis parameters. First, socioeconomic variables from U.S. Census Bureau are static data. We retrieved 2017 data for median house value, percentage of population with no high school degree, percentage of population below poverty level, and percentage of unemployment. We assume these variables did not have significant variation during the study period, however this may lead to slight changes in spatial and temporal correlation results with adjusted rates of ED patients. Second, when running topic modeling analysis using Twitter content, only three variables, crime, depression and drug use were studied. However, there are numerous other topics that could be potentially associated with the locations where the ED patients were residing, for example, racial and sexual discrimination, and cigarette and alcohol activities (Karriker-Jaffe, 2013; Mennis et al., 2012; Molina et al., 2012). An important limitation of the ED data in this paper was that approximately 70% of the patients that would have tested positive for fentanyl were missed in the standard hospital opiate screen (Dezman, Felemban, Bontempo, & Wish, 2019). Therefore there was a possible underestimation of opioid users in a number of locations in the study.

In spatial panel regression model and GTWR analysis, we utilized ZIP code centroids for computing distance-based spatial weights. However, geometric centroids cannot represent the population distribution of each ZIP code. Further sensitivity analysis could improve this model. In terms of Twitter data, in addition to the population biases mentioned in section 1, there are several other issues that could limit the results. Similar to the bias from geometric centroids of ZIP codes, place-based tweets might cover the area of multiple ZIP codes. Currently geographic coordinates of the centroids of place-based tweets were used and could have resulted in underestimation of tweet population in certain ZIP code areas. Twitter API streams a small portion of tweets, indicating the streaming process is still under investigation (Tsou et al., 2013). Although we applied three steps to filter each topic for this study, noise still exists due to the ambiguity of text content (Wang & Stewart, 2015). It was also noted that Twitter from non-human users were removed based on the number of tweets in this paper. The characteristics of non-human accounts could be identified further through other classification methods but these are highly dependent on time and computing environment (Guo & Chen, 2014).

4.6 Conclusion

For this research study, we analyzed neighborhood characteristics in the state of Maryland using both Twitter data and socioeconomic variables from U.S. Census ACS 2017. We described how these socio-environmental factors were associated with adjusted rates of ED patients with drug-related health problems at ZIP code level and 3-month level for the period 2016-2018. It is important to understand the environment in which individuals identified in a hospital emergency department as having a chief complaint of overdose and drug-related health problems were residing, and how these characteristics change over space and time. The dynamic pattern indicates factors that are highly correlated do not appear at the same location all the time. For example, our research indicated poverty was highly correlated with the adjusted rates of ED patients in Baltimore City in early 2016. But the highly correlated variable changed to crime related tweets and drug use in 2017, and unemployment in 2018. In addition, crime related tweets showed a strong association in northern Anne Arundel County in 2018. The changing socio-environmental factors that were associated with adjusted rates of ED patients in different locations provides insights to local health officials to address proper policies to improve psychosocial services and potential economic support in certain risky locations. Using geo-tagged socially sensed data provides a more efficient approach to identify socio-environmental variables compared to collecting survey data, which costs both time and labor. Combining Twitter content and census data offered a comprehensive view of both subjective and objective description of neighborhood. The framework we developed in this research could be applied in modeling built environment for different health outcomes from the perspectives of both space and time.

Chapter 5 Conclusion and future work

5.1 Conclusion and major results

The opioid epidemic has hit the United States hard in the past decade, impacting different population groups and locations and unfortunately, the number of deaths from unintentional overdoses involving illicit drugs is still increasing. This dissertation investigates three different topics that evaluate geographical aspects of the opioid epidemic, focusing on the perspectives of place, time, and spatial context. The datasets used in this dissertation have brought new opportunities for the study of geography and drug addiction. To investigate spatial and temporal pattern of drug poisoning deaths involving heroin, I acquired national mortality data (48 contiguous states) from Center for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) at county level for a 17-year period between 2000 and 2016. In addition to traditional survey data from government agencies, we also collected data from medical examiners, Emergency Department physicians and data on treatment facilities, as well as demographic data from the U.S. Census and data from Twitter, a social media platform. Through accessing socially sensed big data, the research for this dissertation provides a new way to quantify dynamic neighborhood characteristics in relation to data on the residential locations of individuals admitted to Emergency Departments in Maryland with drug-related health problems.

This dissertation presents research undertaken on three aspects regarding geography and opioid epidemic. I first described trends of mortality, specifically how the pattern of drug poisoning deaths involving heroin have evolved across the U.S. between 2000 and 2016. This work also analyzes the disparities in mortality among different population groups (from the perspectives of race, age and gender) as well as locations (urban and rural counties) across space and time. This study found the pattern shifted from the west coast in early 2000s, to the Great Lakes and Mountain regions by 2010, and to the Ohio Valley, New England, and the Mid-Atlantic region by 2014. This research found that while large metro areas had higher rates of deaths overall, there was an increasing trend in small metro and rural counties. In terms of demographic groups, the most impacted population over the study period were Whites, males, and individuals aged 35-54 years old. However, in counties that were predominantly African American, the death rates were higher, exceeding rates for Whites. Death rates among the youngest group studied (ages 25-34) and females also showed an increasing trend.

For this second study in this dissertation, my research investigated spatial variations in access to opioid use treatment services and emergency medical services (EMS) in a state highly impacted by fentanyl, a synthetic opioid 50 times more powerful than heroin, New Hampshire. For this study, significant variations was found in access to both opioid use treatment services and EMS (referred to as *composite access* in this research) across the state during 2015 - 2016. Higher overall access was estimated in metropolitan and micropolitan towns in the southern part of New Hampshire. A key result of this research was that towns with high access to opioid use disorder treatment facilities did not necessarily have similarly high access to EMS. In terms of urban- rural disparities, 85% of towns with the highest composite access were urban, but certain rural locations were also estimated to have high access. This study also found that 40% of individuals who died from unintentional overdoses involving fentanyl during 01/01/2015-9/30/2016 did not reside in towns that were in the highest access zone.

The third study in this dissertation investigated associations between socio-environmental factors discovered through the analysis of topics present in tweets in relation to the residential locations of patients admitted to four Maryland Emergency Departments (The University of Maryland Baltimore Washington Medical Center (BWMC), University of Maryland Medical Center Midtown Campus (MTC), University of Maryland Medical Center (UMH), and University of Maryland St. Joseph Medical Center (SJMC)) for a study using data collected for 01/01/2016 – 12/31/2018 . High rates of ED patients occurred during July - November 2017 in Baltimore City and northeastern Anne Arundel County. This research investigated topics in tweets that were related to crime, depression, and drug use, as well data collected from the American Community Survey on median house value, education (percentage of population with no high school degree), percentage of population below poverty, and percentage of population of unemployment. However, variables with strong correlations were variable with respect to time and locations. For example, in mid-2018 in downtown Baltimore, unemployment was highly correlated with the individuals admitted to the EDs.

However, there are a number of data limitations that must also be noted when working in the domain of public health. These limitations were described in Chapters 2, 3, and 4. A major data limitation in studying drug poisoning deaths involving heroin is the uncertainty associated with the identified drug type causing death, and these uncertainties, which stem from the practice of medical examiners may potentially vary across jurisdictions and professional judgement. In Chapter 3, buprenorphine physicians listed on SAMHSA website are waivered practitioners and have potential issue of over-counting. In addition to health data, the limitation of socially-sensed data should also be noted. The Twitter data in Chapter 4 have the major limitation of population bias. The sample representation from crowd sourced data could also benefit from further study.

5.2 Significant contributions

This dissertation makes a number of significant contributions to the study of geography and the opioid epidemic in the U.S. The unique interdisciplinary collaboration with NDEWS made possible the three studies that comprised this dissertation.

Contribution 1: The first research paper (Chapter 2) investigated the spatial and temporal patterns of drug poisoning deaths involving heroin in the US during the period, 2000-2016. The approach addressed both small area and small number problems by using spatial empirical Bayes' estimation techniques. Scan statistics that detected space-time core clusters were found to be useful for identifying spatial and temporal pattern of drug poisoning deaths involving heroin. The results were significantly robust where clusters with 77% of counties at high risk were identified. The evolving patterns were revealed based on this analysis.

Contribution 2: The results from first research paper also revealed disparities in drug poisoning deaths involving heroin among different demographic groups and among urban and rural counties. An increasing (new) trend in the death rates was found for rural counties, and among younger aged groups, females, and Blacks.

Contribution 3: A significant innovation of the second research study (Chapter 3) is that a comprehensive approach was developed to investigate access to both opioid use disorder treatment facilities that use medications (e.g., methadone and buprenorphine) and emergency medical services in New Hampshire, as state hard hit by the opioid crisis and increasing use of fentanyl. I modified the original E2SFCA model, by adjusting model parameters in terms of driving time and impedance functions, to make it more suitable for the study area and the types of access being studied. The model captured population demand, treatment service and EMS supply side characteristics, street network properties, as well as properties of EMS response, to tailor the study and evaluate spatial access to opioid use disorder treatment services.

Contribution 4: The results of the second study in New Hampshire revealed spatial variation in access to treatment services for opioid use across the state. Disparities between urban and rural locations were also presented. In addition, I compared the spatial pattern of access to the treatment services with fentanyl deaths across the state during 2015-2016 and estimated where the gaps were during the study period.

Contribution 5: The third research study (Chapter 4) created a research framework to investigate spatial and temporal associations between neighborhood socio-environmental factors and adjusted rates of ED patients with drug-related health problems. Instead of using traditional survey data, we collected socially sensed geo-tagged data to identify neighborhood characteristics on a finer spatial and temporal scale.

Contribution 6: The local statistical results returned an indicator for each location-time observation to represent association between neighborhood characteristics and adjusted rates of ED patients with drug-related health problems. The results are able to identify the socio-environmental factors during the time the rates of ED patients is significantly high at certain locations. The lack of social support or psychosocial services can be noted for different locations.

5.3 Future work

Spatial modeling of data on drug-related hospital admissions or deaths offers many new opportunities for understanding a more complete picture of the opioid crisis in the U.S. This dissertation delivered new insights from the perspective of geography and the separate viewpoints of place, time and spatial context. Each of the studies discussed in this dissertation set out several topics for future study, and below I discuss some of the key ideas for future research that have stemmed from my research.

In Chapter 3, we analyzed spatial access to opioid use disorder treatment services. However, the treatment services in this Chapter only include medication treatment (e.g., buprenorphine and methadone). Further work could also consider modeling access to mental health, which is an important treatment for patients with opioid use disorder (Mennis et al., 2012). In addition to improving access to treatment services, another key aspect to reduce burden of opioid crisis is to intervene opioid and other illicit drug use. A topic for future study relates to analyzing spatial social networks among individuals in the context of drug-related topics (Miech et al., 2015), for example, the role of spatial social networks for monitoring and predicting drug traffic patterns over space and time (e.g., understanding drug dealer locations based on social networks) (Hunt, Summer, Scholten, & Frabutt, 2008). In this way, research can contribute to scientific solutions or interventions that help to reduce drug networks. Future research directions would also involve investigating geospatial association between injection drug users and other health problems (e.g., Human Immunodeficiency Virus infection) (Beyrer, 2008; Schwartz et al., 2015). Efforts for intervening drug networks could further prevent related public health issues.

In terms of techniques, the accuracy of opioid use estimates can be improved by quantifying uncertainties. Due to the small quantity of data, this dissertation did estimations for patients and decedent residents involving drug use. However, further probabilistic test for the estimation error could potentially robust the estimation accuracy. In addition, this dissertation indicated the demand of treatment services including medication treatment from Chapter 3 and potential psychosocial services in Chapter 4. Further analysis would include location-allocation analysis to identify where to site these treatment centers, to allow maximum coverage in a study region.

In conclusion, this dissertation contributed to the studies of geography and opioid epidemic from multiple perspectives including describing current trend, modeling access to treatment services and neighborhood characteristics that are associated with locations of opioid use and misuse. The important insights from the discovered patterns are beneficial to local health officials and policy makers for generating solutions in response to opioid crisis. More efforts however are urgent need for scientific estimation of trend and solutions to reduce the burden of tremendous loss of lives and social welfare from opioid epidemic.

Appendix A[21]

Table A1 List of town names by county (population) in New Hampshire

County (Population 2015)	**Belknap (60,424)**	**Carroll (47,853)**	**Cheshire (77,342)**	**Coos (34,562)**		**Grafton (89,415)**		**Hillsborough (404,151)**	**Merrimack (448,153)**		**Strafford (125,396)**	**Sullivan (42,600)**
Towns	Alton	Albany	Alstead	Atkinson and	Jefferson	Alexandria	Landaff	Amherst	Allenstown	Hopkinton	Barrington	Acworth
	Barnstead	Bartlett	Chesterfield	Gilmanton	Kilkenny	Ashland	Lebanon	Antrim	Andover	Kensington	Dover	Charlestown
	Belmont	Brookfield	Dublin	Academy	Lancaster	Bath	Lincoln	Bedford	Atkinson	Kingston	Durham	Claremont
	Center Harbor	Chatham	Fitzwilliam	Beans grant	Low and	Benton	Lisbon	Bennington	Auburn	Londonderry	Farmington	Cornish
	Gilford	Conway	Gilsum	Beans purchase	Burbanks	Bethlehem	Littleton	Brookline	Boscawen	Loudon	Lee	Croydon
	Gilmanton	Eaton	Harrisville	Berlin	Martins	Bridgewater	Livermore	Deering	Bow	New Castle	Madbury	Goshen
	Laconia	Effingham	Hinsdale	Cambridge	Milan	Bristol	Lyman	Francestown	Bradford	New London	Middleton	Grantham
	Meredith	Freedom	Jaffrey	Carroll	Millsfield	Campton	Lyme	Goffstown	Brentwood	Newbury	Milton	Langdon
	New Hampton	Hale's	Keene	Chandlers	Northumberland	Canaan	Monroe	Greenfield	Candia	Newfields	New Durham	Lempster
	Sanbornton	Hart's Location	Marlborough	Clarksville	Odell	Dorchester	Orange	Greenville	Canterbury	Newington	Rochester	Newport
	Tilton	Jackson	Marlow	Colebrook	Pinkhams	Easton	Orford	Hancock	Chester	Newmarket	Rollinsford	Plainfield
		Madison	Nelson	Columbia	Pittsburg	Ellsworth	Piermont	Hillsborough	Chichester	Newton	Somersworth	Springfield
		Moultonborough	Richmond	Crawfords	Randolph	Enfield	Plymouth	Hollis	Concord	North Hampton	Strafford	Sunapee
		Ossipee	Rindge	Cutts	Sargents	Franconia	Rumney	Hudson	Danbury	Northfield		Unity
		Sandwich	Roxbury	Dalton	Second College	Grafton	Sugar Hill	Litchfield	Danville	Northwood		Washington
		Tamworth	Stoddard	Dixs	Shelburne	Groton	Thornton	Lyndeborough	Deerfield	Nottingham		
		Tuftonboro	Sullivan	Dixville	Stark	Hanover	Warren	Manchester	Derry	Pembroke		
		Wakefield	Surry	Dummer	Stewartstown	Haverhill	Waterville	Mason	Dunbarton	Pittsfield		
		Wolfeboro	Swanzey	Errol	Stratford	Hebron	Valley	Merrimack	East	Plaistow		
			Troy	Ervings	Success	Holderness	Wentworth	Milford	Kingston	Portsmouth		
			Walpole	Gorham	Thompson and		Woodstock	Mont Vernon	Epping	Raymond		
			Westmoreland	Greens	Meserves			Nashua	Epsom	Rye		
			Winchester	Hadleys	Wentworth			New Boston	Exeter	Salem		
					Whitefield			New Ipswich	Franklin	Salisbury		
								Pelham	Fremont	Sandown		
								Peterborough	Greenland	Seabrook		
								Sharon	Hampstead	South Hampton		
								Temple	Hampton	Stratham		
								Weare	Hampton	Sutton		
								Wilton	Falls	Warner		
								Windsor	Henniker	Webster		
									Hill	Wilmot		
									Hooksett	Windham		

[21] https://www.census.gov/programs-surveys/acs

Appendix B[22]

Table B1 List of service settings and service types for opioid use disorder treatment centers in New Hampshire

List of service settings	List of service types
Hospital inpatient	substance abuse treatment
Residential	detoxification
Outpatient	methadone maintenance
Short-term residential	methadone maintenance for predetermined time
Long-term residential	methadone detoxification
Residential detoxification	buprenorphine maintenance
Outpatient detoxification	buprenorphine maintenance for predetermined time
Outpatient methadone/buprenorphine or naltrexone	buprenorphine detoxification
Outpatient day treatment or partial hospitalization	relapse prevention from naltrexone
Intensive outpatient treatment	buprenorphine used in treatment
Regular outpatient treatment	naltrexone (oral)
Hospital inpatient detoxification	vivitrol (injectable naltrexone)
Hospital inpatient treatment	methadone
	do not use medication for opioid addiction
	accepts clients on opioid medication
	prescribe/administer buprenorphine and/or naltrexone
	all clients in opioid treatment program
	SAMHSA-certified Opioid Treatment Program

[22] https://findtreatment.samhsa.gov/locator?

Appendix C

Table C1 Parameters for CUSUM statistics

Desired ARL_0	Desired ARL_1	k	h (Equation 7.10)	Actual ARL_0	Actual ARL_1
100	2	1.00	1.50	93	2.2
	3	0.76	2.00	97	3.4
	7	0.40	3.35	100	8.3
	10	0.29	4.11	100	12.6
	20	0.10	6.16	93	34.8
250	2	1.14	1.69	860	2.2
	3	0.88	2.23	238	3.3
	7	0.50	3.70	248	7.4
	10	0.39	4.48	248	11.3
	20	0.22	6.40	249	24.2
	40	0.10	9.24	251	59.7
500	2	1.23	1.82	441	2.2
	3	0.96	2.39	473	3.2
	7	0.56	3.96	494	7.6
	10	0.45	4.80	499	10.9
	20	0.28	6.82	498	22.5
	40	0.16	9.53	501	48.4
1000	2	1.31	1.94	860	2.2
	5	0.76	3.348	976	5.3
	10	0.49	5.11	988	10.7
	20	0.32	7.27	1001	21.7
	40	0.20	10.13	1004	44.9

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