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EXAMINING THE DIFFERENCES IN NARCAN PRESCRIPTION ACROSS STATES

BY

Julie Kramer

A Doctoral project submitted to the faculty of the Medical University of South Carolina
in partial fulfillment of the requirements for the degree
Doctor of Health Administration in the College of Health Professions

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EXAMINING THE DIFFERENCES IN NARCAN PRESCRIPTION ACROSS STATES

BY

Julie Kramer

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Abstract of Dissertation Presented to the
Medical University of South Carolina
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Health Administration

EXAMINING THE DIFFERENCES IN NARCAN PRESCRIPTION ACROSS STATES

by
Julie Kramer

Chairperson: Dr. Jillian Harvey, MPH, PhD

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The problem that we face as a nation is the increasing cases of opiate overdoses (CDC, 2019). Regulations vary across state lines regarding patient needs and prescribing regulations. The current study addresses closing the gaps in opioid use disorder. The overarching research question for this study is—How are Narcan policies related to the drug’s utilization? Other questions in this study will be explored through analysis of national claims data. The study population consist of beneficiaries who have received a prescription for Narcan in 2016. The data includes Narcan prescriptions across state lines as well as the Narcan access law. Using the MarketScan Commercial Database we look at patient claims from states that do not have a Narcan access law and states with a Narcan access law. The study included a total of 3,756,833 prescriptions for naloxone and opioids (14,210, 0.38%), naloxone only (1660, 0.04%), and opioids only (3,740,963, 99.6%) provided to privately insured individuals in 2016. In total, 7448 Naloxone prescriptions by State Policy Status were dispensed in 2016. The odds of receiving a Naloxone prescription in access law states presented 40% greater than the states without the

access law in 2016. This study will add to the literature concerning the misuse of prescription and illicit opioids.

Table of Contents

| | |
|---|----|
| Acknowledgments | 3 |
| Abstract | 4 |
| Table of Contents List of Tables | 7 |
| CHAPTER 1 INTRODUCTION..... | 8 |
| Background and Need | 8 |
| Problem Statement | 9 |
| Research Questions | 9 |
| Population | 9 |
| CHAPTER II SCOPING LITERATURE REVIEW | 10 |
| CHAPTER III METHODOLOGY..... | 24 |
| Research Design | 24 |
| Sample Selection | 24 |
| Data Set Descriptive | 24 |
| Data Analysis | 25 |
| CHAPTER IV RESULTS | 30 |
| CHAPTER V DISCUSSION | 34 |
| References | 38 |
| Appendix A: Raw Data for Descriptive Statistics | 42 |

List of Tables

Table 1. 2018 Drug Overdose Death Rate by State

Table 2. Laws Setting Limits on Certain Opioid Prescriptions

Table 3. States with Narcan Access Laws by Year (2015-2017)

Table 4. Age, Sex and Payments for 3,756,833 Prescription Records from Privately Insured
Individuals with One or More Prescriptions for Naloxone and/or Opioids in 2016

Table 5. Cost and Copays of 3,756,833 Privately Insured Individuals with One or More
Prescriptions for Naloxone and/or Opioids in 2016

Table 6. 2016 Opioid Prescriptions by State Policy Status

Table 7. Odds Ratio of an Opioid Prescription in Access Law States

Table 8. 2016 Naloxone Prescriptions by State Policy Status

Table 9. Odds Ratio of a Naloxone Prescription in Access Law States

CHAPTER I INTRODUCTION

1.1. Background and Need

In the last two decades, there has been a rise in misuse of prescription and illicit opioids (Hodge, Gulinson & Barraza, 2019). During this same time, across the United States, there has been an increase in opioid-induced and opioid-related deaths (Centers for Disease and Control and Prevention [CDC], 2019). Commonly utilized opiates include Vicodin, oxytocin, and heroin. The United States continues to develop programs to reverse opiate overdoses and educate individuals on overdose prevention. Narcan, also known as Naloxone, is a highly effective opiate antagonist and one approach to reversing opiate overdoses. It is a commonly known medication that many doctors and paramedics have used during emergency cases after an opiate overdose and is the only FDA approved method of treatment for potential overdose (Substance Abuse and Mental Health Association [SAMHSA], 2020). In some counties, the public can attend the training, which will teach them how to obtain and use Narcan. In most states, Narcan can be purchased from any pharmacy without a prescription (Hodge, Gulinson & Barraza, 2019). A decade ago, Narcan cost \$1 for the single nasal spray (Hufford & Burke, 2018). The average cost today is \$150 per dose of the nasal spray (Hufford & Burke, 2018). The Narcan auto-injector was approved in 2016 and cost \$4,500 (Hufford & Burke, 2018). Pharmaceutical innovation is not the driving cost of Narcan, but opportunity is (Hufford & Burke, 2018). Costs due to abuse of prescription opioids in the United States as of 2017 consist of \$26 million in health care, along with \$78.5 million in overall cost (Elflein, 2019). One argument against Narcan use, is that it enables continued drug abuse (Elflein, 2019). However, other stakeholder interviews state that intervention may allow that person to live another day (Elflein, 2019).

1.2. Problem Statement

The problem that we face as a nation is the increasing cases of opiate overdoses (CDC, 2019). Regulations vary across state lines regarding patient needs and prescribing regulations. The current study addresses closing the gaps in opioid use disorder.

1.3. Research Questions

The overarching research question for this study was -- How are Narcan policies related to the drug's utilization? In addition, the following sub questions were explored through analysis of national claims data:

1. How do the characteristics of patients who receive a Narcan prescription differ across states that require a prescription and those that do not?
2. Does the likelihood of receiving an opioid prescription differ between states that have a Narcan Access law?
3. Does the dispensing of Narcan vary among states that require a prescription versus those that do not?

1.4 Population

The study population consisted of patients between the ages of 20 to 64 who have an insurance claim for the receipt of Narcan in 2016. This study examined the patient characteristics and prescriptions from commercial insurance claims files.

2 CHAPTER II SCOPING LITERATURE REVIEW

This literature review synthesizes the current research and policy on the opioid epidemic in the United States. This chapter will cover factors driving the opioid epidemic, the impact of opioid use, and policy or medical treatment interventions.

Factors driving the opioid epidemic

In 1980, acute pain was predominantly treated with opioids which are narcotic pain relievers. They were the second-most dispensed drug within the United States at the time (Dasgupta, Beletsky & Ciccarone, 2018). The Carter White House Administration stated, “Diversion, misuse, and abuse of legal drugs may be involved in as many as seven out of ten reports of drug-related injury or death” (Dasgupta, Beletsky & Ciccarone, 2018). A decade later, the US healthcare system was overcome by discoveries of lack of chronic pain treatment, motivating normative practice and policy shifts (Dasgupta, Beletsky & Ciccarone, 2018). The Institute of Medicine attributed the increase in chronic pain management during the chronic pain pervasiveness during the 1990s to the following: (Dasgupta, Beletsky & Ciccarone, 2018).

1. substantial patient expectations for pain relief,
2. musculoskeletal disorders of the aging population,
3. obesity,
4. elevated survivorship post injury and cancer,
5. rising frequency and complications of surgery.

With behavioral pain therapy developing limited coverage, biopharmaceutical manufacturers considered this as an opportunity to formulate extended-release drugs, transdermal patches, nasal sprays, and oral dissolving strips (Dasgupta, Beletsky & Ciccarone, 2018). Innovated pain-modulating implants were also being driven by medical device manufacturers (Dasgupta,

Beletsky & Ciccarone, 2018). By 2000, chronic pain became a big business in the medical industry (Dasgupta, Beletsky & Ciccarone, 2018). Withdrawals became increasingly problematic in these nonopioid analgesics due to cardiovascular risk and acetaminophen toxicity heightened concerns about nonopioid alternatives (Dasgupta, Beletsky & Ciccarone, 2018). It was common for pharmaceutical companies to market improperly by minimizing addiction potential for drugs such as OxyContin and promote off-label use of Actiq, later giving rise to physician kickback schemes, lucrative speaking fees, and lobbying (Dasgupta, Beletsky & Ciccarone, 2018). A small proportion of physicians were dispensing opioids without adequate regard for medical needs (Dasgupta, Beletsky & Ciccarone, 2018). These factors are believed to have contributed to the steady rise in opioid analgesic consumption over the past three decades, causing rates of overdose and addiction to increase (Dasgupta, Beletsky & Ciccarone, 2018).

The second phase started around 2010, with a concern over intertwining of opioid analgesic and heroin use (Dasgupta, Beletsky & Ciccarone, 2018). This remained stable for several years while heroin overdose deaths tripled between 2010 and 2015 (Dasgupta, Beletsky & Ciccarone, 2018). There became an expanded pool of individuals with rising dependency and tolerance to opioid prescription drugs. This led to these individuals transitioning to a more potent and cheaper alternative such as the reformulation of OxyContin (Dasgupta, Beletsky & Ciccarone, 2018). During this phase, clinicians and policymakers reassessed the effectiveness and safety of outpatient use of opioid analgesics (Dasgupta, Beletsky & Ciccarone, 2018).

The third phase developed in late 2013 and continues today (Dasgupta, Beletsky & Ciccarone, 2018). There is an increasingly efficient global supply chains creating the emergence of potent and less bulky products such as illicitly manufactured fentanyl and its analogs, which are increasingly present in counterfeit pills and heroin (Dasgupta, Beletsky & Ciccarone, 2018).

Between 2013 and 2016, deaths related to fentanyl analogs spiked by a shocking 540% nationally (Dasgupta, Beletsky & Ciccarone, 2018). This led to the declaration of as a national public health emergency placing blame on health care (Dasgupta, Beletsky & Ciccarone, 2018). Contradicting the blame placed on health care as the leading cause of addiction, individuals entering drug treatment facilities are now more likely to report having started opioid use with heroin, and not a specific prescription analgesic (Dasgupta, Beletsky & Ciccarone, 2018).

As of 2017, a high percentage of adults in the U.S. contribute the opioid epidemic on the several scenarios (Elfein, 2017). Survey respondents were able to select more than one contributing factor, leading to a complex set of issues to investigate. 79% of adults place majority of the blame on drug dealers selling opioid products. Doctors overprescribing painkillers to patients comes in second with 76% of respondents considering this option as a contributing factor. Individuals without prescriptions acquiring otherwise legal prescription medication make up 75%. Most respondents also believe the pharmaceutical industry is encouraging doctors to prescribe opioids to their patients (72%). Sixty-six percent of respondents stated patients demanding prescriptions to ease their pain as a contributing factor. The smallest category connected the opioid epidemic and the economic crisis of 2008 with 30% of respondents selecting this choice (Elfein, 2017).

Opioid anesthetics remain the most powerful drug class for controlling severe pain, but those medications have potential adverse effects, and pose a risk for misuse, and overdose (Rose, 2018). Poverty and substance abuse can influence the health framework that is extensively known to be significant in responding to public health challenges (Dasgupta, Beletsky & Ciccarone, 2018).

The evidence of chronic pain leading to drug overdose and suicide

Since 1999, age-specific mortality continues to rise from the trends in fatal drug overdose and suicide (Dasgupta, Beletsky & Ciccarone, 2018). This trend is especially predominant among middle-aged White Americans without a college degree, who are now dying earlier, on average, than their parents (Dasgupta, Beletsky & Ciccarone, 2018). Also, on-the-job injuries can contribute to the rise of chronically painful conditions, potentially resulting in a downward spiral of disability and poverty (Dasgupta, Beletsky & Ciccarone, 2018). In the US, the counties with the lowest levels of social capital have the highest overdose rates (Dasgupta, Beletsky & Ciccarone, 2018). Individuals with opioid dependence are likely to have interrupted opioid tolerance and a substantial elevation in overdose risk (Dasgupta, Beletsky & Ciccarone, 2018).

In 2000, chronic pain was big business for pharmaceutical companies and medical device manufacturers (Dasgupta, Beletsky & Ciccarone, 2018). In majority of the country, the counties with the lowest levels of social capital have the greatest overdose rates (Dasgupta, Beletsky & Ciccarone, 2018). Individuals living in low socioeconomic communities were at greater risk to develop chronic pain after car crashes, a process mediated by stress response genes (Dasgupta, Beletsky & Ciccarone, 2018).

Impact of the Opioid Epidemic

Opioid Deaths

One of the greatest public health threats facing the United States today is the misuse of prescription and non-prescription opioids (Hershey, 2019). In 2017, 70,237 opioid overdoses led to injury-related deaths (Hershey, 2019). According to the U.S. Centers for Disease Control and Prevention (CDC), the prescription opioid deaths were five times higher in 2017 than reported in 1999 (Hershey, 2019).

The United States has experienced three distinct waves related to these deaths (Hershey, 2019). The first wave began in 1990s with the overprescribing of prescription medications (Hershey, 2019). The second wave went into effect in 2010 with an increase of overdose deaths due to heroin (Hershey, 2019). The final wave of 2013 occurred with the manufacturing of synthetic opioids such as fentanyl (Hershey, 2019)

Table 1: 2018 drug overdose death rate by state (per 100,000 population) (Elfein, 2020)

| State | Deaths per 100,000 population |
|----------------------|--------------------------------------|
| Alabama | 16.6 |
| Alaska | 14.6 |
| Arizona | 23.8 |
| Arkansas | 15.7 |
| California | 12.8 |
| Colorado | 16.8 |
| Connecticut | 30.7 |
| Delaware | 43.8 |
| District of Columbia | 35.4 |
| Florida | 22.8 |
| Georgia | 13.2 |
| Hawaii | 14.3 |
| Idaho | 14.6 |
| Illinois | 21.3 |
| Indiana | 25.6 |
| Iowa | 9.6 |
| Kansas | 12.4 |
| Kentucky | 30.9 |
| Louisiana | 25.4 |
| Maine | 27.9 |
| Maryland | 37.2 |
| Massachusetts | 32.8 |
| Michigan | 26.6 |
| Minnesota | 11.5 |
| Mississippi | 10.8 |
| Missouri | 27.5 |
| Montana | 12.2 |
| Nebraska | 7.4 |
| Nevada | 21.2 |
| New Hampshire | 35.8 |
| New Jersey | 33.1 |
| New Mexico | 26.7 |
| New York | 18.4 |
| North Carolina | 22.4 |
| North Dakota | 10.2 |
| Ohio | 35.9 |
| Oklahoma | 18.4 |
| Oregon | 12.6 |
| Pennsylvania | 36.1 |
| Rhode Island | 30.1 |
| South Carolina | 22.6 |
| South Dakota | 6.9 |
| Tennessee | 27.5 |
| Texas | 10.4 |
| Utah | 21.2 |
| Vermont | 26.6 |
| Virginia | 17.1 |
| Washington | 14.8 |
| West Virginia | 51.5 |
| Wisconsin | 19.2 |
| Wyoming | 11.1 |

Table 1 depicts the number of drug overdose deaths in the U.S. in 2018, by state (Elfein, 2020). There is considerable variation across the states, ranging from a low of 6.9 deaths per 100,000 in South Dakota to 51.5 in West Virginia. Opioids are considered the primary prescription pain relievers, and heroin is the main driver of overdose deaths (Elfein, 2020).

Health Policy and Treatment Interventions

Emergency Declaration

Various levels of the government announced the opioid crisis as a public health emergency, thereby supplying resources and avoiding undisclosed legal obstacles to response efforts (Hershey, 2019). On October 26, 2017, President Trump advised Acting Secretary Eric Hargan of the Health and Human Services to declare the opioid crisis a national public health emergency (Hershey, 2019). This declaration allowed the federal government to waive specific requirements for Medicaid coverage, supplying prescribing practices and training providers and advancing the National Institutes of Health research funding for treatment for opioid use disorder and overdoses (Hershey, 2019). The United States Department of Health and Human Services developed a five-point comprehensive strategy: (1) better data, (2) better pain treatment, (3) more addiction prevention, treatment, and recovery services, (4) more overdose reversers, and (5) better research (CDC, 2019). On July 17, 2019, the federal government renewed the public health emergency declaration (Hershey, 2019).

Supervised Injection Facilities

Supervised Injection Facilities (SIF) are providing a harm-reduction strategy to preventing opioid-related overdoses and deaths (Hodge, Gulinson & Barraza, 2019). This type of facility provides a safe environment for individuals to use illicit drugs in a clean environment

with immediate access to emergency medical services (Hodge, Gulinson & Barraza, 2019). On February 7, 2019, The Department of Justice filed a lawsuit preventing SIF from opening a facility in Philadelphia, alleging multiple violations of the federal Controlled Substances Act (Hodge, Gulinson & Barraza, 2019).

The evidence supporting Narcan use, versus other interventions

Narcan is an opioid antagonist approved in (1971) by the U.S. Food and Drug Administration (FDA). Narcan reverses the effects of opioid overdose by displacing opioids from their receptors in the brain (Corso &Townley, 2016). By blocking the effects of opioids on the brain, Narcan reverses respiratory depression caused by opioid overdose, which depreciates the possibility of overdose injury or death, including complications caused by non-fatal overdose such as brain and organ damage (Corso &Townley, 2016). Unlike other interventions, Narcan can act quickly and immediately knocking opiate drugs off the receptors in the brain and reversing the effects of opiate overdose (“What Are the Key Differences Between Naltrexone and Naloxone?”, 2020). This works best in particular issues where an individual has decreased heart rate and breathing rate (“What Are the Key Differences Between Naltrexone and Naloxone?”, 2020). Narcan differs from other various treatments in a way that it is not designed to be used for long-term treatment of the abuse of opiate drugs, but instead it is commonly used as an emergency treatment for people who overdose on opiate drugs (“What Are The Key Differences Between Naltrexone And Naloxone?”, 2020).

Various leading agencies and organizations, such as the Substance Abuse and Mental Health Services Administration (SAMHSA), CDC, the World Health Organization, the American Public Health Association, the American Medical Association, and the American Pharmacists Association recommend expanding access to Narcan as a key evidence-based

strategy to reduce opioid overdose injury and death (Corso &Townley, 2016). Addiction services includes stages of treatment, along with detoxification, rehabilitation, and recovery (Corso &Townley, 2016).

- **Detoxification** is a medical intervention that manages acute intoxication and withdrawal with the objective of minimizing physical harm. This process can be broken down into three stages: patient evaluation and assessment, physical and psychosocial stabilization, and facilitating entry into treatment.
- **Rehabilitation** (also referred to as treatment) incorporates ongoing primary medical and behavioral health care with ongoing assessments of the individual's physical and psychosocial status as well as environmental risk factors.
- **Recovery** (also referred to as maintenance) continues the behavioral health support present in the rehabilitation component of care and includes refining and fortifying strategies to encourage prevention against relapse.

Medication-assisted treatment (MAT) incorporates the use of FDA-approved medications to assist individuals overcome alcohol or opioid dependence (Corso &Townley, 2016). The FDA has approved three various medications for the treatment of opioid dependence: methadone, buprenorphine, and naltrexone (Corso &Townley, 2016). The difference between the three types of medications is the way they interact with opioid receptors within the brain: (Corso &Townley, 2016).

- **Methadone** is an opioid *full agonist*. It fully binds with the opioid receptors within the brain and serves as a replacement therapy for heroin or prescription opioids. With creating tolerance, methadone treats symptoms of drug withdrawal and blocks euphoria.

- **Buprenorphine** is an opioid *partial agonist*. Partial agonists produce comparable effects as a full agonist, but the effects are less inducive and involves a “ceiling effect” that predominantly increases the safety profile of the medication while reducing the risk of misuse or dependency.
- **Naltrexone**, similar to naloxone, is an *opioid antagonist*. Opioid antagonists inhibit opioid receptors within the brain, which means an individual using an opioid post taking naltrexone will not feel the opioid’s effects.

The fears, drawbacks, side effects of Narcan use

Side effects

Narcan may precipitate sudden opioid withdrawal in physically dependent individuals; signs and symptoms may include body aches, fever, sweating, sneezing, yawning, nausea, vomiting, sweating, lacrimation, rhinorrhea, cramping, insomnia, chills/hot flashes, piloerection, tachycardia, anxiety, restlessness, irritability, tremulousness, hypertension, seizures, and cardiac arrest (Narcan Nasal Spray Side Effects, 2019). With the use of Narcan nasal spray, nasal dryness, nasal edema, nasal congestion, and nasal inflammation were common adverse reactions that were reported (Narcan Nasal Spray Side Effects, 2019).

Policy and Narcan Overdose Prevention Laws

State lawmakers are developing innovative policies-engaging health, criminal justice, human services, and other sectors- to address the public health crisis while also providing appropriate access to pain management (NCSL, 2019). The access to Narcan can be limited by state laws and regulations (“Preventing Opioid Overdoses Among Rural Americans”, 2018). State laws and regulations have a direct influence on the availability of overdose reversing medicines. Currently, the changing laws continue to increase the access to naloxone in all fifty

states and the District of Columbia. All states have legislation designed to enhance layperson Narcan access, along with protections for health care providers who prescribe or dispense Narcan and for bystanders who administer the drug. The Good Samaritan laws were passed on July 15, 2017, within 40 states and the District of Columbia that protects bystanders who report overdoses from facing their own possible drug possession charges (“Preventing Opioid Overdoses Among Rural Americans”, 2018).

Legislation limited opioid prescriptions in the early 2016, with Massachusetts passing the first law in the nation (National Conference of State Legislatures {NCSL}, 2019).

Massachusetts set a seven-day supply limit for initial (first-time) opioid prescriptions. By the end of 2016, seven states also passed legislation reducing opioid prescriptions, and the movement continued in 2017. More than 30 states expressed over 130 bills related to opioid prescribing in 2016 and 2017. According to NCSL’s tracking, 33 states had executed legislation with limitations, guidance or requirements related to opioid prescribing by October 2018 (NCSL, 2019).

Some state laws allow doctors to provide Narcan to any person who could administer the drug to another person who is at risk for an overdose, also known as third-party prescriptions (“Preventing Opioid Overdoses Among Rural Americans”, 2018). Evidence shows that educating family and/or close friends about the warning signs of overdose and the ability to use Narcan to help the prevention of overdose (“Preventing Opioid Overdoses Among Rural Americans”, 2018).

State laws and regulations determine whether all emergency personnel can administer Narcan to patients (“Preventing Opioid Overdoses Among Rural Americans”, 2018). With the various levels of training for emergency personnel, and emergency medical technicians in rural

areas, they are more likely to be trained to provide only basic-level life support (“Preventing Opioid Overdoses Among Rural Americans”, 2018). This practice law determines which emergency personnel can administer Narcan (“Preventing Opioid Overdoses Among Rural Americans”, 2018).

Senate Enrolled Act 406-2015, “Aaron’s Law”, was signed into law April 2015. This Indiana law allows citizens to obtain a prescription for Narcan if they believe someone they know is at risk of an opioid overdose (Indiana Department of Labor [Indiana], 2020). Aaron’s Law allows Narcan to be available to on-site medical staff, school nurses, supervisors, and anyone responsible for someone at risk of an overdose (Indiana Department of Labor, 2020). Aaron Sims was a young man who lost his battle with a heroin addiction (Indiana Department of Labor, 2020) and the Senate Enrolled Act 406-2015, “Aaron’s Law” was named after Sims (Indiana, 2020).

Most of the legislation limits first-time opioid prescriptions to a determined number of days’ supply, seven days is most common, with some laws set limits at three, five or 14 days (NCSL, 2019). Almost half of the states with limits specify that they apply to treatment of acute pain, and most states set exceptions for chronic pain treatment (NCSL, 2019). Most of the states focus on general opioid prescribing; Alaska, Connecticut, Indiana, Louisiana, Massachusetts, Nebraska, Pennsylvania, and West Virginia also set limits for minors (NCSL, 2019). These laws set limits for any opioid prescription (versus the initial opioid prescription for adults) and may also identify various requirements, including discussing opioid risks with the minor and parent or guardian (NCSL, 2019).

Instead of setting opioid prescription limits in statute, several state laws directed or authorized other entities to do so (such as New Hampshire, Ohio, Oregon, Vermont, Virginia,

Washington, and Wisconsin) (NCSL, 2019). These entities consist of the department of health/state health/state health official, or provider regulatory boards such as the board of medicine, nursing and/or dentistry (NCSL, 2019). Rhode Island and Utah have prescribing limits in statute and allowing other entities to adopt prescribing policies (NCSL, 2019).

State leaders continue to tackle prescription drug misuse with various approaches (NCSL, 2019). While attempting to avert or intervene earlier in misuse, addiction and overdose, states have established various laws regarding prescription drug monitoring programs, access to Narcan, pain clinic regulation, provider education and training (NCSL, 2019). NCSL tracks these bills in the Injury Prevention Database, which shadows six categories of legislation aimed at preventing prescription opioid misuse (NCSL, 2019).

The government from different levels disclosed the opioid crisis as a public health emergency, allowing various resources available across state lines in efforts to reduce opioid related deaths (Hersey, 2019). There are numerous contributing factors throughout this period that places blame on the opioid epidemic. Controlling severe pain is one main purpose for the dispensing of an opioid anesthetic. With this type of controlled substance other health concerns develop such as adverse effects which leads to misuse and overdose (Rose, 2018).

A vast majority of legislation has applied limits on controlled substances to prohibit the ability overdose and addiction. Changes in access laws pertaining to Narcan vary in every state throughout the years. In 2015, six times greater opioids per resident were dispensed in the highest-prescribing counties than in the lowest-prescribing counties (Centers for Disease Control and Prevention, 2017). County-level characteristics, such as rural versus urban, income level, and demographics, are only a third of the differences (Centers for Disease Control and

Prevention, 2017). It is common that patients receive different care depending on where they live. Characteristics of counties with greater opioid prescribing consist of the following:

- Small cities or large towns
- Higher percent of white residents
- More dentists and primary care physicians
- More people who are uninsured or unemployed
- More people who have diabetes, arthritis, or disability

CHAPTER III METHODOLOGY

3.1 Research Design

A descriptive study was conducted to explore how state-level Narcan policies are related to the drug's utilization. The following sub questions were explored through analysis of national claims data:

1. How do the characteristics of patients who receive a Narcan prescription differ across states that require a prescription and those that do not?
2. Does the likelihood of receiving an opioid prescription differ between states that have a Narcan Access law?
3. Does the dispensing of Narcan vary among states that require a prescription versus those that do not?

3.2 Sample Selection

The data sample included 3,756,833 prescriptions from 1.6 million privately insured individuals between the ages of 20 to 64 who have an insurance claim for the receipt of and opioid drug and/or Narcan in 2016.

3.3 Data Set Description

This study uses a sample of retrospective claims for patients with opioid prescriptions and naloxone dispensing from an original study by Dr. Kit Simpson (unpublished data). The retrospective claims analysis utilized data from the Truven Health MarketScan Commercial Database in the calendar year 2016. This data includes Narcan prescriptions and patient demographics for all 50 states. This MarketScan Commercial Database includes patient claims from states that do not have a Narcan access law and states with a Narcan access law. MarketScan is a registered trademark of Truven Health Analytics Inc., an IBM Company.

3.4 Data Analysis

Data were extracted from public data sources on laws and regulations in place for dispensing Narcan. We elected to use the year 2016 because that year marked a major change nationally in recognition of opioid as a major epidemic problem. For each time, period patient claims were coded as 0 if the state does not have a Narcan access law, and 1 for states with a Narcan access law (Table 3). The analysis compared the number of Narcan prescriptions across states with and without Narcan access laws. Descriptive comparisons between the Access Law Group and Non-Access Law was conducted using t-tests for normally distributed continuous variables and Chi Squared Tests or Fishers Exact Test for Categorical Variables, as appropriate. Key outcomes include: Narcan prescriptions filled for patients that live in access law states, Opioid prescriptions for patients that live in access law states, and characteristics of patients who receive a Narcan or opioid prescription. The data covers individuals from various geographic areas across the United States.

Table 2: Laws Setting Limits on Certain Opioid Prescriptions (2018) (Source: NCSL, StateNet, 2019)

| State | Statutory limit: 14 days | Statutory limit: 7 days | Statutory limit: 5 days | Statutory limit: 3-4 days | Statutory limit: Morphine Milligram Equivalents | Direction/authorization to other entity to set limits or guidelines | No Limit |
|----------------------|--------------------------|-------------------------|-------------------------|---------------------------|---|---|----------|
| Alabama | No | No | No | No | No | No | Yes |
| Alaska | No | No | No | No | No | No | No |
| Arkansas | No | Yes | No | No | No | No | No |
| Arizona | No | No | Yes | No | Yes | No | No |
| California | No | No | No | No | No | No | Yes |
| Colorado | No | Yes | No | No | No | No | No |
| Connecticut | No | Yes | No | No | No | No | No |
| Delaware | No | No | No | No | No | No | Yes |
| District of Columbia | No | No | No | No | No | No | No |
| Florida | No | No | No | Yes | No | No | No |
| Georgia | No | No | No | No | No | No | Yes |
| Hawaii | No | Yes | No | No | No | No | No |
| Idaho | No | No | No | No | No | No | Yes |
| Illinois | No | No | No | No | No | No | Yes |
| Indiana | No | Yes | No | No | No | No | No |
| Iowa | No | No | No | No | No | No | Yes |
| Kansas | No | No | No | No | No | No | Yes |
| Kentucky | No | No | No | Yes | No | No | No |
| Louisiana | No | Yes | No | No | No | No | No |
| Maine | No | Yes | No | No | Yes | No | No |
| Maryland | No | No | No | No | No | No | Yes |
| Massachusetts | No | Yes | No | No | No | No | No |
| Michigan | No | No | No | No | No | No | Yes |
| Minnesota | No | No | No | Yes | No | No | No |
| Mississippi | No | No | No | No | No | No | Yes |
| Missouri | No | Yes | No | No | No | No | No |
| Montana | No | Yes | No | No | No | No | No |
| Nebraska | No | No | No | No | No | No | Yes |
| Nevada | Yes | No | No | No | Yes | No | No |
| New Hampshire | No | No | No | No | No | Yes | No |
| New Jersey | No | No | Yes | No | No | No | No |
| New Mexico | No | No | No | No | No | No | Yes |
| New York | No | Yes | No | No | No | No | No |
| North Carolina | No | No | Yes | No | No | No | No |
| North Dakota | No | No | No | No | No | No | Yes |
| Ohio | No | No | No | No | No | Yes | No |
| Oklahoma | No | Yes | No | No | No | No | No |
| Oregon | No | No | No | No | No | Yes | No |
| Pennsylvania | No | Yes | No | No | No | No | No |
| Rhode Island | No | No | No | No | Yes | Yes | No |
| South Carolina | No | Yes | No | No | No | No | No |
| South Dakota | No | No | No | No | No | No | Yes |
| Tennessee | No | No | No | Yes | Yes | No | No |
| Texas | No | No | No | No | No | No | Yes |
| Utah | No | Yes | No | No | No | Yes | No |
| Vermont | No | No | No | No | No | Yes | No |
| Virginia | No | No | No | No | No | Yes | No |
| Washington | No | No | No | No | No | Yes | No |

| | | | | | | | |
|---------------|----|-----|----|----|----|-----|-----|
| West Virginia | No | Yes | No | No | No | No | No |
| Wisconsin | No | No | No | No | No | Yes | No |
| Wyoming | No | No | No | No | No | No | Yes |

Table 2 illustrates the state’s primary opioid prescription limit and does not include additional limits on certain providers or in certain setting (NCSL, 2019). Most of the legislation limits first-time opioid prescriptions to a certain number of days’ supply- seven days is most common, with few laws allow limits at three, five or 14 days (NCSL, 2019).

Table 3: States with Narcan Access Laws by Year (2015-2017) (Source: Naloxone Overdose, 2017)

| State | 2015 | 2016 | 2017 |
|----------------------|------|------|------|
| Alabama | No | Yes | Yes |
| Alaska | No | No | Yes |
| Arkansas | No | No | Yes |
| Arizona | No | Yes | Yes |
| California | Yes | Yes | Yes |
| Colorado | Yes | Yes | Yes |
| Connecticut | Yes | Yes | Yes |
| Delaware | Yes | Yes | Yes |
| District of Columbia | Yes | Yes | Yes |
| Florida | No | Yes | Yes |
| Georgia | Yes | Yes | Yes |
| Hawaii | No | No | Yes |
| Idaho | No | Yes | Yes |
| Illinois | Yes | Yes | Yes |
| Indiana | No | Yes | Yes |
| Iowa | No | No | Yes |
| Kansas | No | No | Yes |
| Kentucky | Yes | Yes | Yes |
| Louisiana | No | Yes | Yes |
| Maine | Yes | Yes | Yes |
| Maryland | Yes | Yes | Yes |
| Massachusetts | Yes | Yes | Yes |
| Michigan | Yes | Yes | Yes |
| Minnesota | Yes | Yes | Yes |
| Mississippi | No | Yes | Yes |
| Missouri | No | No | Yes |
| Montana | No | No | Yes |
| Nebraska | No | Yes | Yes |
| Nevada | No | Yes | Yes |
| New Hampshire | No | Yes | Yes |
| New Jersey | Yes | Yes | Yes |
| New Mexico | Yes | Yes | Yes |
| New York | Yes | Yes | Yes |
| North Carolina | Yes | Yes | Yes |
| North Dakota | No | Yes | Yes |
| Ohio | Yes | Yes | Yes |
| Oklahoma | Yes | Yes | Yes |
| Oregon | Yes | Yes | Yes |
| Pennsylvania | Yes | Yes | Yes |
| Rhode Island | Yes | Yes | Yes |
| South Carolina | No | Yes | Yes |
| South Dakota | No | No | Yes |
| Tennessee | Yes | Yes | Yes |
| Texas | No | Yes | Yes |
| Utah | Yes | Yes | Yes |
| Vermont | Yes | Yes | Yes |
| Virginia | Yes | Yes | Yes |
| Washington | Yes | Yes | Yes |
| West Virginia | No | Yes | Yes |
| Wisconsin | Yes | Yes | Yes |
| Wyoming | No | No | Yes |

All jurisdictions now have laws that address accessibility to Narcan for individuals at risk of opiate overdose (Naloxone Overdose Prevention, 2017). These laws allow distribution beyond the traditional prescriptions (Preventing the Consequences of Opioid Overdose: Understanding Naloxone Access Laws, 2018). This allows individuals to obtain Narcan with flexibility (Preventing the Consequences of Opioid Overdose: Understanding Naloxone Access Laws, 2018). Table 3 illustrates the changes in access laws regarding Narcan within every state through the years of 2015-2017. Starting in 2015 there were more jurisdictions that did not have Narcan access laws. The following year in 2016 more jurisdictions came onboard implementing the new law. By 2017, every state set into motion the Narcan access law. This was a major turning point for the country.

Protection of Human Subjects

This study was classified as non-human subjects by the Medical University of South Carolina Institutional Review Board.

CHAPTER IV RESULTS

This study was a retrospective review of data sets constructed for a previous study of opioid use. The data were originally obtained from Truven Health MarketScan Commercial Database from January through December 2016. This study examined how state-level Narcan policies are related to the drug’s utilization. The data sample included 3,756,833 prescriptions from privately insured individuals between the ages of 20 to 64 who have an insurance claim for the receipt of and opioid drug and/or Narcan in 2016. The Statistical Package for Social Sciences (SPSS) version 24 was used to analyze the data.

The study included a total of 3,756,833 prescriptions. Of these, 14,210 (0.38%) were for naloxone and opioids, 1,660 (0.04%) for naloxone only, and 3,740,963 were for opioids only (99.6%). Data were extracted from prescriptions provided to 1.6 million privately insured individuals in 2016 (Table 4). There was a statistically significant difference ($p < .0001$) in the mean age of those receiving a prescription for Naloxone & Opioids (49.3) versus Naloxone Only (43.7) or Opioids Only (42.6).

Table 4. Age, Sex and Payments for 3,756,833 Prescription Records from Privately Insured Individuals with one or more prescriptions for Naloxone and/or opioids in 2016

| Characteristics | Naloxone & Opioids n=14,210 (0.38%) | Naloxone Only n=1,660 (0.04%) | Opioids Only n=3,740,963 (99.6%) | p-value |
|-------------------|--|----------------------------------|-------------------------------------|---------|
| Age Mean \pm SD | 49.3 \pm 10.9 | 43.7 \pm 14.5 | 42.6 \pm 14.8 | <0.0001 |
| Female Sex N (%) | 8,675 (61.0) | 1,000 (60.2) | 2,174,401 (58.1) | <0.0001 |

The mean prescription copayment for Naloxone and Opioids (14,210, 0.38%) was \$37 (SD \$143) versus \$43 (SD \$275) for Naloxone only (1,660, 0.04%) (Table 5). The mean ingredient cost is higher for Naloxone and Opioids (\$1,060 + 1,782) versus Naloxone only (\$997

$\pm 1,847$). The payment means and standard deviations were similar to ingredient cost at $\$1,061 \pm 1,783$ for Naloxone and Opioids and $\$989 \pm 1,839$ for Naloxone only (Table 5).

Table 5: Cost and Copays of 3,756,833 Privately Insured Individuals with one or more prescriptions for Naloxone and/or opioids in 2016

| Naloxone Cost Variables in Dollars | Naloxone & Opioids n=14,210 (0.38%) | Naloxone Only n=1,660 (0.04%) | Opioids Only n=3,740,963 (99.6%) | p-value |
|------------------------------------|--|----------------------------------|-------------------------------------|---------|
| Copay Mean \pm SD | $\$37 \pm 143$ | $\$43 \pm 275$ | NA | |
| Ingredient Cost Mean \pm SD | $\$1,060 \pm 1,782$ | $\$997 \pm 1,847$ | NA | |
| Payment Mean \pm SD | $\$1,061 \pm 1,783$ | $\$989 \pm 1,839$ | NA | |

Table 6: 2016 Individuals with Opioid and Naloxone Prescriptions by State Policy Status

| | States Without Narcan Access Law | States with Narcan Access Law | Total | P Value |
|--|--|-------------------------------------|-------|----------|
| Opioid & Naloxone Prescriptions n (%) | 350 (5.2%) | 6363 (94.8%) | 6713 | p<0.0001 |

In total, 6713 individuals with opioid prescriptions were also dispensed Naloxone across the United States in 2016 (p<0.0001) (Table 6). There is a statistically significant difference in the number of prescriptions between states with and without the Narcan access law (p<0.0001). Approximately 94.8% of the prescriptions for Opioids and Naloxone were dispensed in states with the Narcan Access Law, while only 5.2% of the prescriptions were dispensed in states without the Narcan Access Law.

Table 7: Likelihood of patients having prescriptions for both Opioid and Naloxone Prescription in Access Law States, adjusting for a state, rate of overdoses, and patient sex, age, and rural residence

| | Odds | 95% CI | P Value |
|-----------------------|-------------|---------------|----------------|
| Access Law | 1.33 | 1.194-1.482 | p<0.0001 |
| Overdose Death | 0.986 | 0.983-0.989 | p<0.0001 |
| Age | 1.034 | 1.032-1.036 | p<0.0001 |
| Sex (Male) | 0.842 | 0.802-0.885 | p<0.0001 |
| Rural | 0.790 | 0.732-0.853 | p<0.0001 |

Patients with an Opioid prescription who live in an Access Law state are 33% more likely to receive Naloxone than patients in states without this legislation. However, for all patients in the data set, patients in states with high overdoses are 1.4% less likely to get Naloxone, as are male and those living in the rural area of the state. However, older patients are more likely to get a Naloxone prescription, with 3% times higher odds of Naloxone per year increase in age.

Table 8: 2016 Naloxone Prescriptions by State Policy Status

| | Without Narcan Access Law | States with Narcan Access Law | Total | P Value |
|-------------------------------------|----------------------------------|--------------------------------------|--------------|----------------|
| Naloxone Prescriptions n (%) | 370 (5%) | 7078 (95%) | 7448 | p<0.0001 |

In total, 7448 Naloxone prescriptions were dispensed in 2016 (p<0.0001) (Table 8). Approximately 5% of the Naloxone prescriptions were dispensed in states without the Narcan Access Law. The states with Narcan Access Law delivered 95% of the Naloxone prescriptions which were dispensed without regards to opioid prescriptions.

Table 9 Odds Ratio of a Naloxone Prescription in Access Law States

| | Odds | 95% CI | P Value |
|-----------------------|-------------|---------------|----------------|
| Access Law | 1.400 | 1.26-1.555 | p<0.0001 |
| Overdose Death | 0.989 | 0.985-0.992 | p<0.0001 |
| Age | 1.030 | 1.028-1.032 | p<0.0001 |

| | | | |
|-------------------|-------|-------------|----------|
| Sex (Male) | 0.850 | 0.811-0.890 | p<0.0001 |
| Rural | 0.819 | 0.762-0.880 | p<0.0001 |

The odds of receiving a Naloxone prescription in Access Law states were 40% greater than the states without the Access Law in 2016 (Table 9) (p<0.0001). This relationship was observed after we controlled for factors, such as a state’s rate of opioid overdoses, and patient demographics, including age, sex, and rural residence. The overdose odds of receiving Naloxone was 1.1% lower in for states with higher rates of opioid overdoses. Across all states, patient age increases the likelihood of receiving Naloxone (OR 1.03). Males have 15% lower odds of a Naloxone prescription. Patients living in rural areas of the country have a 18.1% lower likelihood of getting a Naloxone prescription compared to urban residents living in urban areas.

Chapter V Discussion

This study revealed various important findings, signifying the influence of state Narcan Access Laws on the dispensing of Naloxone and on Opioid-related deaths. In 2016, less than 1% of the study population received a prescription for Naloxone and Opioids or Naloxone only (Table 4). Of the 3,756,833 Opioid prescriptions dispensed, 15,870 Naloxone prescriptions were dispensed. Of the 15,870 Naloxone prescriptions dispensed, 95% were in states with a Narcan Access Law. Those living in a state with a Narcan Access Law were 33% more likely to receive a Naloxone prescription, as were those who were older and female. Additionally, the cost of copays for Naloxone and Opioids was less expensive than the copay for Naloxone alone. When examining individuals with an opioid prescription, there were an extremely low number who also had a Naloxone prescription. However, there was a 40% greater chance of receiving a prescription for Naloxone only in states with the Narcan Access Law. Those residing in rural areas of the country had 18.1% lower odds receiving a prescription for Naloxone only.

Limitations

This research is subject to several limitations. The data were collected from insurance claims data, hence the potential for errors in coding. We were unable to account for differences across state that may also impact Naloxone prescriptions that were not related to patient characteristics or the Narcan Access laws, such as stigma. Finally, the study examines patients age 20-64 with commercial insurance. Results may not be generalizable to other ages or payer types, such as Medicare, Medicaid, or self-pay.

Policy and Research Implications

There are many factors that contribute to rising overdose rates. Previous studies have shown a rise in opioid analgesic and heroin use and overdose (Dasgupta, Beletsky & Ciccarone, 2018). In 2016 deaths related to fentanyl analogs spiked by a shocking 540% nationally (Dasgupta, Beletsky & Ciccarone, 2018). Also, previous studies illustrate that counties with the lowest levels of social capital have the greatest overdose rates (Dasgupta, Beletsky & Ciccarone, 2018). As elucidated in this study, states with higher rates of Opioid overdoses had lower odds of receiving lifesaving Narcan, and those residing in rural areas had decreased odds of receiving a Naloxone prescription. Due to these findings, policy makers should consider laws to increase awareness and education regarding Opioid-use disorder and provide access to supportive services, including Naloxone (Faul, Dailey, Sugerma, Sasser, Levy & Paulozzi, 2015).

While Narcan access policies differ across states, it is unclear which policy components are most helpful in improving access to Naloxone. Future research should examine the differences in Narcan Access Laws across states to examine if specific policy interventions are more effective. Research should also focus on disparities amongst states and rural residence to ensure consistency in adherence to best practices regarding the treatment of opioid use disorder. Further, across all states, male patients and those living in rural communities are less likely to get Narcan prescriptions filled. Future policy work should examine access to Narcan prescriptions for rural residents and male patients, especially for individuals who may be at risk of overdose.

Conclusion

In the last two decades, there has been a rise in misuse of prescription and illicit opioids (Hodge, Gulinson & Barraza, 2019). During this time, across the United States, there has been an increase in Opioid-induced and Opioid-related deaths (Centers for Disease and Control and Prevention [CDC], 2019). We are presently facing an Opioid-use Disorder (OUD) with high rates of deaths from opioid overdoses. The treatment of OUD is complex but the prevention of deaths from opioid overdoses is relatively simple even for lay individuals if they have access to naloxone (Narcan) a drug that reverses opioid overdoses. Narcan is an opioid antagonist approved in (1971) by the U.S. Food and Drug Administration (FDA). Narcan reverses the effects of opioid overdose by displacing opioids from their receptors in the brain (Corso &Townley, 2016). Leading agencies, such as the Substance Abuse and Mental Health Services Administration (SAMHSA), CDC, the World Health Organization, the American Public Health Association, the American Medical Association, and the American Pharmacists Association recommend expanding access to Narcan as a key evidence-based strategy to reduce opioid overdose injury and death (Corso &Townley, 2016). However, access to Narcan can be limited by state laws and regulations (“Preventing Opioid Overdoses Among Rural Americans”, 2018).

The availability of naloxone differs greatly across the fifty states. Results of this study indicate that Narcan policies are related to the drug’s utilization, as commercially insured patients who lived in states with Narcan Access Laws were more likely to receive a Naloxone prescription. States with higher rates of deaths from opioid overdoses had lower likelihood of having Narcan dispensed. The characteristics of patients who receive a Narcan prescription differ in both age and rural residence compared to those who do not. Being male or living in a rural area was associated with decreased odds of receiving a Naloxone prescription.

Results of this study also indicate that Narcan Access Laws are associated with differences in prescribing behaviors. Thus, access to the life-saving medicine is not equal across states in the U.S. Few studies have been conducted with specific focus on the opioid epidemic across state lines and spanning decades. What we have learned through this and prior studies is that the opioid epidemic has continuously advanced over the years. While the effect is modest, there appears to be a relationship between Narcan Access laws, increased Narcan prescriptions, and overdose deaths.

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Appendix A: Raw Data Descriptive
Statistics

| Characteristics | Naloxone & Opioids n=14,210 (0.38%) | Naloxone Only n=1,660 (0.04%) | Opioids Only n=3,740,963 (99.6%) | p-value |
|---------------------|--|----------------------------------|-------------------------------------|---------|
| Age Mean ± SD | 49.3 ± 10.9 | 43.7 ± 14.5 | 42.6 ± 14.8 | <0.0001 |
| Female Sex N (%) | 8,675 (61.0) | 1,000 (60.2) | 2,174,401 (58.1) | <0.0001 |

| Naloxone Cost Variables in Dollars | Naloxone & Opioids n=14,210 (0.38%) | Naloxone Only n=1,660 (0.04%) | Opioids Only n=3,740,963 (99.6%) | p- value |
|---------------------------------------|--|----------------------------------|-------------------------------------|-------------|
| Copay Mean ± SD | \$37 ± 143 | \$43 ± 275 | NA | |
| Ingredient Cost Mean ± SD | \$1,060 ± 1,782 | \$997 ± 1,847 | NA | |
| Payment Mean ± SD | \$1,061 ± 1,783 | \$989 ± 1,839 | NA | |

| | Without Narcan Access Law | States with Narcan Access Law | Total | P Value |
|---|------------------------------|-------------------------------------|-------|----------|
| Opioid Prescriptions n (%) | 350 (5.2%) | 6363 (94.8%) | 6713 | p<0.0001 |

| | Odds | 95% CI | P Value |
|-----------------------|-------|-------------|----------|
| Access Law | 1.33 | 1.194-1.482 | p<0.0001 |
| Overdose Death | 0.986 | 0.983-0.989 | p<0.0001 |
| Age | 1.034 | 1.032-1.036 | p<0.0001 |
| Sex (Male) | 0.842 | 0.802-0.885 | p<0.0001 |
| Rural | 0.790 | 0.732-0.853 | p<0.0001 |

| | Without Narcan Access Law | States with Narcan Access Law | Total | P Value |
|---|------------------------------|-------------------------------------|-------|----------|
| Naloxone Prescriptions n (%) | 370 (5%) | 7078 (95%) | 7448 | p<0.0001 |

Appendix A: Raw Data Descriptive
Statistics Continue

| | Odds | 95% CI | P Value |
|-----------------------|-------------|---------------|----------------|
| Access Law | 1.400 | 1.26-1.555 | p<0.0001 |
| Overdose Death | 0.989 | 0.985-0.992 | p<0.0001 |
| Age | 1.030 | 1.028-1.032 | p<0.0001 |
| Sex (Male) | 0.850 | 0.811-0.890 | p<0.0001 |
| Rural | 0.819 | 0.762-0.880 | p<0.0001 |