The Effect of State Legislation on Opioid Prescribing Practices, Mortality, and Emergency Departments

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Daelon Morais Date

# Table of Contents

## Acknowledgments

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# Abstract

The purpose of this project is to assess how states' laws regarding prescribing opioids affects the prescribing rates of opioid medications. Currently, there is a lack of research on types of prescription opioid related legislation and their effectiveness at combating the opioid epidemic. The effects of state laws regarding opioids on prescribing and mortality rates should be examined since providers' prescribing practices are influenced by local, state, and federal regulations and can affect the rate of opioid abuse.

In this investigation, I conducted a secondary data analysis of using the categories of opioid-related state legislature. The numerical data I used was comprised of state prescribing rates both in the emergency department and in general, and drug-related mortality rates with data provided by the Center of Disease Control and Prevention. Cluster analysis was performed on the numerical data to see if the groups aligned with distinct categories of opioid-related legislation.

The results of the data analysis showed that states that required physical exams for an opioid prescription were correlated with a higher opioid prescribing rate. States that have an overdose emergency law are associated with both a high opioid related emergency department visitation rate and high opioid overdose mortality rate.

An investigation into the effectiveness of opioid-related laws can help policymakers create more effective regulations and guidelines that are bolstered by data analysis. Additionally, states can assess which categories of laws are suitable to implement and direct funding towards.

Some states have had varying levels of success with their legislature and they could be used as models for further reform. Since emergency departments receive a large proportion of opioid overdoses, analyses of legislation affecting the treatment of overdose emergencies can help produce protocols that reduce mortality and possibly increase rehabilitation rates. Furthermore, this may lead to larger scale investigations into opioid prescribing regulations in different regions and at varying jurisdiction to lead to wider scale reform.

**Key Terms**: opioids, physician, beliefs, regulations, guidelines, prescribing

# Introduction

A major issue plaguing society today is the opioid epidemic. Opioid abuse can lead to poor coordination, depression, poor decision making, and death by overdose (Kosten & George, 2002). Opioid abuse presents in many forms ranging from the misuse of prescription opioids to illicit drug use and has social, political, and economic implications. Illicit drug use or prescription abuse of opioid pain medication has led to the death of over 400,000 people in the United States from 1999 to 2017 (Center of Disease Control [CDC], 2020). It has been estimated that the epidemic cost $696 billion in 2018 due to healthcare, treatment, lost productivity, and criminal justice expenses. Over 130 people die every day due to opioid overdose according to the Center of Disease Control and Prevention.

Over 80% of current heroin users first misused prescription opioids (National Institute on Drug Abuse [NIDA], 2019). Efforts to curtail this abuse of prescription opioids has unfortunately driven those addicted to seek out medication in other forms leading to an increase in the use of heroin and fentanyl, illicit, highly addictive, and potent opioids

The tightened regulation of prescription opioids causes users to find substitutes. Aside from on-going research into the development of a new class of pharmaceuticals that would have the same pain-relieving effects of opioids without the addictive drawbacks, the many efforts to abate the opioid epidemic include: recovery programs; education; access to and reducing the stigma surrounding naloxone (an opioid overdose-reversing drug); and revising the practice of

pain management, a multi-disciplinary branch of medicine that treats patients living with chronic pain (CDC, 2020).

Emergency departments can play a major role in the opioid epidemic. About 80% of cases referred to the emergency department are related to pain (Abdolrazaghnejad et al., 2018). The diagnoses that typically receive opioid prescriptions are musculoskeletal back pain, abdominal pain, and extremity fractures and sprains. The most commonly prescribed opioids are hydrocodone, tramadol, and oxycodone (Guarisco and Salup, 2018). Some researchers such as Axeen et al. (2018) argue that emergency departments do not significantly contribute to the opioid epidemic and therefore should not be the focus of opioid-reduction efforts. However, the emergency department sees a high volume of visits, about 139 million visits, and the nature of the cases as stated previously typically require some form of pain management (CDC, 2020). Furthermore, there is the possibility that initial exposure to opiates in the emergency department may be the precipitant to opioid addiction (Butler et al, 2016). In addition to treating pain, the emergency department also sees those who abuse opioids when complications due to overdosing arise. The CDC reported from July 2016 to September 2017, there were over 140,000 suspected opioid-involved overdose emergency department visits (CDC, 2020).

The objective of one study was to assess the impact of state laws that restrict opioid duration for opioid-naïve patients to seven days. The researchers used data from a commercial claims database from Connecticut, Massachusetts, and New-York, the first 3 states to implement such a law. The researchers found that the implementation of the law resulted in a significant reduction in the number of opioid prescriptions longer than 7 days only in Connecticut and Massachusetts (Dave et al., 2019). While there are federal and state laws that regulate some

prescribing practices, many hospitals have additional institutional guidelines that reflect such laws and may be more specific in wording. The effectiveness of a hospital's new clinical practice policy designed to reduce the number of controlled substance prescriptions was the subject of one research article by Chacko and colleagues (2017). The study used a 2012-2014 retrospective chart review of the number of prescriptions, pills, and dosages prescribed. Their analysis showed that there was an overall decrease in the number of prescriptions after the policy was implemented although the number of pills stays the same and the dosage had a small decrease (Chacko et al., 2017).

Based on the research above, it is reasonable to conclude that there is a need for further research into opioid-related policy and opioid-related clinical practice guidelines in the emergency department. To that end, the objectives of this study are to: (1) analyze opioid and other drug related state laws; (2) determine their effect on prescribing patterns; (3) determine their effect on preventing opioid abuse mortality and; (4) recommend changes based on the data. I will perform a secondary data analysis of the laws affecting the ongoing opioid epidemic using opioid prescribing rates and overdose mortality as indicators. In my study, I propose to conduct an analysis of several categories of state laws regarding the prescribing of opioids. Some states have had varying levels of success with their legislature and they could be used as models for further reform. This research can be used by states to assess which types of laws are suitable to implement and fund.

# Background

## Pain

When asked why they sought medical attention,  patients most frequently identify pain as the primary reason. It is defined as an unpleasant sensory and emotional experience that usually is associated with structural or tissue damage. Unfortunately, pain is highly subjective since the perception of pain by individuals is influenced by psychological, situational, and emotional factors and past experiences. Pain is commonly assessed using the PQRST framework which stands for palliative/provocative factors (factors that make the pain worse or better), quality (description of the pain), radiation (location of the pain), severity, and temporal factors (change of pain over time). Severity is typically assessed using a pain scale from 0 to 10 where 0 is no pain and 10 is “the worst pain possible.” However, this assessment, although quantitative, is highly subjective and is based on the individual patient’s past experiences and motivations (Hui and Bruera, 2014).

## Overview of Opioids and Addiction

An opioid is an analgesic agent which means it is a medication that reduces pain. In the 19th century, morphine, the most commonly known opiate, was isolated from opium, which comes from the opium poppy flower, and was used in the clinical setting. The 20th century brought about the advent of more powerful, synthetic and semi-synthetic opioids. Semi-synthetic opioids include hydrocodone, oxycodone, oxymorphone, and hydromorphone (Jones et al.,

2018). Synthetic opioids include methadone and fentanyl. Fentanyl is about 50 times stronger than heroin and about 100 times stronger than morphine (CDC, 2020).

However, in addition to reducing pain, opioids can also reduce consciousness and produce euphoria thus increasing their abuse potential . Opioid addiction arises since they activate reward pathways in the brain that result in the feeling of pleasure. The brain creates conditioned associations between drug use, pleasure, and memories. For that reason, environmental cues can trigger cravings (Pathan and Williams, 2012).

According to Kosten and George (2002), over time, repeated exposure alters the user's brain so that the user feels the need to take escalating doses of the opioids also known as opioid tolerance. Furthermore, over time, neurons adjust to opioid use by increasing noradrenaline to counter the effects of opioids. Then when opioids are introduced, the body produces the normal amount of noradrenaline resulting in a normal feeling; however, when no opioids are present, there is an excess of noradrenaline resulting in restlessness, anxiety, and muscle cramps. Opioid use becomes daily to avoid the negative consequences of opioid withdrawal. This combination of tolerance and dependence cumulates into addiction (Kosten and George, 2002).

Treatment for addiction can include methadone, a long-acting opioid medication. While it results in dependence, it reduces tolerance and cravings. This decreases relapse rates and allows patients to focus on developing a healthy lifestyle. Buprenorphine can also be used since it does not produce as much euphoria or respiratory depression as other opioids including methadone. Additionally, at moderate levels, the effects of buprenorphine plateau reduce the risk of overdosing (Kosten and George, 2002).

**History of The Opioid Epidemic**

In the early 20th century, in response to heroin abuse and morphine dependence, there was an emergence of opiophobia, or an avoidance of opioids when treating pain. Patients with persistent, unexplained pain were stigmatized as drug abusers or pretending to be ill. In 1986, the World Health Organization introduced the Cancer Pain Monograph to highlight the undertreatment of cancer pain. This, in turn, opened up the medical community to questioning of clinical practices in regards to treating pain due to other illnesses aside from cancer. The consensus of the public and patient advocacy groups such as the American Pain Society was that healthcare providers were not doing enough to alleviate patient suffering. Due to this push from the public, the government relaxed regulation to increase opioid prescribing (Jones et al., 2018).

Before the 1990s, opioids had been used to treat chronic and acute pain, but in the 1990s, they were increasingly heavily prescribed. This was due to assurances from pharmaceutical companies that they were not addictive and increasing concerns that physicians were not managing chronic pain appropriately. This combination of the pharmaceutical industry's deception and concern for mismanaged chronic pain spurred the overreliance and misuse of prescription opioids (CDC, 2020). Several manuscripts and unverified articles also pushed the notion that the "therapeutic use of opiate analgesics rarely results in addiction (Jones et al., 2018)." This omission of information and concern spurred the misuse of prescription opioids (CDC, 2020).

In 1997, the Federation of State Medical Boards in the United States developed the "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain" which

encouraged healthcare providers to provide adequate pain management for all patients and reduced regulatory scrutiny. In the early 2000s, the American Pain Society and the Joint Commission pushed for the creation of the Standards for Assessment and Management of Pain which pushed the idea of "pain as the fifth vital sign"; essentially, making pain management a crucial factor of treatment in healthcare. It mandated the routine screening of all individuals for pain regardless of their chief complaint. Healthcare providers were obligated to treat their patients' pain until their patients reported zero pain. From 1997 to 2002, OxyContin prescriptions increased from 670,000 to 6.2 million (Health and Human Services [HHS], 2020). Furthermore, physicians were required to meet quality assurance benchmarks and were pushed by institutions to keep their patients satisfied. Publicity campaigns funded by pharmaceutical companies pushed treatment with opioids as the humane option. If physicians failed to prescribe opioids, they faced public outrage and possible litigation for undertreatment and unnecessary suffering. In 2005, hospitals were required to participate in the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) Survey. This, coupled with the Patient Protection and Affordable Care Act of 2010 (PPACA) increased the role of patient satisfaction in the Hospital Value Based Purchasing program. The Hospital Value Based Purchasing program was designed to incentivize hospitals to provide high-quality care. However, this meant that patient satisfaction was linked to reimbursements. This lead to an over-prescription of opioids out of fear of losing access to federal funding if patients reported low satisfaction with their pain management on their surveys (Jones et al., 2018).

**Strategies to Combat the Opioid Epidemic**

The many efforts to abate the opioid epidemic include recovery programs, education, access to naloxone (an opioid overdose-reversing drug), and revising the practice of pain management (CDC, 2020). Like the CDC, the U.S. Department of Health and Human Services has a plan of increasing access to recovery programs and naloxone as well as increasing public health surveillance, pain and addiction research, and pain management education. Similarly, the National Institute of Health (NIH) is working alongside pharmaceutical companies and researchers to develop strategies to manage chronic pain, investigate the development of a new class of pharmaceuticals that would have the same pain-relieving effects of opioids without the addictive drawbacks, and increase access to overdose reversal drugs (NIDA, 2019).

### *Prescription Drug Monitoring Programs*

However, prescription drug monitoring programs (PDMPs) and the National All Schedules Prescription Electronic Reporting Act (NASPER) (2005) have been instituted to help combat the epidemic. NASPER was enacted to establish controlled substances monitoring programs such as PDMPs (Manchikanti 2005). PDMPs are state-composed electronic databases that monitor controlled substances, such as opioids, prescriptions. The database includes patient and prescribing behavior. For example, a pharmacist can track how many prescriptions a patient has filled in a certain time period. They can flag instances where someone may be abusing opioids if they are filling them too frequently or "pharmacy shopping.". There are currently PDMPs in 49 of the 50 states (Missouri the only state without a statewide PDMP), however an analysis of PDMP implementation in Texas found that the program has not had a "consistent pattern of discernible change" on opioid-related outcomes (Finley et al., 2017).

## Types of Opioid-Related State Legislation

Laws and guidelines can have a significant effect on opioids prescribed. Policies and strategies such as utilization of Prescription Drug Monitoring Programs (PDMP), pain clinic legislation, insurance strategies, motivational interviewing, and patient education in the clinical setting have the strongest evidence for being effective. Researchers investigating possible strategies suggest limiting the dosage and duration of prescriptions, beginning treatment with short-acting opioids, and making use of PDMPs (Haegerich et al., 2019). Broida et al. (2017) analyzed the clinical guidelines regarding prescribing opioids in the emergency department across all 50 states in the U.S and found that there were 67 different guidelines regarding limiting opioid prescriptions, 59 guidelines to prevent opioid abuse, 34 guidelines related to addiction, and 24 guidelines regarding community resources. This underscores the needs for increased clarity and uniformity in addressing this issue. Moreover, they found that while most states' guidelines discouraged opioid prescribing in the emergency department, only 17 states' contain emergency department-specific guidelines highlighting the need for integration of policy decisions with actual clinical practice (Broida et al., 2017).

### *Prescription Drug Time and Dosage Limit Laws*

As of 2015 forty-seven states and the District of Columbia have enacted laws that set dosage or time limits on the prescribing or dispensing of controlled substances. These laws limit opioid prescriptions either in terms of hour's or day's supplied or by the number of pills. The idea behind this law was that patients could not get addicted to opioids if they were used acutely. Furthermore, it would reduce the likelihood of abuse if there were not many leftover pills. As an

example of this type of law, Florida statute states: “the amount or quantity of drug dispensed shall not exceed a [thirty-four]-day supply or standard course of treatment unless subject to the specific limitations in this rule.” The CDC recognizes high-dose prescribing as a high-risk prescribing practice that contributes to the overdose epidemic (CDC, 2018). A review article found that long-term opioid therapy is associated with an increased possibility for opioid abuse or dependence compared to no opioid prescription. Furthermore, it found that higher-dose (6.1%) chronic therapy compared to lower-dose (0.7%) chronic therapy had higher rates of opioid abuse or dependence (Chou et al., 2015).

### *Physical Examination Requirements*

Most examination laws require a ”physical examination” as the basis for prescribing and dispensing a controlled substance (CDC, 2018). Physical exams and checking patients’ past medical history are necessary in order to determine if opioids are necessary to treat the pain, if the patient is a drug seeker, or if there are underlying causes of the pain that have been overlooked. For example, Indiana law states: “[A] physician shall not prescribe, dispense, or otherwise provide, or cause to be provided, any controlled substance to a person who the physician has never personally physically examined and diagnosed (CDC, 2018).”

### *Doctor Shopping Laws*

Doctor shopping is defined as a patient seeing multiple treatment providers, either during a single illness episode or to procure prescription medications illicitly (Sansone and Sansone, 2017). All fifty states and the District of Columbia require disclosure of controlled substances or prescriptions received within a concurrent time frame according to a summary of state laws by

the CDC (CDC, 2018). The Drug Abuse Warning Network (DAWN) claims that emergency department visits involving prescription opioids increased by 146% from 2005 to 2011 (Simone, 2017). Some doctor shopping laws require patients to report to their provider if they have received either any controlled substance from another practitioner in a time frame. California law dictates that "[n]o person shall obtain or attempt to obtain controlled substances, or procure or attempt to procure the administration of or prescription for controlled substances; (1) by fraud, deceit, misrepresentation, or subterfuge; or (2) by the concealment of a material fact (CDC, 2018)."

### *State Laws Related to Prescription Drug Overdose Emergencies*

According to the CDC, 18 states allow immunity from prosecution or mitigation in prosecution or at sentencing when an individual seeks help for themselves or for another person (CDC, 2018). The probability of surviving a drug overdose is associated with how fast medical treatment is received. Rates of calling for medical assistance among drug users is between 21% and 63% according to a study on post-overdose interventions (Wagner, 2019). These laws were enacted in order to remove obstacles to appropriate overdose treatment and make it more likely that emergency services are called.

## Role of the Emergency Departments

As stated previously, a large proportion of cases presented to the emergency department are related to pain. Treatment of pain is not to be delayed and typically, for acute mild to moderate pain, aspirin, acetaminophen, or nonsteroidal anti-inflammatory drugs (NSAIDs) are administered to relieve it (Bonnie, Ford,  and Phillips, 2017). However, these drugs have a

ceiling effect on their pain relief which means that at a certain dose and above, their effect on pain stops increasing. These drugs do not produce tolerance or physiological dependence and the majority of them can be purchased over-the-counter. Opioids are effective for moderate to severe pain and do not have a ceiling effect. There is a lack of analgesics besides the two noted which severely limits physicians' ability to manage pain and reduce risk to their patients. Furthermore, pain management can be a quality-of-care indicator, so although NSAIDs can theoretically have the same effect as opioids after 20 to 30 minutes, opioid agents are used to treat acute moderate to severe pain and are faster acting. (Abdolrazaghnejad et al., 2018). One study found that about 1 in every 6 patients the emergency department received an opioid pain reliever (Barnett et al., 2017).

**Prescribing Patterns**

Although there are guidelines and laws in place to reduce the amount and type of opioids prescribed, there is still a reliance on physicians and other healthcare providers to follow them. Clinical practice guidelines and protocols are enacted in order to limit variation in medical treatment, increase quality of care, and encourage the practice of evidence-based medicine. Unfortunately, according to one systematic review patients received 54.9% of recommended care (Ebben et al., 2013 ). Factors that can influence adherence to clinical practice guidelines and protocols can include the patient's age, race, sex, insurance status, and current disease.

The reliance on physicians to follow policies creates variation in practice. Physicians have varying views on the opioid epidemic, whose responsibility it is, what and how to prescribe medication, the effectiveness of regulation, and other beliefs and attitudes. In one study, the

researchers analyzed 4 years of Medicare data, sorting emergency medicine physicians by low and high-intensity prescribing behaviour and analyzing whether the type of physician resulted in long or short term opioid use (Barnett et al., 2017). The researchers showed that while there was a large variation in physician prescribing practices, there was little difference in the impact of high versus low-intensity prescribing on long-term outcomes. All of these factors can impact how a physician decides what and how much to prescribe. A study found that emergency medicine physicians regarded guidelines as institutional policies that were modeled after state/federal policies. The physicians' views towards the guidelines tended to match their general view towards opioids and any sort of guidelines (Kilaru *et al.,* 2014).

As stated above, emergency departments have been recognized as sources for opioid addiction intervention. According to the NIH, one of the major risk factors for an opioid overdose death is having a previous overdose. Research has shown that if drug users receive medications to treat their opioid use disorder during a visit for a non-fatal overdose, they will be at reduced risk for another overdose in the future. Several studies have shown that initiating opioid use disorder treatment while the patient is still not yet discharged decreases their risk for a repeat overdose (NIDA, 2019). A Journal of the American Medical Association study showed that buprenorphine initiation in the emergency department was associated with improved treatment engagement and decreased opioid use in the 30 days after discharge (NIDA, 2019).

A randomized clinical trial tested the efficacy of different interventions for addressing opioid-dependence in the emergency department ranging from screening and referral for treatment to initiating treatment with buprenorphine/naloxone. Over a course of about four years, the trial enrolled 329 patients. The researchers found that emergency department-initiated

buprenorphine treatment significantly increased patient engagement in addiction treatment compared to brief intervention and referral alone. (D'Onofrio et al., 2015).

## Counter Arguments

### *Policy*

The increase in regulation for prescription opioids has driven some of those who are addicted to opioids to turn to illicit sources of drugs in the form of heroin and fentanyl. This effect, known as the "balloon effect," is a common criticism of the United States' drug policy. When a balloon is squeezed, the air does not disappear, but rather it moves to an area of less resistance (Bonnie, Ford, and Phillips, 2017). In the same way, those with opioid use disorder lose access to legal forms of opioid, they are diverted to more potent, illegal drugs that are unrestricted. Policymakers have to take into account this effect when implementing legislation and assess the risks and benefits of increasing restrictions.

### *Emergency Department's Contribute to the Opioid Epidemic*

Contrary to the idea that policy changes in the emergency department can impact the opioid epidemic, several research studies have demonstrated that emergency departments do not significantly contribute to the opioid epidemic in the first place (Jeffery et al., 2018). The study by Axeen et al. (2018) found that the number of opioids prescribed has drastically increased 471% from 1996 to 2012. However, a large proportion of those prescriptions were office-based with a positive, steady trend over the years. On the other hand, the proportion from the emergency department was small and decreasing over the years. Furthermore, the notion that

high-risk opioid abusers frequently used emergency departments as a source of opioids has been disabused. There is an abundance of emergency departments and lack of an established continuance of care; many people believe that these conditions allow those who abuse opioids to easily obtain prescriptions. However, a study found that the top 5% of annual opioid consumers procured 87.8% of their opioids from office-based settings rather than emergency departments where 2.4% of opioids were sourced. Moreover, chronic opioid users obtain 82% of their opioids from office-based settings compared to 4.5% from emergency departments (Axeen et al. 2018). This led to the conclusion that the emergency department is not a significant source of opioids in the opioid epidemic.The researchers argue that efforts to reduce the quantity of opioids prescribed should be focused on office-based settings rather than in the emergency department.

However, the emergency department and efforts to curtail opioid prescribing/use in the emergency department would still be beneficial to pursue. According to the CDC, in 2017, there were 139.0 million visits to an emergency department, 40.0 million of those were injury-related. In 2016, 25% of adult emergency department patients were either given opioids, prescribed opioids, or both (Rui, 2019). The sheer volume of visits lends itself to the idea that even a small change in opioid policy in emergency departments could potentially have large effects.

Another study sought to determine if exposure to opioids in the emergency department could precipitate opioid addiction. The researchers recruited 59 heroin/opioid abusing patients from a local teaching hospital that reported that they were first prescribed opioids from an ED. They then surveyed this population to find what proportions then sought opioid addiction treatment, used opioids regularly, and started to use opioids for non-medical purposes. They found that 10 (29%) of them reported that they were first exposed to opioids in the emergency

department (Butler et al, 2016). A study based on retrospective data analysis of survey data concluded that since emergency departments negligibly contribute to the opioid epidemic compared to office-based settings, resources in the emergency department should be redirected from reducing the number of opioids to identifying individuals with a high-risk of opioid abuse and referring them to treatment (Axeen et al., 2018). Based on these articles, it can be reasoned that although the emergency department is not a significant contributor to the opioid epidemic, it can still play a role in combating the epidemic by treating patients with opioid addiction and dependence according to the NIH (NIDA], 2019).

As evidenced by the articles cited above, there is plenty of literature regarding possible solutions and policies regarding the opioid epidemic. However, there is a lack of evaluation of the efficacy of such policies. Without this information, it is not known whether these laws have produced their intended results and if they need more funding, to be modified, or removed altogether.

# Methodology

As part of this thesis, I conducted a secondary data analysis to look for associations between implementation of opioid-related state laws and prescribing patterns to determine if regulation decreases healthcare providers' proclivity to prescribe opioid medications. Physicians not only have to contend with the possibility of undertreatment of pain, but now, due to the publicity and scope of the opioid epidemic, they also have to contend with increased scrutiny, raids by Drug Enforcement Agency swat teams, and medical record seizure. Furthermore, I will look for associations between the implementation of these laws that are associated with opioid

overdose mortality. These laws were instituted to abate the opioid epidemic so lower mortality rates would be expected in higher regulated states. However, due to the "balloon effect", those with opioid addiction will seek alternative, often illicit sources of opioids. These unregulated opioids are harder to measure doses or are sometimes combined with other chemicals making them more dangerous. As evidenced by the multiple opposing outcomes to every decision, a solution to the opioid epidemic may be just as complex. Using these measures of prescribing rates, mortality, and emergency department visit rates, I will determine which categories of opioid-related legislation are most effective at abating the opioid crisis as to identify one possible avenue for relief.

## Descriptions of Data Sources

Due to the importance of the opioid epidmeic, data on various factors has been collected for years and is readily accessible. This also means that a large volume of data is available and increases statistical power of tests, decreases variance, and increases the generalizability. Furthermore, it allows me to pick and vet the source of data to determine how data was collected to ensure its validity.

### *State Laws*

In order to create the categories of state laws, I found the United States' governmental agency, The Center of Disease Control and Prevention's State Laws on Prescription Drug Misuse and Abuse. The Center of Disease Control and Prevention's National Center for Injury Prevention and Control and the Center of Disease Control and Prevention's Public Health Law Program worked together to create summary sheets of the laws that states have implemented in

order to combat prescription opioid abuse, misuse, and opioid overdose. There are eight categories of laws, but for the purposes of this project, I chose the following summary sheets: "Menu of Prescription Drug Time and Dosage Limit Laws"; "Menu of Physical Examination Requirements"; "Menu of Doctor Shopping Laws"; "Menu of State Laws Related to Prescription Drug Overdose Emergencies."

For the purpose of this thesis study, a state was recorded to have a law for dosage and time limits if it had a statute that set time or dosage limits for controlled substances. A state was recorded to have a law for physical exams requirements if it required a "physical examination" as the basis for prescribing and dispensing a controlled substance. All fifty states and the District of Columbia have a version of a doctor shopping law; however, only twenty states have more specific doctor shopping laws the CDC categorizes as laws that "prohibit a patient from knowingly withholding information from the practitioner the patient is currently seeing about controlled substances or prescriptions they have received from other healthcare practitioners." States identified as providing "immunity to prosecution are defined as states that "grant immunity to an individual seeking help for himself or for another person experiencing an overdose and can facilitate the receipt of emergency medical assistance by people experiencing prescription drug overdoses." Furthermore, eight states offer mitigation in prosecution or sentencing. If a state has at least one type of these two laws, it is called an "emergency law."

***Opioid Overdoses***

The data on the number of opioid overdoses by state was also obtained from the Center of Disease Control and Prevention's National Center for Health Statistics. The data came from the

mortality data in the National Vital Statistics System which gathers data from contracts between the National Center for Health Statistics and various vital registration systems. It is comprised of provisional counts for drug overdose deaths by state, month and year, and drug classes. Some of the missing data is attributed to the cause of death pending investigation.

I reorganized the data to group by year and state while excluding non-opioid abuse deaths. This was done by removing the columns Month, State, Period, Percent Complete, Percent Pending Investigation, Footnote, Footnote Symbol, and Predicted Value. Data is available for 2015-2019. Since data on prescribing rates is only available for 2006-2017, I only used the data from the years that overlap: 2015. 2016. and 2017. Additionally, due to the discrepancy in population sizes between states, I used population estimates from the U.S. Census to calculate the mortality rate as per 100 people to keep it consistent with the prescribing rate data.

***Prescribing Rates***

Data on the prescribing rates in each state was found through the Center of Disease Control and Prevention's pages on Opioid Overdoses. The U.S. State Prescribing Rates are presented for 2017 and earlier. The data shows the number of retail opioid prescriptions dispensed per 100 persons per U.S. state. Since the data is provided by each county, I took the average of these data by state. The source of prescription data is a sample of 50,000 retail pharmacies, which dispense nearly 90% of all retail prescriptions in the U.S. The data on population were acquired from the U.S. Census Bureau.

***Emergency Department Visits***

Another dataset was from the Healthcare Cost and Utilization Project (HCUP) which is a collection of health databases. The data is collected from a variety of data collection organizations that have partnered with the Agency for Healthcare Research and Quality (AHRQ) which is a federal program under the Department of Health and Human Services (DSHS) (HCUP, 2017). This data is of U.S. hospital emergency departments and inpatient visits related to opioids. For this project, I focused on emergency department visits related to opioids. The rate of visits are reported per 100,000 people. I divided this data by 1000 in order to keep it on the same scale (per 100 people) as the other two response variables.

**Description of Data**

After reorganizing and creating my dataframe, I created new variables and subsets to analyze the data on various levels. The data is independent since a state having a certain type of law does not impact another state's legislature; additionally, the observations for the same state are temporally spaced a year apart. I also created another independent variable, a categorical variable that consisted of the laws each state had. For example, Alabama has the designation TPD which means it has a time/dosage law, physical exam law, and doctor shopping law. Since there ended up being nine categories, I decided to not analyze the data separated by year in order to increase the sample size. After combining the data, I came up with two data sets. The first one consisted of state laws, opioid overdose mortality rate, and opioid prescribing rate (Table 2). The second one included the same variables as the first except it also included the opioid-related emergency department visit rate for each state. The second data set was created independently from the first due to incomplete data regarding opioid-related emergency department visit rates for 2017 (Table 2). I decided to drop the entire year of 2017's data to prevent misrepresentation.

Moreover, the survey only covers 35 of 50 states which reduced the sample size from 150 observations to 70 observations.

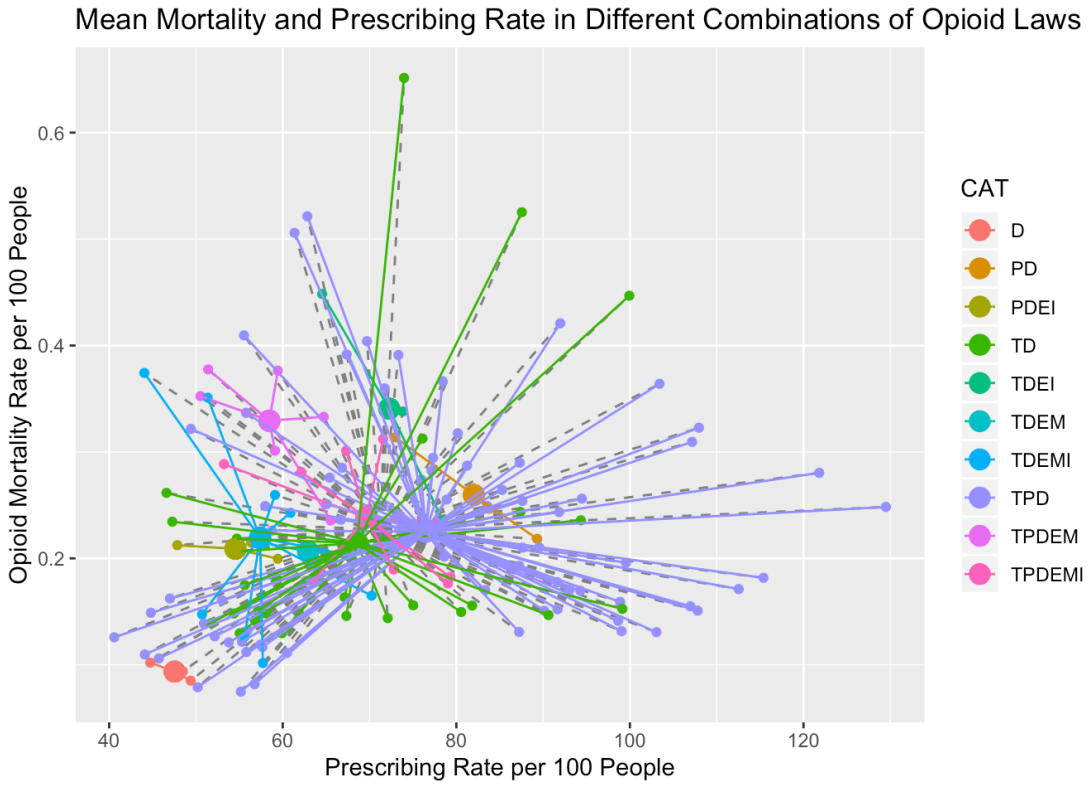
**Types of Analyses**

In order to test differences between groups, I elected to use a PERMANOVA (permutation MANOVA) test because of the multivariate normal distribution of the numeric response variables and the less restrictive assumptions associated with PERMANOVAs . This type of analysis allows me to answer: are there any differences across all nine categories of instituted laws? Since my response variables are continuous, numeric variables, I elected to use Euclidean distance over Bray-Curtis dissimilarity which is better for categorical data. For post-hoc analysis, I used a pairwise PERMANOVA to compare between categories. Due to the multiple comparisons, the p-value was adjusted using the Hochberg method since the hypothesis tests were independent.

In order to determine the effects of each of the laws on prescribing rate and opioid overdose mortality rate, I constructed a generalized linear model since the laws are categorical explanatory variables. The laws were then dummy-coded as binary, numeric variables. Regression on a binary variable is a t-test and therefore, would show where the institution of a certain type of law has a significant impact on the response variables. This linear model would also show the amount of variation in each of the dependent variables that could be explained by the institution of each law. I conducted these tests twice, once for each dataset: the larger one lacking emergency visit rate and the smaller one with emergency department visit rate.

# Results

## PERMANOVA




The permutation multivariate analysis of variance was conducted to determine the effect of the types of laws (Dosage and Time, Physical Exam, Doctor Shopping, Laws, Emergency, Immunity to Prosecution, Mitigation in Prosecution or at Sentencing) on two dependent variables (prescribing rate and opioid overdose mortality). Examination of bivariate density plots for each group revealed stark departures from multivariate normality thus a PERMANOVA based on euclidean distances was considered to be an appropriate analysis technique. Significant differences were found among the 9 categories of enacted laws on the two dependent measures (degrees of freedom = 9; sum of squares = 8261; Pseudo-F = 3.0875, $R^2 = 0.16561$, $p < .01$,

based on 999 permutations). Based on the analysis of multivariate homogeneity of group variances, the data was found to have violated the similar multivariate dispersion assumption ($p < .001$). Therefore, it can be concluded that the average prescribing rate and average opioid overdose mortality rate differed among the categories. However, no conclusions regarding the variance nor which specific categories differed could be drawn.

Table 3

First Permanova Results

| | Df | SumsOfSqs | MeanSqs | F.Model | $R^2$ | Pr(>F) |
|---|---|---|---|---|---|---|
| Categories | 9 | 8261 | 917.88 | 3.0875 | 0.16561 | **0.002** |
| Residuals | 140 | 41620 | 297.28 | | 0.83439 | |
| Total | 149 | 49881 | | | 1.00000 | |

*Df - degrees of freedom; Sum Sq - sum of squares; MeanSqs - mean of squares; F.Model - F value by permutation, boldface indicates statistical significance with P<0.01, P-values based on 999 permutations (lowest P-value possible 0.001)*

Post hoc analysis was performed conducting pairwise comparisons to determine which categories differed in prescribing rate and opioid overdose mortality rate. However, there were no significant findings after adjusting for multiple comparisons using the Hochberg method.

```
 Pairwise comparisons using permutation MANOVAs on a distance matrix

data:  dists by opRes$CAT
999 permutations

        D    PD   PDEI TD   TDEI TDEM TDEMI TPD  TPDEM
PD      0.19 -    -    -    -    -    -     -    -
PDEI    0.40 0.19 -    -    -    -    -     -    -
TD      0.11 0.24 0.24 -    -    -    -     -    -
TDEI    0.19 0.40 0.19 0.74 -    -    -     -    -
TDEM    0.19 0.19 0.31 0.66 0.31 -    -     -    -
TDEMI   0.18 0.10 0.68 0.16 0.11 0.40 -     -    -
TPD     0.11 0.70 0.16 0.16 0.75 0.40 0.10  -    -
TPDEM   0.11 0.11 0.52 0.24 0.17 0.41 0.79  0.11 -
TPDEMI  0.10 0.18 0.11 0.84 0.70 0.37 0.10  0.40 0.11

P value adjustment method: fdr
```

A second PERMANOVA was conducted to determine the effect of the types of laws on three dependent variables (prescribing rate, opioid overdose mortality, opioid-related emergency department visit rate). PERMANOVA was once again determined to be the appropriate analysis due to violation of MANOVA assumptions. Significant differences were not found among the nine categories of enacted laws on the three dependent measures (degrees of freedom = 7; sum of squares = 4240; Pseudo-F = 1.8716, $R^2$ = 0.31521, $p > .05$, based on 999 permutations). Based on the analysis of multivariate homogeneity of group variances, the data was found to have violated the similar multivariate dispersion assumption.

| | Df | SumsOfSqs | MeanSqs | F.Model | $R^2$ | Pr(>F) |
|---|---|---|---|---|---|---|
| Categories | 7 | 4240 | 605.71 | 1.8716 | 0.17444 | 0.087 |
| Residuals | 62 | 20066 | 323.64 | | 0.82556 | |

| | | | |
|---|---|---|---|
| Total | 69 | 24306 | 1.00000 |

*Df - degrees of freedom; Sum Sq - sum of squares; MeanSqs - mean of squares; F.Model - F value by permutation, boldface indicates statistical significance with P<0.01, P-values based on 999 permutations (lowest P-value possible 0.001)*

**Generalized Linear Model**

A generalized linear model (GLM) was used to determine which laws could explain variation in prescribing rate. Upon checking assumptions, it was found that the data was not heteroskedastic; however, GLMs are robust and I decided to proceed with caution using robust standard errors. Controlling for all other laws, there is a significant effect of physical exams laws on opioid prescribing rate. There is a difference of 8.197 more opioid prescriptions per 100 people in states that enacted a physical exam law ($t = 2.9931$, $df = 144$, $p < .01$). No other laws were found to have a significant effect on prescribing rate. Since there is more than one explanatory variable in my model, I selected the Adjusted R-squared which means the model explains 9.8% of the variation in opioid prescribing rate.

A second GLM was used to determine which laws could explain variation in opioid overdose mortality rate. Upon checking assumptions, it was found that the residuals were not normally distributed; I proceeded with using bootstrapped standard errors. However, there were no significant differences between those and the pre-bootstrapped standard errors. Controlling for all other laws, there is a significant effect of emergency exams laws on opioid overdose mortality rate. There is a difference of 0.14444 more fatal overdoses per 100 people in states that

enacted an overdose emergency law ($t = 2.403$, $df = 144$, $p < .05$). No other laws were found to have a significant effect on mortality rate. Since there is more than one explanatory variable in our model, I will use the Adjusted R-squared which means the model explains 3.2% of the variation in opioid overdose mortality rate.

A third GLM was used to determine which laws could explain variation in opioid-related emergency department visit rate. Although there were fewer observations than the previous two models, no assumptions were violated. Controlling for all other laws, there is a significant effect of emergency exams laws on opioid-related emergency department visit rate. There is a difference of 291.22 more opioid-related emergency department visits per 100,000 people in states that enacted an overdose emergency law ($t = 2.874$, $df = 64$, $p < .01$). No other laws were found to have a significant effect on mortality rate. Since there is more than one explanatory variable in our model, I will use the Adjusted R-squared which means the model explains 19.2% of the variation in opioid-related emergency department visit rate.

## Discussion

The first PERMANOVA test confirmed my hypothesis that the institution of opioid-related laws does in fact affect opioid prescribing rate and overdose mortality rate. However, the following post hoc analysis did not help determine what combination of laws created this difference. The assumption violation could have impacted the PERMANOVA leading to a Type I Error, a rejection of the null hypothesis that there was no difference in opioid prescribing rate and overdose mortality rate among the different combination of laws.

I, therefore, proceeded with the GLM to see differences between instituting a law or not and to ascertain the magnitude of an impact that law had on the response variables. The only significant law that had an impact on opioid prescribing rate was the one concerning the requirement of physical exams for an opioid prescription. However, contrary to my original belief, according to the model, this led to an increase in the number of prescriptions rather than a decrease. Although the heteroskedastic assumption was violated, I used robust standard errors to correct for this. Upon a closer look at the data I found that 46 of 50 states have a physical exam law; therefore, it is possible that there is an unknown lurking variable.

The GLM for the mortality rate indicated that the only significant law that had an impact was the category of having an overdose emergency law. Once again, contrary to my belief, this was correlated with an increase in the number of deaths rather than a decrease. No assumptions were violated this time, however. It is possible that the increased reporting of overdose emergencies has just increased the visibility of these deaths rather than causing inefficacious effects. Another possibility is that these states already had a high mortality rate which is why they then implemented these laws making this a problem of causality. However, since the GLM is a correlation test, I cannot prove causality. Additionally, this trend could be the product of "safety net" overconfidence similar to the concern that access to naloxone would lead to heavier drug use (Beheshti et al., 2015). However, there is not sufficient research on the subject.

The GLM for the opioid-related emergency department rate indicated that the only significant law that had an impact was the category of having an overdose emergency law. Once again, no assumptions were violated this time. This time, the model confirmed my belief and the

original intention of removing barriers to treatment. It is shown that the institution of these laws is associated with the increased likelihood that bystanders will call 911.

**Recommendation for Change**

The analysis has made evident, from the adjusted $R^2$ values (ranging from approximately 3-19%), that the laws analyzed, the explanatory values, do not explain a large proportion of variation in any of the response variables. This means that there are more variables to consider when making an accurate prediction of opioid prescribing, mortality, and emergency department visit rate. While this offers another avenue for exploration, changes in policy may still have an impact.

An increase in opioid overdose emergency laws in states that do not currently have them may lead to increased treatment in emergency departments. As proposed before, emergency departments can serve as sites of the beginning of opioid abuse treatment with the administration of buprenorphine and follow up. Therefore, I believe it would be prudent to also institute clinical practice guidelines that encourage this therapy and patient education.

Furthermore, although not found significant in this study, time and dosage laws for opioid prescriptions may be beneficial. There has been plenty of literature associating the number of days' supply of opioid with and increased risk of overdose. There is not, however, sufficient research on the impact of these types of laws and therefore more research is needed to augment policy (Bonnie, Ford,  and Phillips, 2017). Doctor shopping laws have become ubiquitous and every state has some form of prescription drug monitoring program (CDC, 2020). However, increased provider education is necessary to see the benefits of implementation. According to

one study, utilization of these programs among providers is about 35%. Therefore, there is a need to mandate use of these programs and education to maximize their benefit (Haffajee, Jena, and Weiner, 2015).

**Limitations and Future Directions**

It is important to acknowledge that there are a number of limitations in this study. One such limitation was the number of observations. In order to increase sample size, data from several years had to be combined. Ideally, though, each year could be separated; however, it was difficult to discern when each type of law was enacted in each state since some states instituted new laws while others modified pre-existing ones. This data would require even more separation of data. Therefore, it would be recommended that this study be repeated on a smaller scale than national, possibly by regional or even on a state by state basis. That way, data can be analyzed before and after each law is instituted, rather than assuming that all laws for all states were instituted before 2015.

Additionally, the emergency department visit rate data was incomplete for 2017 and thus the models had to be split apart which made an overall analysis difficult. The tradeoff was either losing a response variable or losing proceeding with a smaller sample size. Therefore, it is recommended that the study be repeated with as big of a range of years as possible. Such data required to conduct a complete analysis requires funding as statewide healthcare data is sold by governmental agencies such as the Healthcare Cost and Utilization Project (HCUP) and private companies.

# Conclusion

On average, approximately 130 Americans die every day from opioid overdose which means since the conceptualization of this thesis almost four years ago, about 172,000 people have possibly died from this epidemic (CDC, 2018). Although the epidemic is incredibly intricate and has no simple solutions, one front of attack is through public policy. Although there is promise in the legislature, more data on state-by-state scales need to be analyzed because even though this is a national problem, the profile of opioid abuse is different in every case. Moreover, it is evident that while policy can impact the epidemic, there are various additional components that need to be addressed and therefore, broad data collection across a plethora of possible explanatory variables needs to take place and then analyzed to determine the most crucial targets for change. The data I have analyzed has shown that opioid overdose emergency laws are associated with increased utilization of the emergency department where addiction treatment can be initiated. Additionally, the high emergency department visitation rate proves that the emergency department has a role to play in the mitigation of the opioid epidemic. Although my data analysis did not show dosage and time laws and physical exam requirement laws to be significant in reducing overdose mortality, I believe that they may still yet play another role in prevention. Curbing the increase of the number of people suffering from opioid abuse disorder will save numbers resources and lives downstream.

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# Appendix

Opioid-Related Law and Emergency Visit Data

## Author Biography

I grew up in the suburbs of the Dallas-Fort Worth Metroplex with my parents and elder sister. I am an Honors Biology major at the University of Texas at Austin with a transcript certificate in the Business of Healthcare. I am interested in medicine and my experiences as an EMT influenced me to write this thesis. I also have an interest in computational biology and bioinformatics which influenced the analysis of this paper. My future plans include attending Baylor College of Medicine.