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Demographics, Naloxone Accessibility, and Repeat Opioid Overdose in the United States

Craig Hamp Booker
Walden University

Walden University

College of Health Sciences

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Craig Booker

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Abstract

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MPH, University of New England, 2016

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Dissertation Submitted in Partial Fulfillment

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Abstract

Approximately 2.1 million people in the United States suffer from opioid use disorder, and over 47,600 people die from opioid-related overdoses each year. Opioid overdose is often treated with naloxone, a quick-acting medication that counteracts the effects of an overdose. This quantitative, correlational study was conducted to determine whether demographics (gender, age, and race) and naloxone accessibility were predictors of repeat opioid overdose in a Tennessee county in the United States. The study was developed and conducted using principles of the diffusion of innovations theory. Descriptive and inferential analyses were conducted using secondary, county-level data (n = 967) from emergency medical services (EMS) overdose rescues and a community-based naloxone education and distribution program. Results of multiple logistic regression and Poisson regression analyses indicated gender was the only demographic variable to be a statistically significant predictor of repeat opioid overdose. The odds ratio of females was .37 times that of males, indicating females were 63% less likely to experience a repeat opioid overdose compared to males (p = .02). Naloxone accessibility, as measured by the distribution of naloxone kits through the community-based program and the naloxone dose administered by EMS first responders, was not a statistically significant predictor of repeat opioid overdose. The results of this study could be used to craft appropriate interventions to minimize overdose mortality statistics and curtail the deadly opioid epidemic.

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Chapter 1: Introduction to the Study

Opioid overdose, which can be nonfatal or fatal, is a daunting public health concern affecting individuals globally. Although approaches such as multidisciplinary treatment and prevention efforts are underway to address the problem, opioid-related morbidity and mortality rates continue to rise (Blanco & Volkow, 2019). Fatal and nonfatal opioid overdoses are often associated with opioid use disorder, which is the continual use of opioids despite their adverse effects, resulting in a spectrum of mental, physical, and social problems (Blanco & Volkow, 2019). The disorder involves cravings to use opioids, increased tolerance to usual dose of opioids, and withdrawal symptoms when attempting to reduce or cease the use of opioids (Blanco & Volkow, 2019). In 2016, approximately 27 million people worldwide suffered from opioid use disorder, and 118,000 opioid overdose deaths were attributed to such disorders (World Health Organization [WHO], 2018). Approximately 2.1 million people in the United States suffer from the disorder, and 130 people die each day from opioid-related overdose (U.S. Department of Health and Human Services [HHS], Substance Abuse and Mental Health Services Administration [SAMHSA], 2018). The severity of the opioid overdose problem in the United States led to its declaration as a national public health emergency by the nation's president in October 2017 (The White House, n.d.).

Two types of opioids are associated with the current opioid overdose crisis: prescription opioid pain relievers and illicit opioids. The pain-relieving opioids are categorized as natural, semisynthetic, or synthetic (Centers for Disease Control and Prevention [CDC], 2018). Natural opioids are derivatives of opium poppy and include

such drugs as codeine and morphine (CDC, 2018). Semisynthetic opioids are synthesized from natural opioids and include prescription drugs such as hydrocodone and oxycodone (CDC, 2018; Seither & Reidy, 2017). Synthetic opioids are made in laboratories, are highly potent, and may not have a similar chemical structure as natural opioids, although they are designed to produce the same effect as natural opioids (Seither & Reidy, 2017). Fentanyl, methadone, and tramadol are examples of synthetic opioids (CDC, 2018). The pain-relieving opioids are licit because they are prescribed legally by physicians in the treatment of pain.

Illicit opioids are prohibited by law. Such opioids include heroin, which is synthetic, and illegally manufactured synthetic opioids such as fentanyl and carfentanil, a derivative/analog of fentanyl (CDC, 2018; HHS, National Institutes of Health [NIH], National Institute on Drug Abuse [NIDA], n.d.-a). All opioids are agonists that activate the opioid receptors—particularly the mu receptor—in the brain, causing the increased release of dopamine, which triggers the rewarding or feel-good effects of the drug (Kreek, 2002). The interaction is illustrated in Figure 1. The feeling of euphoria caused by opioids makes them extremely addictive, which can lead to opioid use disorder or a fatal overdose (Kolodny et al., 2015).

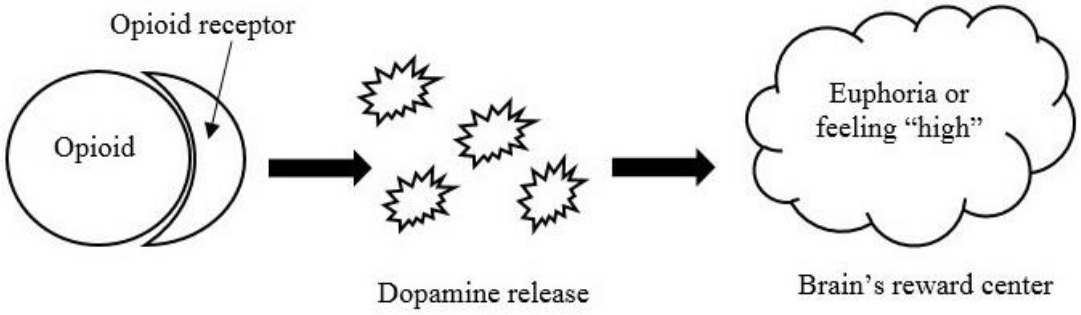

Figure 1. Effect of opioid use on the brain.

In 2017, opioids were involved in 47,600 drug overdose deaths in the United States (Scholl, Seth, Kariisa, Wilson, & Baldwin, 2019). The use of prescription opioids was attributable to 35.8% of these deaths (Scholl et al., 2019). Synthetic opioids (excluding methadone) and the illicit opioid heroin were attributable to 59.8% and 32.5%, respectively, of the opioid-related deaths (Scholl et al., 2019). Over 142,500 people visited emergency departments between July 2016 and September 2017 as a result of opioid-related overdose, a rate of 15.7 per 10,000 visits (Vivolo-Kantor et al., 2018). During this same observation period, the emergency department visits involving opioid overdose increased by 29.7% (Vivolo-Kantor et al., 2018). Monitoring these opioid overdose statistics is only one method of attempting to quantify the extent of the nation's opioid epidemic (Warfield, Pollini, Stokes, & Bossarte, 2019). Examining the nature of repeat overdose, which is the focus of this study, is also important. Such information can help provide needed metrics regarding the potency of opioids being used illicitly and the efficacy of naloxone, which is used to reverse the effects of an overdose (Warfield et al., 2019). Such data can also be used to craft policies and programs designed to alter the behavior of opioid misuse, thereby reducing opioid-related illnesses and deaths.

The background information regarding opioid overdose, the problem statement, and the purpose of the study are discussed in this chapter. Next, the research questions, along with their respective hypotheses, and the theoretical framework are discussed. Finally, the nature of the study, the definitions, the assumptions, and the scope and delimitations of the study are discussed.

Background

To understand the current status of the opioid overdose problem in the United States, it is necessary to understand several previous events and current factors associated with the public health issue. Discussions regarding the nation's progression of opioid overdose mortality and risk factors associated with the problem are included in this section. Detailed information about naloxone and its accessibility and role in the prevention of opioid overdose are also presented. Lastly, a discussion of the knowledge gap associated with the research topic and why this current study was necessary are presented.

Progression of Opioid Overdose Mortality

Seth, Scholl, Rudd, and Bacon (2018) observed that the United States is experiencing the third wave of opioid overdose deaths. The first wave began in the 1990s with prescription opioids at the forefront of the overdose crisis (Seth et al., 2018). By 2010, U.S. physicians were prescribing opioids at a rate of 81.2 prescriptions per 100 patients (Guy et al., 2017). The historic overprescribing of opioid pain relievers is believed to be the source of the current opioid epidemic, as many people became addicted to opioids (Kolodny et al., 2015). The prevalent availability of the pain relievers made

them easily accessible by individuals who used the drugs for nonmedical reasons (Compton, Jones, & Baldwin, 2016; Kolodny et al., 2015). Many of the people who became addicted to prescription opioids and lacked access to them (i.e., discontinued prescription or unable to afford the pharmaceuticals) often turned to heroin as a substitute (Compton et al., 2016; Kolodny et al., 2015).

Pharmacologically, heroin has the same effect as prescription pain relievers, and it is cheaper, which makes it attractive to those who abuse opioids (Compton et al., 2016). Heroin became the prominent opioid associated with the second wave of overdose fatalities that began in 2010 (Seth et al., 2018). Law enforcement reports indicated that heroin use increased continually in the United States from 2006 to 2015 (O'Donnell, Gladden, & Seth, 2017). The fatality rate involving heroin increased during this period as well, with a more pronounced increase observed between 2010 and 2015 (O'Donnell et al., 2017). In 2010, heroin overdose claimed the lives of 3,036 U.S. individuals (O'Donnell et al., 2017). By 2015, the annual death toll had quadrupled to 12,989 (O'Donnell et al., 2017). After 2013, many of the heroin-related deaths were associated with illicit fentanyl, which is much more potent than heroin (O'Donnell et al., 2017). Drug traffickers began adding fentanyl to their heroin supplies, creating an extremely deadly combination (O'Donnell et al., 2017).

The third wave of opioid overdose deaths began in 2013 and has been driven by the prevalent misuse of extremely potent synthetic opioids (O'Donnell et al., 2017; Seth et al., 2018). From 2014 to 2015, the rate of overdose deaths involving synthetic opioids increased by 72.2% from 1.8 to 3.1 deaths per 100,000 population (Rudd, Seth, David, &

Scholl, 2016). Fentanyl was the main opioid associated with the rise in opioid overdose-related deaths. Fentanyl is classified as a Schedule II drug, meaning it has a high risk of abuse and is likely to cause physical or psychological dependence (U.S. Drug Enforcement Agency, n.d.). Compared to morphine, fentanyl is approximately 100 times more potent (Volpe et al., 2011). Analogs of fentanyl, such as carfentanil, can be as much as 100 times more potent than fentanyl and 10,000 times more potent than morphine (HHS, NIH, National Library of Medicine [NLM], n.d.-a). Carfentanil was synthesized to be used as an anesthetic for large animals and not for use in humans (HHS, NIH, NLM, n.d.-a). However, between July 2016 and June 2017, carfentanil was detected in 1,236 people who died from opioid overdose (O'Donnell, Gladden, Mattson, & Kariisa, 2018). The use of carfentanil and other illicitly manufactured fentanyls has been at the center of recent increasing outbreaks of opioid overdose deaths (O'Donnell et al., 2018). The emergence of these illicit drugs represents an added component to the current opioid epidemic with which law enforcement, health, and public health personnel must contend.

Recent surveillance data indicated that opioid-related deaths are increasing. The increase, according to O'Donnell et al. (2017), continues to be attributed to illegally produced fentanyl and its analogs. The rate of death from all opioids increased from 13.3 to 14.9 deaths per 100,000 from 2016 to 2017 (Scholl et al., 2019). Overdose fatalities involving synthetic opioids increased from 6.2 to 9.0 deaths per 100,000 population from 2016 to 2017, which was cause for alarm as the fatalities represented a 45.2% increase in just 1 year (Scholl et al., 2019). During this same period, prescription pain relievers and heroin continued to contribute to the opioid epidemic with stabilized overdose death rates

of 5.2 and 4.9 per 100,000, respectively (Scholl et al., 2019). Prevention efforts are necessary to minimize these statistics and to help control the opioid overdose crisis. For such efforts to be effective, it is important that public health practitioners understand the populations affected by the problem.

Opioid Overdose Risks Factors

There are overdose risk factors associated with the use of licit prescription opioids (i.e., pain relievers) and illicit opioids (i.e., heroin and fentanyl). The risk factors of overdose among users of prescription pain relievers include older age, lower socioeconomic status, being male, multiple prescriptions for pain relievers, and a history of mental illness or substance use disorder (WHO, 2018). Users of illicit opioids who are at risk of overdose tend to be male, 18 to 25 years of age, White, reside in metropolitan areas, and suffer from opioid, cocaine, marijuana, and alcohol use disorders (C. M. Jones, Logan, Gladden, & Bohm, 2015).

People who are at greater risk of opioid overdose include those who suffer from opioid use disorder, use opioids intravenously, take high doses of prescription opioids, combine fentanyl or its analogs with other opioids (i.e., heroin), combine opioids with other sedating drugs, or have a history of overdose (i.e., repeat overdose), psychiatric disorders, or suicide ideations (Blanco & Volkow, 2019). Opioid use disorder, which is the greatest risk of opioid overdose, has risk factors associated with it (WHO, 2018). Some of the factors include being male, younger in age, unemployed, having a history of psychiatric disorders, and having a lower income and educational level (Blanco & Volkow, 2019).

Naloxone

Naloxone hydrochloride (commonly known as naloxone) is a synthetic derivative of oxymorphone and was discovered in 1961 (Handal, Schauben, & Salamone, 1983). As a medication, naloxone is quick acting in counteracting the effects of an opioid overdose (WHO, 2014). An overdose involves the excessive intake of a drug that causes bodily injury or death (American Society of Addiction Medicine, 2015). An opioid overdose manifests as pinpoint pupils, depression of the respiratory system, or loss of consciousness (Weaver, Palombi, & Bastianelli, 2018). Naloxone acts as an antagonist, competing with the opioid drug to bind the opioid receptor, thereby temporarily reversing the depressed respiration, sedation, and unconsciousness caused by the overdose (CDC, 2018; Weaver et al., 2018). Administering naloxone as soon as possible to an individual experiencing an opioid overdose increases the individual's chances of survival (ADAPT Pharma, n.d.; Heavey, Chang, et al., 2018). Because naloxone has an affinity for the mu opioid receptor in the brain, it rarely activates other receptors and, therefore, is ineffective for use with other nonopioid drugs such as cocaine or alcohol (Weaver et al., 2018).

Naloxone is regulated as a prescription drug (Sherman et al., 2009). The medication is available in different forms for administration to an opioid overdose victim. The form approved by the Food and Drug Administration (FDA) in 1971 was for injection, which can be administered intravenously, intramuscularly, or subcutaneously (HHS, NIH, NLM, n.d.-b; Weaver et al., 2018). An intramuscular (or subcutaneous) auto-injector form with the brand name Evzio® was approved by the FDA in 2014 (Weaver et al., 2018). In 2015, the FDA approved Narcan®, which is the brand name of a naloxone

nasal spray, for the use in reversing opioid overdose (WHO, 2015). As a form that is more user-friendly to laypersons, Narcan® offers the advantage of administration without the use of needles, thereby eliminating the risk of infections resulting from needle sticks (WHO, 2015).

Naloxone is considered a relatively safe, innocuous pharmaceutical that does not have addictive properties (HHS, NIH, NLM, n.d.-b). There are, however, some adverse effects associated with the medication, including rare instances of hypertension, hypotension, pulmonary edema, cardiac arrest, and convulsions (HHS, NIH, NLM, n.d.-b). Acute withdrawal syndrome, another adverse effect of the medication, is experienced more frequently in resuscitated individuals (McDonald & Strang, 2016). The condition occurs when the reversal of the opioid overdose is abrupt in individuals who are physically dependent on opioids (HHS, NIH, NLM, n.d.-b). Some of the symptoms often experienced during acute withdrawal syndrome include agitation, nausea, sweating, body aches, fever, and weakness (HHS, NIH, NLM, n.d.-b; McDonald & Strang, 2016). Considering its life-saving capability, the potential to precipitate a rare adverse effect or acute withdrawal syndrome is an acceptable trade-off.

Naloxone Accessibility

The continued misuse of prescription opioids and the proliferation of illicit opioids have necessitated legislation and policies addressing increased access to naloxone on a broad scale. Naloxone access refers to the possession of or ability to obtain naloxone to treat or prevent opioid overdose (Heavey, Chang, et al., 2018). On July 22, 2016, the U.S. Congress enacted the Comprehensive Addiction and Recovery Act (2016) in

response to the nation's opioid epidemic. The Act authorized the Attorney General and Secretary of Health and Human Services to award grants to the states to help them establish or improve opioid overdose education and prevention initiatives, to provide opioid training to law enforcement personnel, and to improve access to opioid use disorder treatment and recovery (Comprehensive Addiction and Recovery Act, 2016). On April 5, 2018, the U.S. Surgeon General issued a public health advisory that urged Americans to learn how to administer naloxone and emphasized that the medication should be available when needed to prevent an opioid overdose (HHS, Office of the Surgeon General, 2018). The Surgeon General encouraged health care practitioners to review their state's requirements regarding the use of standing orders or collaborative agreements and work with pharmacists in ensuring that individuals most at risk of opioid overdose and their friends and families can obtain naloxone (Adams, 2018). Additionally, the Surgeon General encouraged health care providers to adhere to the CDC's opioid-prescribing guidelines and learn the risk factors associated with opioid overdose (Adams, 2018). Expanding the access to naloxone and implementing opioid prevention, treatment, and recovery programs were deemed crucial elements by the Surgeon General in helping to reduce opioid overdose mortality (HHS, Office of the Surgeon General, 2018).

As of 2017, all 50 states and the District of Columbia had instituted legislation improving access to naloxone by laypersons, including family members and friends of the opioid users (Lewis et al., 2016; Network for Public Health Law, n.d.). Included among the laws and policies are Good Samaritan laws and provisions for naloxone standing orders and collaborative practice agreements. Good Samaritan legislation

provides immunity from criminal charges to individuals who witness and report an overdose event (McClellan et al., 2018). The objective of Good Samaritan laws is to save lives by encouraging bystanders who witness an opioid overdose to call for emergency medical services, even if they were also using opioids (Keane, Egan, & Hawk, 2018). Standing orders and collaborative practice agreements allow clinicians to designate other health care professionals as dispensers of naloxone without a patient-specific prescription (Adams, 2018; Davis & Carr, 2017). The orders and agreements expand the role of individuals such as pharmacists who occupy positions that can help in treating opioid overdose so that they can prescribe naloxone (Adams, 2018; Davis & Carr, 2017).

Standing orders, collaborative practice agreements, and Good Samaritan laws are being adopted or transformed to ensure that individuals in need of naloxone have access to it (Davis & Carr, 2015). Currently, 47 states and the District of Columbia have standing orders and collaborative practice agreements that permit the prescribing and the dispensing of naloxone by pharmacists to individuals other than the person at risk of an opioid overdose (Network for Public Health Law, n.d.). The individuals can be family members or friends of the at-risk person. Statewide naloxone standing orders or collaborative practice agreements that allow laypersons to purchase naloxone in the form of Naran® from major pharmacy chains without a doctor's prescription exist in every state (ADAPT Pharma, n.d.). As of 2018, Good Samaritan laws that provide at least some level of protection to individuals who, in good faith, report an opioid overdose from arrest or prosecutions exist in 46 states and the District of Columbia (Network for Public Health Law, n.d.). Legislation and policies like these can help achieve the Surgeon

General's goal of expanding access to naloxone to at-risk opioid overdose populations. Increasing the accessibility of the medication to vulnerable populations may help reduce the pervasiveness of opioid-related deaths.

Role of Naloxone in Opioid Overdose

The FDA approved the use of naloxone in 1971 to treat respiratory depression caused by opioids (Faul et al., 2017). Emergency medical service (EMS) providers have used the medication for more than 30 years to treat overdose patients (Kim, Irwin, & Khoshnood, 2009). The rapid rise in opioid overdose deaths since 1999 prompted policy makers to include other professional emergency first responders, such as law enforcement officers (LEOs) and firefighters, in the efforts to expand the accessibility of naloxone to individuals in need of the medication (Davis, Carr, Southwell, & Beletsky, 2015; Davis, Ruiz, Glynn, Picariello, & Walley, 2014; O'Donnell et al., 2017).

An analysis of 2012–2016 data by Cash et al. (2018) revealed a relationship between naloxone use and opioid-related fatalities in the United States. As the death rate increased by 79.7% from 7.4 to 13.3 deaths per 100,000 during the observation period, the number of naloxone administrations increased as well (Cash et al., 2018). From 2012 to 2016, naloxone administrations by EMS personnel increased from 573.6 administrations per 100,000 to 1,004.4, an increase of 75.1% (Cash et al., 2018). The North Carolina Harm Reduction Coalition (NCHRC, n.d.) estimated that by the end of 2016, there were 1,216 law enforcement programs nationwide that had incorporated the use of naloxone in their emergency response practices. By November of 2018, the total number of programs nationally more than doubled, increasing to 2,482 (NCHRC, n.d.).

The increasing prevalence of naloxone administrations by emergency response professionals helps save lives by reversing the effects of an opioid overdose. However, it is not a solution to the addiction problem associated with opioids, which is a risk marker for repeat opioid overdose and opioid-related mortality (Haug, Bielenberg, Linder, & Lembke, 2016).

Gap in Knowledge and Rationale for the Current Study

As Heavey, Chang, et al. (2018) discussed, little is known about the effect of naloxone on opioid use behavior from a social and health perspective, thereby representing a gap in knowledge. The current study, which included an examination of the correlation between demographics, naloxone accessibility (as measured by the doses administered by professional first responders and naloxone rescue kits distributed via a community naloxone program), and repeat overdose, may help fill the gap in knowledge. This study may help quantify the relationship between repeat overdose and naloxone accessibility, and it may help determine whether the accessibility of naloxone has an impact on repeat overdose. Health and public health practitioners may use the results to understand the depth of the opioid epidemic. Additionally, the findings may be useful in crafting appropriate interventions to minimize overdose mortality statistics and curtail the deadly opioid epidemic.

Problem Statement

Opioids are valuable in managing pain associated with cancer, surgery recovery, and other medical conditions. Their use, however, involves risks that include misuse, opioid use disorder, overdose, and death (Dowell, Haegerich, & Chou, 2016). Globally,

the annual incidence of fatal opioid overdose is 0.65% among those who misuse opioids (WHO, 2018). In the United States, the opioid overdose death rate of 14.9 deaths per 100,000 in 2017 represented an increase from the 2016 rate of 13.3 and the 2015 rate of 10.4 and was an indication of the progression of the opioid misuse problem (Scholl et al., 2019; Seth et al., 2018). Almost 1% of the U.S. population ages 12 years and older has an opioid use disorder (HHS, SAMHSA, 2018). In 2017, over 11 million individuals acknowledged using opioids that were not prescribed for them (HHS, SAMHSA, 2018).

From an economic perspective, opioid misuse and its consequences can be a considerable burden. Prescription opioid misuse costs the United States $78.5 billion annually in health care, substance use treatment, and criminal proceeding expenditures (Florence, Luo, Xu, & Zhou, 2016). In a comparison between opioid abusers and nonabusers, Kirson et al. (2017) found that abusers cost taxpayers an average of $14,810 per patient in incremental health care expenditures each year. Included in the total cost were the costs for inpatient, outpatient, emergency department, and rehabilitation facility treatment (Kirson et al., 2017). The cost represented a cumulative amount, meaning the expenditures accrued up to and after the initial diagnosis of opioid abuse, dependence, or overdose (Kirson et al., 2017). Approximately 6 months before the diagnosis of abuse, the health care incremental cost for abusers was $3,084, and within 6 months after the diagnosis, it was $11,726 (Kirson et al., 2017). The cost began increasing rapidly about 5 months before the diagnosis of abuse and was attributed to treatment for alcohol abuse and nonopioid drug dependence (Kirson et al., 2017).

Naloxone is valuable in preventing opioid-related deaths, but little research has been conducted to determine whether the ease of access to the medication is associated with opioid misuse, specifically repeat opioid overdose. Only one study that addressed the impact of the accessibility of the medication on repeat opioid overdose was found during the literature review. The study, which is discussed in detail in Chapter 2, was qualitative in design and focused on a small sample. Therefore, I concluded there was a gap in the research addressing the impact of naloxone's accessibility on opioid use behavior, particularly from a quantitative perspective. The current study may help to fill this gap through the quantitative examination of the relationship between opioid overdose demographics, naloxone accessibility, and repeat opioid overdose.

Purpose of the Study

The purpose of this quantitative, correlational study was to determine the relationship between demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county. In doing so, five independent variables (age, gender, race, naloxone doses administered by professional first responders, and distribution of naloxone rescue kits) and one dependent variable (repeat opioid overdose) were examined. Each of the variables is discussed in-depth in Chapter 2.

Research Questions and Hypotheses

Research Question 1: What is the association between age and repeat opioid overdose?

$H_0$1: There is no statistically significant association between age and repeat opioid overdose.

H_a1: There is a statistically significant association between age and repeat opioid overdose.

Research Question 2: What is the association between gender and repeat opioid overdose?

$H_0 2$: There is no statistically significant association between gender and repeat opioid overdose.

$H_a 2$: There is a statistically significant association between gender and repeat opioid overdose.

Research Question 3: What is the association between race and repeat opioid overdose?

$H_0 3$: There is no statistically significant association between race and repeat opioid overdose.

$H_a 3$: There is a statistically significant association between race and repeat opioid overdose.

Research Question 4: What is the association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose?

$H_0 4$: There is no statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

H_a4: There is a statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

Research Question 5: What is the association between the distribution of naloxone rescue kits and repeat opioid overdose?

H_05: There is no statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

H_a5: There is a statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

Theoretical Framework

The diffusion of innovations, popularized by Rogers in 1962, served as the theoretical foundation for this study. Subjective information about a new idea is often communicated among members of a social group (Rogers, 2003). The diffusion of innovations focuses on how, why, and how quickly the subjective information associated with the idea is spread—or diffused—among individuals within the social group over time (Rogers, 2003). Such focus renders the theory useful in analyzing changes in human behavior (Rogers, 2003).

The four elements on which the diffusion of innovations is premised are the innovation, a communication system, time, and a social system composed of individuals, groups, or organizations (Rogers, 2002, 2003). An innovation, as discussed by Rogers (2002, 2003), is a physical item, idea, or way of doing things perceived by a person or

people as something new. Diffusion is the process by which the innovation is perceived and communicated over time among a population or social system (Rogers, 2002, 2003).

The diffusion of innovations posits that the adoption of an innovation is a process that typically follows predictable, ordered stages over time (Rogers, 2002, 2003). The stages include awareness (learning about or being exposed to the innovation), persuasion (forming an opinion—whether positive or negative—about the innovation), decision (choosing to accept or reject the innovation), implementation (practicing the innovation), and confirmation (seeking validation about the selected innovation decision and deciding whether to continue using the innovation; Rogers, 2002, 2003). The increased access to and use of naloxone over time may be representative of the stages.

The stages of adoption of naloxone were evident in many studies. For example, Heavey, Chang, et al. (2018) reported that there was naloxone awareness among some at-risk populations. Cash et al. (2018) demonstrated that naloxone use by EMS professionals in opioid overdose rescues was increasing. According to Wheeler, Jones, Gilbert, and Davidson (2015), the number of community organizations that advocated and distributed naloxone rescue kits was increasing as well.

Regarding the four elements of the diffusion process, the innovation is naloxone, the communication system includes venues such as public health notices from the CDC and U. S. Surgeon General that provide the public information about naloxone, time is the extent and acceptance of naloxone use, and the social system is the group of individuals and organizations (i.e., U. S. Surgeon General, CDC, President, policy makers, health and public health professionals, community activists, and members of the

public) working to minimize opioid use disorder and mortality. Another component of the diffusion of innovations that is often disregarded is understanding what consequences are associated with the adoption of the innovation (Rogers, 2003). Because this study focused on the progression of naloxone accessibility and how this accessibility relates to repeat opioid overdose over a period of time, the choice of the diffusion of innovations as a theoretical basis was appropriate to answer the research questions and to address the hypotheses. Further details regarding the theory and its applicability are included in Chapter 2.

Nature of the Study

The nature of this study was quantitative with a correlational, cross-sectional design. A quantitative approach includes numerical data that can be analyzed with statistical tests to generalize the findings (Creswell, 2014). The correlational design is a nonexperimental design used to describe and measure the relationship between two or more variables (Creswell, 2014). Creswell (2014) discussed that quantitative data collection methods were either longitudinal, in which data about study participants are collected over time, or cross-sectional, in which data are collected at one point in time. Numerical data collected on the variables in the current study represented a single point in time, which made the cross-sectional design appropriate. Because the objective of the study was to determine whether relationships existed between the dependent and independent variables, the quantitative, correlational approach was appropriate.

The secondary data used in the study were obtained from a county's EMS and a community-based program that provides opioid overdose training and naloxone kits to

community members. Permission to use data from the organizations was obtained through data use agreements, which are included in the Appendix. The organizations de-identified their data before providing the data sets for this study.

There were five independent (or predictor) variables in this study: age, gender, race, the naloxone dose administered by professional first responders, and the distribution of naloxone rescue kits. Age, gender, and race were considered covariates and were analyzed as independent variables. Repeat opioid overdose was the only dependent (or outcome) variable in the study. Logistic regression was used to assess the relationships between age, gender, race, administered naloxone dose, and repeat opioid overdose during a specific time frame. Poisson regression was used to examine the relationship between distributed naloxone rescue kits and repeat opioid overdose during the same time frame. The operationalization of the variables and the rationale for selecting the statistical tests are described in Chapter 3.

Definitions

The terms used in this study were defined or clarified as follows:

Emergency Medical Services personnel: Health care professionals who, under medical oversight, are trained to provide medical care and transportation in prehospital settings and out-of-hospital settings (National Highway Traffic Safety Administration, 2019). The professionals, in order of their licensure levels, include the emergency medical responder, emergency medical technician, advanced medical emergency technician, and paramedic (National Highway Traffic Safety Administration, 2019).

Index opioid overdose: The first nonfatal opioid overdose experienced by an individual (Olfson, Wall, Wang, Crystal, & Blanco, 2018).

Naloxone access: The possession of naloxone or the ability to readily obtain it (Heavey, Chang, et al., 2018).

Naloxone administration event: The administration of at least one dose of naloxone while providing rescue care to an opioid overdose patient (Cash et al., 2018).

Naloxone rescue kit: An emergency kit used by laypersons to administer naloxone to reverse an opioid overdose (Panther, Bray, & White, 2017). There are various types of kits, but typically a kit consists of two doses of a 1-mg/mL vial of injectable naloxone, a nasal atomizer, a rescue breather, and instructions (Panther et al., 2017). Currently, Narcan® Nasal Spray is the rescue kit that is broadly marketed and contains a single intranasal spray of 2 mg or 4 mg with instructions (ADAPT Pharma, n.d.).

Nonfatal opioid overdose: The resuscitation with naloxone of a patient from an opioid overdose in which the patient survives at least 1 day following the resuscitation (Ray, Lowder, Kivisto, Phalen, & Gil, 2018).

Opioid: Pain-relieving drugs that are categorized as natural, semisynthetic, or synthetic. Natural opioids—also known as opiates—are derivatives of opium poppy and include such drugs as codeine and morphine. Semisynthetic opioids include prescription drugs such as hydrocodone and oxycodone as well as heroin, an illicit drug. Fentanyl and its analogs (i.e., carfentanil), methadone, and tramadol are examples of synthetic opioids (CDC, 2018).

Opioid misuse: The use of heroin or nonmedical use of prescription pain medication (McClellan et al., 2018).

Opioid overdose: The accidental ingestion or administration of an opioid drug that causes decreased mental status and/or respiratory depression and requires the administration of naloxone, and the patient survives at least 1 day (Samuels et al., 2018).

Opioid use disorder: The continual use of opioids, notwithstanding the adverse consequences, causing significant impairment or distress and manifesting as mental, physical, and social problems or increased mortality (Blanco & Volkow, 2019).

Repeat opioid overdose: The first nonfatal or fatal opioid overdose occurring more than 1 day after the first overdose treatment with naloxone (Olfson et al., 2018).

Take-home naloxone: An intervention that makes naloxone available to nonmedically trained individuals to administer to those experiencing an opioid overdose (Farrugia et al., 2019).

Assumptions

Several assumptions were associated with this study, including one regarding the use of secondary data. There was an assumption that the data sets obtained from the county's EMS and the community-based naloxone program were accurate. Both data sets contained information about the variables assessed in this study. An accurate measure of the variables was important to the accuracy of the results.

The administration of naloxone by the professional emergency first responders was assumed to have been an indication of an opioid overdose. The first responders could have administered naloxone to a patient suspected of experiencing an overdose, but the

patient's condition was not confirmed to be an opioid overdose (see Lindstrom et al., 2015). Such a scenario could have positively skewed the repeat opioid overdose events. Such an assumption was likely more of a concern among the LEOs than the EMS personnel, as LEOs do not have the same level of training and medical expertise as EMS personnel in accurately recognizing an opioid-involved overdose (Rando, Broering, Olson, Marco, & Evans, 2015).

Another assumption regarding the study was that the naloxone administrations by the professional emergency first responders were an appropriate proxy measure of the county's public health issue of repeat opioid overdose. Ray et al. (2018) used the same approach in their study to examine mortality associated with nonfatal overdoses. Ray et al. concluded that the naloxone administrations were suitable proxy data for assessing repeat opioid overdose. In the current study, this assumption was necessary because the EMS data were the only available measure of the variable of repeat opioid overdose. Finally, the individuals who were administered naloxone by the professional first responders were assumed to be residents of the county, and the naloxone rescue kits distributed through the community-based program were assumed to have been for use solely by individuals who resided in the county.

Scope and Delimitations

The intent of this study was to determine whether relationships existed between demographics, naloxone accessibility, and repeat opioid overdose. The relationships were assessed using secondary data collected on a county in Tennessee. The data were collected from two sources: the reports of professional first responders who responded to

emergency calls regarding a potential opioid overdose and data collected through a community-based naloxone program. The target population included anyone in the county who was treated with naloxone by a professional first responder during an opioid overdose emergency. There were no other delimitations regarding the target population.

Internal validity refers to the degree of assurance that conclusions about the dependent variable are attributed to the independent variables rather than some other alternative explanation (Babbie, 2017). The measures of the naloxone dose administered by professional first responders and the distribution of naloxone rescue kits were the two main independent variables tested for a relationship with repeat opioid overdose. Because the literature indicated that the variables of age, gender, and race were risk factors of opioid overdose, these variables were treated as potential confounders, which meant they could have influenced the outcome variable and threatened the internal validity of the study. These demographics were included as independent variables to preclude potential confounding and to improve the study's internal validity.

The ability to generalize the results that are based on a sample of a population to the general population refers to the study's external validity (Babbie, 2017). In this study, the focus was a sample population from a county in Tennessee. Opioid overdose is a public health problem in the county. The state has one of the highest opioid-prescribing rates in the United States and a rate of opioid overdose deaths that is higher than that of the national average (HHS, NIH, NIDA, n.d.-b). Restricting the data collection and analysis to a single county meant the results may not be generalizable to other geographical locations.

Limitations

The lack of access to patients' medical history of substance abuse and related information was a limitation of this study. I relied on data from the professional emergency first responders for the measure of repeat opioid overdose. Emergency department data that involved individuals who were not transported via EMS were not included in the study. Also, resuscitations that might have occurred in residences were not included, as these data may never be quantified unless information regarding the overdose and resuscitated individual is reported to medical professionals. In light of these limitations, the measure of repeat opioid overdose could have been understated, which could have biased the results.

The measure of access to naloxone was limited to the distribution of naloxone kits through the community-based program and the administrations of naloxone by professional first responders. There are other venues within the county that contribute to the accessibility of naloxone, such as local pharmacies, emergency departments, and other community-based naloxone distribution programs. Although data from these other sources might have increased the strength of the findings in the study, these data sources were not part of the study's scope.

Another limitation of this study included the correlational design. This design precludes the determination of causality. In other words, the design does not allow researchers to conclude that the change in one variable was caused by another variable (Asamoah, 2014). Because correlational research is useful in determining whether an

association exists between variables that occur naturally (Asamoah, 2014), the limitation was an acceptable trade-off to achieve the purpose of the study.

Misclassification bias was also a limitation of this study. As a type of information bias that can affect a study's validity, misclassification bias refers to the accurate categorization of observational measurements (Althubaiti, 2016). Professional first responders could have incorrectly classified an emergency rescue as an opioid overdose when the overdose did not involve an opioid. Such a misclassification could have skewed the relationship estimates between the study's variables (see Althubaiti, 2016). Ensuring the thoroughness of the data collection procedures and definitions of the variables can help minimize misclassification bias (Szklo & Nieto, 2014). The use of adequately defined variables and the reliance on the robustness of the professional first responders' procedures for recording data were measures implemented in this study to mitigate the bias.

Significance

The expansion of public access to naloxone has improved with the implementation of naloxone access laws (Xu, Davis, Cruz, & Lurie, 2018). Such broad-scale access, however, has been criticized by some who consider it a barrier that precludes the cessation of opioid abuse (Rudski, 2016). Some contend that opioid abusers will continue or increase their risky use behaviors if naloxone is available to revive them if they overdose (Rudski, 2016). Little evidence exists that confirms or refutes the claim. Also, there has been little research, especially of a quantitative nature, conducted to determine whether the efforts to expand the general public's access to naloxone have had

unintended consequences (i.e., increased overdoses or repeat overdoses). The results of the current study may help to advance that knowledge.

The use of local-level data is important in developing community prevention programs (Madah, Clausen, Myrmel, Brattebø, & Lobmaier, 2017). The current study, which included use of local data, may be useful to the respective local community. Public health practitioners may use the findings to gauge the prevalence of repeat opioid overdose and design prevention and intervention programs. The study addressed naloxone access policies and legislation that clinicians and pharmacists may use for awareness. The data provided by the county's EMS were valuable in studying naloxone accessibility and repeat opioid overdose. The first responder professionals may use the results to evaluate the effectiveness of their efforts in saving lives. Finally, educators and the local media, partnered with public health practitioners, may use findings from this study to educate the community about opioid overdose and naloxone.

The current opioid overdose mortality statistics are alarming, yet they represent only part of the complex, enduring opioid epidemic. According to the WHO (2018), nonfatal overdoses occur in approximately 45% of opioid users. Applying the percentage to the current estimate of 2.1 million people in the United States who suffer from opioid use disorder (Scholl et al., 2019) suggests that there may be as many as 945,000 nonfatal opioid overdoses annually in the United States. The importance of the phenomenon is that nonfatal overdose is a risk factor for repeat opioid overdose, which increases the potential for opioid overdose mortality (Olfson et al., 2018; Ray et al., 2018). From a social change perspective, this study provided evidence about the public health problem

of repeat opioid overdose, and the findings may be used to reduce the morbidity and mortality associated with the opioid crisis.

Summary

Opioid overdose is a formidable worldwide public health issue. The United States, which has been impacted heavily by the problem since the 1990s, recently elevated to the problem to the level of a national public health emergency (Seth et al., 2018; The White House, n.d.). Approximately 47,600 American deaths are attributable to opioid overdose each year (Scholl et al., 2019). Laws and policies have been, and continue to be, implemented to address the problem. Ensuring that the public has access to naloxone, which is a medication that reverses the effects of an opioid overdose, is one of the objectives of the laws and policies. Research on the effectiveness of naloxone indicated that the medication is effective in treating opioid overdose (Chou et al., 2017). However, little is known about the impact of broad-scale accessibility of naloxone on opioid use behavior. The current study was conducted to fill the gap in knowledge and in the literature. The in-depth literature review, which was conducted to identify the gap, is presented in Chapter 2. The strategy used to conduct the literature review, the theoretical basis that guided the review, and a discussion of the variables assessed in this study are also presented in Chapter 2.

Chapter 2: Literature Review

The opioid epidemic continues to claim lives worldwide. The purpose of this study was to examine the relationship between demographics, naloxone accessibility, and repeat opioid overdose. In this chapter, I present the strategy of conducting my literature review followed by a discussion of the theoretical framework that I used to guide my study. Next, I discuss prominent topics associated with the variables in my research questions that surfaced in my in-depth literature review. The topics include repeat opioid overdose, the demographics of opioid overdose, naloxone dose, the role of professional first responders in administering naloxone during opioid overdose emergencies, and the venues associated with the distribution of naloxone. Finally, I discuss opposing perspectives regarding the expanded access to naloxone and the gap that I observed in the literature. I conclude with a summary.

Literature Search Strategy

Sources for this literature review were retrieved from electronic databases available through the Walden University library and Google Scholar. Additionally, printed book literature was also used. The databases included MEDLINE, CINAHL Plus, ProQuest Central, PubMed, SAGE Journals, PsycINFO, ScienceDirect, and the National Center for Biotechnology Information. The key terms included in the search were *naloxone*, *Narcan*, *opioid*, *overdose*, *recidivism*, *nonfatal overdose,* and *repeat* OR *recurrent overdose*. The inclusion criteria were articles that were published in English, available in full-text academic journals that were peer-reviewed, published within the past 5 years (2015–2019), and had an available abstract. Articles that were more than 5

years old were included if they provided a historical perspective to the current research. Studies were excluded if they did not meet the inclusion criteria. Additionally, articles appearing as reviews, case reports, commentaries, opinions, and debates were excluded. The titles and abstracts of the remaining articles were reviewed for relevance to this study. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines discussed by Moher, Liberati, Tetzlaff, and Altman (2010) were used in the selection of studies for my research. Figure 2 depicts the flow diagram of the selection process.

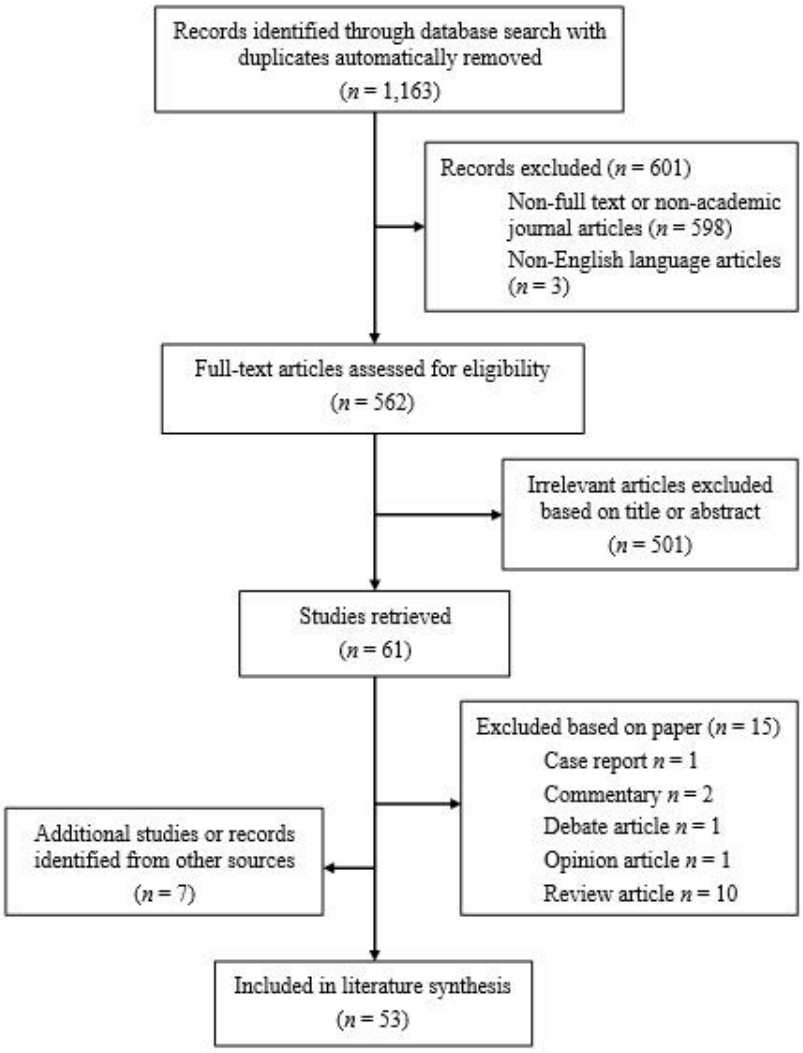

Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) study selection process.

Theoretical Foundation

The diffusion of innovations served as the theoretical framework of this study. Although discussed initially in historical literature by Tarde, a French sociologist, the theory became popular through the *Diffusion of Innovations* textbook written by Rogers in 1962 (Kaminski, 2011). The diffusion of innovations theory is beneficial in the understanding of behavioral change among humans (Rogers, 2003). The theory's

applicability is useful in improving programs aimed at social change (Rogers, 2003). Rogers (2003) discussed that an understanding of the characteristics of the innovation and the potential adopters is necessary when assessing the viability of the innovation's diffusion.

Innovation Characteristics

According to the diffusion of innovations theory, some innovations are diffused faster and more pervasively than others. There are five characteristics of an innovation that help to explain its rate and extent of adoption: relative advantage, compatibility, observability, complexity, and trialability (Rogers, 2002, 2003). Each of these characteristics is based on the perception of the individual.

Relative advantage refers to the individual's perception of the innovation, specifically whether the innovation is more advantageous to the individual than the idea or object it replaces (Rogers, 2002, 2003). Innovations with greater relative advantage tend to be adopted at a higher rate (Rogers, 2003). Comparability refers to the perception about whether the innovation is consistent with the individual's values and normative beliefs (Rogers, 2002, 2003). An innovation that aligns with the individual's beliefs and values is adopted with less resistance than one that requires the individual to change their belief/value system (Rogers, 2003). Observability is the degree to which the innovation's benefits or outcomes are evident to the potential adopter (Rogers, 2002, 2003). Seeing the results of an innovation, whether positive or negative, generates discussion by the adopter and others in the adopter's social system, thereby further diffusing the innovation (Rogers, 2003).

The characteristic of complexity, which refers to the perception about the ease of use or understanding of the innovation, is straightforward (Rogers, 2002, 2003). Simple ideas are easier to understand and, therefore, are adopted quicker than those based on complex knowledge or require the development of new skills (Rogers, 2003). Trialability is the extent to which the innovation can be tried before committing to adopt it fully (Rogers, 2002, 2003). Trialability helps the individual determine whether the innovation is a good fit. An innovation that lends itself to a trial run has a better chance of being adopted (Rogers, 2003).

Characteristics of Innovation Adopters

The diffusion of innovations theory addresses characteristics about the people of a social system as they evaluate an innovation for adoptability. The first 2.5% of people within the system to adopt an innovation are identified as innovators (Rogers, 2002, 2003). These individuals are knowledge seekers who are not afraid of the uncertainty regarding the innovation, nor do they bind themselves by adhering to social norms (Rogers, 2002, 2003). The next group is the early adopters who constitute 13.5% of the social system (Rogers, 2002, 2003). As visionaries and trendsetters, early adopters are well connected socially and are viewed as role models (Kaminski, 2011; Rogers, 2003). Early adopters are highly respected within the social system and are capable of influencing opinions and norms (Rogers, 2003). With their knowledge, their respected opinions, and their ability to influence large peer groups, the innovators and early adopters are valuable in launching an effective and successful innovation (Rogers, 2003).

The early majority is the next category in the diffusion process, followed by the late majority. Each of these two categories constitutes 34% of the social system (Rogers, 2002, 2003). Those in the early majority category are pragmatic and prefer proof—usually from the innovators and early adopters—that the innovation is worthwhile and reliable (Kaminski, 2011; Rogers, 2003). The early majority individuals have frequent interactions with their peers, and their opinions are valued by their peers (Kaminski, 2011; Rogers, 2003). The late majority members, on the other hand, are conservative (Kaminski, 2011; Rogers, 2003). These individuals tend to be skeptical about the innovation and will adopt it only if it is an economic necessity and only if it is endorsed by a trusted peer (Kaminski, 2011; Rogers, 2003).

The last category is the laggards, representing 16% of the social system (Rogers, 2002, 2003). The laggards are the most skeptical among the categories and prefer traditionalism over new things, ideas, or behaviors (Kaminski, 2011; Rogers, 2003). Because the laggards are often isolated from those in other categories, they have little knowledge about the innovation and, therefore, are the last ones to adopt it (Kaminski, 2011; Rogers, 2003). As late adopters in the diffusion of innovations process, the early majority, the late majority, and the laggards share the behavior of adopting the innovation only if it has been adopted and endorsed by their close peers (Rogers, 2002, 2003).

Applications of the Diffusion of Innovations Theory

Myriad research studies incorporating the diffusion of innovations theory have been conducted in various disciplines. Economics, organization, social psychology, sociology, anthropology, and political science are social science disciplines in which the

theory has been used as a framework of research projects (Rogers, 2003). Very few articles in the literature included discussions on the theory as it relates to naloxone accessibility and repeat opioid overdose.

Bowles and Lankenau (2019) used the diffusion of innovations theory in their qualitative study of 30 individuals who reported injecting heroin. The innovation was an opioid overdose prevention program (OOPP) operated by a harm reduction facility. OOPPs, sometimes referred to as opioid overdose prevention and response (OOPR) programs, overdose prevention and naloxone distribution (OPND) programs, or opioid overdose education and community naloxone distribution (OEND) programs, are venues where laypersons can obtain naloxone rescue kits and opioid overdose prevention training. The training helps individuals to identify and respond to an overdose and to administer naloxone if necessary (Bowles & Lankenau, 2019; Heavey, Chang, et al., 2018; Koester, Mueller, Raville, Langegger, & Binswanger, 2017; Lambdin, Zibbell, Wheeler, & Kral, 2018; Prabhu et al., 2017; Sherman et al., 2009).

Bowles and Lankenau (2019) applied the diffusion of innovations theory to determine the effectiveness of an OOPP in reaching a community of people in Philadelphia who inject drugs. Although subject to social desirability bias and recall bias, the study indicated that the participants were receptive to the OOPP when the innovation was championed by workers within the harm reduction facility (Bowles & Lankenau, 2019). The influence of the harm reduction workers as champions of the innovation underscores a strategy discussed by Rogers (2002). Champions who are skilled in

persuading and negotiating with people can be valuable in attracting potential adopters, thereby expediting the innovation's rate of diffusion (Rogers, 2002, 2003).

The diffusion of innovations theory was also employed by Sherman et al. (2009) who conducted a qualitative study to examine the diffusion of information by 25 participants who attended an OPND program. Sherman et al. sought to understand the nature of the information that was diffused throughout a community of injection drug users in Baltimore, Maryland. Sherman et al. found that 90% of the participants experienced at least one overdose (with a median of two overdoses) and that 20% of the participants died from an overdose.

Sherman et al. (2009) found that the OPND program was effective in training people to recognize and respond to an overdose and in diffusing program information within the community. The participants who attended the program were more likely to promote the program to their peers when they administered naloxone during an overdose that they witnessed or when they discussed their own overdose experiences. Sherman et al. concluded that information from the program diffused faster when the participants had personal experiences to share than it did when the participants had only on the information they learned in the training. The participants in Sherman et al.'s study were likely late majority adopters of the OPND program (i.e., the innovation), as they might have been skeptical about the program or might have required proof that it was helpful.

Theory Relevance to Current Study

The surge of opioid-related deaths that began in the late 1990s gave rise to general public awareness of naloxone (Humphreys, 2015). There is a dearth of literature in which

the diffusion of innovations theory served as a framework for studies involving naloxone. Only two such studies were found, and they were qualitative in design. The theory was selected as a basis for this current study because of its temporal aspect. The use of naloxone has progressed from being administered solely by medically trained professionals to being administered by peers and family members of people who misuse opioids (McDonald, Campbell, & Strang, 2017). The aim of this current study was to examine the distribution of naloxone during a specific time frame to determine whether it correlated with repeat opioid overdoses during the same time frame. According to the diffusion of innovations theory, time is one of the four key elements associated with the diffusion of a new idea; the innovation, channels of communication, and social system are the other three elements (Rogers, 2002, 2003). Because the focus of this study entailed the examination of the effect of naloxone's accessibility on repeat opioid overdose during a period of time, the theoretical framework was appropriate.

Repeat Opioid Overdose

Repeat opioid overdose is an insidious public health problem that is a component of the current opioid epidemic. In 2016, of those who died from an overdose involving illicit, prescription, or a combination of illicit and prescription drugs, 15.1%, 13.5%, and 9.3%, respectively, had experienced at least one previous opioid-related overdose (Mattson et al., 2018). Not all users of opioids embrace the notion of abstaining from opioids even when they experience an overdose (Keane et al., 2018). Some studies suggest that repeat opioid overdose is a growing public health problem. Lasher, Rhodes, and Viner-Brown (2019) conducted a study in Rhode Island to quantify EMS dispatches

involving opioid overdose. Lasher et al. (2019) found that 13.2% of the 1,288 patients treated by EMS first responders for opioid overdose in 2018 had experienced between one and nine repeat overdoses within the past year and that 2.6% of the patients had experienced two or more prior overdoses. Klebacher et al. (2017) found that 27.2% of 2,166 patients treated for opioid overdose by EMS first responders between 2014 and 2016 in New Jersey had experienced a previous overdose.

Dahlem et al. (2017), evaluated the naloxone training provided to 114 LEOs in a Michigan county and found that two of the 32 overdoses that required the administration naloxone were repeat overdoses. Warfield et al. (2019), found that 18.2% of the 833 patients admitted to a hospital system in West Virginia between 2008 and 2016 for opioid overdose experienced at least one repeat opioid overdose within the past year and that the repeat overdoses increased annually on average by 13%. Ray et al. (2018) examined opioid overdose mortality outcomes in an Indiana county and found that 13.4% of the 4,726 patients revived with naloxone by EMS first responders between 2011 and 2016 had experienced between one and 12 repeat opioid overdoses. Such evidence seems to indicate that the problem is not negligible or isolated.

The studies conducted by Lasher et al. (2019), Klebacher et al. (2017), Dahlem et al. (2017), and Warfield et al. (2019) addressed the problem of repeat opioid overdose at the county and state levels. Olfson et al. (2018) examined the problem from a national-level perspective. Olfson et al. conducted a retrospective cohort study with data collected from 45 states to examine risk factors of repeat opioid overdose occurring within the first year of an index opioid overdose. The sample consisted of 75,556 Medicaid patients

between the ages of 18 and 64. Within the first year following the index overdose, 18.9% of the patients had a repeat opioid overdose, and 1% had a repeat opioid overdose that was fatal (Olfson et al., 2018). The rate of repeat opioid overdose in the cohort was 295.0 per 1,000 person-years (Olfson et al., 2018). The hazard ratio of repeat opioid overdose among those patients who overdosed on heroin was higher than the hazard ratio of those patients who overdosed on prescription opioids (Olfson et al., 2018). Those patients who took prescription opioids within 180 days of their index opioid overdose had a higher hazard ratio of repeat opioid overdose than those patients who did not (Olfson et al., 2018). Although Olfson et al. used data that were more than 10 years old, the findings support the notion that a nonfatal opioid overdose often results in a repeat opioid overdose within 1 year.

Another retrospective cohort study in which national-level data were used was conducted by Larochelle, Liebschutz, Zhang, Ross-Degnan, and Wharam (2016). Larochelle et al. (2016) examined the opioid prescriptions of 2,848 patients who experienced an index opioid overdose to determine whether there was a relationship between the prescription dosage and repeat opioid overdose. Larochelle et al. found that 7% of the patients experienced a repeat opioid overdose and that opioid prescriptions continued to be written for patients after their index overdose. The risk of repeat opioid overdose was higher among the patients who received prescriptions for higher opioid dosages (Larochelle et al., 2016). Although the design of the study by Larochelle et al. precluded a causal determination, the results were consistent with the findings from

Olfson et al. (2018). Both studies provided evidence to indicate that individuals who experience their first nonfatal opioid overdose are likely to experience a repeat overdose.

Opioid Overdose Demographics

Opioid overdose, whether nonfatal or fatal, affects all demographic groups. Olfson et al. (2018) analyzed national data from the Centers for Medicare and Medicaid Services and found that individuals who experienced a nonfatal opioid overdose were predominantly White (71.1%), female (59.2%), and over 34 years of age (70.3%). National EMS data examined by Cash et al. (2018) indicated that of the 207,548 rescues involving the administration of naloxone by EMS first responders in 2016, 61.3% of the patients were male; 72.0%, White; and 21.4%, Black. Among the age groups, those who were 25–34 years of age had the largest proportion of naloxone administration events with 23.0%, followed by the 45–54 age group with 17.6%, the 35–44 age group with 16.5%, and the 55–64 age group with 15.7% (Cash et al., 2018).

A cross-sectional analysis of national data by Scholl et al. (2019) indicated that the rate of death from opioid overdose (i.e., all opioids overdose) per 100,000 population in 2017 was 20.4 for men and 9.4 for women. The age groups with the highest rates of death were those 25–34, 35–44, 45–54, and 55–64, with rates of 29.1, 27.3, 24.1, and 17.0, respectively (Scholl et al., 2019). The analysis of the age and sex subgroups indicated that males and females who were 25–44 years of age had the highest rates of death at 40.0 and 16.3, respectively (Scholl et al., 2019). Among the race groups, the rates were 19.4 among Whites, 12.9 among Blacks, 6.8 among Hispanics, 15.7 among American Indians/Alaska Natives, and 1.6 among Asian/Pacific Islanders (Scholl et al.,

2019). Scholl et al. compared the 2017 data to the 2016 data and found that the rates of death from opioid overdose increased overall within the demographic groups.

Scholl et al. (2019) found that Whites had a higher rate of opioid overdose mortality than that of Blacks and that the rate of opioid overdose mortality was increasing among Blacks. The phenomenon was reversed at the beginning of the opioid epidemic. The Black population sustained the heavier burden of opioid overdose mortality from the late 1970s to the mid-1990s, an era in which opioid-related mortality was driven by heroin use (Alexander, Kiang, & Barbieri, 2018). From the mid-1990s to 2010, the racial gradient shifted such that the White population had the greatest burden of opioid overdose mortality (Alexander et al., 2018). The fatalities during this period were advanced by the use of licit opioid pain relievers (Alexander et al., 2018). Since 2010, the rate of opioid-related deaths continues to be highest among Whites than among any other racial group but is increasing in all groups (Alexander et al., 2018). Heroin and synthetic opioids (i.e., fentanyl and its analogs) are the current drivers of opioid-related mortality (Alexander et al., 2018). The annual increase in fatality rates involving heroin is 31% among Whites and 34% among Blacks (Alexander et al., 2018). The heroin statistics may be alarming, but they pale to those involving synthetic opioids, which are responsible for mortality rates that are increasing among Whites and Blacks annually at 79% and 107%, respectively (Alexander et al., 2018).

Naloxone Dose

The dose of naloxone necessary to achieve resuscitation from an opioid overdose depends on the formulation of the pharmaceutical. The initial recommended dose is 0.4–2

milligrams (mg) for intravenous injections; 2 mg or 4 mg (depending on how the pharmaceutical is supplied) per single spray in each nostril for Narcan® nasal spray, and 2 mg intramuscularly or subcutaneously for Evzio® (HHS, NIH, NLM, n.d.-b). Naloxone has an onset of action of 2–3 minutes and a half-life in the body of 1–1.5 hours (Handal et al., 1983; WHO, 2014). The half-life (i.e., plasma half-life) of naloxone is shorter than that of many opioids, including OxyContin®, fentanyl, morphine, codeine and methadone (Willman, Liss, Schwarz, & Mullins, 2017; WHO, 2014). Overdoses involving opioids with longer half-lives may require additional doses of naloxone to prevent opioid rebound toxicity, which is the return of opioid overdose symptoms after the initial overdose reversal (WHO, 2014). Regaining consciousness and breathing normally are indications that the administered naloxone was effective in reversing the overdose (Lasher et al., 2019). If the signs of recovery are not observed, the dose can be repeated every 2 to 3 minutes as needed (HHS, NIH, NLM, n.d.-b).

Different doses and multiple administrations of the doses are often necessary during the rescue of opioid overdose patients. Lasher et al. (2019) observed that of the 1,006 doses of naloxone administered by EMS first responders between 2016 and 2018 in Rhode Island, 44.3% of the administrations were intravenous deliveries; 46.5%, intranasal; and 7.3%, intramuscular. Lasher et al. found that 26.4% of the patients required multiple administrations of naloxone and that the mean total dose of naloxone administered was 2.7 mg. Klebacher et al. (2017) found that 91% of the 2,166 study participants required one 2-mg dose of intranasal naloxone, 9% required two doses, and 2.4% required three doses. Klebacher et al. also found that of the patients who received

intravenous doses of naloxone, 51% received 2 mg, 26% received 0.4 mg, and 21% received 1 mg. Neither Lasher et al. nor Klebacher et al. included information about the type of opioid that was involved in the overdoses in their studies.

Information collected on naloxone doses during opioid overdose rescues can improve understanding of the opioid epidemic. Heavey, Delmerico, et al. (2018) found that LEOs and firefighters administered an average of 1.76 doses of 2-mg intranasal naloxone to 800 overdose victims and that the first responders noted the presence of heroin at 79.1% of the overdose scenes. Although the collection of data about the involved opioid was not within the scope of the studies by Lasher et al. (2019) and Klebacher et al. (2017), such information might have provided valuable insight regarding the efficacy of the naloxone doses. According to Faul et al. (2017), multiple administrations of naloxone doses during an attempt to resuscitate an overdose victim may be a proxy for gauging the potency of the ingested opioid.

Professional First Responders

EMS personnel and LEOs are professional emergency first responders uniquely positioned to perform crucial roles in reducing opioid overdose fatality rates. If these professionals are contacted in time, they can administer naloxone as a prehospital treatment to prevent or reverse an opioid overdose. Policy changes in Massachusetts, which broadened the role of many of these first responders, advanced the expansion of naloxone access in the state, which reduced opioid overdose emergency response times (Davis et al., 2014). Additional studies have since been published that provide evidence of the effectiveness of naloxone administrations by EMS and LEO professionals.

Emergency Medical Services

EMS personnel are typically the first medically trained professionals to arrive at an overdose scene (Faul et al., 2017). Depending on their level of certification, EMS personnel can administer naloxone as part of standard care, revive patients in cardiac arrest, and perform procedures such as tracheal intubations when naloxone administration attempts by bystanders or other first responders are unable to revive the overdose victim (Banta-Green et al., 2017; Cash et al., 2018; Faul et al., 2017; National Highway Traffic Safety Administration, 2019). As of 2015, the administration of naloxone was limited to EMS personnel with advanced life support training (i.e., paramedics), with only 12 states allowing those responders with basic life support training to administer the pharmaceutical (Faul et al., 2015).

Faul et al. (2015) discussed the importance of expanding the use of naloxone to include other EMS personnel in helping to reduce opioid-related deaths. The rationale focused on the greater likelihood that EMS personnel with basic life support training would be the first to arrive at opioid overdose scenes in rural areas (Faul et al., 2015). Recent research indicated that as many as 35 states authorized those EMS first responders with basic life support training to administer naloxone and that the responders in rural areas demonstrated improved knowledge of opioid overdose and naloxone administration after training (Zhang, Marchand, Sullivan, Klass, & Wagner, 2018). EMS personnel in the United States administer naloxone at the rate of 1,004.4 per 100,000 EMS naloxone administration events (Cash et al., 2018). When called to respond to an opioid overdose, EMS personnel perform life-saving procedures at the scene, provide overdose victims

with referrals to opioid misuse treatment programs, and stabilize critical patients while transporting them for additional care at emergency departments.

Law Enforcement Officers

LEOs often arrive at the scene of an overdose before EMS first responders (Davis et al., 2014; Davis et al., 2015). In rural areas, which typically have a higher burden of overdose, LEOs who perform routine patrols are often the first to respond to an overdose (Faul et al., 2015; Rando et al., 2015; Wagner, Bovet, Haynes, Joshua, & Davidson, 2016). With adequate naloxone training, LEOs can be key components in the multifaceted approach to solve the opioid overdose crisis.

Rando et al. (2015) conducted a prospective intervention study in an Ohio county to determine whether LEOs could administer naloxone to help reduce the county's opioid overdose mortality rate. The intervention was a 2-hour training session in which the LEOs practiced performing basic life-saving procedures, identifying potential opioid overdose victims, and administering intranasal naloxone (Rando et al., 2015). Rando et al. found that the rate of opioid overdose deaths before and after the LEO training was 1.5 ($p < .002$) and -4.1 ($p < .025$) deaths per quarter, respectively, which indicated a decrease in the mortality rate. There were few limitations associated with the study, the primary one being an issue regarding the LEO's ability to accurately identify an opioid overdose. An accurate identification of an opioid overdose can be problematic even for well-trained EMS personnel because depressed respiration—a typical indication of overdose—could result from other etiologies or nonopioid drugs ingested by the victim (Williams et al., 2019). The results observed by Rando et al. indicated a statistically significant decrease

in the number of opioid overdose deaths in the county, which was attributed to the naloxone administration training provided to the LEOs.

Whereas Rando et al. (2015) measured the effectiveness of the LEO naloxone administration training by the change in opioid overdose mortality rate, other researchers have since conducted studies in which they measured the effectiveness through pretest–posttest training measurements of the LEOs' knowledge and abilities regarding naloxone use. For example, in a pilot program evaluation, Wagner et al. (2016) provided training to 81 LEOs that involved recognizing and responding to an overdose and administering intranasal naloxone. Pretest–posttest training surveys of the 81 LEOs and qualitative interviews with four of the LEOs indicated improvements in the knowledge and confidence of the LEOs in identifying an opioid overdose and administering naloxone (Wagner et al., 2016). The LEOs administered naloxone to 11 overdose victims within the first 4 months after training and revived nine of the victims successfully (Wagner et al., 2016). The pilot program was a positive indication that LEOs could manage opioid overdose situations (Wagner et al., 2016).

Another study in which the pretest–posttest measurement approach was used was conducted by Dahlem et al. (2017). Dahlem et al. evaluated a naloxone training program by administering pre-opioid overdose knowledge surveys to 98 LEOs, training the officers on opioid overdose and naloxone education, and administering posttest opioid overdose knowledge surveys to the officers. The training included information regarding the benefits of naloxone, how to recognize an opioid overdose, and how to administer intranasal naloxone (Dahlem et al., 2017). The LEOs were instructed on how to link an

overdose victim to substance use treatment, and the LEOs listened to a testimony of a recovering opioid overdose victim who had been guided to treatment by an LEO (Dahlem et al., 2017). The testimony, which was added to address the stigmatization associated with active addiction, and the instructions regarding linkage to care were training components that were not included in the training program evaluated by Wagner et al. (2016).

Similar to the findings from Wagner et al. (2016), the results from Dahlem et al. (2017) indicated statistically significant improvements in all measured knowledge areas of the LEOs. Within the first year of completing the training, the LEOs administered naloxone to 32 overdose victims, revived 31 of the victims successfully, and linked six of the victims to treatment services (Dahlem et al., 2017). As in the study by Wagner et al. (2016), the sample size in Dahlem et al.'s study was small, which limited the study's generalizability. Despite the limitation, Dahlem et al.'s study provided evidence that the naloxone training approach improved the LEOs' knowledge of the medication and provided the first responders with the skills to reverse an opioid overdose by administering the life-saving naloxone. Additionally, the study indicated that LEOs were valuable in facilitating the overdose victim's linkage to treatment (Dahlem et al., 2017).

Heavey, Delmerico, et al. (2018) used county opioid overdose reports to examine the effectiveness of the training that had been provided to LEOs and firefighters on how to administer naloxone in opioid overdose situations. The opioid overdose reports had been completed by LEOs and firefighters who had completed naloxone training. Heavey, Delmerico, et al. found that the officers and firefighters administered naloxone to 800

overdose victims during a 2-year period and revived 653 (81.6%) of the victims successfully. The training provided to the LEOs and firefighters helped reduce the overdose-related deaths in the county (Heavey, Delmerico, et al., 2018).

Distribution of Naloxone

National, state, and local public health efforts ensure that the public is knowledgeable about naloxone and that those individuals who need the overdose reversal medication have access to it. Community-based programs, emergency departments, and pharmacies are among the institutions associated with naloxone expansion efforts.

Community-Based Programs

Community-based organizations (i.e., homeless shelters, substance abuse treatment facilities, health care setting, HIV testing and linkages to care centers, harm reduction centers, and health care providers) have provided naloxone through OOPP, OOPR, OPND, and OEND programs in the United States since 1996 (Bagley, Forman, Ruiz, Cranston, & Walley, 2018; Wheeler, Davidson, Jones, & Irwin, 2012). The programs provide support services to individuals with opioid use disorders as well as to their family members and friends (Wheeler et al., 2012). Linking individuals who suffer from opioid use disorder to treatment centers is a key service provided by the programs (Wheeler et al., 2012). In addition to naloxone, training that helps the participants understand the risk factors associated with opioid overdose, recognize opioid overdose signs, call 911 for medical assistance, and administer naloxone to overdose victims is also provided through these programs (Wheeler et al., 2012). The effectiveness of such programs has been evaluated in many studies.

The Massachusetts Department of Public Health (MDPH) operates a state OEND program that supports community-based organizations in providing opioid overdose education and naloxone rescue kits to individuals at risk of overdose and to the family members of the individuals (Bagley et al., 2018). Bagley et al. (2018) used data collected via the MDPH OEND to study the characteristics of 10,827 family members who accessed the naloxone resource between 2008 and 2015. The MDPH OEND program reported 4,373 successful opioid overdose reversals during this period, with 860 (20%) of the reversals attributed to the quick response of family members (Bagley et al., 2018). Although the use of self-report data was a limitation of the study, the large sample size enabled an extensive analysis of the characteristics of the families (Bagley et al., 2018). Bagley et al. concluded that family members could perform crucial, active roles in reducing opioid overdose. Community-based naloxone programs engage family members who are willing to learn about opioid overdose and administer naloxone to help save lives (Bagley et al., 2018). The family is an important social network component of the individuals who are dependent on opioids and should be leveraged by public health practitioners in the fight against the opioid epidemic (Bagley et al., 2018).

Pade, Fehling, Collins, and Martin (2017) examined the impact of an OEND program established within a substance use residential treatment facility in Colorado. The study participants included 47 opioid-dependent patients from the treatment facility and their family members (Pade et al., 2017). Training was provided to the participants, and a pretest–posttest training questionnaire was used to assess the family members' knowledge and perception about opioid overdose (Pade et al., 2017). Pade et al. (2017)

concluded that the OEND program was implemented successfully within the treatment facility and that the family members demonstrated proficiency in recognizing and managing an opioid overdose situation. Pade et al. emphasized that OEND programs were important as a harm reduction approach and that the caregivers in treatment facilities should consider implementing such programs rather than relying solely on an abstinence-based care approach. Substance use treatment facilities can incorporate OEND programs and leverage them as harm reduction tools to manage high-risk patients and empower the family members with the skills and abilities to save lives (Pade et al., 2017).

Rowe et al. (2015) conducted a study to examine the demographic characteristics of the participants who attended the Drug Overdose Prevention Education Project, a community-based naloxone program in San Francisco. Identifying the predictors associated with the participants' reporting of naloxone refills and overdose reversals was also a focus of the study (Rowe et al., 2015). Training, naloxone, and health services were provided through the program to individuals who were likely to experience or witness an opioid overdose (Rowe et al., 2015). The program was dynamic in that it was used to service high-risk opioid users at needle exchange locations, opioid treatment facilities, and pain management clinics (Rowe et al., 2015). High-risk users who resided in single-room occupancy hotels were serviced through the program as well (Rowe et al., 2015). Rowe et al. found that program participants who were White, used illicit opioids, and experienced or witnessed an overdose were more likely to obtain naloxone refills. The participants who used illicit opioids and experienced or witnessed an overdose were more likely to report an overdose reversal (Rowe et al., 2015). The program was effective

in reaching high-risk opioid users and in training them to use naloxone to reverse an opioid overdose (Rowe et al., 2015). Rowe et al. used self-report data in their study, which meant the results were subject to social desirability and recall bias limitations. The study provided evidence that community-based naloxone programs could reach high-risk populations and educate them on opioid overdose prevention.

Emergency Departments

Emergency departments are opportune venues for the provision of naloxone education and rescue kits to opioid overdose survivors and to their family and friends. Between July 2016 and September 2017, opioids were suspected in 15.7 per 10,000 overdoses assessed during emergency department visits (Vivolo-Kantor et al., 2018). This statistic equated to 142,557 suspected opioid overdoses, all of which represented opportunities to provide the patients with take-home naloxone kits, education them on opioid overdose, and link them to treatment centers or other needed services. (Vivolo-Kantor et al., 2018). Taking advantage of such opportunities may help save lives, as a repeat opioid overdose or an opioid overdose-related fatality is often the outcome of a nonfatal opioid overdose (Olfson et al., 2018).

Samuels et al. (2018) conducted a retrospective cohort study to evaluate the impact that an emergency department intervention program had on repeat opioid overdose, linkage to care timeliness, and opioid overdose mortality. The program was called Lifespan Opioid Overdose Prevention, and it was the collaborative initiative of several public health organizations in Rhode Island (Samuels et al., 2018). Naloxone, opioid overdose education, and a peer recovery coach were provided to the opioid

overdose patients through the program, which was established in two emergency departments within the state (Samuels et al., 2018). The role of the peer recovery coach—who was an individual enrolled for at least two years in addiction treatment—was to motivate and navigate the opioid overdose patient to seek substance use treatment (Samuels et al., 2018). The sample was composed of 151 opioid overdose patients who received treatment from the two emergency departments, and the treatments consisted either of usual care, take-home naloxone along with educational materials, or a combination of take-home naloxone and a peer recovery coach (Samuels et al., 2018). The usual care treatment included stabilizing the patient from the overdose and providing the patient with printed information about substance use treatment programs (Samuels et al., 2018).

Samuels et al. (2018) found that the all-cause mortality and the incidence of repeat opioid overdose were lowest among the take-home naloxone group, followed closely by that of the take-home naloxone plus recovery coach group. Patients in the take-home naloxone plus recovery coach group sought linkage to care sooner than the patients in the other two treatment groups (Samuels et al., 2018). The study provided evidence that the distribution of naloxone kits by emergency departments were associated with reductions in the repeat opioid overdose visits to the emergency department, reductions in the length of time that an individual chose to seek substance use treatment, and reductions in the opioid overdose mortality (Samuels et al., 2018).

Gunn et al. (2018) conducted a systematic review of the literature to summarize the evidence available on the role of emergency departments in the distribution of

naloxone. Gunn et al. found that emergency departments were valuable as harm reduction mechanisms in the efforts to improve naloxone access and reduce opioid overdose. As points of entry for urgent care, emergency departments serve as a venue for educating individuals with opioid use disorders who do not have access to other health care facilities (Gunn et al., 2018). To be effective in this role, emergency departments require support from senior management in overcoming barriers such as the insufficient time to train the staff and the lack of staff to distribute naloxone and counsel overdose patients (Gunn et al., 2018).

Papp and Schrock (2017) hypothesized that the provision of naloxone kits by emergency departments would reduce repeat opioid overdose as well as opioid-related morbidity and mortality. Papp and Schrock conducted a retrospective cohort study of 291 patients who presented with heroin overdose to an urban emergency department from 2013 to 2016. Papp and Schrock compared the composite outcomes (i.e., at 3 months and at 6 months) of patients who received naloxone kits at discharge to the outcomes of the patients who did not and found no significant difference between the groups. Papp and Schrock discussed that the small sample was a limitation of the study that could have influenced the results. Confounders, though not discussed as limitations by Papp and Schrock, might have accounted for the observation of no significant difference between the groups. For example, patients who did not receive naloxone kits from the emergency department might have enrolled in substance use treatment facilities where the distribution of naloxone kits was part of the treatment program.

Pharmacies

The role of pharmacies in the expansion of access to naloxone was emphasized in the Comprehensive Addiction and Recovery Act (2016). States were encouraged to implement standing orders that would allow pharmacists to supply naloxone to individuals needing the medication (Comprehensive Addiction and Recovery Act, 2016). Xu et al. (2018) conducted a cross-sectional study to analyze naloxone dispensing based on state-level naloxone access legislation. Xu et al. found that such legislation was associated with national increases in naloxone dispensed by retail pharmacists. From 2007 to 2016, naloxone dispensed via prescriptions increased by over 9,800%, with the greatest upsurge occurring between 2015 and 2016 (Xu et al., 2018). Similar results were observed by Freeman, Hankosky, Lofwall, and Talbert (2018), who used national naloxone prescription data to examine the impact of access legislation on the dispensing rate of naloxone by states. Freeman et al. (2018) found a nearly eightfold increase in dispensed naloxone prescriptions by states from October 2015 through June 2017. Freeman et al. attributed the phenomenon to the diffusion of legislation designed to make naloxone accessible to the public through the availability of Narcan® and Evzio®.

Despite the positive influence of naloxone laws on increased prescriptions by pharmacies, the expansion of access to pharmacy-provided naloxone has not been as progressive in many locations. For example, Freeman et al. (2018) found that while dispensing rates were as high as 244 prescriptions per 100,000 persons in states such as Virginia, the rates were as low as 2.2 prescriptions per 100,000 in other states such as Hawaii. In many communities in North Carolina, naloxone is neither offered nor

dispensed by pharmacists (Carpenter et al., 2019). According to Carpenter et al. (2019), many community pharmacists who did not offer naloxone indicated they lacked the time or adequate training to do so. Some pharmacists also indicated they felt that their patients would not comprehend the use of naloxone and, therefore, did not offer the medication (Carpenter et al., 2019). The limited expansion of access to naloxone might have been isolated to these instances. Regardless, additional efforts by national, state, and local policy makers are necessary to ensure universal and consistent implementation of pharmacy-based naloxone distribution programs (Bachyrycz, Shrestha, Bleske, Tinker, & Bakhireva, 2017).

Controversy Regarding Broad Distribution of Naloxone

The effectiveness of naloxone in reversing an opioid overdose may not be a controversial topic, but the perceived impact of the medication on the misuse of opioids is. Not everyone supports the public health measures of expanding the access of naloxone to laypersons. Some opponents of publicly available naloxone believe that increasing laypersons' accessibility to the pharmaceutical may cause an increase in the use of opioids (Keane et al., 2018). This conception is premised on risk compensation, which is a belief that the provision of naloxone will encourage opioid misuse (Keane et al., 2018). In a cross-sectional study of 276 online participants, Rudski (2016) found that 59.1% of the participants believed that expanded access to naloxone caused opioid users to perceive the medication as a safety net and that it encouraged the opioid users to engage in reckless drug use. Additionally, 58.0% of the participants believed that making naloxone easy to access by laypersons discouraged the cessation of drug use, 43.8%

believed that promoting naloxone represented condoning the use of opioids, and 39.5% believed that easy access to naloxone undermined the emphasis on abstaining from opioid misuse (Rudski, 2016).

Negative perceptions regarding easy access to naloxone by laypersons have been discussed in some studies. Haug et al. (2016) found that health care providers, particularly nurses and emergency medical technicians, often stigmatized their opioid overdose patients and maintained the opinion that naloxone did little to reduce opioid addiction. Some physicians were reluctant to prescribe naloxone to patients who were dependent on opioids because they believed that their peers or their patients might perceive the action as encouraging or enabling opioid misuse behaviors (Gatewood, Van Wert, Andrada, & Surkan, 2016). Other physicians had misgivings that access to naloxone by laypersons would preclude seeking proper treatment after an overdose resuscitation (Gatewood et al., 2016). The physicians felt that underlying problems might not be identified or addressed if patients believed they could treat themselves with naloxone (Gatewood et al., 2016). Such perceptions and beliefs regarding the expanded access to naloxone may not be the norm among the medical community. The provision of training that highlights prescribing and using naloxone may help to alleviate the concerns that some health care professionals have regarding laypersons' access to and administration of naloxone (Gatewood et al., 2016).

Whether or not the expansion of naloxone access increases reckless behavior or discourages the cessation of opioid misuse remains a point of contention (Heavey, Chang, et al., 2018). Several studies indicated that expanded access to naloxone was not

associated with opioid misuse behaviors. For example, Marco et al. (2018) conducted a study of patients who presented to the emergency department with opioid overdose. The intent of the study was to understand the patients' experiences involving the use of naloxone. Marco et al. found that the patients who had access to naloxone did not alter their opioid dose or frequency of opioid use as a result of the access. Among those patients who had possessed naloxone, 33% of them indicated they used opioids less often (Marco et al., 2018).

Another example is a study conducted by J. D. Jones, Campbell, Metz, and Comer (2017) who observed current and former heroin users who were in and out of substance use treatment. J. D. Jones et al. sought to determine whether the provision of naloxone and opioid overdose training changed the participants' drug use behaviors. J. D. Jones et al. used repeated-measures analysis of variance and found that heroin use decreased among the active users at the conclusion of the first and third months after the training and the provision of naloxone. J. D. Jones et al. concluded that access to naloxone did not increase opioid misuse behavior.

The studies conducted by Marco et al. (2018) and J. D. Jones et al. (2017) were subject to several limitations. Marco et al. used a qualitative design and relied on self-report data from patients of a single emergency department. The study lacked generalizability, and the results were based on the accuracy of the information provided by the patients, which might have biased the results. J. D. Jones et al. relied on self-report data and used a correlational design study, which precluded a causal inference determination. Despite these limitations, these studies provided evidence that supported

the expansion of public access to naloxone and refuted the claims that expanded access to naloxone promoted risky opioid use behavior.

Gap in the Literature

A search of the literature for studies that addressed how access to naloxone affected opioid use behavior regarding repeat overdose yielded only one study, which was conducted by Heavey, Chang, et al. (2018). To understand opioid use behaviors among patients enrolled in opioid use treatment, Heavey, Chang, et al. conducted in-depth interviews with 20 inpatients to explore the patients' perceptions regarding access to naloxone and the patients' behavior, awareness, and attitude regarding the medication. Heavey, Chang, et al. found that all the patients except one were aware of naloxone and its purpose and that less than one half of the patients knew how to obtain naloxone or had ever possessed or administered the medication. Some of the patients, despite their knowledge about the life-saving ability of naloxone, prioritized maintaining the euphoric feeling from the opioid above that of reviving someone—or being revived—from a potential overdose (Heavey, Chang, et al., 2018). The accessibility to naloxone was a factor in several of the participants' opioid use behavior in that the individuals reported increasing their usual dose of heroin when naloxone was present (Heavey, Chang, et al., 2018).

The study by Heavey, Chang, et al. (2018) was qualitative in nature and limited to a small sample of people who were undergoing opioid use treatment. Although repeat opioid overdose was not the outcome variable of interest in the study, the results provided insight that naloxone might be perceived as a safety net for those individuals who choose

to misuse opioids. The paucity of research focused on the accessibility of naloxone and the medication's impact on opioid use behavior represented a gap in the literature. This current study may help fill that gap through a quantitative analysis of the relationship between opioid overdose demographics, naloxone accessibility, and repeat opioid overdose.

Summary

Preventing opioid overdose-related mortalities is an ongoing public health effort. The use of naloxone, an opioid antagonist, is a common practice used in reversing the effect of an opioid overdose (Klebacher et al., 2017; Rowe et al., 2015; Wheeler et al., 2015). The literature is rife with studies involving opioid overdose and naloxone. A surge in studies published on these topics occurred within the past decade, which likely stemmed from the opioid epidemic in the United States. There was not, however, an abundance of studies published in which the diffusion of innovations theory served as the basis for research on naloxone use and repeat opioid overdose. The four elements of the theory, along with parenthetical entries that show how they related to the current study, are as follows: the innovation (naloxone), a communication system (public health communications about the importance of naloxone), time (the acceptability and extent of naloxone use), and a social system (the interconnected individuals and organizations involved in combating the opioid overdose crisis). The diffusion of innovations theory was appropriate as a framework because it focuses on behavioral changes (i.e., repeat opioid overdose) among people over time.

Professional emergency first responders such as LEO and EMS personnel provide timely, prehospital treatment with naloxone to revive opioid overdose victims. These professionals are also well positioned to provide overdose victims with information about treatment options for substance misuse disorder. The rescue roles of these emergency first responders are beneficial in other ways as well. For example, the data collected by these professionals may be used to monitor overdose and repeat overdose trends in communities (Lasher, et al., 2019). Additionally, the data collected on the number of doses required to revive overdose victims may help local public health officials monitor the potency of ingested opioids (Lasher et al., 2019).

Historically, naloxone was reserved for administration by those within the medical profession. The medication has since been made available for use by members of the public via venues such as emergency departments, pharmacies, and community-based programs. The role of pharmacies in improving naloxone access is evolving, consistent with the provisions addressed in the Comprehensive Addiction and Recovery Act (2016). Pharmacies are located throughout communities, which makes the venues beneficial in providing accessibility to naloxone, particularly to opioid users in rural and underserved areas (Bachyrycz et al., 2017). Emergency departments are uniquely oriented to educate opioid users at risk for overdose and to provide the opioid users with take-home naloxone (Gunn et al., 2018). Such a unique opportunity is often unexploited by emergency departments because the departments lack adequate staffing or because the staff members lack the time to attend the requisite naloxone training (Gunn et al., 2018). If emergency

departments can overcome these barriers, they can help reduce community overdoses and repeat overdoses involving opioids (Gunn et al., 2018).

Community-based naloxone programs can be used to distribute naloxone to populations in need of the medication, provide training on recognizing and responding appropriately to an opioid overdose, and link patients to support and recovery programs. Community-based naloxone programs are effective in improving the knowledge and confidence of family members of individuals who use opioids (Bagley et al., 2015). Also, the programs help public health policy makers communicate opioid overdose prevention strategies to communities and social networks (Bagley et al., 2015). Family members, community-based naloxone programs, emergency departments, and pharmacies are examples of the components of the social system described by Rogers (2003) in the diffusion of innovations theory.

Deaths associated with opioid overdose continue to rise, making the problem a high priority among health and public health policy makers. Expanding the access of naloxone to laypersons is one approach in addressing the opioid overdose problem. The approach has not been well received by some people, including some health care professionals. Despite the beliefs by some that misbehaviors are associated with the expanded access to naloxone, ready access to the medication is crucial because not all opioid overdoses stem from the use of illicit opioids (Rudski, 2016).

Little is known about the impact of the expanded accessibility of naloxone on opioid use behavior, including repeat opioid overdose. There is a dearth of research literature addressing the topic. Understanding the epidemiology of repeat opioid overdose

is beneficial in understanding the depth of the current opioid epidemic. The intent of this current study was to extend the literature regarding what is known about the impact of naloxone on opioid use behavior. This study was conducted to determine the relationship between the demographics (gender, age, and race), naloxone accessibility, and repeat opioid overdose. Information regarding the collection and analysis of data on the variables in the study is presented in Chapter 3. The research design, rationale, and methodology used in conducting the study are presented in Chapter 3 as well.

Chapter 3: Research Method

The purpose of this study was to determine whether relationships existed between demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county. The selection of the research design for this study and the methodology that was used to test the research questions and their associated hypotheses are discussed in this chapter. Discussions of the research population, sampling strategy and procedures, operationalization of each variable, and data analysis plan are included as part of the methodology. Additionally, threats to the validity of the study and the ethical procedures employed in the study are presented. The chapter concludes with a summary.

Research Design and Rationale

In this study, there were five independent variables (age, gender, race, naloxone doses administered by professional first responders, and distribution of naloxone rescue kits) and one dependent variable (repeat opioid overdose). The independent variables of age, gender, and race were covariates. The variables were components of the research questions, which were structured to support the study of the effect of naloxone on opioid use behavior from a social and health perspective. The focus of the study's research questions was on the quantitative examination of the predictor variables (age, gender, race, the naloxone dose administered, and the distribution of naloxone rescue kits) and their relationship to the outcome variable (repeat opioid overdose).

A study is guided by its research questions and hypotheses, which, together with the study's purpose, dictate the appropriate choice of research design (Crawford, Burkholder, & Cox, 2016). The research design provides a detailed strategy that will be

used to answer the research questions (Crawford et al., 2016). Typically, the research design comprises an inquiry approach, a design specific to that approach, and a rationale for selecting the approach and design (Crawford et al., 2016). The research's approach to inquiry can be quantitative, qualitative, or a combination of the two, which is known as mixed methods.

The quantitative approach involves the use of large amounts of numerical data along with statistical analyses to objectively and systematically explain an observation (McCusker & Gunaydin, 2015; Queirós, Faria, & Almeida, 2017). The approach's strengths include its ability to make statistical comparisons between samples and test hypotheses; weaknesses include its inability to focus on contextual details and the need for complex statistical analysis procedures (McCusker & Gunaydin, 2015). The qualitative approach, on the other hand, involves the use of words as the data. Such data are generated during researcher-participant dialogues conducted to understand the perceptions, attitudes, and experiences of study participants (McCusker & Gunaydin, 2015). Although the approach allows for a deeper understanding of the topic of interest, it is susceptible to emotional and subjective biases associated with the active, intimate role of the researcher (McCusker & Gunaydin, 2015). The mixed-methods approach includes a combination of the quantitative and qualitative methods and is beneficial in answering research questions that tend to be complex (McCusker & Gunaydin, 2015). Combining the quantitative and qualitative attributes is a strength of the mixed-methods approach; however, doing so can be time-consuming and expensive (McCusker & Gunaydin, 2015).

Of the three approaches, the quantitative approach was the most appropriate choice for the current study because the data collected to answer the research questions were numerical and analyzed using statistical tests. Additionally, the use of de-identified, secondary data and the restricted access to interview patients who overdosed on opioids more than one time precluded the selection of a qualitative or mixed-methods approach. The next step after determining the approach is to choose a design consistent with the approach. Selecting the appropriate design for a quantitative study is crucial in answering research questions. Descriptive, experimental, and correlational are three commonly used quantitative designs.

Consistent with its nomenclature, the descriptive design is used to describe observed occurrences (i.e., the variables). With the design, statistical data such as frequencies/counts, means, and standard deviations are collected on the variables and examined (Cook & Cook, 2016). Although the descriptive research design does not permit the determination of relational or causal inferences between the variables, it offers the benefit of providing reliable measures of phenomena, formulating theory, and serving as a basis for subsequent research using qualitative or other quantitative research designs, such as relational and experimental designs (Cook & Cook, 2016).

Experimental designs are used to examine causal inference between the variables, specifically whether a change in the independent variable is responsible for a change in the dependent variable (Cook & Cook, 2016). The design includes use of experimental and control samples partitioned by the researcher, and the researcher systematically manipulates the independent variable and measures its effect on the dependent variable

(Cook & Cook, 2016; Queirós et al., 2017). Despite their use in determining causality, experimental designs can be expensive, difficult to replicate, and susceptible to ethical concerns (Cook & Cook, 2016; Queirós et al., 2017). Additionally, the small sample often employed in the design might not be representative of the population from which participants were selected (Queirós et al., 2017).

Correlational research is the third quantitative design. Correlational research is exploratory in that it is used to determine whether relationships exist between variables (Queirós et al., 2017). The design does not involve the manipulation of variables or a determination of whether the independent variable causes a change in the dependent variable (Cook & Cook, 2016; Queirós et al., 2017). Instead, the design is used to examine whether and how the variables are related, whether the variables are responsible for differences observed among groups, and whether there is enough evidence to explore causality through experimental research (Cook & Cook, 2016).

In light of the goal of the current study to examine the relationships between demographics, naloxone dose administrations, naloxone kit distributions, and repeat opioid overdose, the correlational research design was the appropriate quantitative design. The descriptive design was not appropriate because examining the relationship between variables is not part of its design feature. Because there was no manipulation of the variables or an intent to make a causal determination, the experimental design was inappropriate. An additional rationale that made the choice of the correlational design appropriate was the efficiency associated with the time and resources necessary to conduct the study. The design permitted the exploration of a large amount of data on

different variables in a short time frame, as the data on each variable were collected simultaneously and at one point in time.

Methodology

The research methodology includes the steps that will be followed to obtain answers to the research questions (Crawford et al., 2016). Typically, the methodology addresses the study participants, sampling strategy, data instrumentation, and data collection procedures (Crawford et al., 2016). Such procedures should include how the data will be obtained, structured, cleaned, and analyzed (Crawford et al., 2016).

Population

The setting of this study was a county in Tennessee. The population of interest was the county's approximately 80,000 residents (U.S. Department of Commerce [DOC], U.S. Census Bureau [USCB], n.d.). Racially, the population was 91.7% White, 4.0% Black, 3.1% Hispanic, 1.5% Asian, 0.5% American Indian/Alaska Native, and 0.1% Native Hawaiian/Pacific Islander (DOC, USCB, n.d.). There were slightly more females than males in the population, with ratios of 51.3% and 48.7%, respectively (DOC, USCB, n.d.). The median age was 43.3 years, with 21% of the population under 18 years of age, 58.9% between 18 and 64 years of age, and 20.1% 65 years of age and older (DOC, USCB, n.d.).

Sampling and Sampling Procedures

A sampling strategy that is well planned and carefully executed is necessary to ensure that the results of the study are not biased by the participant selection process (Martínez-Mesa, González-Chica, Duquia, Bonamigo, & Bastos, 2016). The strategy

includes establishing the sampling unit, target population, sampling frame, and sample. Understanding the sampling strategy helps contextualize the sample's representativeness of the population from which it was selected (Lohr, 2010). The sampling unit is the element under observation (i.e., an individual, household, or community) that has the potential to be included in the sample (Lohr, 2010). The collection of the sampling units constitutes the target population, which is used to make inferences (Lohr, 2010). The sampling frame is a listing of the sampling units in the study population (Lohr, 2010). Finally, the sample is a subset of the sampling units selected from the target population (Martínez-Mesa et al., 2016). Results from the sample are used to make inferences to the target population with a degree of accuracy (Lohr, 2010).

Secondary data were used in this study. The data were obtained from two sources: the county's EMS and a community-based naloxone program. Data use agreements, which described the criteria necessary for the sample, were used to obtain the data sets. The data sets were de-identified before they were provided for use in the study.

The individual was the sampling unit in this study. The sampling frame was a listing of the individuals to whom the EMS professionals responded based on 911 calls that involved suspected opioid overdose during a specified time frame. The individuals who did not require the administration of naloxone were excluded from the sampling frame. The remaining individuals represented the sample.

Erdfelder, Faul, and Buchner's (1996) power analysis program G*Power was used to calculate the size of the two samples that were used in the current study. In calculating the first sample, binary logistic regression was used as the statistical test to

examine the relationships between the independent variables (age, gender, race, and the naloxone dose administered) and the dependent variable (repeat opioid overdose). Choosing the two-tailed *z*-tests option in G*Power allowed the selection of logistic regression for the statistical test. The effect size was specified to be measured as an odds ratio. The two-tailed test was selected because there was no presumption about the direction of an observed difference regarding the independent and dependent variables (Parab & Bhalerao, 2010).

Assumptions were made regarding the logistic regression power analysis calculation of the first of two samples used in the study. The assumed event rates under the null and alternative hypotheses were .5 and .6, respectively, which corresponded to an odds ratio of 1.5. Because there were multiple independent variables in the study, the squared multiple correlation value was assumed to be 0.1. Additionally, a normal distribution of the independent variables was assumed. The probability of error (or alpha) of .05 and the statistical power of .80, a value recommended by Cohen (1992) when rationales for other power values are unavailable, were selected. Statistical power, which refers to the probability of rejecting the null hypothesis when it is false, is a function of the alpha level of significance, the sample size, and the size of the effect (Cohen, 1992). Using .80 for the power is commonly accepted as the value necessary to select an adequate sample size that will detect a statistically significant effect size with confidence (Undersander, Kettler, & Stains, 2017). Anything lower than .80 will likely diminish the level of confidence that the study results are truly reflective of the sample (Undersander et al., 2017). Based on the input parameters, the minimum sample size necessary to detect

a statistically significant relationship between the independent variables and the dependent variable was determined to be 231.

In calculating the second sample with G*Power, Poisson regression was used as the statistical test to examine the relationship between the independent variable (distribution of naloxone rescue kits) and the dependent variable (repeat opioid overdose). Other selections included the *z*-test, which allowed the selection of the Poisson regression test; 80% for the power; and .05 for the probability of error. Assumptions made in selecting the parameters were that the distribution of the independent variables was normal, the event base rate was equal to 1, the change in the dependent variable with each unit increase of the independent variable was 10%, and the independent and dependent variables was examined in 7-day increments (i.e., the mean exposure). With the input parameters, a minimum sample size necessary to detect a statistically significant relationship between the independent and the dependent variables was determined to be 123.

Operationalization

Naloxone access was operationalized as two variables: the naloxone dose administered by professional first responders and the distribution of naloxone rescue kits through a community-based program. Although there were other means by which individuals could access naloxone (i.e., pharmacies, emergency departments, and local health departments), the venues represented by the two variables were chosen because they were included in the literature along with results that were used as comparisons to the findings of the current study. The demographics of interest in this study were the age,

gender, and race of individuals who received naloxone because of an opioid overdose. Age, gender, race, the naloxone dose administered by professional first responders, and the distribution of naloxone rescue kits were the independent variables in the current study; repeat opioid overdose was the sole dependent variable. Age can be a continuous or categorical variable, depending on how the data are collected and coded. Nominal variables, which can have two or more categories in no particular order; dichotomous variables, which have two mutually exclusive categories; and ordinal variables, which have two or more ranked levels, are the types of categorical variables.

So that the variable of age could be compared with results in the literature, age was analyzed as a categorical, ordinal variable with eight levels in the current study. The levels of the variable, which were age groups in years, were coded as 1 = less than 15, 2 = 15–24, 3 = 25–34, 4 = 35–44, 5 = 45–54, 6 = 55–64, 7 = 65–74, and 8 = 75 or older. Gender was a categorical, dichotomous variable that was coded as 1 = male and 2 = female. Race was a categorical, nominal variable with three categories coded as 1 = White, 2 = Black, and 3 = Other. The variable that represented the naloxone dose administered by professional first responders was analyzed as a continuous variable. The unit of measure of the administered dose was in milligrams (mg). The distribution of naloxone rescue kits was also analyzed as a continuous, interval variable because it was a measure of the number of kits distributed through the community naloxone program. The dependent variable, which was repeat opioid overdose, represented the number of nonfatal or fatal opioid overdoses that occurred more than one day after the first overdose

in which naloxone was administered (Olfson et al., 2018). Repeat opioid overdose was analyzed as a categorical, dichotomous variable that was coded as 1 = no and 2 = yes.

Data Analysis Plan

The descriptive and inferential statistical analyses in this study were performed using IBM SPSS Statistics (Version 25). The software was used also to screen and clean the data sets. The screening and cleaning processes included a visual examination of the data sets to determine whether there were outliers among the data or whether any of the data were missing or seemed abnormal. Missing data can reduce the size of the study's sample and affect the reliability of the study if the results were biased by the missing information (Kwak & Kim, 2017). Outliers can also introduce bias in a study's results, especially results derived from standard deviation and mean calculations (Kwak & Kim, 2017). The mean and standard deviation are sensitive to outliers in that the outliers can cause the statistics to be overestimated or underestimated (Kwak & Kim, 2017).

Determining the relationship between demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county was the purpose of this study. The research questions and the hypotheses that guided the examination of the relationships are as follows:

Research Question 1: What is the association between age and repeat opioid overdose?

$H_0$1: There is no statistically significant association between age and repeat opioid overdose.

H_a1: There is a statistically significant association between age and repeat opioid overdose.

Research Question 2: What is the association between gender and repeat opioid overdose?

$H_0 2$: There is no statistically significant association between gender and repeat opioid overdose.

$H_a 2$: There is a statistically significant association between gender and repeat opioid overdose.

Research Question 3: What is the association between race and repeat opioid overdose?

$H_0 3$: There is no statistically significant association between race and repeat opioid overdose.

$H_a 3$: There is a statistically significant association between race and repeat opioid overdose.

Research Question 4: What is the association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose?

$H_0 4$: There is no statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

H_a4: There is a statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

Research Question 5: What is the association between the distribution of naloxone rescue kits and repeat opioid overdose?

H_05: There is no statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

H_a5: There is a statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

Descriptive analysis. Descriptive statistics are useful in summarizing observations so that the information can be conveyed in a manner that is easy to understand (Mishra et al., 2019). The three types of descriptive statistics are measures of frequency (i.e., frequencies and percentages), measures of central tendency (i.e., mean, median, or mode), and measures of variability (i.e., variance, standard deviation, standard error, range, interquartile range, and percentile; Mishra et al., 2019). The measures of frequency were used to summarize the characteristics of age, gender, race, and repeat opioid overdose because the variables were categorical. The variables that represented the distribution of naloxone rescue kits and the naloxone dose administered by professional first responders were continuous variables, so their characteristics were described using the measures of central tendency or the measures of variability.

Inferential analysis. Inferential statistics help researchers draw conclusions from data used in the study. The intent of such statistics is to make inferences—or

generalizations—about a larger population based on the statistical analyses conducted on a sample selected from the population (Mishra et al., 2019). Researchers rely on statistical tests to help make the inferences. The level of measurement of a study's variables is important in determining which statistical test is best to analyze the quantitative data (Parab & Bhalerao, 2010). Multiple logistic regression can be used to analyze the relationship between a dichotomous dependent variable and several independent variables that are categorical, continuous, or a combination of the two (Daniel & Cross, 2013; Warner, 2013). The dependent variable (repeat opioid overdose) in the first four research questions was categorical and dichotomous; the independent variables of age, gender, and race in Research Questions 1, 2 and 3, respectively, were categorical; and the independent variable (the naloxone dose administered by professional first responders) in Research Question 4 was continuous. The use of multiple logistic regression to analyze the data and to answer Research Questions 1 through 4 was appropriate.

Predicting the odds of the dependent variable on the measures of the independent variable is the goal of using multiple logistic regression as an analysis test (Warner, 2013). Multiple logistics regression yields an odds ratio, which is a measure used to determine the strength of an association between the independent and dependent variables. In the current study, the odds ratios were interpreted as how much greater or lesser the odds were that the sample characterized by the independent variable would experience the dependent variable (see Daniel & Cross, 2013).

Multiple logistic regression requires adherence to the assumptions that (a) the dependent variable be dichotomous; (b) the categories on the dependent variable be statistically independent of each other, exhaustive, and mutually exclusive; and (c) one or more independent variables be categorical or continuous (Warner, 2013). The dependent variable (repeat opioid overdose) was dichotomous in that the variable had two categories (yes and no), which were independent of each other, exhaustive, and mutually exclusive. The first two assumptions were satisfied. The four independent variables were categorical or continuous, which fulfilled the requirement of the third assumption.

Another assumption of multiple logistic regression requires that the model predicted by SPSS be consistent with the outcome data, a verification process known as the goodness of fit test (Warner, 2013). In the current study, this assumption was tested using the Hosmer-Lemeshow goodness of fit (H-L) test in SPSS. The observed and the expected frequencies predicted by the logistic regression were compared using a chi-square test, which helped assess the level of deviation between the two sets of frequencies (see Warner, 2013). A large H-L chi-square value and a test statistic (i.e., *p* value) that is less than .05 mean that the model's expected frequencies deviate significantly from the observed frequencies, which indicates a poor model fit (Warner, 2013). A good-fitting model has a small H-L chi-square value and a *p* value greater than .05, which is interpreted to mean the model's expected frequencies fit the observed frequencies at an acceptable level (Warner, 2013).

The Poisson regression analytical test, which is useful in determining whether an independent variable influences the rate of events (i.e., the dependent variable) over a

period of time, was used to answer Research Question 5. Poisson regression is also useful when the dependent variable is represented as frequency or count data. In Poisson regression, the independent variable can be categorical or continuous and is used to predict the dependent variable measure, which is expected to vary as a log-linear function of the independent variable (Chakraborty, Maiti, & Strecher, 2018). Because the independent variable (distribution of naloxone rescue kits) in Research Question 5 was continuous and the dependent variable (repeat opioid overdose) was measured as count data, the use of Poisson regression was appropriate to answer the research question.

The measure of effect size in Poisson regression analysis is the rate ratio. In SPSS, the effect size is reported as the exponentiated value of the regression coefficient (i.e., ExpB), which represents the change in the expected dependent variable when the independent variable increases by one unit (Chakraborty et al., 2018). In the current study, the rate ratio value was interpreted as the change in repeat opioid overdose events for each extra naloxone rescue kit that was distributed.

Poisson regression requires adherence to the assumptions that (a) the dependent variable is composed of count data, (b) the observations on the dependent variable are independent of each other, (c) the counts demonstrate a Poisson distribution, and (d) the mean and variance distributions are equivalent (Huang & Cornell, 2012). The dependent variable (repeat opioid overdose) in Research Question 5 was measured as count data, which satisfied the first assumption. An individual can have multiple repeat opioid overdoses as long as the events are treated as independent observations. The definition of

repeat opioid overdose used in the current study, ensured the independence of observation assumption was met. The last two assumptions were tested using SPSS.

A *p* value of .05 was used as the level of statistical significance during the hypothesis testing in this study. The *p* value, also known as the alpha level, represents the probability of observing the results if the null hypothesis were true (du Prel, Hommel, Roehrig, & Blettner, 2009). Confidence intervals, which provide a range of the accuracy of the estimate that is likely to contain the true value of the population parameter of interest (Frankfort-Nachmias & Leon-Guerrero, 2015), were used in reporting the odds ratios and rate ratios in the study. The 95% confidence interval is frequently used in research, and it was used in this present study. The measured effects were statically significant at the .05 alpha level if the value of 1 (which means no discernible difference) was not contained within the confidence interval.

Threats to Validity

The quality of a quantitative study depends on its validity, i.e., the ability to depict the real meaning of the phenomenon that is under observation (Babbie, 2017). The traditional components of validity are internal validity and external validity. Other components include construct validity and statistical conclusion validity. The components of validity characterize the representativeness of the sample, the attributes of the population from which sample was obtained, the data collection and analysis, and the study methods in such a way that allows inferences to be drawn from the results of the study (Stewart & Hitchcock, 2016). Conditions referred to as threats to validity can interfere with the outcome of the study. Threats to validity minimize the internal,

external, construct, and statistical conclusion validities of a study (Holgado-Tello, Chacon-Moscoso, Sanduvete-Chaves, & Perez-Gil, 2016).

Internal Validity Threats

Internal validity refers the extent to which the independent variable made a significant difference in the dependent variable (Campbell, 1957). Seven types of extraneous variables can impact the internal validity of a study: (a) selection, which is the potential bias associated with how the participants are selected; (b) history, which refers to the specific events experienced by the participants; (c) maturation, which refers to the biological changes that occur among the participants; (d) regression, which is the statistical regression of measures on the participants toward the mean value; (e) testing or measuring outcomes associated with the participants; (f) instrument decay, which involves changes in an instrument that affect the instrument's ability to measure accurately; and (g) mortality, which is the differential loss of participants from the study (Campbell, 1957; Flannelly, Flannelly, & Jankowski, 2018). Controlling the extraneous variables is crucial in achieving a high degree of internal validity, meaning any measured changes in the dependent variable were most likely influenced by the independent variable (Flannelly et al., 2018).

Selection can threaten a study's internal validity. Choosing study participants through randomization procedures can minimize the threat. Because the sample in the current study included all of the individuals who met the selection criteria, selection had no impact on the internal validity. Three variables (i.e., age, gender, and race) associated with the participants in the current study could have been confounders and could have

influenced the dependent variable. In a systematic literature review and meta-analysis, Brady, Giglio, Keyes, DiMaggio, and Li (2017) found that being White, male, and among the 35–44 age group were statistically significant risk factors of nonfatal and fatal prescription opioid overdose. To minimize the potential threat to the internal validity of the current study, the variables of age, race, and gender were included as independent variables and were examined during the statistical analyses. Doing so minimized confounding as a selection threat to this study's internal validity.

As discussed by Campbell (1957), the threat of history refers to specific events or stimuli that occur during the study's observation period and are experienced by the participants such that the events or stimuli influence the results of the study. In the strictest sense of the term, the threat of history was not applicable in the current study because anonymous data were collected only once on the participants and only at a single point in time. Because Research Question 5 focused on the distribution of naloxone rescue kits and repeat opioid overdose observed over time, history might have been a threat to the internal validity. For example, unmeasured environmental confounders such as the variations in opioid prescriptions written by physicians, the availability of opioid misuse treatment facilities, and the illicit opioid market trends could have influenced the outcome measure (see McClellan et al., 2018; and Wagner et al., 2016). Because anonymous data were collected only once on the participants and only at a single point in time, the threats associated with maturation and mortality were not applicable in the current study. Also, there were no threats related to testing, regression, or instrument

decay in this study because no tests or examinations were administered to obtain biological or psychological information about the participants.

External Validity Threats

The extent to which the study's results can be applied to other populations or settings is known as external validity (Campbell, 1957). The credibility of research relies on its external validity, meaning that the study results, with a high level of confidence, can be extrapolated to other populations, places, and times (Pound & Ritskes-Hoitinga, 2018). Selection can affect external validity through interaction with the sample units (i.e., the study participants). For example, the study results may be different if another group of participants is used (Campbell, 1957; Stewart & Hitchcock, 2016). The interaction effects of selection reduce the representativeness of the sample and, thereby, the generalizability of the results to the target population if there are effects in the environment that can influence the outcome (Campbell, 1957).

Because all eligible overdose events were included in the sample of the current study, a sampling selection procedure was unnecessary. The external validity associated with representativeness, therefore, was not compromised. On the other hand, the results of this study may not be generalizable to other populations or environments. Target populations in which individuals overdose on opioids may have demographic compositions that are different from those in the current study. Additionally, other target populations may have more or less access to opioids (i.e., via physician prescriptions or illegal drug markets), naloxone (i.e., via community-based programs or pharmacies that dispense naloxone under standing orders), or substance use treatment facilities, all of

which are factors that may influence the rates of opioid overdose and repeat overdose. To address the potential validity threat associated with generalizability to other populations or settings, a strategy suggested by Stewart and Hitchcock (2016) was employed in the current study. The strategy included conducting a thorough literature review for studies related to the variables in the current study and comparing the findings from those studies with the findings of the current study (see Stewart & Hitchcock, 2016).

Construct Validity Threats

Construct validity is the extent to which the conclusions of a research study truly reflect the construct that was operationalized, meaning that the construct (or idea) was translated into something real or tangible (Trochim & Donnelly, 2008). Failure to analyze and to develop the construct of interest adequately can threaten construct validity (Holgado-Tello et al., 2016). The threat of construct validity in the current study was mitigated by the use of a clear definition of the dependent variable (repeat opioid overdose) that was based on the literature. Additionally, naloxone access was defined based on prior research, and the phenomenon was operationalized as two independent variables that were measurable and analyzable.

Statistical Conclusion Validity Threats

Statistical conclusion validity refers to the extent to which a statistical inference can be made about the measured relationship between the dependent and independent variables (Cor, 2016). Statistical conclusion validity focuses on whether the observed relationship between the predictor and outcome variables was attributed to a true effect or to chance (Cor, 2016). Threats to statistical conclusion validity can result in type I and

type II errors, which can result in inaccurate inferences from the data (Creswell, 2014). A type I error, also known as the alpha risk, occurs when the null hypothesis—a determination of no statistically significant difference—is rejected although it is true (Daniel & Cross, 2013). Such an error means that what was detected was due solely to chance and that the researcher incorrectly interpreted the data to mean there was a difference when there was not a difference. A type II error, known as the beta risk, occurs when the null hypothesis is not rejected when it is false (Daniel & Cross, 2013). A type II error means that the observed difference was not due solely to chance and that the researcher incorrectly interpreted the data to mean there was no difference when there was a difference.

Statistical conclusion validity threats are caused by choosing a statistical power that is inadequate, selecting an incorrect statistical technique based on the characteristics of the data (i.e., parametric versus nonparametric tests), or failing to ensure that statistical assumptions are not violated (Cor, 2016; Creswell, 2014). In conducting the statistical power analysis to determine the sample size for this current study, .80 was used for power. According to Dorey (2011), the power of .80 is sufficient to use in correlational studies of a retrospective nature. Because the sample used in this current study comprised at least the number of participants calculated in the G*Power analysis, the statistical conclusion validity was not threatened by an inadequate statistical power. The threat of inappropriate use of statistical techniques was not a concern in this study. The dependent variable in Research Questions 1 through 4 was categorical and was analyzed using logistic regression. The dependent variable in Research Question 5 was a measure of

count data and was analyzed using Poisson regression. The assumptions associated with multiple logistic regression and Poisson regression used in the current study were identified. Measures were implemented to ensure the assumptions were not violated, which reduced the threat to the statistical conclusion validity in this study.

Ethical Procedures

Research should always be conducted ethically, ensuring the protection of study participants and the organizations associated with the research. Obtaining informed consent and making certain that the participants are not physically or mentally harmed are crucial aspects associated with the use of participants in research (Rudestam & Newton, 2015). The prevention of harm subsumes the assurance that the participants' anonymity and their confidentiality will be maintained. The integrity, reputation, and copyright interests of the organizations involved with the research must be protected as well (George, 2016).

Secondary data were used in this quantitative study. The data were de-identified, and there were no interactions with the subjects of the study, which assured anonymity of the participants. Data were collected from a county's EMS and from a community-based naloxone program. I had no affiliation with the organizations. There were no conflicts of interest regarding power differentials or conducting research in my work environment. Because there were no interactions with the study participants, the use of incentives was not applicable.

Data from the EMS and the community-based naloxone program were collected through the use of data use agreements. The data use agreements indicated that only a

limited data set of the variables in the study was needed and that the data set must contain only de-identified data (i.e., no names or any other direct identifiers to the individuals). The results of this study will be shared with the organizations. Because there were no interactions with the subjects of this study and because there was no collection of primary data, obtaining confidentiality disclosures and written informed consents was not applicable to the study.

The data use agreements specified that the data sets would be safeguarded to prevent disclosure. The data sets were stored and accessed only by me on my personal computer. Encryption software was installed on my computer and was used to encrypt the data sets. Analyses of the data sets were performed using SPSS software on my computer. No software that was linked directly to the internet was used to analyze the data sets. The data will be retained for 5 years and then will be deleted permanently from my computer.

The reporting aspect of research, which is often overlooked, can jeopardize the anonymity of study participants (Babbie, 2017). For example, responses provided by members of a small community might be recognizable by others in the community even if the data were de-identified (Babbie, 2017). There were no responses or personal information collected on the participants in this study, and the results were discussed as an aggregate (i.e., an age group) rather than at the level of the individual, a precaution that represented another mechanism of ensuring the anonymity of the participants.

Conducting research ethically also means that researchers are responsible for being objective in their reporting, meaning they should report undesirable results as well

as the desirable results (Babbie, 2017). The undesirable (or negative) findings may benefit future research by indicating, for example, that there may not be a relationship between certain variables (Babbie, 2017). Positive and negative findings were included and discussed in this current study.

Approval from the institutional review board (IRB) was a prerequisite to the collection of any data in this study despite that secondary, de-identified data were used and despite that no participants were recruited for the study. After approval from the IRB, the secondary data were collected and analyzed. Adherence to the ethical considerations ensured that this study was conducted ethically.

Summary

To determine whether relationships existed between opioid overdose demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county, a quantitative, correlational study with a cross-sectional design was conducted. Five research questions and their associated hypotheses guided the examination of the relationships. In the study, there were five independent variables (age, gender, race, the naloxone dose administered by professional first responders, and distribution of naloxone rescue kits) and one dependent variable (repeat opioid overdose). The variables were analyzed using descriptive and inferential statistics. The nature of the variables warranted the use of multiple logistic regression and Poisson regression in the inferential analyses.

Validity threats can jeopardize the quality of a quantitative study. Internal, external, construct, and statistical conclusion are types of validity threats that should be recognized and managed before and during a study. Adherence to ethical procedures is

critical when planning and conducting a study as well as when reporting the results of a study. In Chapter 4, the data collected for this current study and the results of the statistical analyses are discussed.

Chapter 4: Results

Naloxone is a life-saving pharmaceutical that is widely known to be effective in reversing an opioid overdose. However, what is not widely known, nor has been fully explored, is whether the medication precipitates opioid abuse (i.e., repeat overdose behavior). The purpose of this quantitative, correlational study was to examine the relationship between demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county. The research questions and their associated null and alternative hypotheses were as follows:

Research Question 1: What is the association between age and repeat opioid overdose?

$H_0$1: There is no statistically significant association between age and repeat opioid overdose.

H_a1: There is a statistically significant association between age and repeat opioid overdose.

Research Question 2: What is the association between gender and repeat opioid overdose?

$H_0$2: There is no statistically significant association between gender and repeat opioid overdose.

H_a2: There is a statistically significant association between gender and repeat opioid overdose.

Research Question 3: What is the association between race and repeat opioid overdose?

$H_0$3: There is no statistically significant association between race and repeat opioid overdose.

H_a3: There is a statistically significant association between race and repeat opioid overdose.

Research Question 4: What is the association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose?

$H_0$4: There is no statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

H_a4: There is a statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

Research Question 5: What is the association between the distribution of naloxone rescue kits and repeat opioid overdose?

$H_0$5: There is no statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

H_a5: There is a statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

This chapter includes the process employed in collecting and analyzing the data used in this study and the results of the statistical analyses. Information about the data source and the sample related to the target population is presented first. Next, the

descriptive statistics of the sample and the findings of the statistical analyses are discussed. The chapter concludes with a summary and segue to Chapter 5.

Data Collection

After approval from the Walden University IRB (#02-21-20-0670103), data were requested and received from a Tennessee county's EMS and a community-based naloxone program. The community-based program data set consisted of the number of naloxone kits distributed and the dates of the distributions, which ranged from November 2017 to December 2019. In total, there were 791 naloxone kits distributed on 40 days during the time frame. Each kit contained two 4-mg doses of naloxone. The EMS data set consisted of a database printout of 971 de-identified records of dispatches associated with overdoses from July 2016 to December 2019.

Data Screening and Cleaning

An examination of the data received from the community-based naloxone program in an Excel spreadsheet indicated seven duplicate line items. The duplicate entries were removed. There were 674 naloxone kits (representing 5,392 mg of naloxone) distributed during the time frame. The initial distribution of the naloxone kits via the program began on November 28, 2017. Figure 3 displays the monthly distribution of the kits from this start date through December 2019.

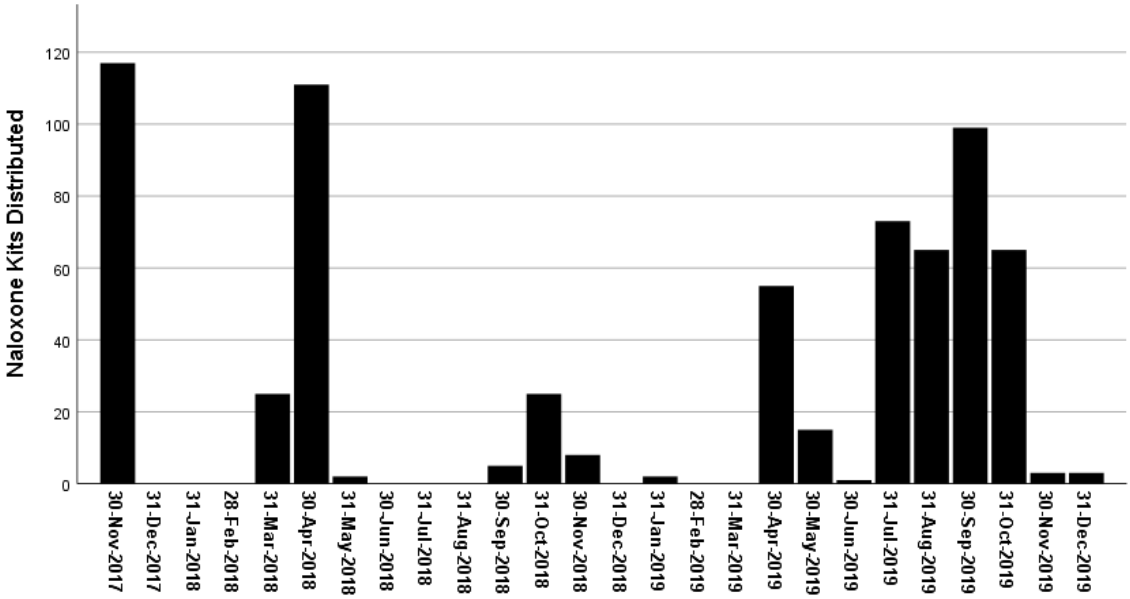

Figure 3. Naloxone kits distributed by month (November 2017 to December 2019).

The EMS data set was transferred to a Microsoft Excel spreadsheet and examined for missing information regarding the study variables. In two of the recorded overdose events, the dose of naloxone administered was recorded in units other than milligrams, so the records were removed from the data set. The gender was not listed on two recorded overdose events, so the two entries were removed as well. There were no other discrepancies or missing data identified in the EMS data set. The remaining 967 recorded overdose events represented the sampling frame. The characteristics of the sampling frame are listed in Table 1.

Table 1

Characteristics of Sampling Frame

Characteristics	Overdose dispatches (*N* = 967)
Gender, no. (%)	
Male	483 (49.9)
Female	484 (50.1)
Age (in years)	
Mean	40.4
Median	38.0
Range	1–99
Race, no. (%)	
White	920 (95.1)
Black	28 (2.9)
Other	19 (2.0)
Repeat overdose, no. (%)	
0 repeat overdoses	884 (91.4)
1 repeat overdose	63 (6.5)
2 repeat overdoses	16 (1.7)
3 repeat overdoses	3 (.3)
4 repeat overdoses	1 (.1)
Naloxone administered, no. (%)	
Yes	386 (39.9)
No	581 (60.1)
Naloxone dose, mg	
Mean ± SD	1.80 ± .98
Median	2.0
Range	0.5–8.0

Note. No. = number; mg = milligram; SD = standard deviation.

Figure 4 depicts the opioid overdose events recorded by month by the county EMS from July 2016 through December 2019. Figure 5 displays the repeat opioid overdose events by months that occurred during that same time frame.

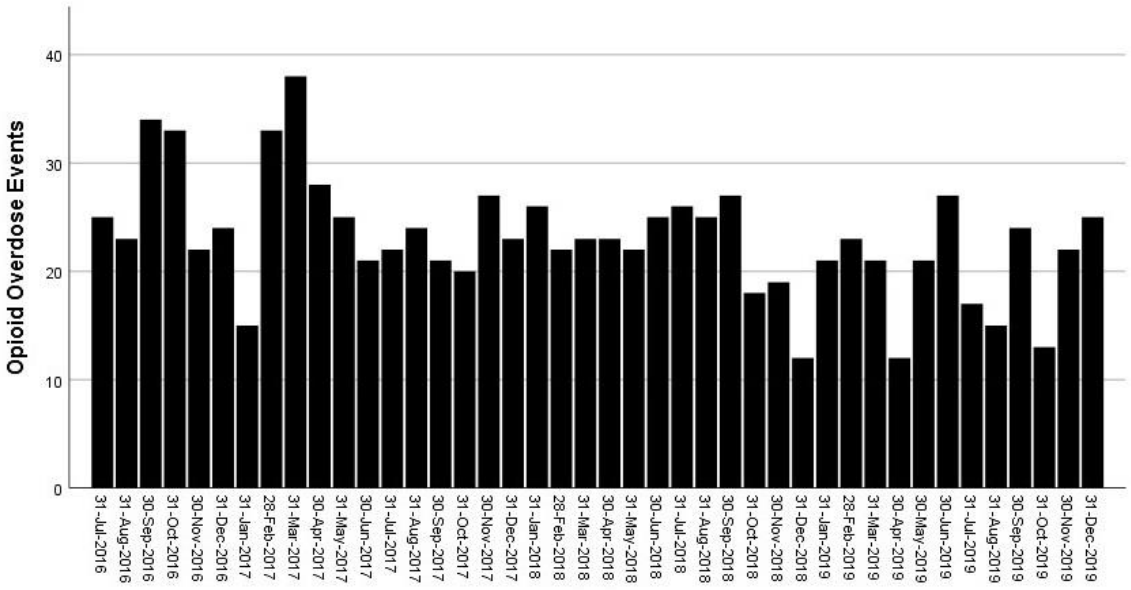

Figure 4. Opioid overdose events by month (July 2016 to December 2019).

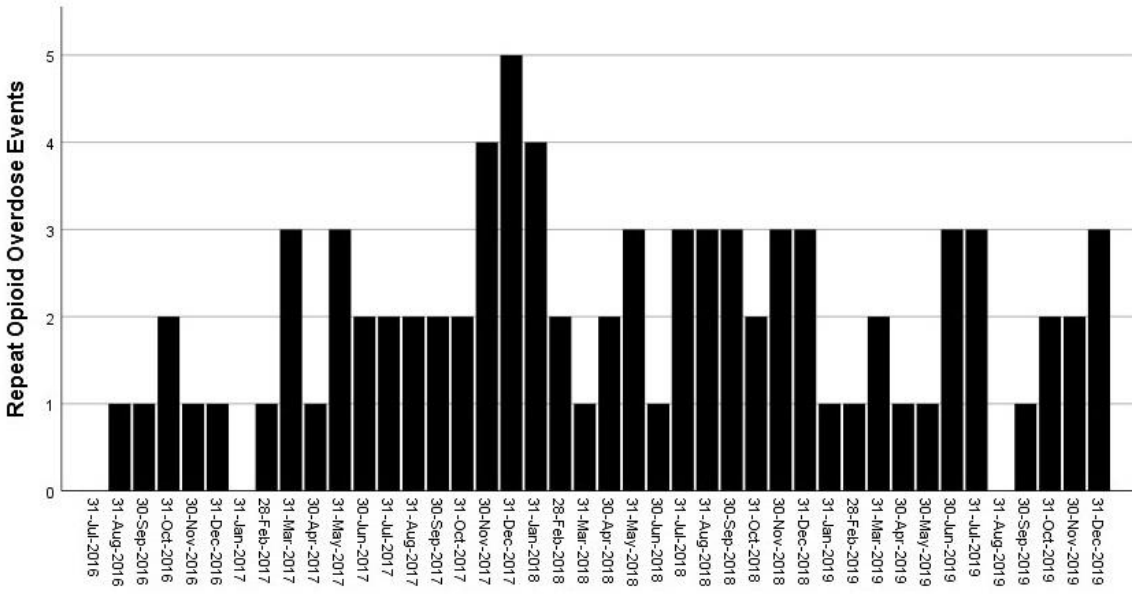

Figure 5. Repeat opioid overdose events by month (July 2016 to December 2019).

An examination of Figure 4 indicated that more than 10 opioid overdose events occurred each month, and more than 20 events occurred in over 80% (n = 34) of the months. The annual means of the opioid overdose events in 2016 (based on 6 months), 2017, 2018, and 2019 were 26.8, 24.8, 22.3, and 20.1, respectively, which indicated that the opioid overdose events decreased compared to the prior year. Contrastingly, Figure 5 shows a consistent increase in the repeat opioid overdose events through 2018, followed by a decrease in 2019. The average number of repeat events in 2016, 2017, 2018, and 2019 were 1, 2.3, 2.5, and 1.7, respectively. The peak number of repeat opioid overdose events in a single month during the observation period was five, which was in December 2017.

Data Manipulation

Microsoft Excel was used to create and code dummy variables for the independent categorical variables of gender and race and for the dependent variable, repeat overdose. The spreadsheet was also used to transform the independent continuous variable of age into a categorical, ordinal variable with eight levels. No data manipulation was necessary for the independent continuous variable, which was the naloxone dose administered by professional first responders during opioid overdose events. The Excel spreadsheet data were imported into SPSS, which was used to select and analyze only the cases (i.e., overdose events) in which naloxone was administered. The 386 selected cases represented the study sample and were used in conducting a multiple logistic regression analysis to answer Research Questions 1 through 4.

Two samples were used in the current study. The first sample was derived from the recorded overdose dispatches that were included in the EMS data set. To answer Research Question 5, it was necessary to create a new data set (i.e., the second sample) using the EMS data set and the community-based naloxone program data set. The date variable was the key variable in both data sets that permitted the linking procedure. Each record included the date (i.e., the end date of each week) associated with the distribution of naloxone kits and the number of repeat overdoses from January 2017 to December 2019. The new data set had 156 records, which represented the 156 weeks of the study's time frame. Because the sampling unit was the week, the size of the second sample was 156.

Univariate Analysis

A univariate analysis was conducted using SPSS to determine whether to include the covariates (i.e., the independent variables of gender, age, race, and the naloxone dose administered by professional first responders) in the multiple logistic regression model. The results of each independent variable analysis are listed in Table 2. Gender was the only independent variable of statistical significance.

Table 2

Independent Variables in the Univariate Analysis

Factors	Exp(*B*)	*p* value (Wald test)
Gender (male-female comparison)	.35	.01
Age (compared to 15–24)		
25–34	.88	.84
35–44	1.13	.85
45–54	.72	.62
55–64	.42	.28
65–74	.96	.96
75 and over	.00	1.00
Race (compared to White)		
Black	1.90	.42
Other	.00	1.00
Naloxone dose	1.17	.34

Conducting univariate analyses helps determine which independent variables are best to use in predicting the dependent variables. Typically, the multiple logistic regression analysis is conducted using only the independent variables that are statistically significant in the univariate analyses. Although gender was the only statistically significant variable in the univariate analyses, all covariates were included in the multiple logistic regression analysis.

Data Analysis Results

Descriptive Statistics – Sample 1

The descriptive statistics associated with the first sample are presented in Table 3. The sample consisted of more males (55.2%) than females (44.8%), the reverse of the county's population in which there were more females (51.3%) than males (48.7%). Unlike the sampling frame, the sample comprised no individuals younger than 15 years

of age. The largest age category was the 25–34 (23.6%), followed by the 35–44 and 45–54 categories, both of which represented 18.9% of the sample. The two smallest categories were the 75 and over (15.5%) and the 65–74 (7.3%). The sample was predominantly White (95.1%). Blacks and other races accounted for less than 5% of the sample.

Most of the individuals [91.2% (n = 352)] treated with naloxone by the EMS first responders in this study experienced only one opioid overdose. The remaining individuals [8.8% (n = 34)] had frequencies of repeat opioid overdose events that ranged from one to three. The dose of naloxone administered by the professional first responders during the overdose events ranged from 0.5 mg to 8.0 mg per overdose dispatch. The mean dose was 1.80 ± .98 mg, and the median was 2.0 mg.

Table 3

Characteristics of Study Sample

Characteristics	Dispatches involving naloxone administration (*N* = 386)
Gender, no. (%)	
Male	213 (55.2)
Female	173 (44.8)
Age, no. (%)	
15–24	36 (9.3)
25–34	91 (23.6)
35–44	73 (18.9)
45–54	73 (18.9)
55–64	60 (15.5)
65–74	28 (7.3)
75 and over	25 (6.5)
Mean, years	45.3
Median, years	44.0
Range, years	15–99
Race, no. (%)	
White	367 (95.1)
Black	13 (3.3)
Other	6 (1.6)
Repeat overdose, no. (%)	
0 repeat overdoses	352 (91.2)
1 repeat overdose	26 (6.7)
2 repeat overdoses	7 (1.8)
3 repeat overdoses	1 (.3)
Naloxone dose, mg	
Mean ± SD	1.80 ± .98
Median	2.0
Range	0.5–8.0

Note. No. = number; mg = milligram; SD = standard deviation.

Descriptive Statistics – Sample 2

The size of the second sample was 156, which represented the weeks of the time frame from January 2017 through December 2019. During this time frame, 674 naloxone kits were distributed, and there were 77 repeat overdose events.

Figure 6 shows that there were 30 occurrences (i.e., weeks) of naloxone distributions during the 3-year study period, with as many as 117 kits distributed in a single week. One repeat opioid overdose event occurred in 53 of the weeks, and two repeat events occurred in 12 of the weeks. There were no repeat events recorded in 91 of the weeks. Compared to the prior year, the number of weeks with repeat opioid overdose events increased in 2018 but decreased in 2019. There were 23, 24, and 18 weeks with repeat opioid overdose events in 2017, 2018, and 2019, respectively. An analysis of the naloxone distributions and the repeat opioid overdose events during the 3-year observation period indicated that there was no discernable pattern of association between the two measures. In other words, there were no definitive periods of increases or decreases in the number of repeat opioid overdose events following the distribution of the naloxone kits.

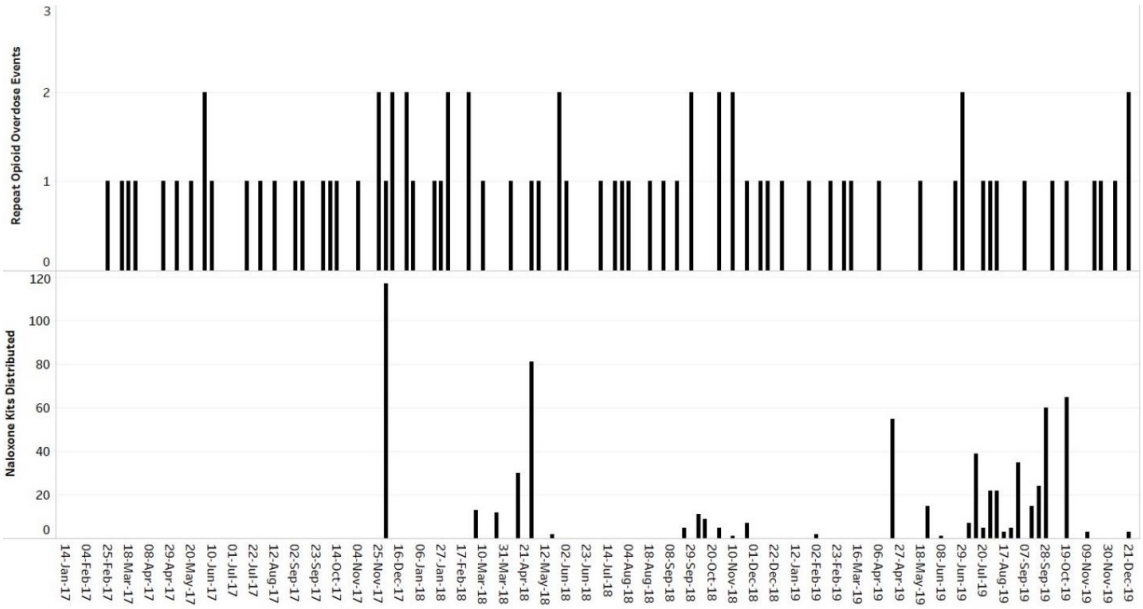

Figure 6. Repeat opioid overdose events and naloxone kits distributed by week (January 2017 to December 2019).

Figure 7 depicts the same data used to generate Figure 6, but the data were aggregated by month to provide a different perspective of the data. A logarithmic line graph was used to accommodate the full range of the quantities of the naloxone kits that were distributed during the study period. A visual examination of the descriptive data indicated no apparent relationship between the distributed naloxone kits and repeat opioid overdose events.

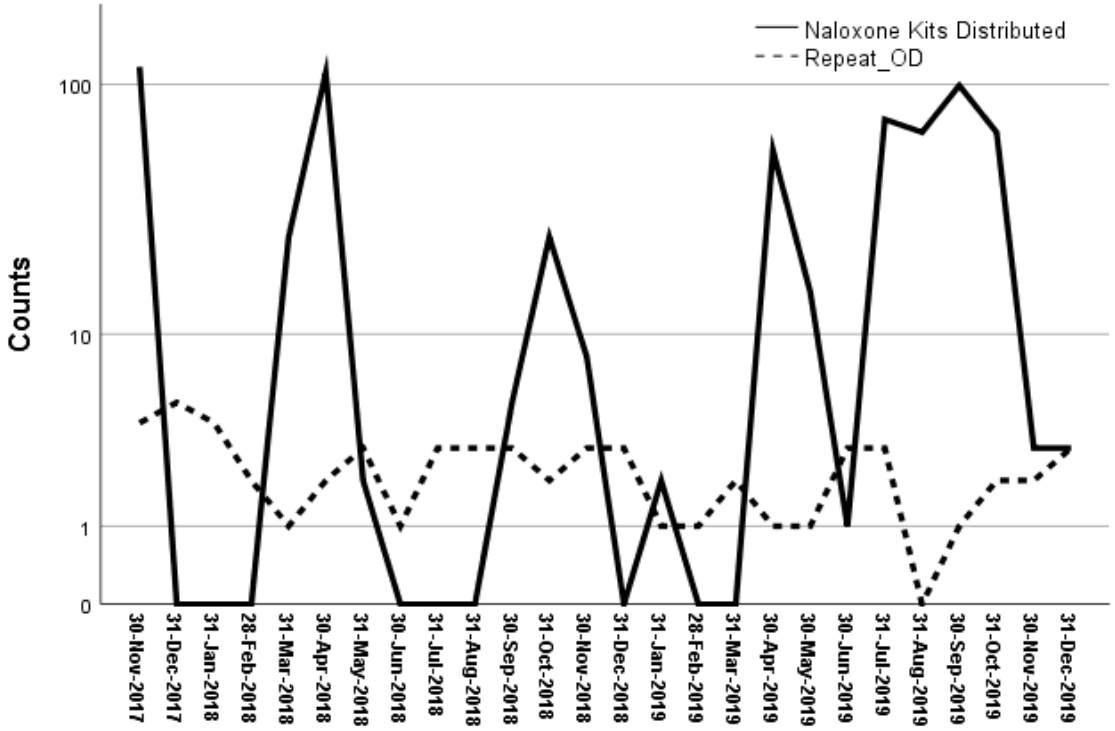

Figure 7. Repeat opioid overdose events and naloxone kits distributed by month (January 2017 to December 2019).

Statistical Assumptions

Multiple logistic regression. Research Questions 1 through 4 were assessed using multiple logistic regression. The accuracy of the statistical test in predicting the odds of the dependent variable on the measures of the independent variable depends on the adherence to assumptions. The assumptions are that (a) there is only one dichotomous dependent variable, (b) the categories of the dependent variable are independent of each other, (c) there are one or more independent variables that are measured on the continuous or nominal scale, (d) the independent variables are not too correlated to each other (i.e., the absence of multicollinearity), (e) the relationship between the independent

variable and the logit (or log odds) of the dependent variable is linear, and (f) the predicted model is consistent with the measured outcome data (Warner, 2013).

The dependent variable, repeat opioid overdose, was measured at the nominal level and had only two categories in which the observations could fall, which satisfied the first two assumptions. Four independent variables were included in the multiple logistic regression analysis: gender (a nominal, dichotomous variable), age (an ordinal variable with eight levels), race (a nominal variable with three categories), and the naloxone dose administered by professional first responders (a continuous variable). The independent variables with their respective levels of measurement satisfied the third assumption.

In evaluating the multicollinearity assumption, SPSS was used to conduct cross-tabulation tests of independence between the three categorical independent variables. A chi-square (or Pearson's chi-square) test or a Fisher's exact test can be used to examine the association or relationship between categorical variables in a cross-tabulation analysis (McHugh, 2013). A Cramer's *V* test is used to measure of effect size of the association between variables. A Fisher's exact test produces a statistic that tends to be more precise than the statistic produced by a chi-square test, but unlike a chi-square test, the Fisher's exact test can only be used for 2-by-2 (or 2 x 2) cross-tabulation tables (McHugh, 2013). A chi-square test assumes that at least five observations (or counts) are in the expected cells of the cross-tabulation process (McHugh, 2013). If the assumption cannot be met, then a Fisher's Exact test must be used instead (McHugh, 2013). The chi-square test, Fisher's exact test, and Cramer's *V* test are statistical procedures within SPSS. The results

of the cross-tabulation tests of independence between the variables are displayed in Table 4.

Table 4

Test of Independence Between Categorial Predictor Variables

Cross tabulation tables	Statistical test	Value	*df*	Sig.
Gender x Age	Chi-square	13.75	6	.03
	Cramer's *V*	.19		.03
Gender x Race	Chi-square	.08	2	.96
	Fisher's exact	.21		1.00
Race x Age	Chi-square	5.64	12	.93
	Fisher's exact	4.92		.98

In a test of independence between predictor variables, the variables are independent of each other if the *p* value of the test statistic is greater than the acceptance level of significance (i.e., greater than .05). As indicated in Table 4, there was no statistically significant association between gender and race ($p = 1.00$) or between race and age ($p = .98$). The test of independence between gender and age was statistically significant, $\chi^2 (6) = 13.75$, $p = .03$, which meant that there was an association between these variables. The Cramer's *V* statistic of this association was .19, which was indicative of a small (or low) association between gender and age as determined by Cohen's (1988) effect size guidelines. A determination was made that the categorial variables of gender, age, and race were not too closely associated with each other, which satisfied the fourth assumption.

The assumption regarding the linearity between the continuous independent variable (i.e., the naloxone dose administered by professional first responders) and the

logit of the dependent variable (i.e., repeat opioid overdose) was assessed using SPSS. A test statistic that is greater than the .05 level of statistical significance means that the independent variable is linearly related to the log odds of the dependent variable. Based on the *p* value of .84 of the Naloxone Dose x Ln-Naloxone Dose interaction term, the variable of the naloxone dose administered by first responders was linearly related to the log odds of the variable of repeat overdose, which satisfied the fifth assumption.

The sixth assumption of whether the model predictions of outcomes in SPSS were consistent with the measured outcomes in the data was assessed using SPSS's Hosmer-Lemeshow goodness of fit (H-L) test. The null hypothesis of the H-L test is that the model is a good fit for predicting observed outcomes. The alternative hypothesis is that the model is poor (i.e., not a good fit) in predicting the observed outcomes (Warner, 2013). A *p* value less than .05 means poor model predictions; therefore, a *p* value greater than .05 is preferred. The SPSS analysis yielded a *p* value of .33, which meant the model was a good fit for predicting the outcomes at an acceptable level. The sixth multiple logistic regression assumption was satisfied.

Poisson regression. Poisson regression was used to answer Research Question 5. Adhering to Poisson regression assumptions is necessary to achieve valid research results that can be used to determine whether an independent variable has a significant effect on a dependent variable. The assumptions associated with Poisson regression require that (a) the dependent variable be represented by count data, (b) the observations on the dependent variable be independent of each other, (c) the mean and variance distributions

be equivalent, and (d) the counts demonstrate a Poisson distribution (Huang & Cornell, 2012).

Count data were collected on the dependent variable (repeat opioid overdose) in Research Question 5, which satisfied the first assumption. The dependent variable was measured at the nominal level and had only two categories (i.e., yes and no). Because each observation could fall in only one of the two categories, the second assumption of independence was met.

The final two Poisson regression assumptions were tested using SPSS. The descriptive statistics indicated that the mean and variance were .49 and .41, respectively. These values were similar and, therefore, satisfied the third assumption.

The null hypothesis of the Kolmogorov-Smirnov test, which is a statistical test in the SPSS software, is that the dependent variable's count data follow a Poisson distribution. The preferred statistic of the Kolmogorov-Smirnov test is one with a *p* value greater than the .05 acceptance level of significance. The SPSS test yielded a Kolmogorov-Smirnov test statistic of .34 with a *p* value of 1.00, which meant that the repeat opioid overdose count data followed a Poisson distribution. The fourth assumption was satisfied.

Statistical Analysis Findings

The results of the multiple logistic regression analysis that was conducted to answer Research Questions 1 through 4 are displayed in Table 5. The full predictive model was not statistically significant, $\chi^2(10) = 15.82$, $p = .11$. The Cox and Snell's $R^2 = .04$ and Nagelkerke's $R^2 = .09$ indicated that the variables of gender, age, race, and the

naloxone dose administered by first responders were weak predictors of repeat opioid overdose and accounted for only 4% and 9%, respectively, of the variance in the dependent variable. The results of the Poisson regression analysis that was conducted to answer Research Question 5 are displayed in Table 6. The full predictive model, compared to the intercept only model, was not statistically significant, $\chi^2(1) = .10$, $p = .75$.

Table 5

Multiple Logistic Regression Analysis of Predictor Variables on Repeat Opioid Overdose

							95% CI	
Variables	*B*	*SE*	Wald	*df*	Sig.	Exp(*B*)	Lower	Upper
Gender (female)	-1.00	.43	5.54	1	.02	.37	.16	.85
Age			1.92	6	.93			
25–34	-.08	.65	.02	1	.90	.92	.26	3.28
35–44	.17	.66	.07	1	.80	1.18	.33	4.28
45–54	-.13	.69	.04	1	.85	.88	.23	3.40
55–64	-.73	.80	.83	1	.36	.48	.10	2.32
65–74	.24	.83	.08	1	.78	1.27	.25	6.39
75 and over	-18.82	7869.35	.00	1	1.00	.00	.00	.
Race			.73	2	.70			
Black	.70	.82	.73	1	.39	2.02	.40	10.10
Other	-18.88	15989.35	.00	1	1.00	.00	.00	.
Naloxone dose	.11	.18	.41	1	.52	1.12	.79	1.59
Constant (intercept)	-2.07	.62	11.09	1	.00	.13		

Note. *B* = regression coefficient; *SE* = standard error; *df* = degrees of freedom; Sig. = significance; Exp(*B*) = exponential of *B*; CI = confidence interval.

Table 6

Poisson Regression Analysis of Naloxone Kits Distributed on Repeat Opioid Overdose

			Wald				95% CI	
Parameter	*B*	*SE*	chi-square	*df*	Sig.	Exp(*B*)	Lower	Upper
(Intercept)	-.71	.12	35.49	1	.00	.49	.39	.62
Naloxone kits distributed	.00	.01	.00	1	.97	1.00	.99	1.01

Note. Dependent variable: Repeat overdose events; *B* = regression coefficient; *SE* = standard error; *df* = degrees of freedom; Sig. = significance; Exp(*B*) = exponential of *B*; CI = confidence interval.

Research Question 1. What is the association between age and repeat opioid overdose?

$H_0$1: There is no statistically significant association between age and repeat opioid overdose.

H_a1: There is a statistically significant association between age and repeat opioid overdose.

Six dummy variables represented the variable of age, and the 15–24 age category was set as the reference category in the multiple logistic regression analysis. As indicated in Table 5, those in the 65–74 and 35–44 age categories had the highest odds ratios. The odds of repeat opioid overdose among those 65–74 were 1.27 times the odds of repeat opioid overdose in the 15–24 category, and the odds of repeat opioid overdose among those 35–44 were 1.18 times the odds of repeat opioid overdose in the 15–24 age category. In other words, those individuals who were 65–74 years of age and 35–44 years of age were 27% and 18%, respectively, more likely to experience a repeat opioid overdose than those individuals who were 15–24 years of age. The odds of repeat opioid

overdose of those in the 25–34, 45–54, and 55–64 age categories were .92, .88, .48, respectively, times the odds of repeat opioid overdose of the reference group, which meant that those individuals were 8%, 12%, 52%, respectively, less likely to experience a repeat opioid overdose than those in the 15–24 age category. The odds ratio of those individuals in the 75 and older age category was close to zero, which meant that they were less likely to experience a repeat opioid overdose than those in the 15–24 age category. The odds ratios of all age categories had *p* values greater than the .05 level of significance, which meant that the null hypothesis was not rejected. There was no statistically significant association between age and repeat opioid overdose. In other words, age was not a significant predictor of repeat opioid overdose.

Research Question 2. What is the association between gender and repeat opioid overdose?

$H_0$2: There is no statistically significant association between gender and repeat opioid overdose.

H_a2: There is a statistically significant association between gender and repeat opioid overdose.

Table 5 indicates that the odds of repeat opioid overdose among females were .37 times the odds of repeat opioid overdose among males, which meant that the odds decreased. Females in the sample were 63% less likely to experience a repeat opioid overdose than males. The odds ratio's *p* value of .02 was less than the .05 level of significance; therefore, the null hypothesis was rejected, and the alternative hypothesis was accepted. There was a statistically significant association between gender and repeat

opioid. In other words, gender was a significant predictor of repeat opioid overdose. The 95% CI [.16, .85] meant that in 95 out of 100 samples, the odds ratio could be as low as .16 and as high as .85.

Research Question 3. What is the association between race and repeat opioid overdose?

$H_0$3: There is no statistically significant association between race and repeat opioid overdose.

H_a3: There is a statistically significant association between race and repeat opioid overdose.

The variable of race was represented by two dummy variables, with the White race set as the reference category. As displayed in Table 5, the odds of repeat opioid overdose among Blacks were 2.02 times the odds of repeat opioid overdose among Whites. Blacks were 102% more likely to experience a repeat opioid overdose than Whites. All race categories had *p* values that were greater than the .05 level of significance, which meant that the odds ratios were not statistically significant. The null hypothesis was not rejected, which indicated that there was no statistically association relationship between age and repeat opioid overdose. In other words, age was not a significant predictor of repeat opioid overdose.

Research Question 4. What is the association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose?

$H_0$4: There is no statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

H_a4: There is a statistically significant association between the naloxone dose administered by professional first responders during opioid overdose events and repeat opioid overdose.

As indicated in Table 5, the variable of the naloxone dose administered had an odds ratio of 1.12, which meant that for every 1 mg increase in the naloxone dose, the odds of repeat opioid overdose increased by a factor of 1.12. In other words, the odds of repeat opioid overdose increased by 12% for every 1 mg increase in the naloxone dose. The *p* value of the odds ratio was .52, which was not statistically significant. The null hypothesis was not rejected, which meant that there was not a statistically significant association between the naloxone dose administered and repeat opioid overdose. The dose of naloxone administered by professional first responders was not a significant predictor of repeat opioid overdose.

Research Question 5. What is the association between the distribution of naloxone rescue kits and repeat opioid overdose?

$H_0$5: There is no statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

H_a5: There is a statistically significant association between the distribution of naloxone rescue kits and repeat opioid overdose.

An odds ratio of 1 means there is no association between the dependent and independent variables (Daniel & Cross, 2013). As displayed in Table 6, the odds ratio of naloxone kits distributed was 1.00, which meant there would not have been an association between repeat opioid overdose and the naloxone kits distributed had the odds ratio been statistically significant. The odds ratio's *p* value of .97 exceeded the .05 level of significance, and the null hypothesis was not rejected. The distribution of naloxone kits was not a significant predictor of repeat opioid overdose.

Summary

Multiple logistic regression was used to analyze the relationship between the independent variables of gender, age, race, and the naloxone dose administered by professional first responders and the dependent variable of repeat opioid overdose. The predictive model was not statistically significant, and the independent variables were weak predictors of the dependent variable. Gender was the only independent variable that had a significant association with repeat opioid overdose. Females in the sample were or 67% ($p = .02$) less likely to experience a repeat opioid overdose compared to the males in the sample.

Poisson regression was used to analyze the relationship between the independent variable of the distribution of naloxone kits and the dependent variable of repeat opioid overdose. The predictive model was not statistically significant. The distribution of naloxone kits was not a significant predictor of repeat opioid overdose.

The interpretations of these findings and the limitations that may affect the interpretations of these findings are discussed in Chapter 5. Implications for positive

social change and recommendations for future research regarding the accessibility of naloxone and repeat opioid overdose are addressed in Chapter 5 as well.

Chapter 5: Discussion, Conclusions, and Recommendations

Quelling the morbidity and mortality associated with opioid dependence, abuse, and overdose remains a significant focus of public health authorities. A multifaceted approach, including increasing access to naloxone, is necessary to effectively address the problem (Rudd et al., 2016). This quantitative, correlational study with a cross-sectional design was conducted to determine the relationship between demographics, naloxone accessibility, and repeat opioid overdose in a Tennessee county. There is a paucity of research evidence that links the accessibility of naloxone with continued risky use behaviors by opioid users, particularly whether those individuals rely on naloxone as a safety net to revive them if they overdose (Rudski, 2016). The intent of this study was to expand the literature regarding what is known about the role of naloxone as an enabler in such behavior.

The results of this current study indicated that there was a statistically significant association between gender and repeat opioid overdose. There was no statistically significant relationship between repeat opioid overdose and the independent variables of age, race, the distribution of naloxone kits, and the naloxone dose administered by professional first responders during opioid overdose events. This chapter includes the interpretation of the findings presented in Chapter 4. Discussions of the limitations of the study and recommendations for future research are also presented. Finally, implications for positive social change are examined, followed by a conclusion of the study.

Interpretation of the Findings

Repeat Opioid Overdose Analysis

Recent studies support the notion that the first nonfatal opioid overdose is often the precursor to repeat overdose. Of the opioid overdose cases treated with naloxone by the EMS responders in this current study, 8.8% represented repeat events, and 2.1% had two or more repeat events. The statistics were similar to those observed by Lasher et al. (2019), which indicated that 13.2% of the patients had a previous opioid overdose, and 2.6% had two or more previous events. The statistics were also similar to those reported by Ray et al. (2018) in their 6-year study of EMS naloxone administration outcomes. Ray et al. found that 9.1% of the patients had at least one repeat opioid overdose, and 2.4% had at least two repeat opioid overdoses.

Contrastingly, the repeat events observed in the current study were lower than those observed by Klebacher et al. (2017), who found that 27.2% of the patients treated with naloxone by EMS first responders had experienced a prior opioid overdose. Various factors could account for the difference in the results, but an obvious factor was the sample size difference. Klebacher et al. used a sample of 2,166 patients, which was over five and a half times greater than the sample size in this current study (N = 386).

Demographics Analysis

A review of the literature indicated that the demographic variables of age, gender, and race were rarely studied as predictors of repeat opioid overdose. Relevant studies contained analyses of the variables in which only descriptive statistics were applied. One study, in which the variables were assessed as predictors, was conducted recently by

Lowder, Amlung, and Ray (2020). Lowder et al. (2020) analyzed race, gender, and age as individual-level predictors of repeat nonfatal opioid overdose and fatal opioid overdose. Lowder et al. found that gender was a statistically significant predictor of repeat opioid overdose in that males were more likely to experience a repeat overdose compared to females ($OR = .86$, $p < .001$). Older age groups (i.e., 35–44, 45–54, 55–64, 65–74, 75–84, and 85 and older) were significantly less likely to experience a repeat overdose compared to the 15–24 age group, but race was not a significant predictor (Lowder et al., 2020).

Consistent with the findings from Lowder et al. (2020), the current study indicated a statistically significant higher likelihood of repeat opioid overdose among males compared to females and that race was not a significant predictor of repeat opioid overdose. Unlike Lowder et al.'s study, however, the results of the current study did not indicate a significant association between the variables of age and repeat opioid overdose. Various factors could account for the difference in the studies' results, including variations in the designs of the studies, behaviors of the populations, sample sizes, and unidentified confounders.

Naloxone Administrations Analysis

Outcomes associated with the administration of naloxone by EMS first responders have been documented in several studies. Lindstrom et al. (2015) compared the frequency of naloxone administrations by EMS providers to emergency department data to determine whether the prehospital administrations of naloxone were indicators of community opioid overdoses. Faul et al. (2017) evaluated national-level EMS data to assess the number of naloxone administrations during an opioid overdose rescue by EMS

first responders. Ray et al. (2018) used county EMS naloxone administration data to study opioid overdose mortality among patients with a recent nonfatal opioid overdose. Cash et al. (2018) also used national-level EMS data in an examination of annual naloxone administration frequencies and opioid-related mortality rates. In a recent study, Ashburn et al. (2020) evaluated the long-term mortality associated with EMS-provided naloxone. None of these studies or others reviewed in the literature focused on the dose of naloxone administered by EMS professionals as a predictor of a repeat opioid overdose. In that respect, the current study was novel.

In the current study, the average dose of naloxone administered to a patient by EMS first responders during an opioid overdose dispatch was 1.8 mg. The finding was similar to that observed by Heavey, Delmerico, et al. (2018) who found that 1.76 mg of naloxone was the average dose administered by professional first responders (i.e., police officers and firefighters). The result was also similar to the mean dose of 2.7 mg of naloxone administered by EMS responders per opioid overdose observed by Lasher et al. (2019). The logistic regression analysis in the current study suggested that the odds of repeat opioid overdose increased, albeit slightly, as the dose of naloxone administered by EMS first responders increased ($OR = 1.12$). The finding, however, was not statistically significant, $p = .52$. Nevertheless, further research on the topic is recommended. Perhaps the use of a larger population and a longer period of analysis would yield different results.

Naloxone Distribution Analysis

Research involving community-based naloxone programs, like the one addressed in the current study, has been conducted to examine outcomes associated with such programs. For instance, the quantities of naloxone refills and overdose reversals among community-based programs were the outcomes studied by Rowe et al. (2015). Walley et al. (2013) focused on opioid-related death rates associated with the programs as the outcome. Additionally, Bagley et al.'s (2018) outcomes of interest included a characterization of family members who accessed community naloxone distribution programs, the types of community naloxone programs the families accessed, and the rescues performed by the family members. Neither of these studies nor others reviewed in the literature included an analysis of repeat opioid overdose as the outcome variable associated with the implementation of the community-based naloxone program. In that respect, the current study was novel.

This study's results indicated no statistically significant relationship between the distribution of naloxone kits through a community-based naloxone program and repeat opioid overdose. A determination of whether naloxone access—using naloxone distributions through a community-based program as a proxy—was a predictor of repeat opioid overdose could not be substantiated by the results of this study. The study's inability to demonstrate a statistically significant finding regarding the role of the naloxone distribution program in the repeat opioid overdose phenomenon was not expected. Nevertheless, the study's finding has value in that it provides a basis for subsequent research on the topic. The use of a larger sample size or a different

population, location, or method of measuring naloxone accessibility may yield a different result that is statistically significant.

Theoretical Framework Analysis

The diffusion of innovations theory was the theoretical framework used to develop and conduct this study. The main emphasis of the theory is diffusion, which Rogers (2003) described as the process by which something new (i.e., an item or idea) is perceived and communicated over time among a group of people. The theory is premised on the interplay of four elements: the innovation, a communication system, time, and a social system of people and organizations (Rogers, 2003). In the current study, naloxone was the innovation, the community-based naloxone program was the venue through which the importance of naloxone was communicated, the progression of naloxone use (measured by the distribution of naloxone kits and EMS-administered naloxone) was the representation of time, and the county observed in this study was the social system.

The diffusion of innovations theory is instrumental in helping to understand behavioral changes in people, particularly how well an innovation is adopted and spread among society members (Rogers, 2003). The theory is also beneficial in understanding that there could be consequences associated with the adoption of an innovation (Rogers, 2003). Examining the progression of naloxone accessibility over time and the nature of repeat opioid overdose as a potential consequence of this accessibility was the aim of this study. Given the aim, the diffusion of innovations theory was befitting as the framework.

One finding of this study suggested that the odds of a repeat opioid overdose might increase with naloxone doses. The finding, however, was not statistically

significant. Another finding of the study indicated that the distribution of naloxone rescue kits did not have a statistically significant influence on the observed repeat opioid overdose events. The comparison of the results of this study to the results of similar studies was limited. The search of the literature did not yield any quantitative studies that addressed how access to naloxone affected opioid use behavior regarding repeat overdose. Only a qualitative study conducted by Heavey, Chang, et al. (2018) was found that addressed the topic. Heavey, Chang, et al. found that some participants contemplated naloxone availability when seeking to amplify their drug high by increasing their heroin dose.

An application of the finding from Heavey, Chang, et al. (2018) could be extended to the current study. For instance, a significant increase in the repeat opioid overdose events following the distribution of naloxone kits might have suggested an increase in the adoption of naloxone use, particularly among sensation seekers. Sensation seekers are individuals who rely on the medication as a safety net as they venture to increase the dose of their opioid of choice (Heavey, Chang, et al., 2018). On the other hand, a significant decrease in the repeat opioid overdose events following the distribution of the kits also might have suggested an increased in the adoption of naloxone use, but for a different reason. The notifications to EMS first responders regarding an opioid overdose event might have been displaced by naloxone rescues performed by bystanders (i.e., family members or friends of the overdose victim) who chose not to notify the EMS, a phenomenon described by Keane et al. (2018). In both scenarios, the influence of confounding, mediating, or moderating factors would be

considered as potential explanations as well. Neither scenario, however, was manifested by the results of this current study. Therefore, the process of innovation adoption described in the diffusion of innovations theory was not supported by the results of this current study.

Limitations of the Study

The intent of this study was to contribute to the literature regarding what is known about the impact of naloxone on opioid use behavior. The results, which were subject to several limitations, should be interpreted with caution. The first limitation was that the correlational design used in this study was observational, which meant the findings did imply a causal effect. Contributing to the design limitation was the inability to identify and include every variable in the study that could have been an effect modifier or confounder.

Second, the measure of repeat opioid overdose was based solely on data from the county EMS, which was necessitated by the inability to access the medical records of the patients treated by the county EMS first responders. In the absence of such information, confirming each repeat overdose case or determining whether a patient suffered from a substance use disorder or other conditions that might have contributed to the emergency event was infeasible. The measure of repeat opioid overdose could have been overstated and could have biased the study results. Alternatively, the repeat opioid overdose cases were just as likely underestimated. Not all of the opioid overdoses in the sampling frame required the administration of naloxone. In many instances, the overdose events involved the use of oxygen—a standard of care practice when patients are not breathing (Banta-

Green et al., 2017)—or other medications as the method of treatment rather than naloxone. Despite the limitation, the use of EMS data offered the advantage of being timesaving and cost-effective because the data were already collected and easier to search and analyze than reviewing numerous hospital charts from multiple hospitals (see Lindstrom et al., 2015).

A third limitation, which was linked to the second limitation, was potential misclassification bias. Lasher et al. (2019) discussed the importance of accurately assessing the rescue situation to ensure the administration of naloxone only when warranted, which can minimize the bias. There could have been misclassifications of an emergency rescue as an opioid overdose when it was not. However, the potential was less likely because the rescue efforts by the county's EMS first responders were governed by prescribed state EMS protocols and guidance from the local EMS medical director. Additionally, adequately defined variables were incorporated in this study to mitigate the concern of misclassification bias.

A fourth limitation involved the measure of naloxone accessibility. The measure was limited to the distribution of naloxone rescue kits and the administration of naloxone by the county's EMS first responders. Local pharmacies, emergency departments, and clinics are other venues that provide naloxone to patients. These venues, however, were not part of the scope of this study. A related limitation was the limited amount of data available from the community-based naloxone program. Naloxone and the related training had only been provided through the program in the county since November 2017.

There were several extended periods (i.e., months) where no kits were distributed, which likely affected the statistical analysis.

Finally, the data were collected and analyzed on a single county in the state. The study's small scale and geographical specificity limited the generalizability of the results to larger populations.

Recommendations

Part of the rationale for using the diffusion of innovations theory as a framework for the current study was the theory's emphasis on unanticipated consequences that might occur with the adoption of an innovation. The phenomenon of repeat opioid overdose was the outcome variable examined as a potential unanticipated consequence of efforts to improve naloxone's accessibility (i.e., the innovation) and reduce opioid overdose mortality. A quantitative approach was used to help address the lack of quantitative studies in the literature in which the phenomenon has been explored.

Although the current study did not indicate a statistically significant association between repeat opioid overdose and the measure of naloxone accessibility, the study may inform the design of future research conducted to examine the relationship. A mixed-methods approach is recommended because the qualitative aspect of the design may provide contextual information regarding the repeat opioid overdose events. Also, an observation period longer than 3 years is recommended. A long-range approach allows for a more in-depth analysis of subtle consequences such as repeat opioid overdose (see Rogers, 2003).

Although a true accounting of repeat opioid overdoses may never be known, the incorporation of data from other sources may help quantify the elusive statistic. Community LEOs represent such a source. The expansion of naloxone access efforts has included equipping LEO first responders with rescue naloxone (NCHRC, n.d.). The LEOs often arrive at emergency scenes involving an opioid overdose and administer naloxone before EMS responders arrive (Davis et al., 2015). Family members and friends of individuals who use opioids—either licitly or illicitly—represent another data source. Naloxone access has been expanded to include family members and friends of opioid users because these laypersons are often first to witness the opioid overdose. Although the naloxone training requires calling 911 in addition to administering the medication, some laypersons do not call, which means many repeat opioid overdoses are likely undisclosed (Bagley et al., 2018). Additional sources of repeat opioid overdose data include emergency department visits and community medical examiner records. Future research should explore incorporating data from these sources to provide a comprehensive measure of repeat opioid overdose.

Community-based naloxone programs represent only one venue that makes naloxone accessible to people who need it. The diffusion of the medication throughout a community via naloxone programs effectively reduces opioid-related mortality (Keane et al., 2018). In this study, naloxone access was restricted to data on the naloxone administrations by EMS first responders and data on the distribution of naloxone rescue kits by a singular community-based naloxone program. Health departments, medical clinics, hospital emergency departments, and pharmacies are other organizations that

provide the medication—in emergency and nonemergency conditions—to individuals who need it as well as to the families and friends of these individuals. Collecting data on naloxone dispensed via these organizations may provide a better measure of naloxone accessibility and, therefore, should be considered in future studies.

Demographic information is important in helping public health practitioners understand the populations at risk of repeat opioid overdose. The sample used in the current study was smaller than other relevant studies in the literature and lacked racial diversity. The demographic variables included in this study (particularly race and age) and their relationship to repeat opioid overdose warrant further research. The research should include the use of data from a larger, racially diverse county or the use of statewide data.

Implications

Providing naloxone to laypersons and training them to recognize and to respond to an opioid overdose are public health efforts aimed at reducing opioid-related mortality (McDonald & Strang, 2016). Such efforts create opportunities to link individuals with substance use disorders to treatment programs (Vivolo-Kantor et al., 2018). J. D. Jones et al. (2017) discussed that the provision of naloxone to people known to abuse drugs is often critically scrutinized as a potential contributor to compensatory drug use. Some people believe that providing naloxone to individuals who misuse drugs such as opioids may cause them to engage in riskier drug behaviors.

Perhaps the opposition to increasing the public's access to naloxone stems from a belief that all individuals suffering from opioid use disorder can quit using opioids at any

time. What is often misunderstood or unknown is that opioid use disorder involves the addiction to opioids, which is a disease that is chronic and recurring (Leshner, 1997). Individuals who use opioids for long periods tend to experience a reduction in the brain's functional connectivity and a volumetric loss of the amygdala, which is responsible for the recognition of fear and social judgment (Rasia-Filho, Londero, & Achaval, 2000; Upadhyay et al., 2010). Discontinuing the use of the opioids may be beyond the self-efficacy of many individuals. Ready access to naloxone may help save the lives of these individuals until they receive substance use treatment.

Research indicates that opioid overdoses that are nonfatal are often precursors to repeat overdoses, which are associated with opioid overdose mortality (Olfson et al., 2018; Ray et al., 2018). The relationship between naloxone use and repeat overdoses involving opioids has rarely been explored. Positive or negative consequences of naloxone adoption were not evident in the results of the current study as was expected in accordance with the diffusion of innovations theory. A follow-up search of the literature revealed a recent study in which the relationship was explored. Ashburn et al. (2020) examined the 1-year mortality associated with patients revived with naloxone by EMS first responders. Ashburn et al. found that of the 72.2% (n = 2,244) overdose patients with improved conditions after being administered naloxone by the EMS professionals, 12.0% of the patients were dead within 1 year. Of the patients who died, the mortality rates of the patients who were treated with naloxone during one, two, and three or more overdose events were 13.0% (n = 234/1,804), 11.5% (n = 17/148), and 6.8% (n = 3/44), respectively (Ashburn et al., 2020).

The repeat opioid overdose statistics from Ashburn et al. (2020) and from this current study provide further evidence that the opioid overdose crisis remains an urgent problem in need of an expeditious solution. Overdoses involving opioids claim the lives of over 47,000 people in the United States each year (Scholl et al., 2019). According to Chen et al. (2019), the annual opioid-related mortality in the United States is projected to reach 82,000 by 2025. The findings of the current study may help prevent the projected statistic.

The use of local data was a strength of this study. Such data are crucial in developing of community programs aimed at prevention (Madah et al., 2017). The administrators of the community-based naloxone program may use the results of this study to gauge the effectiveness of their program. Other public health practitioners may use the findings to assess the prevalence of repeat opioid overdose within the community and to design and implement prevention and intervention programs. Clinicians and pharmacists may use the findings to improve their awareness of naloxone access policies and legislation. The clinicians and pharmacists may also use the findings to help identify patients at risk opioid overdose (and repeat opioid overdose) and to help educate these patients about opioids and naloxone. The local EMS first responders may use the findings for program evaluation purposes. This study provided statistics on repeat opioid overdose and on the characteristics of the opioid overdose patients. Such information may be useful to EMS first responders in evaluating the effectiveness of their protocols used to identify and treat opioid overdose patients. Finally, this study may be used as a reference

source to help educators and the media inform community members about opioid overdose and naloxone.

Conclusion

Naloxone saves lives. Community-based naloxone education and distribution programs are valuable in helping the public understand, recognize, and respond to opioid overdoses using naloxone rescue kits. The broad distribution of naloxone to the general public is not without controversy. The long-term effects of the medication's accessibility on opioid use behaviors are yet to be determined. More research, particularly of a quantitative nature, is needed to help understand the relationship. This study was conducted to provide such information.

Consistent with the literature, this study indicated a statistically significant association between gender and repeat opioid overdose. Among the participants in the study, males were more likely to experience repeat opioid overdose compared to females. Unlike many studies in the literature, this study indicated that the association between the predictor variables of age and race and the outcome variable of repeat opioid overdose was not statistically significant. Additionally, there was not a significant association between naloxone accessibility (i.e., as measured by the distribution of naloxone kits and administration of naloxone by EMS first responders) and repeat opioid overdose. The finding does not mean that a relationship between naloxone accessibility and repeat opioid overdose does not exist, only that the design, methods, and sample used in this study were unable to detect an association that was statistically significant. In light of this finding, further research aimed at exploring the relationship between naloxone

accessibility and repeat opioid overdose is warranted. This study can serve as the basis for such research.

The loss of 47,000 U.S. lives each year to opioid-related overdose (Scholl et al., 2019) is preventable. Finding a solution to the current opioid crisis will require a concerted effort from contributors such as policy makers, health and public health practitioners, researchers, local communities, and law enforcement professionals. As suggested by Wheeler et al. (2012), such comprehensive measures must include educating the public and health care practitioners, strengthening the guidelines for prescribing and monitoring prescription opioids, and ensuring access to naloxone and substance use disorder treatment facilities.

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Appendix: Data Use Agreements

DATA USE AGREEMENT

This Data Use Agreement ("Agreement"), effective as of 1/31/2020 ("Effective Date"), is entered into by and between Craig Booker ("Data Recipient") and [redacted] Emergency Medical Services ("Data Provider"). The purpose of this Agreement is to provide Data Recipient with access to a Limited Data Set ("LDS") for use in research in accord with the HIPAA and FERPA Regulations.

1. Definitions. Unless otherwise specified in this Agreement, all capitalized terms used in this Agreement not otherwise defined have the meaning established for purposes of the "HIPAA Regulations" codified at Title 45 parts 160 through 164 of the United States Code of Federal Regulations, as amended from time to time.

2. Preparation of the LDS. Data Provider shall prepare and furnish to Data Recipient a LDS in accord with any applicable HIPAA or FERPA Regulations

Data Fields in the LDS. **No direct identifiers such as names may be included in the Limited Data Set (LDS).** The researcher will also not name the organization in the doctoral project report that is published in Proquest. In preparing the LDS, Data Provider or designee shall include the **data fields specified as follows**, which are the minimum necessary to accomplish the research:

For each EMS deployment involving a reported or suspected drug overdose, between January 1, 2015, and December 31, 2019, please provide:

(1) The date (i.e., DD/MM/YYYY) of the event,
(2) Whether or not naloxone was administered during the event (i.e., Yes/No),
(3) Total dosage of naloxone in milligrams administered during the event,
(4) The gender of the patient (i.e., Male/Female),
(5) The age in years of the patient,
(6) The race of the patient (i.e., Black, White, Hispanic, etc.), and
(7) Whether or not the EMS deployment for drug overdose was a repeat event for the patient (i.e., Yes/No).

3. Responsibilities of Data Recipient. Data Recipient agrees to:

a. Use or disclose the LDS only as permitted by this Agreement or as required by law;

b. Use appropriate safeguards to prevent use or disclosure of the LDS other than as permitted by this Agreement or required by law;

c. Report to Data Provider any use or disclosure of the LDS of which it becomes aware that is not permitted by this Agreement or required by law;

d. Require any of its subcontractors or agents that receive or have access to the LDS to agree to the same restrictions and conditions on the use and/or disclosure of the LDS that apply to Data Recipient under this Agreement; and

e. Not use the information in the LDS to identify or contact the individuals who are data subjects.

4. Permitted Uses and Disclosures of the LDS. Data Recipient may use and/or disclose the LDS for its research activities only.

5. Term and Termination.

a. Term. The term of this Agreement shall commence as of the Effective Date and shall continue for so long as Data Recipient retains the LDS, unless sooner terminated as set forth in this Agreement.

b. Termination by Data Recipient. Data Recipient may terminate this agreement at any time by notifying the Data Provider and returning or destroying the LDS.

c. Termination by Data Provider. Data Provider may terminate this agreement at any time by providing thirty (30) days prior written notice to Data Recipient.

d. For Breach. Data Provider shall provide written notice to Data Recipient within ten (10) days of any determination that Data Recipient has breached a material term of this Agreement. Data Provider shall afford Data Recipient an opportunity to cure said alleged material breach upon mutually agreeable terms. Failure to agree on mutually agreeable terms for cure within thirty (30) days shall be grounds for the immediate termination of this Agreement by Data Provider.

e. Effect of Termination. Sections 1, 4, 5, 6(e) and 7 of this Agreement shall survive any termination of this Agreement under subsections c or d.

6. Miscellaneous.

a. Change in Law. The parties agree to negotiate in good faith to amend this Agreement to comport with changes in federal law that materially alter either or both parties' obligations under this Agreement. Provided however, that if the parties are unable to agree to mutually acceptable amendment(s) by the compliance date of the change in applicable law or regulations, either Party may terminate this Agreement as provided in section 6.

b. Construction of Terms. The terms of this Agreement shall be construed to give effect to applicable federal interpretative guidance regarding the HIPAA Regulations.

c. No Third Party Beneficiaries. Nothing in this Agreement shall confer upon any person other than the parties and their respective successors or assigns, any rights, remedies, obligations, or liabilities whatsoever.

d. Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

e. Headings. The headings and other captions in this Agreement are for convenience and reference only and shall not be used in interpreting, construing or enforcing any of the provisions of this Agreement.

IN WITNESS WHEREOF, each of the undersigned has caused this Agreement to be duly executed in its name and on its behalf.

DATA PROVIDER	**DATA RECIPIENT**
Signed: Nathan Sweet	Signed:
Print Name: Nathan Sweet	Print Name: Craig H. Booker
Print Title: Director	Print Title: Walden University Student Researcher

DATA USE AGREEMENT

This Data Use Agreement ("Agreement"), effective as of 1/22/2020 ("Effective Date"), is entered into by and between Craig Booker ("Data Recipient") and ASAP of [redacted] ("Data Provider"). The purpose of this Agreement is to provide Data Recipient with access to a Limited Data Set ("LDS") for use in research in accord with the HIPAA and FERPA Regulations.

1. Definitions. Unless otherwise specified in this Agreement, all capitalized terms used in this Agreement not otherwise defined have the meaning established for purposes of the "HIPAA Regulations" codified at Title 45 parts 160 through 164 of the United States Code of Federal Regulations, as amended from time to time.

2. Preparation of the LDS. Data Provider shall prepare and furnish to Data Recipient a LDS in accord with any applicable HIPAA or FERPA Regulations

Data Fields in the LDS. **No direct identifiers such as names may be included in the Limited Data Set (LDS).** The researcher will also not name the organization in the doctoral project report that is published in Proquest. In preparing the LDS, Data Provider or designee shall include the **data fields specified as follows**, which are the minimum necessary to accomplish the research:

(1) The date (i.e., as DD/MM/YYYY) and (2) the quantity (i.e., in milligrams) of naloxone (i.e., Narcan) rescue kits distributed by ASAP of Anderson County between January 1, 2015, and December 31, 2019.

3. Responsibilities of Data Recipient. Data Recipient agrees to:

a. Use or disclose the LDS only as permitted by this Agreement or as required by law;

b. Use appropriate safeguards to prevent use or disclosure of the LDS other than as permitted by this Agreement or required by law;

c. Report to Data Provider any use or disclosure of the LDS of which it becomes aware that is not permitted by this Agreement or required by law;

d. Require any of its subcontractors or agents that receive or have access to the LDS to agree to the same restrictions and conditions on the use and/or disclosure of the LDS that apply to Data Recipient under this Agreement; and

e. Not use the information in the LDS to identify or contact the individuals who are data subjects.

4. Permitted Uses and Disclosures of the LDS. Data Recipient may use and/or disclose the LDS for its research activities only.

5. Term and Termination.

a. Term. The term of this Agreement shall commence as of the Effective Date and shall continue for so long as Data Recipient retains the LDS, unless sooner terminated as set forth in this Agreement.

b. Termination by Data Recipient. Data Recipient may terminate this agreement at any time by notifying the Data Provider and returning or destroying the LDS.

c. Termination by Data Provider. Data Provider may terminate this agreement at any time by providing thirty (30) days prior written notice to Data Recipient.

d. For Breach. Data Provider shall provide written notice to Data Recipient within ten (10) days of any determination that Data Recipient has breached a material term of this Agreement. Data Provider shall afford Data Recipient an opportunity to cure said alleged material breach upon mutually agreeable terms. Failure to agree on mutually agreeable terms for cure within thirty (30) days shall be grounds for the immediate termination of this Agreement by Data Provider.

e. Effect of Termination. Sections 1, 4, 5, 6(e) and 7 of this Agreement shall survive any termination of this Agreement under subsections c or d.

6. Miscellaneous.

a. Change in Law. The parties agree to negotiate in good faith to amend this Agreement to comport with changes in federal law that materially alter either or both parties' obligations under this Agreement. Provided however, that if the parties are unable to agree to mutually acceptable amendment(s) by the compliance date of the change in applicable law or regulations, either Party may terminate this Agreement as provided in section 6.

b. Construction of Terms. The terms of this Agreement shall be construed to give effect to applicable federal interpretative guidance regarding the HIPAA Regulations.

c. No Third Party Beneficiaries. Nothing in this Agreement shall confer upon any person other than the parties and their respective successors or assigns, any rights, remedies, obligations, or liabilities whatsoever.

d. Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

e. Headings. The headings and other captions in this Agreement are for convenience and reference only and shall not be used in interpreting, construing or enforcing any of the provisions of this Agreement.

IN WITNESS WHEREOF, each of the undersigned has caused this Agreement to be duly executed in its name and on its behalf.

DATA PROVIDER	**DATA RECIPIENT**
Signed:	Signed:
Print Name: Stephanie A. Strutner	Print Name: Craig H. Booker
Print Title: Executive Director	Print Title: Walden University Student Researcher