The Impact of Prescription Drug Monitoring Programs on the Dynamics of the Opioid Epidemic

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By
Samuel Gatley

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Science, Technology, and Public Policy

Department of Public Policy
College of Liberal Arts

Rochester Institute of Technology
Rochester, New York
March 1, 2017
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Samuel Gatley

Masters of Science, Science, Technology and Public Policy
Thesis Submitted in Partial Fulfillment of the Graduation Requirements for the

College of Liberal Arts/Public Policy Program at
ROCHESTER INSTITUTE OF TECHNOLOGY
Rochester, New York

March 1, 2017

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<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AG</td>
<td>Attorney General</td>
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<td>APS</td>
<td>American Pain Society</td>
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<tr>
<td>AOR</td>
<td>Adjusted Odds Ratio</td>
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<tr>
<td>BJA</td>
<td>Bureau of Justice Assistance</td>
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<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CME</td>
<td>Continuing Medical Education</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CSMD</td>
<td>Controlled Substance Monitoring Database (Tennessee)</td>
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<td>EMPPR</td>
<td>Extra-Medical Pain Prescription Reliever</td>
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<tr>
<td>DEA</td>
<td>Drug Enforcement Agency</td>
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<td>FDA</td>
<td>Federal Drug Administration</td>
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<td>GAO</td>
<td>General Accounting Office</td>
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<td>HDR</td>
<td>Health Department Region</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HRPDMP</td>
<td>Harold Rogers PDMP Grant Program</td>
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<tr>
<td>HVC</td>
<td>Hepatitis C</td>
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<tr>
<td>I-STOP</td>
<td>Internet System for Tracking Over-Prescribing (New York State)</td>
</tr>
<tr>
<td>MAT</td>
<td>Medication Assisted Treatment</td>
</tr>
<tr>
<td>MME</td>
<td>Morphine Milligram Equivalent</td>
</tr>
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<td>NIDA</td>
<td>National Institute on Drug Abuse</td>
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<tr>
<td>NSDUH</td>
<td>National Survey on Drug Use and Health</td>
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<tr>
<td>NASPER</td>
<td>National All Schedules Prescription Electronic Reporting</td>
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<tr>
<td>N.Y.P.D</td>
<td>New York Police Department</td>
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<tr>
<td>NYS</td>
<td>New York State</td>
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<tr>
<td>PPR</td>
<td>Pain Prescription Reliever</td>
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<td>PDMP</td>
<td>Prescription Drug Monitoring Program</td>
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<tr>
<td>PDMP-TTAC</td>
<td>The PDMP Training and Technical Assistance Center</td>
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<tr>
<td>TN</td>
<td>Tennessee</td>
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<td>TNCSMP</td>
<td>Tennessee Controlled Substances Monitoring Program</td>
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<tr>
<td>UN</td>
<td>United Nations</td>
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<tr>
<td>UT</td>
<td>Utah</td>
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<td>VHA</td>
<td>Veterans Health Administration</td>
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<td>WV</td>
<td>West Virginia</td>
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Abstract

The forces driving the prescription opioid epidemic currently raging across the United States include aggressive marketing, weak regulation, addiction, freely prescribing doctors, a glut of pills available for sharing, and easy access to illicit drugs like heroin. This thesis aims to quantitatively analyze the interactions between these drivers through construction of a System Dynamics model, in order to determine the efficacy of policy intervention through Prescription Drug Monitoring Programs. The System Dynamics model simulates the flow of doctors’ prescriptions to the two very different classes of prescription opioid patients. One class is the long-term pain patients whose tolerance and appetite for opioids grows over time, leading them to higher doses, often dangerously high, and yet also frequently to feeling under-medicated; the other is those patients prescribed opioids for short-term pain, who typically find that they have been given more pills than they need.

These “extra” pills find their way into the hands of friends and family who, in common with the patients who received prescriptions, are in jeopardy of addiction to the opioids. Those addicted repeatedly visit doctors, shopping for more. Sensitivity analysis results reveal that drug diversion is a major contributor to the opioid death rate; that mandatory PDMP use will slow but not stop opioid proliferation, and will cause long term pain patients to be under-treated in larger numbers; that a significant number of people addicted to prescription opioids will transition to heroin use for reasons of price and availability; and that the rate of opioid overdose deaths will remain high until and unless society is better educated about the risks of addiction. Overall, the study helps conclude that the efforts of state governments and the FDA will be insufficient to stem the flow of opioids, and that there is no simple intervention to thwart drug diversion and sharing of pills.
1. Introduction

An epidemic of prescription opioid abuse is raging across the United States. The news reports daily about the tragic costs in human suffering and death. The purpose of this paper is to investigate how this terrible situation arose, and to ask if the policies being proposed and enacted have the potential to bring the problem under control. The approach taken begins with a thorough review of the literature. From this review I will synthesize the most salient issues into a simple model that attempts to capture the dynamics of the epidemic. The reality of the problem is very complex, and so the model will necessarily be naïve. Yet it is my hope that the model will lead to the identification of some recommendations that may prove useful to understanding and remediating the epidemic.

Since the year 2000 the rate of opioid prescription overdose deaths in the U.S.A. has doubled. More than a hundred thousand people have died. Opioid deaths are the second leading cause of accidental death. They are more numerous than deaths from falling, fires, choking, or accidental gunshot. Deaths from opioids are second only in number to motor vehicle deaths. In 2014 the number of deaths from legal prescription opioid overdose was 20,000. This is greater than the number of overdose deaths from the illegal drugs cocaine and heroin combined. (https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates).

In order to combat the problem, the White House Office of Drug Control Management https://www.whitehouse.gov/ondcp/national-drug-control-strategy published and annually updates the prescription drug abuse action plan called “Epidemic: Responding to America’s Prescription Drug Abuse Crisis” (2011). This plan calls for action regarding opioids through education, monitoring, safe storage & disposal, and enforcement. The second of these four strategies – monitoring – is the focus of this thesis. Specifically, I focus on the use of Prescription Drug Monitoring Programs (PDMPs).
Responsibility for monitoring of prescription drugs lies at the level of the states. PDMPs are state-run electronic databases used by prescribers, pharmacies and law enforcement to track particular prescription medications. State policy makers have embraced the use of PDMPs in the last decade. Forty-nine states (all except Missouri) have operational PDMPs. The specifics of implementation vary widely from state to state. In particular, the use of PDMPs is not mandatory in every state. Many users and abusers of opioids have gathered lethal amounts of the drugs legally. They obtain their drugs from prescribing doctors by the simple tactic of visiting several doctors. They receive multiple prescriptions, and fill them at different pharmacies, to avoid attracting unwanted attention. This practice is known as “doctor shopping” (McDonald & Carlson 2014). The resultant glut of prescription opioids leads to widespread illicit use. The excess drugs are spread through diversion to friends and family, and to drug sellers.

In this thesis I will assess the efficacy of PDMPs. I will study the role of PDMPs in stopping opioid abuse through diversion and doctor shopping. I will compare and contrast best practices between the states. I will place a particular emphasis on the impact of New York State’s PDMP, which is called I-STOP. An important distinguishing feature of I-STOP is that doctors and pharmacists dispensing opioids must use the system. Many other states have not made their PDMPs mandatory. Utilization is found to be much higher when participation is mandatory, as described in detail later.

Implementation of internet-based PDMPs is still in its infancy. Government agencies have been quick to claim success for PDMPs. Yet their analyses are still very preliminary, and generally rather superficial. For example, a recent review by Joshua Vinciguerra, New York Director of the Bureau of Narcotic Enforcement, reports that since I-STOP’s inception (1) over 34 million PMP searches on more than 12 million patients by over 96,000 searchers have been performed (2) that a comparison of opioid prescribing during the year prior to mandated PMP use and the year post implementation shows an 8.72% decrease in total prescriptions, (3) that the number of patients with a prescription has decreased 10.4%, (4) that in the first year of the mandated use of the PDMP the number of “doctor-shoppers” decreased by 75%, and (5) that that trend has
continued with a further drop from the fourth quarter of 2012 to the third quarter of 2015 to 86%. (http://www.nascsa.org/Conference2015/Presentations/vinciguerra1.pdf)

Closer examination reveals that the definition of “doctor shopper” in this presentation is “individuals receiving Rx from 5 or more prescribers & dispensed by 5 or more pharmacies”. By this definition the number of doctor shoppers in New York State is only a few hundred (Figure 1). Yet the number of prescribers in New York State exceeds 100,000, and the number of prescriptions written in New York City alone exceeds 2,000,000. Clearly, such a crude algorithm as the Bureau of Narcotic Enforcement’s “five prescribers and five pharmacies” only identifies the most egregious examples of doctor shopping. Yet this definition will arise repeatedly in other publications cited later.

Figure 1  http://www.slideshare.net/OPUNITE/pdmp-5-hopkins-dreyzehneroleary

Despite early claims of success in fighting doctor shopping, opioid deaths and illicit opioid use continue to rise. Two major challenges arise in studying this problem. Firstly, PDMPs are new (and so there is not much data yet). Secondly, the system of opioid migration and use within which PDMPs operate is not well understood.

Nevertheless there is strong evidence of time delays between cause and effect. For example, (1) between first writing a patient’s prescription and subsequent opioid dependency, and (2) between the increase in prescription rate and the increase in death rate; and (3) through accumulations of “stocks & flows” of drugs and their subsequent illicit uses. Time delays and stocks & flows are well modeled by System Dynamics (e.g.
Sterman 2000). In this thesis I therefore build and employ a system dynamics model of opioid use. This approach will reveal the context in which PDMPs operate. It will also model the impact of PDMPs on the use and abuse of opioids.
2. Literature Review

This literature review is organized in five sections. (1) The History of Opioid Use, (2) The Need for Government Intervention and Current Policy Proposals, (3) Prescription Drug Monitoring Programs, (4) PDMP Performance Measures, and (5) Support for and Continuous Improvement of PDMPs.

2.1 A History of Opioid Use: Opioids have been used as medicine for thousands of years. A timeline of opioid use with many sources cited is give at:


The Drug Enforcement Administration Museum recounts that

_The Sumerians referred to opium as Hul Gil, the "joy plant" [and] soon passed it on to the Assyrians, who in turn passed it on to the Egyptians. As people learned of the power of opium, demand for it increased. Many countries began to grow and process opium to expand its availability and to decrease its cost. Its cultivation spread along the Silk Road, from the Mediterranean through Asia and finally to China where it was the catalyst for the Opium Wars of the mid-1800s. In order to fund their ever-increasing desire for Chinese produced tea, Britain, through their control of the East India Company, began smuggling Indian opium to China. This resulted in a soaring addiction rate among the Chinese and led to the Opium Wars of the mid-1800s. Subsequent Chinese immigration to work on the railroads and the gold rush brought opium smoking to America._

(https://www.deamuseum.org/ccp/opium/history.html)

Laudanum (tincture of opium in alcohol) was widely used by the Victorians. They used it for recreation, for inspiration, for pain relief, and to quiet babies. Morphine was derived from opium in the early 19th century. Like laudanum, morphine was named after a joyful Latin word, this time the god of dreams. Used widely, it became especially prevalent with soldiers during the civil war. After the war, addiction was so widespread amongst veterans, that it became known as “soldiers disease”. The US found itself in the midst of its first opioid epidemic. Around this time the hypodermic needle was developed. The medical community embraced the widespread use of morphine.
Because of the addiction concerns associated with morphine, a safer “non-addictive” alternative was sought. This was the reason why Bayer developed heroin. In fact heroin was first marketed as a cough suppressant and non-addictive morphine alternative. The name itself is derivative of the word heroine, female hero, or savior.

According to Inciadi & Cicero (2009),

_Thomas Dover, a student of British physician Thomas Sydenham, is considered the “father” of clinical medicine, and a strong advocate of the use of opium for the treatment of disease. Dover developed a form of medicinal opium known as Dover’s Powder, that contained one ounce each of opium, ipecac (the dried roots of a tropical creeping plant), and licorice, combined with saltpeter, tartar, and wine. Dover’s Powder was introduced in 1709 and soon made its way to America, where it remained one of the most widely used opium preparations for almost two centuries (Inciardi, 2008; Souhami, 2001; Terry & Pellens 1928). The introduction of Dover’s Powder apparently started a trend. By the latter part of the eighteenth century, similar patent medicines containing opium were readily available throughout urban and rural America. They were sold in pharmacies, grocery and general stores, at traveling medicine shows, and through the mail (Terry & Pellens, 1928). This patent medicine industry eventually provided the backdrop for the abuse of prescription drugs and other pharmaceuticals (Inciardi, 2008)._ 

This was the age of patent medicines -- a medicine sold without a prescription in drugstores or by sales representatives, and usually protected by a trademark. At that time you could throw whatever you wanted into a bottle -- usually with alcohol, cocaine, opioids, and some other euphoric drugs -- and claim it was medicine. Addiction was not understood well at all during this time. Some doctors even substituted opioids for alcohol, claiming it was a way to treat alcoholism.

The first federal drug law was the opium exclusion act in 1909. This law specifically targeted opium smokers, typically Chinese immigrants. It made provision for opium derivatives including morphine and laudanum still to be consumed. In December
1908 an international commission met in Shanghai to discuss ending the international opium trade. This was the first step in creating the modern international drug prohibition framework. As with many other instances of prohibition, when opium was outlawed, criminals stepped in to meet the demand. Initially the supply dropped considerably, driving the price up dramatically. Soon after, criminals were matching and even exceeding the previous supply.

In 1914 Congress passed the Harrison Act, which levied taxes on the non-medical use of opium, cocaine, marijuana and their derivatives. In 1924 the Heroin Act outlawed all use, manufacturing and possession of heroin, even medically. A series of laws followed in an attempt to gain control of the drug market, both for tax purposes and in order to protect consumers and patients. Finally, in 1938, the Food, Drug, and Cosmetic Act brought cosmetics and medical devices under control. This law required that drugs be labeled with adequate directions for safe use. Moreover, it mandated pre-market approval of all new drugs. Now a manufacturer would have to prove to the FDA that a drug was safe before it could be sold.

A summary of one hundred years of drug control efforts was published by the UN on the centennial of the 1909 opium convention in Shanghai.

The Durham-Humphrey amendment to the Federal Food, Drug, and Cosmetic Act became effective on April 26 1952 (JAMA. 1952;149(4):371), mandating that

*Drugs that cannot be used with relative safety in self-medication must bear the legend Caution: Federal law prohibits dispensing without prescription on their labels. The pharmacist is liable to prosecution if he makes an over-the-counter sale of any such drug to a customer without obtaining a bona fide prescription or oral authorization from a licensed practitioner.*

The Durham-Humphrey amendment marked the beginning of written prescriptions. Now prescriptions were slowly adopted across the states. During the 1970s
the federal scheduling system was implemented. From then on, the federal government provided more direction on how prescription drugs should be distributed.

In 1970 President Nixon declared war on drugs. The Controlled Substances Act established the current prescription scheduling system in place to this day in the US. This was the beginning of the modern problems. Nixon’s *Special Message to the Congress on Drug Abuse Prevention and Control* on June 17, 1971 included these words:

> It is the production of morphine and codeine for medical purposes which justifies the maintenance of opium production, and it is this production which in turn contributes to the world's heroin supply. The development of effective substitutes for these derivatives would eliminate any valid reason for opium production. While modern medicine has developed effective and broadly used substitutes for morphine, it has yet to provide a fully acceptable substitute for codeine. Therefore, I am directing that Federal research efforts in the United States be intensified with the aim of developing at the earliest possible date synthetic substitutes for all opium derivatives. At the same time I am requesting the Director General of the World Health Organization to appoint a study panel of experts to make periodic technical assessments of any synthetics which might replace opiates with the aim of effecting substitutions as soon as possible.

[http://www.presidency.ucsb.edu/ws/?pid=3048](http://www.presidency.ucsb.edu/ws/?pid=3048)

The repetitive nature of the drug problem over the last 150+ years is ominously clear. In particular, the claims that Purdue Pharma made about Oxycontin in the 1990s echo Nixon’s mandate from 1970. They are in turn the same claims used to market heroin a century earlier. This repetition of historical patterns must be borne in mind when considering modern changes such as the implementation of PDMPs. The repetitive nature of the issues makes it easier for us to understand their nature, their likely pitfalls, and the ways in which they will likely prove intractable.

### 2.2 The Need for Government Intervention and Current Policy Proposals

The current prescription drug model, and the prohibition of Schedule 1 drugs, was born out of a market failure. Before the implementation of any regulation during the last century people were free to manufacture, trade, and consume any substances they wanted. As a
result many people died or became terribly addicted to substances whose dangers they did not understand. Over time the current framework was established in order to address this market failure and gain control of the situation. Despite all of the unintended consequences associated with the modern drug control framework, we are better off today than before drug control began (as demonstrated in the UN Report cited above).

On May 01, 2015 Nora D. Volkow, Director, National Institute on Drug Abuse House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations testified that

*The misuse of opioids is ... a public health epidemic with devastating consequences including not just opioid use disorders and related overdoses, but also the rising incidence of newborns who experience neonatal abstinence syndrome because their mothers used these substances during pregnancy; and increased spread of infectious diseases including HIV and hepatitis C (HCV).*

*Existing evidence based prevention and treatment strategies are highly underutilized across the United States. The recently announced initiative ... emphasizes the implementation of these evidence based prevention and treatment strategies which include not only better prescription practices but also deployment of medication to combat overdoses and medication-assisted treatment (MAT) to treat opioid use disorders. ... [This] initiative and will focus on supporting research and disseminating findings to improve opioid prescribing practices, to expand the use of the opioid overdose reversal drug naloxone, to improve the integration of pharmacotherapies into treatment services in specialty care and primary care, and to develop pain treatments with reduced potential for misuse and diversion.*


Given that the government has to be involved in regulating drugs, it is imperative that they do so effectively. Being better off than the Wild West drug market of the late 18th century is hardly a success. Even though we are clearly better off today than before any drug control was in place, the staggering death rate from prescription drugs shows
that today’s form of drug control is inadequate and must be improved. The government is obligated to enact effective policy. The fact that more people in the US die from medicine prescribed by a doctor than from illicit cocaine and heroin combined is frequently framed as a success for illicit drug control. In fact it is a clear sign that the medical community and prescription drug system urgently needs to be reformed. The current drug policy from the White House emphasizes specifically that the preferred intervention for prescription drug abuse should be to improve information sharing, in other words to establish PDMPs.

Very recent policy proposals reflect a growing awareness of the need for government intervention. In Oct 2015 Massachusetts Governor Charlie Baker proposed a bill that would limit practitioners to prescribing no more than a 72-hour supply of opioids to patients the first time they prescribe an opioid to them. In Feb 2016 The White House proposed $1 billion in new funding over two years to fight heroin and prescription drug abuse. Almost all of the new money, $920 million, would be for mandatory funding over two years for states to increase medication-assisted treatment, which also involves therapy, for people with opioid use disorders. (http://thehill.com/policy/healthcare/267895-white-house-proposes-1-billion-to-fight-opioid-epidemic)

Also in Feb 2016 the National Governors Association, frustrated by a perceived lack of effective action, resolved to propose treatment protocols to reduce the use of opioid painkillers. (http://www.nytimes.com/2016/02/22/us/politics/governors-devise-bipartisan-effort-to-reduce-opioid-abuse.html?_r=0) In March 2016 the CDC issued comprehensive new guidelines for the prescription of opioids for chronic pain (Dowell, Haegerich, and Chou, 2016). These guidelines addressed many of the issues raised in this thesis, specifically (1) when to initiate or continue opioids for chronic pain, (2) opioid selection, dosage, duration, follow-up, and discontinuation, and (3) the risks and harms of opioid use.
http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

2.3 Prescription Drug Monitoring Programs: The rationale for New York Attorney General Eric T. Schneiderman’s 2012 proposal to address the prescription drug crisis was that a modernization of the state’s Prescription Monitoring Program
would exponentially enhance the effectiveness of New York's existing PMP to increase detection of prescription fraud and drug diversion [and] establish an on-line, real-time, controlled substance reporting system that requires prescribers and pharmacists to search for and report certain data at the time a controlled substance prescription is issued, and at the time such substance is dispensed.


The legislation, which passed both Assembly and Senate unanimously in June 2012:

- requires the Department of Health to establish and maintain an on-line, real-time controlled substance reporting system to track the prescription and dispensing of controlled substances;
- requires practitioners to review a patient's controlled substance prescription history on the system prior to prescribing;
- requires practitioners or their agents to report a prescription for such controlled substances to the system at the time of issuance;
- requires pharmacists to review the system to confirm the person presenting such a prescription possesses a legitimate prescription prior to dispensing such substance;
- requires pharmacists or their agents to report dispensation of such prescriptions at the time the drug is dispensed.

With the introduction of I-STOP, New York State has mandated the involvement of prescription writers in PDMPs along with the pharmacies that fill those prescriptions. Now, with very few exceptions, whenever a medical professional writes a prescription in New York State they must first check I-STOP to look for suspicious behavior. This new regulation is intended to fight doctor shopping, where a patient seeks drugs from many different doctors in a short span of time either to source serious personal abuse or to sell the drugs. With the extra involvement of doctors this behavior should be discovered. However it will require extra time from the doctors, and the extra scrutiny and effort may
result in doctors writing fewer legitimate prescriptions. In turn people with legitimate medical needs may not receive medicine. In this thesis I will evaluate I-STOP’s effectiveness. A particular focus will be the mandated involvement of prescription writers. The newness of I-STOP limits the amount of data available. The opportunities inherent in cross-state comparisons led me to the methodology used in this paper.

The Federal Government funds substance abuse surveys (e.g., the National Survey on Drug Use and Health (NSDUH) [https://nsduhweb.rti.org/respweb/project_description.html]). Criminal justice departments, hospitals and health departments at the state and federal level also collect data. The rising abuse of prescription drugs has been identified in all of these different sources. These sources of data can also serve to help evaluate the effects of PDMPs. By looking at the admission to emergency rooms for overdoses, drug arrests, and drug related deaths, in different states, before and after the implementation of different forms of PDMPs, we can hope to get a look at how effective the different policies are. The PDMPs themselves will also serve as sources of data.

For example, the BJA Prescription Drug Monitoring Program Performance Measures Report states that:

*The performance measures ask for the number of patients who have obtained prescriptions from five or more prescribers and filled them at five or more pharmacies in each reporting period (initially, six months; after July 1, 2010, three months). The measures also ask for the number of non-liquid doses associated with these patients, broken out by drug class—pain relievers, sedatives, stimulants, and tranquilizers. We report these threshold measures as ratios—of the number of patients meeting the five prescriber/five pharmacy threshold to the total number of patients who received a prescription during the reporting period, and of the number of non-liquid doses associated with the threshold-meeting patients to the total number of non-liquid doses dispensed in the reporting period, overall and by drug class. A parallel set of performance measures, and ratios, is based on a 10 prescriber and 10 pharmacy threshold. Each of these measures is asked for Schedule II*
prescriptions only, Schedule II and III prescriptions only, and Schedule II, III, and IV prescriptions. These threshold measures are thought to be indicators of questionable activity.

**Terminology and Methodology.** In my literature search I made a complete searches for the terms “doctor shopping”, “bad doctors”, “stolen scripts”, “opioid prescription surveys”, “prescription opioid deaths”, “opioid epidemic”, “pill mills” and “prescription mills”.

**Footnote:** The latter two terms, “pill mills” and “prescription mills” are used to describe doctors’ offices that specialize in freely providing opioid prescriptions with lax or no checks in place. For example, Florida was plagued by such operations until recently. Specifically, 49 of the 50 largest prescribers in the USA were located within two Florida counties. In 2010 and 2011 Florida took important legislative and enforcement steps to bring the problem under a degree of control. $3M was allocated for enforcement in Florida House Bill 7095 which

> provides mandatory administrative penalties for certain violations related to prescribing; requires prescriptions for controlled substances to be written on counterfeit-resistant pad produced by approved vendor or electronically prescribed; provides conditions for being approved vendor; requires certain physicians to designate themselves as controlled substance prescribing practitioners on their practitioner profiles.

The enforcement effort was sweeping. As reported in the press,

> Agents went undercover and posed as patients. They tapped phones to record calls and text messages. They seized security video from cameras installed by the owners of the clinics, recorded their own undercover videos and used the IRS to follow the money. They eventually raided the South Florida clinics, known as ‘pill mills,’ and amassed more than 1.2 million pages of records and statements…

[http://www.huffingtonpost.com/2013/07/06/south-florida-pill-mill_n_3553196.html](http://www.huffingtonpost.com/2013/07/06/south-florida-pill-mill_n_3553196.html)

--- end of footnote
The papers identified in these literature searches show there is a strong consensus that

*access to healthcare generally, and to dentists and pharmacists in particular, increases the availability of prescription opioids in communities, which, in turn, is associated with higher rates of opioid abuse*” (Wright et al 2014).

That is, that the opioid epidemic is (at least in part) a self-inflicted problem within the health care system.

Efforts to implement PDMPs are under way across the nation. There are many papers that discuss the evaluation of their effectiveness, but the quality of such studies has so far been poor. In a comprehensive literature review, Haegerlich et al (2014) searched for evaluations of state policy or systems-level interventions that used “non-comparative, cross-sectional, before–after, time series, cohort, or comparison group designs or randomized/non-randomized trials”. They confirmed that overall study quality is low, and identified limitations including

*lack of baseline data and comparison groups, inadequate statistical testing, small sample sizes, self-reported outcomes, and short-term follow-up.*

Often the scope of these evaluative studies lies within a single state. In this thesis I take the view that inter-comparison of data from different states provides an important opportunity to identify policies and practices that will improve prescribing practices and opioid use protocols, both of which are crucial to the protection of patient health.

Responsibility for monitoring and controlling prescription drugs lies at the level of the state. There are large differences both in the time and in the specifics of implementation from state to state. This means that in practice fifty different experiments
are being conducted on how to build a PDMP. Table 1 shows examples of variations in PDMP implementation by state (from [http://www.pdmpassist.org](http://www.pdmpassist.org)).

**Table 1: Examples of Variations in Implementation of PDMPs by State**

Empty fields mean the program may be recently established and/or may not yet be collecting data.

<table>
<thead>
<tr>
<th>State</th>
<th>#Prescribers</th>
<th>#Pharmacies</th>
<th>#Prescriptions</th>
<th>Frequency</th>
<th>Agency Type</th>
<th>Start</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>15,178</td>
<td>1,437</td>
<td>13,703,512</td>
<td>Daily</td>
<td>Department of Health</td>
<td>2006</td>
</tr>
<tr>
<td>Alaska</td>
<td>4,364</td>
<td>107</td>
<td>585,290</td>
<td>Monthly</td>
<td>Pharmacy Board</td>
<td>2011</td>
</tr>
<tr>
<td>Arizona</td>
<td>28,970</td>
<td>1,162</td>
<td></td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2008</td>
</tr>
<tr>
<td>Arkansas</td>
<td>10,059</td>
<td>775</td>
<td></td>
<td>Weekly</td>
<td>Department of Health</td>
<td>2013</td>
</tr>
<tr>
<td>California</td>
<td>166,333</td>
<td>6,337</td>
<td>45,136,908</td>
<td>Weekly</td>
<td>Law Enforcement Agency</td>
<td>1939</td>
</tr>
<tr>
<td>Colorado</td>
<td>25,787</td>
<td>820</td>
<td></td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2007</td>
</tr>
<tr>
<td>Delaware</td>
<td>4,733</td>
<td>223</td>
<td></td>
<td>Daily</td>
<td>Professional Licensing Agency</td>
<td>2012</td>
</tr>
<tr>
<td>Florida</td>
<td>67,588</td>
<td>4,882</td>
<td>24,842,120</td>
<td>Weekly</td>
<td>Department of Health</td>
<td>2011</td>
</tr>
<tr>
<td>Georgia</td>
<td>34,973</td>
<td>2,429</td>
<td></td>
<td>Weekly</td>
<td>Law Enforcement Agency</td>
<td>2013</td>
</tr>
<tr>
<td>Guam</td>
<td>253</td>
<td>24</td>
<td></td>
<td>Bi-Weekly</td>
<td>Department of Health</td>
<td>2013</td>
</tr>
<tr>
<td>Hawaii</td>
<td>6,343</td>
<td>245</td>
<td></td>
<td>Weekly</td>
<td>Law Enforcement Agency</td>
<td>1943</td>
</tr>
<tr>
<td>Idaho</td>
<td>7,204</td>
<td>313</td>
<td>2,599,175</td>
<td>Weekly</td>
<td>Pharmacy Board</td>
<td>1967</td>
</tr>
<tr>
<td>Illinois</td>
<td>54,404</td>
<td>2,414</td>
<td>17,578,503</td>
<td>Daily</td>
<td>Department of Health</td>
<td>1968</td>
</tr>
<tr>
<td>Indiana</td>
<td>25,991</td>
<td>1,275</td>
<td>12,922,497</td>
<td>Weekly</td>
<td>Professional Licensing Agency</td>
<td>1998</td>
</tr>
<tr>
<td>Iowa</td>
<td>13,989</td>
<td>778</td>
<td>4,499,508</td>
<td>Weekly</td>
<td>Pharmacy Board</td>
<td>2009</td>
</tr>
<tr>
<td>Kansas</td>
<td>13,894</td>
<td>673</td>
<td></td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2011</td>
</tr>
<tr>
<td>Kentucky</td>
<td>17,425</td>
<td>1,162</td>
<td></td>
<td>Daily</td>
<td>Other</td>
<td>1999</td>
</tr>
<tr>
<td>Louisiana</td>
<td>17,168</td>
<td>1,230</td>
<td>12,723,870</td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2008</td>
</tr>
<tr>
<td>Maine</td>
<td>7,484</td>
<td>313</td>
<td>2,532,441</td>
<td>Daily</td>
<td>Substance Abuse Agency</td>
<td>2004</td>
</tr>
<tr>
<td>Maryland</td>
<td>30,906</td>
<td>1,232</td>
<td>3 Days</td>
<td>Sub</td>
<td>Substance Abuse Agency</td>
<td>2013</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>43,115</td>
<td>1,170</td>
<td></td>
<td>Daily</td>
<td>Department of Health</td>
<td>1994</td>
</tr>
<tr>
<td>Michigan</td>
<td>43,139</td>
<td>2,480</td>
<td></td>
<td>Daily</td>
<td>Professional Licensing Agency</td>
<td>1989</td>
</tr>
<tr>
<td>Minnesota</td>
<td>27,806</td>
<td>1,130</td>
<td>6,700,000</td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2010</td>
</tr>
<tr>
<td>Mississippi</td>
<td>10,293</td>
<td>840</td>
<td>6,000,000</td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2005</td>
</tr>
<tr>
<td>Missouri</td>
<td>22,430</td>
<td>1,318</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montana</td>
<td>5,102</td>
<td>269</td>
<td></td>
<td>Weekly</td>
<td>Pharmacy Board</td>
<td>2012</td>
</tr>
<tr>
<td>Nebraska</td>
<td>9,429</td>
<td>499</td>
<td></td>
<td>Daily</td>
<td>Other</td>
<td>2011</td>
</tr>
<tr>
<td>Nevada</td>
<td>9,846</td>
<td>475</td>
<td>3,932,259</td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>1997</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>7,697</td>
<td>270</td>
<td></td>
<td>Weekly</td>
<td>Pharmacy Board</td>
<td>2014</td>
</tr>
<tr>
<td>New Jersey</td>
<td>44,064</td>
<td>2,048</td>
<td>4,000,606</td>
<td>Weekly</td>
<td>Law Enforcement Agency</td>
<td>2011</td>
</tr>
<tr>
<td>New Mexico</td>
<td>9,627</td>
<td>329</td>
<td></td>
<td>Daily</td>
<td>Pharmacy Board</td>
<td>2005</td>
</tr>
<tr>
<td>New York</td>
<td>108,256</td>
<td>5,019</td>
<td></td>
<td>Daily</td>
<td>Department of Health</td>
<td>1973</td>
</tr>
</tbody>
</table>
2.4 PDMP Performance Measures: In 2005, the Bureau of Justice Assistance (BJA) convened state representatives and BJA consultants to develop performance measures for PDMPs. Over the following three years, an initial set of measures was adopted, consistent with federal reporting requirements mandated by the Government Performance Results Act (Bureau of Justice Assistance 2013). Measures were developed in each of four areas: input, output, outcomes and impacts.

Inputs include training of prescribers, dispensers, and individuals authorized to conduct investigations in how to access and use PDMP data.

Outputs are solicited reports in response to a request from a prescriber, pharmacist, investigator, regulatory agency or other authorized end user of the PDMP, while unsolicited reports result from the PDMP’s having identified questionable prescription patterns.

<table>
<thead>
<tr>
<th>State</th>
<th>PDMPs</th>
<th>Weekly/Daily</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oregon</td>
<td>19,793</td>
<td>Weekly</td>
<td>2011</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>63,002</td>
<td>3 Days</td>
<td>1973</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>5,881</td>
<td>3 Days</td>
<td>1979</td>
</tr>
<tr>
<td>South Carolina</td>
<td>18,589</td>
<td>Daily</td>
<td>2008</td>
</tr>
<tr>
<td>Tennessee</td>
<td>30,064</td>
<td>Daily</td>
<td>2006</td>
</tr>
<tr>
<td>Texas</td>
<td>91,727</td>
<td>Weekly</td>
<td>1982</td>
</tr>
<tr>
<td>Utah</td>
<td>12,082</td>
<td>Daily</td>
<td>1996</td>
</tr>
<tr>
<td>Vermont</td>
<td>3,707</td>
<td>Weekly</td>
<td>2009</td>
</tr>
<tr>
<td>Virginia</td>
<td>38,227</td>
<td>Weekly</td>
<td>2003</td>
</tr>
<tr>
<td>Washington</td>
<td>37,145</td>
<td>Weekly</td>
<td>2011</td>
</tr>
<tr>
<td>West Virginia</td>
<td>8,052</td>
<td>Daily</td>
<td>1995</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>28,273</td>
<td>Weekly</td>
<td>2013</td>
</tr>
<tr>
<td>Wyoming</td>
<td>2,641</td>
<td>Weekly</td>
<td>2004</td>
</tr>
</tbody>
</table>

Crucially, participation in PDMPs by prescribers and pharmacies is not mandatory in every state. The impact of this very important factor will be considered in detail later.
Outcomes focus is on consumers who fill prescriptions in a manner that may indicate inappropriate use of prescription drugs. Measures in this area relate to the number of individuals who exceed certain thresholds of prescribers and pharmacies, and to the number of doses of drugs associated with these individuals.

The primary impact measure is the prevalence of inappropriate use of prescription drugs by the general population, to be obtained from the National Survey on Drug Use and Health (NSDUH). Secondary impact measures are overdoses and deaths attributable to misuse of controlled substances. Reporting on these measures has been required of BJA Harold Rogers PDMP grantees beginning in 2008 (see chapter 6). The measures have been updated and improved since that time, as described in the next section.

The first comprehensive compilation of the measures, across the three and one-half years from January 2009 through June 2012 showed:

• grantees provided formal trainings to several hundred prescribers and somewhat fewer pharmacists over a typical 12-month period,
• registration rates increasing for four or more years after implementation of online access, reaching an average of 58% in the first half of 2012 for the six states where online access began prior to 2007,
• large increases in the number of solicited reports provided to in-state prescribers (more than 400%), pharmacists (more than 200%), and law enforcement (more than 100%), and
• rates of individuals who had obtained Schedule II prescriptions from five or more prescribers and five or more pharmacies in a three-month reporting period less than 1/10th of 1%.

http://www.pdmpeXcellence.org/sites/all/pdfs/BJA_PDMP_Performance_Measures_1_09_6_12_fdbk.pdf

This report also contained the following extraordinary paragraph:
We explored associations between non-medical use of pain relievers and rates of drug-related overdose deaths for the grantee states. We found that all years of non-medical use were correlated with all years of overdose death rates. However, the highest correlations were between non-medical use in 2002/2003 and overdose death rates in 2008, 2009, and 2010 (correlation coefficients of .725, .747, and .754, respectively). (The correlation between non-medical use in 2009/2010 and overdose death rates in 2010 was .654.) This finding suggests that the relationship between these two impact measures may be complex...

This empirically determined time lag of several years in the correlation between non-medical use of opioids and overdose deaths is one of the strong motivations for the construction of my System Dynamics model below: specifically, my model shows that the mean time from initial opioid addiction to death is several years.

2.5 Support for and Continuous Improvement of PDMPs: The PDMP Training and Technical Assistance Center (PDMP-TTAC) is a partnership between the Bureau of Justice Assistance (BJA) and the Heller School for Social Policy & Management at Brandeis University. The PDMP-TTAC provides assistance with developing policy and information for PDMPs, collecting and reporting performance measurements, hosting regional and national conferences, participating in interstate data sharing, and planning & implementing new PDMPs.

http://pdmpassist.org/content/about-training-and-technical-assistance-center-ttac

Since 2010, the TTAC has conducted three State Surveys of PDMPs (2010, 2012, 2014). The surveys have gathered data on PDMP statutes, regulations, policies and procedures, tracked their changes over time, and identified program trends and candidate practices. In September 2012, the PDMP Center of Excellence (COE) published a white paper entitled “Prescription Drug Monitoring Programs: An Assessment of the Evidence for Best Practices”. Drawing on published research, consensus statements of expert opinion, and accumulated experience among states, this report identified 35 best and
promising practices likely to help maximize PDMP effectiveness. These fell into 7 major categories:

- Data collection and data quality
- Data linking and analysis
- User access and report dissemination
- PDMP recruitment, utilization, and education
- Inter-organizational best practices for PDMPs
- Evaluation of PDMPs
- Funding PDMPs


The best practices identified and recommended for implementation in all PDMPs were:

- Collect positive identification for the person picking up prescriptions
- Collect data on method of payment, including cash transactions
- Reduce data collection interval; move toward real-time data collection
- Integrate PDMP reports with health information exchanges, electronic health records, and pharmacy dispensing systems
- Send unsolicited reports and alerts to appropriate users
- Mandate enrollment
- Mandate utilization
- Delegate Access
- Enact and implement interstate data sharing among PDMPs
- Secure funding independent of economic downturns, conflicts of interest, public policy changes, and changes in PDMP policies

A federal program created by the FY 2002 U.S. Department of Justice Appropriations Act (Public Law 107-77) and continued to date under each subsequent year’s
Funding is a perennial problem for PDMPs, because there is no steady supply. Some states prohibit using general state revenues for the programs. Private funding supports some PDMPs, but many are supported only by federal grants. There have only been two Federal PDMP grant-funding programs. The Substance Abuse and Mental Health Services Administration (SAMHSA) administered The National All Schedules Prescription Electronic Reporting (NASPER) grant. No funds have been appropriated for the NASPER program since fiscal years 2009 and 2010, and NASPER grants are not currently available. The Bureau of Justice Assistance (BJA) Harold Rogers PDMP Grant Program (HRPDMP) has made grants available to states since 2003 for the purpose of planning, implementing and enhancing PDMPs. HRPDMP grant programs, however, are a competition between states. They generally place a limit on the amount a state may receive. They specify a funding period, and place restrictions on how the funds are to be used. A state receiving an HRPDMP grant may not be eligible for future support.

A state’s legislature may allocate General Revenue funds for a PDMP. General revenue funds come from state sales, income, and property taxes. The demands on state revenues are many and the funds are limited. Passing legislation allocating sufficient funds for PDMP operation requires persistent advocacy by those who might benefit from effective prescription monitoring. Examples are medical groups and law enforcement. The NYS AG testified in his case for I-STOP that 1/5th of the state budget in the years leading up to I-STOP was spent on dealing with consequences of the opioid epidemic. He suggested that savings from dealing with this epidemic effectively could offset some or all of the costs incurred by I-STOP. This argument could also be advanced in every state.

http://www.pdmpassist.org/pdf/PDMP_Funding_Options_TAG.pdf
In order to be effective PDMPs’ prescription data must be completely and accurately collected, analyzed appropriately, and made available in a proactive and timely manner to all appropriate end users. Prescription data generally include information on the date written and dispensed, patient, prescriber, pharmacy, medicine, day’s supply, dose, and source of payment. PDMP reports are made available on request from end users. These are typically prescribers and pharmacists, but also include medical licensure boards, law enforcement and drug control agencies, medical examiners, drug courts, addiction treatment programs, and, in some states, third party payers.

http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_COE_PDMP_3rd_pty_payer_mtg_rpt.pdf

2.6 The Tension between Treatment of Pain and Regulation of Abuse: The regulatory ideas inherent in PDMPs and regulation in general, unless implemented with great subtlety and forethought, will run headlong into the problems both of actually causing under-treatment and of being accused of causing under-treatment by those eager to proliferate the use of opioids.

An underlying belief implicit in the creation of PDMPs is that of the “bad patient”, a villain whose drug-seeking propensities must be held in check by regulation. Certainly such characters exist (Inciardi et al 2007). An assessment of blame throughout the entire supply chain for prescription drug abuse, however, must include many other actors, including doctors, dentists, pharmacists, family members (of both negligent and well-intentioned types), robbers, and drug pushers (of both criminal and other types).

Chief among the advocates for increased use of opioids are the drug manufacturers. One specific brand, OxyContin, was marketed with unprecedented vigor under the (later proved to be false) claim that it had less than a 1% chance of leading to addiction. After protracted investigations before congress (“EXAMINING THE EFFECTS OF THE PAINKILLER OXYCONTIN, FOCUSING ON FEDERAL, STATE AND LOCAL EFFORTS TO DECREASE ABUSE AND MISUSE OF THIS PRODUCT WHILE ASSURING AVAILABILITY FOR PATIENTS WHO SUFFER DAILY FROM CHRONIC MODERATE TO SEVERE PAIN” February 12, 2002) the
manufacturers of OxyContin, Purdue Pharma, eventually pleaded guilty in 2007 to the criminal charge of “misbranding” the product and agreed to pay $600 million in fines.

By then the damage was done. Furthermore, as part of the settlement, the GAO (General Accounting Office) recommendations stated, “In addition to developing a risk management plan, Purdue has initiated several OxyContin-related educational programs. They have taken disciplinary action against their own sales representatives who they say improperly promoted OxyContin. They have referred physicians suspected of improper prescribing practices to the authorities”. In this way they have succeeded in perpetuating a system by which they, the manufacturers, are allowed to “educate” doctors and others to market their products. Such education is a major factor in creating a climate of opinion in which doctors freely prescribe opioids; it began decades ago, and its influence still persists to this day in medical schools and doctor’s offices.

The role of the Federal Drug Administration (FDA) has been similarly compromised through “education” and the provision of funding from the pharmaceutical industry. The FDA approved OxyContin labeling that read, “Delayed absorption, as provided by OxyContin tablets is believed to reduce the abuse liability of a drug.” In retrospect it is also clear that the approved labeling contained a recipe for abuse:

\[
\text{OxyContin tablets are to be swallowed whole, and are not to be broken, chewed, or crushed. Swallowing broken, chewed, or crushed OxyContin tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone.}
\]

The medical community has long used four primary vital signs: body temperature, blood pressure, pulse (heart rate), and breathing rate (respiratory rate) to monitor a patient’s condition. In 1996, coincident with the aggressive marketing of OxyContin, the American Pain Society (APS) created the idea of “pain as the 5th vital sign”. James Campbell, in his presidential address, said,

\[
\text{Vital Signs are taken seriously. If pain were assessed with the same zeal as other vital signs are, it would have a much better chance of being treated properly. We need to train}
\]
doctors and nurses to treat pain as a vital sign. Quality care means that pain is measured and treated.

The logic of this syllogism – vital signs are taken seriously; pain is a vital sign; therefore pain is taken seriously -- so appealed to the Veterans Health Administration (VHA) that they created a task force to initiate “a comprehensive national strategy for pain management” based upon it. Thus was born the VHA’s “Pain as the Fifth Vital Sign Toolkit”

http://www.va.gov/PAINMANAGEMENT/docs/Pain_As_the_5th_Vital_Sign_Toolkit.pdf

Many of us have direct personal experience of the protocol “requiring a pain intensity rating (0 to 10) at all clinical encounters.” The idea of pain as the 5th vital sign made so much sense to so many people that it spread like wildfire. It led to proliferation in the use of opioids, and to patients demanding opioids as a right.
3. Research Questions

There are clear recurrent trends shown by my literature review of opioid use that lead to the questions to be addressed in this thesis. For much more than a century people have persistently used opioids, and during all of that time the use of opioids has been justified by arguments implying their safety and efficacy. President Nixon was just one in a long line of apologists claiming extenuating circumstances for continued opioid production. Purdue Pharma is merely the latest. The historical perspective is therefore that the opioid problem is likely to prove intractable, and that PDMPs will face familiar pitfalls.

Given that people will use opioids, the pressing questions facing PDMPs become (1) when should doctors initiate or continue opioids for chronic pain, (2) what are the appropriate strategies for opioid dosage, duration, and discontinuation, and (3) what are the risks and harms of opioid use?

Given that people will abuse opioids, which of the possible modalities of abuse should raise greatest concern? The possibilities include doctor shopping, sharing of drugs by family and friends, purchase of drugs from dealers, and transitioning from prescription drugs to heroin.

My review has shown that, before government regulation, many people died or became terribly addicted to substances whose dangers they did not understand. We are better off today than before drug control began, but the situation is extremely problematic. Given that the government has to be involved in regulating drugs, it is imperative that they do so effectively. The current drug policy from the White House emphasizes specifically that the preferred intervention for prescription drug abuse should be to improve information sharing, in other words to establish PDMPs.

Information sharing in the information age naturally means online Prescription Drug Monitoring Programs. With I-STOP, New York State has mandated the involvement of prescription writers in PDMPs, along with the pharmacies that fill those
prescriptions, with a primary intent to fight doctor shopping. A particular focus is the mandated involvement of prescription writers. Specifically, are PDMPs more effective when mandatory?

The near-simultaneous launch of PDMPs in almost every state provides important contrasting data, both because each state has its own perspective on the best way to proceed, and because the specific problems of the opioid epidemic are different in different states. The intrinsic opportunities inherent in cross-state comparisons led me to the methodology used in this thesis.

There are identifiable problems with mandatory regulation. Compliance will require extra time from the doctors. The extra scrutiny and extra effort may result in doctors writing fewer legitimate prescriptions. Attempts to curb usage means that people with legitimate medical needs may not receive medicine.

Which, if any, of the possible metrics for PDMP performance found in the literature will prove most effective? The possibilities include (1) reports that respond to requests from a prescriber, a pharmacist, an investigator, a regulatory agency or another authorized end user of the PDMP, (2) patterns in the data from the PDMP’s having questionable prescription behaviors, such as consumers who fill prescriptions in a manner that may indicate inappropriate use of prescription drugs, or the number of individuals who exceed certain thresholds of prescribers and pharmacies, or the number of doses of drugs associated with these individuals (3) a prevalence of inappropriate use of prescription drugs by the general population, or (4) overdoses and deaths attributable to misuse of controlled substances.

In this thesis I will construct, analyze, calibrate, and extrapolate a system dynamics model of the opioid epidemic. This research will focus on the following four questions:
1. Are Prescription Drug Monitoring Programs an effective tool in curbing opioid abuse?

2. How does the mandatory use of Prescription Drug Monitoring Programs affect the supply of opioids to long-term pain sufferers, many of whom already contend that their pain is under-treated?

3. How large a factor in the opioid epidemic is sharing of drugs with family and friends?

4. Does a System Dynamics analysis provide an adequate description for the onset and subsequent unfolding of the opioid epidemic?
4. Methods

4.1 A System Dynamics Approach: In order to evaluate I-STOP and the effectiveness of PDMPs I will first establish a system dynamics model of prescription drug distribution and use, and the opioid addiction that results. The model will show how the treatment of pain and the diversion of drugs interact with each other. Once this model is established and calibrated, I will introduce into it different instances of PDMPs based on actual practices within individual US states. For example, some states mandate use of PDMPs while others do not. These variations in the implementation of PDMPs lead to variation in outcomes from the model I have created. The resultant set of model outcomes and extrapolation of the models to more extreme parameter values is the basis for my sensitivity analysis.

4.2 The Complexities of Addiction: Opioids are addictive, and so, whenever an individual first takes a prescription pain pill, for whatever reason (legal or illegal, given by a friend or family member, sold by a drug dealer, stolen, prescribed by a well-intentioned doctor or dentist, delivered as part of post-operative care, or for any other reason whatsoever), there is a chance of addiction. Therefore a fundamental strategy for this study will be to follow the trajectory of the pills from creation to consumption, an approach that will also provide a robust test of my assumption that any exposure to opioids carries an inherent risk of addiction.

The title of the GAO hearing quoted in section 2.6 contained an interesting statement of the problem: “…TO DECREASE ABUSE AND MISUSE … WHILE ASSURING AVAILABILITY FOR PATIENTS WHO SUFFER DAILY FROM CHRONIC MODERATE TO SEVERE PAIN.”

This is only one of many examples of the kind of dichotomy inherent in the opioid epidemic: in this case, to decrease supply (abuse) while ensuring supply (to pain sufferers). In order to tease apart the numerous often-conflicting interests and motives involved in the opioid epidemic, a useful tactic is to model the extremes of a distribution as two populations, for example long-term and short-term pain sufferers, heavy and light
drug users, under-supplied and over-supplied patients, parsimonious and profligate prescribers, and so on. This simplifying assumption proves sufficient to explain important trends, and facilitates construction of a model simple enough to appreciate intuitively yet robust enough to make specific policy predictions, in line with the standards and expectations of the System Dynamics modeling community (Sterman 2000).

The literature on the opioid epidemic abounds with examples of presuppositions that result from narrowness of focus regarding such inherently dichotomous distributions, when typically only one half of the distribution is considered. Examples include the stigmatization of some opioid dependent patients as blameworthy rather than as inadvertent and unknowing victims, and the failure to appreciate that some doctor shoppers want more drugs to treat their pain while others want more drugs to sell from their prescriptions for financial gain. Another important reason to build a system dynamics model is to address dichotomous issues of this kind.

Tracking the prescription drugs from the doctors’ offices leads directly to two kinds of opioid patients. The first are those with long-term pain and increasing tolerance to opioids. The second are those with short-term needs from sports injury, dental procedures, minor surgery, falls, and so on. On first examination it might seem sufficient to model the latter class of patients as the source for all proliferation of opioids into society, simply because they often have pills left over from their prescription. Meanwhile the long-term pain patients, especially because they become increasingly habituated to the drug over time, will generally consume all of their prescriptions.

While this is perhaps a reasonable first approximation, the reality is considerably more complex. Long-term pain sufferers may choose to sell some or all their prescription, suffer targeted theft, or choose to give pills to friends and family despite the pain (Inciardi et al 2007). Some short-term pain patients may dispose of their prescription pill excesses responsibly (Baumblatt et al 2014).

For the purposes of modeling I therefore distinguish two trajectories from the doctors’ office: one into homes with a de facto excess of pills available for distribution.
and the other into homes where the primary users consumes the entire prescription. The fraction of prescriptions entering each of these two channels is empirically determinable through comparison between the model and published data. There are huge variations in the numerical value of this fraction from place to place and over time. Factors including the doctors’ susceptibility to persistent marketing and their prior education regarding opioids, the rate at which doctors write prescriptions, and the number of prescriptions they write per patient all affect the number of pills leaving their offices. Meanwhile the activities of the patients in requiring drugs (such as feigning pain, doctor shopping, current degree of opioid dependency, or refusing to take opioids because of concerns about their risks) affect the number of pills received by patients.

Evidence accumulated over the past two decades shows the use of opioids in the United States springing up in isolated pockets, increasing over time, and spreading into adjacent geographic regions exactly like a contagious disease, and therefore amply justifying the term “epidemic” to describe its course.

4.3 Lessons from Prior Epidemics: Prior drug epidemics have been successfully modeled (Everingham & Rydell, 1994; Caulkins, 2002) by the assumed existence of two populations of users (usually called “light users” and “heavy users”) initiated into drug use and so entering the light user class, with a few subsequently escalating over time into heavy use. The ability of such simple models to fit the data on initiation and use (of cocaine in the references cited), using only three parameters (rate of quitting from light use, escalation from light to heavy use, and rate of quitting from heavy use) is impressive, and part of the inspiration for the approach taken in this work.

Figure 2: Model #1. Implementation of the Everingham & Rydell and Caulkins model.
My implementation of the Everingham & Rydell and Caulkins model is shown in Fig 2. The arrow on the left side of the figure indicates the boundary of the model, beginning with initiation. As expected, my implementation (Model #1) can successfully reproduce the published results of Everingham & Rydell (1994) and Caulkins (2002). In subsequent sections of this thesis I will model the system that causes and sustains the opioid epidemic. With that model in hand, I will then be in position to investigate the effectiveness of PDMPs through sensitivity analyses within the world of the model in which variables that describe the behavior of the actors in the model are adjusted between two perceived extremes.

4.4 Modeling the Opioid Epidemic: I begin my modeling of opioid addiction with a specific focus on illicit use. Time series data documenting the rate of initiation into the illicit use of opioids (http://www.samhsa.gov/data/) are published annually, as are death rates from opioid poisoning (CDC_Deaths.pdf). Having developed a preliminary model for the addiction component of the system, I proceed to construct the rest of the opioid epidemic system model in a series of logical steps. In particular, I add components to the system motivated by answers to three questions:

• Where specifically are the doctor-prescribed drugs consumed or hoarded?
• When the user’s appetite grows, where do the additional drugs come from?
• If doctors, having habituated their patients, turn off the supply, how will their patients react?

Despite a welter of confusion about possible causes, effects, and trends in the published opioid epidemic literature, I found it possible to identify a set of six self-consistent assumptions, listed below, from which I built my system dynamics model in several steps. Working in steps helped me to think through the logic of the model. Calibration of the variables in the model will be accomplished from comparison with published data once the logical interconnections of the model are all in place.
The six assumptions underlying my System Dynamics modeling are:

1. A population exposed to opioids exhibits dependency and death at an empirically determinable rate. The original reason for exposure to opioids is not a factor.

2. When the number of pills prescribed exceeds patient needs, exposure of family and friends leads to non-medical use. Initially the excess of pills is greater than any demand for this diversion of supply.

3. Recreational users supplied by family and friends give pills to their peers. Initially the excess of pills is greater than any demand for this diversion of supply.

4. As tolerance to the drug grows in an individual dependent user, doctor shopping arises in order to meet increasing individual need.

5. For long-term pain sufferers who develop dependency, their supply from a single doctor becomes insufficient to meet their needs. Patients with expectations that this need should be fulfilled within the medical system voice complaints about under-treatment while the world nevertheless sees an ongoing epidemic.

6. The purity and reputable source of pharmaceutical opioids makes them preferable to heroin when they are free and readily available. When cost and scarcity become factors, use of heroin (which is cheaper but riskier) rises.

**Step 1 implements my assumption number 1:** A population exposed to opioids exhibits dependency and death at an empirically determinable rate. The original reason for exposure to opioids is not a factor.

I first extended the model of Figure 2 to begin consideration of opioid deaths, shown in Figure 3. The input data (initial use of illicit drugs, http://www.samhsa.gov/data/) are entered into the model through tabulation in a text file (called OpioidTimeSeries) that
lists year and annual initiation rate. The inclusion of a mortality rate for heavy users (called rate of heavy users dying) completes this naïve opioid addiction and death model. The reason for the omission of a mortality rate for light users is explained below.

Figure 3: Model #2 Light and Heavy Users; Deaths from Heavy User Population

What values should be used for the rates of quitting from light and heavy drug use, and for the rate of escalation to investigate the opioid data? Close examination of the epidemic trend lines gives a clue. Both the opioid prescription rate and the opioid death rate had been slowly growing since the 1970s but an abrupt steepening, signaling the onset of the epidemic, happened around the year 2000.

The uptick in prescription rate from aggressive OxyContin marketing surged in 1997 (as data from the GAO hearings, described in section 2.6, confirm). Equally clearly, the sudden change in slope of the death rates trajectory happened later: specifically, in the year 2001. This lag in response is characteristic of stock and flow models, where accumulation (in this case, of opioid users) precedes an observed flow (here “deaths”). That is, in a model of this kind, it takes some time for users to transition to the points of addiction, overdose, and death.

The data from the cocaine epidemic of the 1980s (cited above) showed similar behavior. Because both cocaine use and opioid use lead to physiological addiction, I
hypothesized that the rate coefficients might be similar in the two epidemics, and so I had the idea to begin with precisely those (cocaine-determined) escalation and quitting parameters as a first guess with which to attempt to model the opioid data.

![Graphs](image)

**Figure 4:** Model #2 output vs CDC data

Graphs of number of heavy users of opioids and number of light users of opioids generated from this model are shown in figure 4 (upper). Because the appearance of the curves for each of these two classes of users turns out to be significantly different, a simple comparison of the appearance of these graphs with a plot of annual number of deaths from opioids (figure 4, center, dashed line) yields an interesting result -- the model curve for the number of heavy users of opioids is similar in appearance (in both time of onset and rate of increase) to the curve for number of deaths. Yet the curve for number of light users of opioids -- specifically, with regard to the time of onset of the steep rise in numbers of opioid users and the persistence of upward trend all the way to the end of the time line -- is very different.

Therefore, within this simple model, and assuming a constant rate of deaths per user population, the deaths are found to arise preponderantly from the heavy user
population. This allows an immediate calculation of a value for my model parameter “rate of death of heavy user” from a ratio of the death rate to the number of heavy users. That ratio is indeed constant with time (the curves of the two quantities are the same shape) and corresponds to an annual probability of one death per 133 heavy users.

This numerical result from my model can be directly compared with data presented by Dr. Tom Frieden, the Director of the Centers for Disease Control and Prevention (CDC). (http://ireta.org/2015/04/07/high-risk-opioid-use/)

![Infographic from Dr. Tom Frieden of the CDC](image)

Figure 5: Infographic from Dr. Tom Frieden of the CDC

Even though Director Frieden’s model is a static “snapshot” and my model is dynamic -- from a comparison between the numerical result of my model calculation (one death per 133 heavy users) and the data from figure 5 (115 who abuse/are dependent per death) -- it seems reasonable to conclude that the “heavy users” in my model can reasonably be equated those “who abuse/are dependent” in Director Frieden’s model.

There are two obvious shortcomings in my model of addiction to this point. I have considered only illicit drug use, and I have used the rates from the cocaine model. I will later remedy the first defect below by modeling the rate of opioid initiation from the published prescription rates, but before doing that I will consider the question of whether
it is possible to find published research that determines appropriate rates directly from the opioid data themselves.

In their paper “Epidemiological evidence on extra-medical use of prescription pain relievers: transitions from newly incident use to dependence among 12–21 year olds in the United States using meta-analysis, 2002–13”, Parker & Anthony write,

*In this report, by joining previously published age-specific estimates for prevalence of EMPPR [Extra-medical pain prescription reliever] use with this study’s newly published age-specific estimates of incidence rates through 2013, it has been possible to discover that for the most part the mean duration of extra-medical PPR [pain prescription reliever] use is on the order of 2–4 year...*

The rate coefficient from the cocaine model for light users quitting, and therefore also the rate in my opioid model, is 0.28/year, implying a duration of use of the inverse of this number, that is $1/0.28 = 3.6$ years, in *good agreement* with Parker & Anthony.

Parker & Anthony also report,

*Previously published estimates suggest that many EMPPR users try these compounds no more than a few times and then stop, with duration far shorter than the estimated mean, whereas others become persistent users, with duration considerably longer than the estimated mean (e.g., those who become opioid dependence cases).*

In other words, a few light opioid users escalate to become heavy users. The escalation rate I used, 0.04/year, is again *consistent with the range* given by Parker & Anthony.

I therefore conclude that it is justified to continue to include my simple model of addiction as a component of my larger system model. My search of the literature failed to find any description of potential similarities between the dynamics of the present opioid epidemic and those of the cocaine epidemic of the 1980’s and 90’s. Therefore, as far as I can determine, my comparison of these two epidemics (cocaine and opioid) represents a
novel contribution. Furthermore, my model result regarding exposure to opioids is consistent with my primary assumption: that any exposure to opioids carries an inherent risk of addiction.

**Step 2 implements my assumptions number 2 and 3:** When the number of pills prescribed exceeds patient needs, exposure of family and friends leads to non-medical use. Initially the excess of pills is greater than any demand for this diversion of supply. Recreational users supplied by family and friends give pills to their peers. Initially the excess of pills is greater than any demand for this diversion of supply.

That the number of pills available within the population exceeds the needs of those to whom they were prescribed is vividly demonstrated by the astonishing amount of drugs turned in at so-called “take-back” events (figure 6). These opioids are dispensed in units of tens of milligrams per dose, and returned in units of thousands of pounds left over.

![Figure 6: Drugs collected at a Tennessee “take back” event](https://tn.gov/assets/entities/behavioral-health/sa/attachments/Prescription_For_Success_Full_Report.pdf)

My model for this wild excess of pills in the population is shown in the upper half of the diagram in figure 7 -- while the lower half of the diagram attaches to the addiction module developed in step 1.
Figure 7: Model #3: Supply of pills is abundant, friends and family are supplied

From the prescription rate, I determine new initiates to opioid use as a fraction of the number of prescriptions written (assuming the rise in prescription rate is largely a consequence of new patients, consistent with this being an epidemic situation). The fraction of those new opioid patients who do not require all of their pills (do not have long term pain) are held responsible in the model for exposure of family and friends to the excess pills (in medicine cabinets, for example).

The product of three variables within this model -- “mean fraction of new patients per prescription”, (1 – “fraction of patients with long-term pain”), and “rate of use per home with extra pills per year” -- determines the normalization of the output parameter “opioid deaths per 100,000”, and the three parameters can be adjusted
until a good fit is obtained to the published data. Figure 8 shows the result from a typical run.

**Figure 8:** Input to and output from a typical run of model #3

Although it was a useful step in developing my thinking, this model is of very limited use both because it is seriously incomplete and because it only captures one of the possibilities regarding where the prescriptions go; therefore I will not consider it further, but will proceed directly to the inclusion of the rest of my six assumptions into a completed model.

One parameter I used in this model #4, enclosed here in parentheses (1 - fraction of patients with long-term pain), might seem a clumsy choice (why not “fraction of patients with no long-term pain”?), yet it was chosen this way in this model characterization of drug diversion to friends and family for a very specific reason. Patients with long-term pain generally will not have pills to share. It is well documented that opioid addiction progresses in the case of long-term use by way of ever-increasing doses as tolerance to the drug grows: below (section 4.5) I will describe a survey of deaths in Utah in which decedents routinely sought more drugs than their first doctor provided. Which brings me to the next step in building a model of the opioid epidemic system.

**Step 3 implements my assumptions number 4, 5 and 6:** As tolerance to the drug grows in an individual dependent user, doctor shopping arises in order to meet increasing individual need. For long-term pain sufferers who develop dependency,
their supply from a single doctor becomes insufficient to meet their needs. Patients with expectations that this need should be fulfilled within the medical system voice complaints about under-treatment while the world nevertheless sees an ongoing epidemic. The purity and reputable source of pharmaceutical opioids makes them preferable to heroin when they are free and readily available. When cost and scarcity become factors, use of heroin (which is cheaper but riskier) rises.

At this point I include all six assumptions of my model, as shown in figure 9. Now the distinction implied by the parameter “fraction of patients with long-term pain” becomes fully explicated. Parallel to the “oversupply” stock and flow that I introduced in the previous model above, I now add a “potential undersupply” stock and flow for the patients with long term pain, whose growing habituation and long-term need for pain relief are the perennial driver toward higher doses, and therefore potential undersupply and collateral risk of death. Taken together, the oversupply and undersupply channels consume all the pills: there is simultaneously a glut and a shortage.

Figure 9: Model #4 of the epidemic system based on my six underlying assumptions
In an important refinement from the model of figure 7, I found it was preferable to enter the data on prescription rate by using the year-over-year increase rather than the rate itself; this led to a more straightforward formulation of the parameter called “initiation” - -that is, to the part of the model that describes transition from light to heavy drug use – which was easier to compare with published data for the purpose of calibration.

The rest of the assumptions made in building this version of my model are straightforward. Long-term pain patients naturally complain about the pain when they are under-supplied relative to their growing tolerance and increasing need. They seek more prescriptions from other doctors, becoming “doctor shoppers”. Also joining the ranks of doctor shoppers are those heavy users whose habit was initiated through exposure to opioids by family and friends.

A nice point of modeling arises here, in that a person who has never seen a doctor, yet who joins the ranks of heavy users using illicit opioids, might well now be driven by addiction to seek a doctor’s prescription, and will almost certainly receive one -- given no prior record within the system and presenting as being in pain. I call such a person a doctor shopper, as logic demands; but the algorithms of a PDMP will not detect such an individual, and indeed will only discover the most egregious examples. The model suggests that the number of “one doctor shoppers” may in fact be large, a situation perhaps to be expected in the midst of an epidemic of addiction in a medical system that denies the prevalence of addiction.

The parameter called “likelihood doctor will prescribe to a shopper” allows me to model the number of doctor shoppers, and will later serve as a point of inclusion for PDMPs because, in the case of an ideal PDMP (of which none presently exist), this parameter would take the value zero. Addiction then drives thwarted would-be doctor shoppers to go in search of heroin. Some (perhaps many) heavy users will not even attempt doctor shopping -- but will go directly towards heroin, driven to do so by considerations of cost.
4.5 Calibrating the Model with Real World Data: Tennessee suffers the misfortune of having one of the most severe cases of over-prescription of opioids in the nation, and so it has been closely studied. In order to calibrate a baseline model against which to compare the differences between states I will therefore use data from the state of Tennessee. One especially useful set of data comes from a five-year-long, complete, statewide sample in which Baumblatt et al (2014) conducted a matched case-control study (matching deceased opioid victims with living patients from the state database) finding that

From January 1, 2007, through December 31, 2011, one-third of the population of Tennessee filled an opioid prescription each year, and opioid prescription rates increased from 108.3 to 142.5 per 100 population per year. Among all patients in Tennessee prescribed opioids during 2011, 7.6% used more than 4 prescribers, 2.5% used more than 4 pharmacies, and 2.8% had a mean daily dosage greater than 100 MME’s [Morphine Milligram Equivalents]. Increased risk of opioid-related overdose death was associated with 4 or more prescribers (adjusted odds ratio [aOR], 6.5; 95% CI, 5.1-8.5), 4 or more pharmacies (aOR, 6.0; 95% CI, 4.4-8.3), and more than 100 MMEs (aOR, 11.2; 95% CI, 8.3-15.1). Persons with 1 or more risk factor accounted for 55% of all overdose deaths.

The Baumblatt et al analysis did not consider the system dynamics of the epidemic. In fact few studies of the system dynamics exist in the literature, as I will discuss below. My analysis of these same data therefore addresses a unique aspect of the epidemic in Tennessee that has received relatively little scrutiny.

<table>
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<th>Year</th>
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<th>JMR</th>
<th>KKR</th>
<th>MCR</th>
<th>MSR</th>
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Table 2: Tennessee Prescription Rate per 100 Population by Health Department Regions 2007-2011: data from Prescription Opioid Use and. Opioid-Related Overdose Death —
In Table 2 the prescription rate is tabulated by Health Department Regions, whose geographic distribution within the state is shown in Figure 10.

Figure 10: Tennessee Health Department Regions

Table 2 shows that the annual rate of prescriptions is high (more than 100 prescriptions per 100 population) and varies by almost of factor of three from highest to lowest. (For comparison, the average rate per state varies from a low of 53 to a high of 143.) When I plot the Tennessee regions (figure 11), the rates are seen to be increasing in every district across the five-year timeline.
Figure 11: Tennessee Prescription Rate by Health Department Regions 2007-2011
The overdose death rate for 2008-2011 is also available from the same source, as follows:

<table>
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<tr>
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<th>JMR</th>
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Table 3: Tennessee Overdose Death Rate per 100,000 Population by Health Department Regions 2008-2011: data from *Prescription Opioid Use and Opioid-Related Overdose Death — TN, 2009–2010*. Jane A.G. Baumblatt, MD. Centers for Disease Control and Prevention. [https://www.etsu.edu/.../Baumblatt%204](https://www.etsu.edu/.../Baumblatt%204)

Figure 12: Regions with higher prescription rates have higher death rates
In Figure 12 I binned the data from tables 2 and 3 into four bins from lowest to highest prescription rate (based on the 2011 rate) -- see the legend on the right. The reason for binning the data was to demonstrate that there is a trend towards higher death rates where prescription rates are higher. This tendency is present in every case I have examined, not only in Tennessee.

Two plausible explanations for this trend in the data are (1) opioid patients in some regions are prescribed successively larger amounts over time in the form of additional prescriptions, and the larger dose kills them – consistent with Baumblatt’s conclusion, quoted above, that a dose of more than 100 MMEs (aOR, 11.2; 95% CI, 8.3-15.1) is a risk factor; and/or (2) that new patients are added within the population over time, and since each opioid patient has a risk of dying, the death rate therefore rises. Both of these factors are present as parameters in my model.

The reason why I chose Tennessee for the initial calibration of my model now comes into sharper focus, because data exist to identify not only the contributions of these two factors but also the third and final variable that deconstructs how the input of prescriptions flows into my model: that third parameter is the mean number of patients per prescription.

<table>
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<tr>
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<tr>
<td>2007</td>
<td>1761168</td>
<td>6272409</td>
<td>1760</td>
<td>14828</td>
</tr>
<tr>
<td>2008</td>
<td>1913416</td>
<td>7176542</td>
<td>1801</td>
<td>15525</td>
</tr>
<tr>
<td>2009</td>
<td>1959246</td>
<td>7460239</td>
<td>1827</td>
<td>16316</td>
</tr>
<tr>
<td>2010</td>
<td>1959923</td>
<td>7739698</td>
<td>1885</td>
<td>17054</td>
</tr>
<tr>
<td>2011</td>
<td>2024551</td>
<td>8449105</td>
<td>1919</td>
<td>17555</td>
</tr>
</tbody>
</table>

*Table 4:* the total numbers of unique patients, unique prescriptions, unique pharmacies, and unique providers for each year from 2007 through 2011 from the Tennessee Controlled Substances Monitoring Program (TNCSMP); data from *Prescription Opioid Use and Opioid-Related Overdose Death* — TN, 2009–2010. Jane A.G. Baumblatt, MD. Centers for Disease Control and Prevention. [https://www.etsu.edu/.../Baumblatt%204](https://www.etsu.edu/.../Baumblatt%204)
From Table 4, it is straightforward to calculate the following values for my model of Tennessee:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of patients per prescription</td>
<td>4.0</td>
</tr>
<tr>
<td>Annual rate of increase of patients</td>
<td>3.3%</td>
</tr>
<tr>
<td>Annual rate of increase of prescriptions</td>
<td>6.4%</td>
</tr>
<tr>
<td>Annual rate of increase of pharmacies dispensing</td>
<td>2.1%</td>
</tr>
<tr>
<td>Annual rate of increase of providers</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

Table 5: Input parameters for Tennessee model, calculated from TNCSMP data

From Table 5 it is also straightforward to calculate the change in number of patients and the change in number of prescriptions over time. The ratio of these two quantities is found to differ by a factor of two from the quantity mean number of patients per prescription, a result that is simply interpreted to mean that half of the growth in prescriptions written between 2007 and 2011 is due to more patients in the population, and the other half to more opioids per patient.

I will assume these numbers calculated from the Tennessee data for my baseline model, and now proceed to find data to calibrate the remaining parameters of my model for the entire opioid system.

Modeling the factors underlying the death rate. The astonishing glut of prescriptions distributed nationally leads to a lot of deaths, and because a lot of people die from opioid overdose, I expected to find a lot of survey data about the circumstances of those people who died: were they taking the drug as prescribed by their doctor, or did they obtain the drug illegally? In fact, I found only two rigorous surveys, details of which can be summarized as follows:

In West Virginia only 44.4% of the 295 who died had been prescribed the drugs that killed them, while in Utah 87.4% of the 254 deceased had been prescribed prescription pain medication in the year before they died, almost all
(91.8%) from a healthcare source. Yet in both cases strong evidence of drug misuse, diversion, and doctor shopping were also present.

The large difference between these two surveys – that in one state the majority of deaths were from drug abuse, while in the other state most resulted quite directly from doctors’ prescriptions – indicates the presence of that large state-to-state variation in prescription drug abuse that I anticipated in choosing my research topic. Less formal information, in the form of innumerable anecdotal accounts no less heart-rending for their lack of rigor, confirms this same trend across the nation. Some people come to opioids through prescriptions from their doctor, while others get them elsewhere – frequently from friends and family. This fact is clearly established through surveys of the living regarding their drug use:

Figure 13: Sources of prescription opioids for non-medical use
http://www.cdc.gov/drugoverdose/data/prescribing.html
The Utah survey is important because almost all of the subjects (87.4%) fall into the “doctor-initiated” category, and yet widespread signs of addiction are clearly seen. This is a survey of close relatives of the people who died, giving an intimate glimpse into the realities of the opioid epidemic -- a complete and unbiased survey that finds 75% of those close relatives had expressed concern about medication use even though the deceased got their drugs as prescriptions from their doctors. They were right to be concerned, because 52.9% had taken pills more often than their prescription specified; 31.6% had obtained prescriptions from more than one doctor during the previous year; and 29.8% had used for reasons other than treating pain, almost half of which “to get high”.

In contrast, the West Virginia survey had a minority of doctor-initiated users (44.4%). This sample had pharmaceutical diversion in 63.1% of the deaths, and doctor shopping in 21.4%. The rate of doctor shopping was therefore less in the West Virginia sample than in the Utah sample. That is, those who got their first opioids from doctors continued to get their drugs from doctors as their appetite for the drugs grew, in line with the fact that people think drugs they get from their doctors are safe.

The fraction of drug diverters in the West Virginia survey of deaths was so large that it was possible to investigate the age distribution within the sample. Drug diversion was greatest among those aged 18-24 and decreased across each successive age group. This age distribution for diversion, skewed as it is to younger users in West Virginia, is significantly different from the national average (figure 14), again demonstrating significant variations from state to state.
Figure 14: National average of opioid overdose death rates by age group
http://www.cdc.gov/drugoverdose/data/overdose.html

This variation in the age distribution of opioid deaths by geographic region is a key indicator of a crucial factor in the epidemic. The press is full of reports of young people abusing drugs (like those who died in West Virginia), and yet the national average distribution of those who die peaks in the age range of 45 – 54 years old (Figure 14).

Earlier, I learned from Baumblatt et al (2014) that higher doses of opioids “more than 100 MMEs (aOR, 11.2; 95% CI, 8.3-15.1)” are a risk factor for death. I struggled to find data on dosage levels until I found the information I needed outside of the peer-reviewed literature in a report called “A Nation in Pain” written by Express Scripts Holding Company, a pharmacy claims processing business. In fact Express Scripts is the largest pharmacy benefit management (PBM) organization in the United States, with 2013 revenues of $104.62 billion, and so the sample size for these data, while not explicitly stated, is probably very large. Figure 15 shows the age distribution of patients receiving 120 mg or more opioid more than 50% of the time.
Figure 15: Patients receiving 120 mg or more opioid more than 50% of the time

*A Nation in Pain* also reports that

*The quantity of opioids contained in each prescription increased for both women and men over the study period, rising 6.5% in five years.*

Taken together, the data in this section hint at an alarming dichotomy that deserves much more study, namely that **young people are in most jeopardy from diverted drugs** and that **older people are in most jeopardy from their prescribed drugs**. This is perhaps not surprising based on the assumptions doctors make about doctor shoppers and drug seekers. Many doctors assume they know what doctor shoppers look like, which is in part why PDMP participation is low when voluntary systems are in place. Doctors know best, in their own minds. Yet the doctors’ frequent assumption that doctor shoppers are young is incorrect. Many turn out to be middle age or senior citizens, as the Utah survey showed. Furthermore, older people statistically are more likely to be prescribed multiple drugs, and the prospect of drug interaction must be factored in; specifically, benzodiazepines are known to be hazardous in combination with opioids.

Although not a prescription drug, alcohol is also known to pose a similar hazard. That drug interaction is a very significant problem, has been demonstrated by a very large statistical analysis from the year 2010: of the 92,209 emergency room opioid overdose
cases reviewed by Yokell et al (2014), 23.2% had a concurrent diagnosis of acute benzodiazepine intoxication, and 7.6% of acute alcohol intoxication.

(Footnote: This rate of alcohol intoxication is not elevated relative to national levels of alcoholism, and so cannot reasonably be expected to be lowered further by any policy intervention aimed at prescription drugs. The fact that approximately a quarter of emergency room case are found to be under the influence of other prescription drugs is very troubling, however, and offers a clear possibility for effective intervention, which could be a highly effective addition to the best practices of PDMPs.
-- end of footnote)

In my baseline model I will set the parameter fraction of patients who use every pill at the middle of its range (0.5), because the data presented above clearly indicate that both the “oversupply” and the “undersupply” channels of the model are populated, yet the values for West Virginia and Utah, for example, are clearly different. The sensitivity analyses below will address this question further.

The number of new extra-medical users per year can be modeled using the very same data on first use of illicit opioids that I used earlier when first developing my model of addiction (Model #2 in Figure 3), this time predicting that rate of first use from the prescription rate. This happens in the model by drug diversion. Specifically, from the number of prescriptions the model calculates the number of homes with an excess of pills, from which the diversion of prescriptions is estimated (I set the baseline model at a value of 50% of the homes suffering diversion of a prescription), and finally multiply by a factor called proliferation of pills that accounts for the fact that prescriptions comprise a bottle of pills, but sharing (probably) happens by the pill. I will vary proliferation of pills but strictly mathematically I could equally well vary the number of homes suffering diversion because only the product of these two terms enters: I modeled the situation with this apparently redundant parameter in order to make explicit the counting of number of prescriptions on one hand, and the number of pills on the other.
When the value of the parameter *proliferation of pills* is set to a value of 4 the model number of non-medical users is similar to the data (Figure 16). The difference in detail between the shapes of the two curves may be an artifact of the precision of the data or demonstrate a limitation of this simple model. Both because the shapes of the two curves are somewhat different, and because I will consider not the absolute values of parameters like this one but rather the effect of changing them from the baseline model values in my sensitivity analyses below there is little motivation to make any further attempt at a best fit for a model like this. I will discuss the issue of goodness of fit in system dynamics models below.

![Non-Medical Users (millions)](image)

**Figure 16:** The model can approximate the number of non-medical users given the prescription rate as input when *proliferation of pills* is set to a value of 4.

The model value for *rate of shortfall per patient per year* modulates the number of *shortfalls and complaints* which also depends on the (calculated) number of *Long-term patients who use every pill prescribed, and so have long-term access issues*. The number of long term pain sufferers complaining of under-treatment numbers 1.1 million (ref), and that value is matched by my model for *rate of shortfall per patient per year = 0.15/year*.

I now proceed to set all of the baseline parameters to the values established in this section. Running the model now gives a prediction for opioid deaths per 100,000 that matches the published data when the *rate of heavy users dying = 0.004*, a value almost a
factor of two different from that obtained from my naïve model #2; but that earlier model #2 was **incomplete**, because it did not include first use of opioids by patients with **prescriptions**. Its sole purpose having been served in allowing an early approximation to the modeling of addiction, model #2 will not be considered further.

The number of heroin users in the country is variously estimated to be between 60,000 and a million. When I set *rate of heavy users affected by price* to 0.1/year, the *number of heavy users per year who switch to heroin because of price* in the model has a value of 300,000 in 2010. This is comfortably within the target range, and so these parameters are adopted into the baseline model.

The rate at which heavy users seek extra prescriptions is unknown. People who become habituated to illicit (diverted) prescription opioids and then go to see a doctor for more are almost invisible to the present medical system. If such a person tells a doctor that his or her back hurts, having no prior prescriptions, that person will probably get opioids. For the baseline model I set the *rate at which heavy users seek extra prescriptions* = 0.5/year. These people are doctor shoppers, and yet are not countable by any PDMP algorithm. They do make a contribution to my model, however, and so their contribution will contribute fully in my sensitivity analyses below. This is a good example of the kind of effect that might be elucidated from a system dynamics model, but not from a more static statistical analysis.

<table>
<thead>
<tr>
<th>Baseline model parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>fraction of prescriptions that represent dose increase</td>
<td>0.5</td>
</tr>
<tr>
<td>mean number of patients per prescription</td>
<td>0.25</td>
</tr>
<tr>
<td>fraction of patients who use every pill</td>
<td>0.5</td>
</tr>
<tr>
<td>proliferation of pills</td>
<td>4</td>
</tr>
<tr>
<td>rate of shortfall per patient per year</td>
<td>0.15</td>
</tr>
<tr>
<td>rate of use per home with extra pills per year</td>
<td>0.5</td>
</tr>
<tr>
<td>rate at which heavy users seek extra prescriptions</td>
<td>0.5</td>
</tr>
<tr>
<td>rate of heavy users affected by price</td>
<td>0.1</td>
</tr>
<tr>
<td>likelihood doctor will prescribe to shopper</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**Table 6**: Parameter values for the baseline model
The final parameter requiring calibration in my model is *likelihood doctor will prescribe to shopper*. This parameter changes downwards by design when PDMPs are introduced, and declines further when PDMPs become mandatory. I will adopt a mid-range value of 0.5 for the baseline model, in order to accommodate extreme variations in either direction from this mid-point. In particular, pill mills and ideal PDMP regulation lie at opposite ends of this range.

A first test of the performance of baseline model can be conducted by using the data from Tennessee for the various Health Department Regions. Earlier, in order to demonstrate the correlation between prescription rates and death rates region by region, I was obliged to bin the data, because the death rate data are based on relative small numbers (in the sense of statistics, not humanity) and so are noisy. The prescription rates, however, are based on much bigger numbers, and are not nearly so noisy. Therefore I can usefully run the time series prescription rate data (Table 1) through my model to predict death rates region by region. (Because I use year over year increase as the input, I first extrapolated the data back to the beginning of the epidemic using the shape of the national prescription rate trend as a template.) The actual death rates (binned, as before) are plotted in the left frame of Fig 17, and the model death rates (less noisy because predicted by the model from prescription rates) are plotted in the right frame. One parameter, *rate of death of heavy user*, was varied to create this fit, and it was necessary to double the value relative to the baseline model. Higher doses are a risk factor, and per capita consumption is high in TN; of course, other explanations are possible, as I will explore further below.

![Fig 17: death rates, data as a function of prescription rates (left); model death rates (right)](image-url)
5. Findings

5.1 Learning about System Dynamics Models: I decided to investigate a System Dynamics model for this study (1) because there is evidence for time delays between cause and effect in the opioid epidemic, (2) because of the accumulation of stocks and flows within the system of opioid distribution, and (3) because I had read that System Dynamics models are considered an effective tool in the study of epidemics. As described in section 4.2, the data show that it is accurate to describe the opioid crisis as an epidemic because opioid abuse is seen springing up in isolated pockets, increasing over time, and spreading into adjacent geographic regions exactly like a contagious disease.

I therefore identified a software package to meet my modeling needs. The software I chose to use, Vensim, comes with many useful learning examples (https://www.researchgate.net/figure/277158047_fig1_Figure-1-Stock-flow-diagram-for-a-simple-epidemic-model) including models of epidemics such as Figure 18.

![Figure 18: A Stock-flow diagram for a simple epidemic model](https://www.researchgate.net/figure/277158047_fig1_Figure-1-Stock-flow-diagram-for-a-simple-epidemic-model)

As I learned to use the software by studying examples like this, I asked myself which of the many variables and interconnections that were raised by my literature search could form the basis for my model of the opioid epidemic. I wondered how I would know that I had chosen “correctly”. I tried to use Figure 18 as an inspiration for my own work. I thought initially that a “good” model would surely have many interlocking feedback...
loops. As I worked to develop such a feedback-dominated model, the first effort I produced was the model shown in Figure 19. It provided me with a major surprise.

![Figure 19: An unsuccessful System Dynamic model of the opioid epidemic](image)

The concept underlying figure 19 is that the doctors and their patients infect each other with the idea of opioids as a panacea for pain relief, and that the spread of this infectious idea leads to the writing of the many opioid prescriptions that fuel the epidemic. Comparison of figure 19 with my final model presented earlier (chapter 4, figure 9) shows that the two are very different in detail, because they are based on very different philosophies. Yet they contain many of the same individual elements.

The model in figure 19 turns out to have a fundamental problem. Through repeated attempts, I discovered that it is not possible to fit the data with this kind of model including any of its variants that I constructed. I was astonished by this failure. To be candid I had thought it was inevitable that any sufficiently complicated diagram would yield a fit. Or equivalently, I might say that I underestimated system dynamics. I thought
perhaps it was little more that a clever didactic tool to illustrate relationships within an interconnected system. I spent a lot of time trying to adjust the interconnections and relationships of figure 19 to fit my data, until repeated failure and further reading led me to a very different perspective. The paper crucial to my improved understanding of the issues was “Optimisation of System Dynamic Models” (Dangerfield 2009), which specifically addresses the example of the model in figure 18. Dangerfield writes

A separate improvement to the model may be sought where it is required to fit the model to past time series data. Optimisation here involves minimising a statistical function which expresses how well the model fits a time-series of data pertaining to an important model variable. In other words a vector of parameters are explored with a view to determining the particular parameter combination which offers the best fit between the chosen important model variable and a past time series dataset of this variable. This type of optimisation might be generically termed model calibration.

Dangerfield’s identification of the fundamental role of calibration proved to be key to my building a successful model. I shifted my focus to follow the trajectory of the drugs themselves, using the rate of prescriptions written as the time-series of data from which the rest of my model should flow. From the perspective offered by Dangerfield, it became clear that the ability to calibrate my baseline model (chapter 4) is an important validation of the model’s appropriateness and usefulness. Specifically, my baseline model fits the national averages for prescription rate of opioids and death rates due to opioid poisoning. This simple model includes over-prescription by doctors, recreational drug use, drug diversion, doctor shopping, under treatment of pain, escalation to the use of heroin, addiction, dependency, and death. In the language of Dangerfield, my baseline model is “the particular parameter combination which offers the best fit” to the time series of the prescription data.

When the parameters of this model are varied away from the baseline values, we enter the realm of “what if”, because the baseline model fits the real world data, and so variations shift us into a hypothetical, imaginary domain of “what might have happened”.
It is of course useful to consider such parameter variations, so that each of the driving factors in the model can be studied in detail in a series of “what if” scenarios, often called “sensitivity analyses”, as follows:

5.2 Drug Sharing: My model directly links the number of prescriptions written to the number of people annually initiated into opioid abuse. It is important to realize that it was by no means a foregone conclusion that these two data sets could be modeled concordantly with the set of assumptions I made. Therefore, the concordance found in my model corroborates the idea that a major source of illicit drugs is diversion of legally prescribed opioids from family and friends. The baseline model value, determined from real world data, is four people per diverted prescription, an entirely plausible number, since drug sharing is known to be very common (Inciardi et al 2007).

By varying this drug-sharing parameter the model can answer the questions, “What if the number of pills diverted were different? How specifically would the death rate change?” Because, within the model -- as prescriptions are taken from medicine cabinets and spread into the world -- some people become initiated to opioid use, some of them become addicted, and some of them die. The parameter proliferation of pills models the issue of how many people are infected from a single prescription. What if it changed from its present real-world value of 4?

Figure 20 shows the effect of varying the parameter proliferation of pills.

![How Death Rate Depends on Proliferation](image)

**Figure 20:** The effect of varying model parameter proliferation of pills (the number of individuals who share from one diverted prescription; called “pills” in the figure).
There are two noteworthy facts about Figure 18. Firstly, the size of the effect is large – a tremendous number of lives would be saved if pill sharing were stopped. Secondly, the death rate is not linearly proportional to the parameter proliferation of pills. Because system dynamics models are non-linear, it would be simplistic to think that the changes predicted by the model with regard to this or other parameters can be accurately anticipated by simple scaling. Specifically, in this case, the predicted death rate would have decreased by almost a factor of two in the year 2010 if proliferation had been reduced by a factor of 4. This non-linearity follows from the fact that proliferation of pills is not the only channel through which victims get their drugs. Sad to say, every patient who ever receives an opioid prescription from a doctor is also another potential addict.

5.3 Long Term Pain: In my model a significant fraction of patients do not share their pills. This is the population that includes long term pain sufferers whose tolerance grows over time, and who therefore tend to consume all the drugs they can obtain. What if doctors only prescribed for this population? What change in the death rate would result? Qualitatively, it is obvious that the number of pills available to be diverted would be smaller, and so the death rate would go down. Quantitatively, Figure 21 shows the model results for four values of the parameter fraction of patients who use every pill.

![Image](image.png)

**Figure 21:** The effect of varying model parameter fraction of patients who use every pill (called “fraction” in the figure).

My model therefore concludes that the death rate would be sharply decreased if
prescription patterns were such that the patient for whom the drugs were intended consumed all of the drugs provided. That is, drug diversion is a major cause of death.

5.4 Transition to Use of Heroin: In a recent article in The New Yorker, Agent James J. Hunt, the head of the New York Division of the Drug Enforcement Agency, gave his opinion about heroin in Staten Island, NY:

\[
\text{Agent Hunt’s office chair at his big desk in D.E.A. headquarters in Manhattan is black and high-backed. He wore a black shirt and a muted tie. His blue eyes and his blond, wavy hair parted almost in the middle made his face stand out as if in an Old Master dark-background oil portrait. I asked if the plan to push large quantities of cheap heroin and undersell the illegal pill market had been the idea of a particular person—like El Chapo Guzmán (the Sinaloan cartel leader who went to jail, escaped, and was recently recaptured). Hunt thought a minute and said, “Yes, it probably was his idea, or the idea of four or five cartel leaders like him.”}
\]

http://www.newyorker.com/magazine/2014/09/08/antidote

When heroin is cheaper than prescription opioids, some heavy users will switch to heroin. Because the precise relationship between rate and price is unknown (no data are available on this issue), I can offer only an order of magnitude estimate. My model indicates that cheaper product could create hundreds of thousands of heroin users nationally.

Nor is price the only driver away from prescription drugs and towards heroin. From the same New Yorker article quoted above:

Within a few months, evidence seemed to show that ISTOP had reduced the amount of illegal opioids on the market. Critics said the law would create a greater demand for heroin, and that seemed to have occurred. According to N.Y.P.D. Captain Dominick D’Orazio, commanding officer of Staten Island Narcotics, seizures of pills had gone down forty-four per cent, while seizures of heroin had gone up by the same amount.

A similar trend is seen in King County, Washington (Figure 22).
5.5 Doctor Shopping: A primary motivation for the creation of PDMPs is to abridge the practice of doctor shopping. In my model the parameter $L$, the likelihood doctor will prescribe to shopper, captures this desired change with an assigned value between 0 and 1. Figure 23 shows the number of doctor shoppers given by the model for three cases of $L$: reducing the probability of a prescription from 70% to 30% in the year 2011 would have reduced the number of doctor shoppers by a million.

Figure 23: The effect of varying model parameter likelihood doctor will prescribe to shopper (called “L” in the figure).
Since about 200 million opioid prescriptions were written in 2011, and doctor shopping is believed to be rampant, it should be expected that the size of the reduction would be of the order of millions. But PDMPs generally define doctor shoppers as individuals seeking more than some specified number of prescriptions (typically five). The PDMP algorithm makers use that kind of definition because they have no choice: their algorithms can only control the things they can count. System dynamics modelers are, however, not constrained by such artificial limitations.

In my model, therefore, people addicted to opioids obtained by illegal means and subsequently seeking a legal prescription to satisfy their habit are classified as doctor shoppers (as are people who simply heard about these drugs on the news and want to try them; for, in the same way that warning labels have unintended consequences, news reports outlining the dangers and potency of these drugs will have varied results). Consequently I expect that the reduction in doctor shopping activity reported by a PDMP will necessarily be very much smaller than predicted by my model, but the trends in the data should be similar to the model prediction.

Data are just beginning to become available. Figure 24 is from Tennessee, while Figure 25 shows trends from ten other states, comparing and contrasting those states that have mandated PDMPs with those that so far have not. Clearly, prescribers do not use PDMPs until and unless they become mandatory, as Figures 25 and 26 so vividly illustrate.

Figure 24 http://www.slideshare.net/OPUNITE/pdmp-5-hopkins-dreyzehneroleary
Figure 25: http://www.slideshare.net/OPUNITE/rx15-pdmp-wed11151kreiner2ringwalt?next_slideshow=1

Figure 26: http://www.slideshare.net/OPUNITE/pdmp-5-hopkins-dreyzehneroleary

5.6 Future Course of the Epidemic: My model is able to predict the future course of the epidemic by assuming the future rate of new prescriptions and any assumed changes in the various parameters of the baseline model as a result of assumed policy changes.
For example, I consider the extreme and unrealistic assumption that no doctor writes an opioid prescription for a new opioid patient after 2011, and that no heavy user switches to heroin. This counter-factual case is considered as a limiting condition -- to show that the pool of heavy users persists for a long time under any assumption in my model, as shown in Figure 27. Therefore my model shows that the effects of the epidemic would linger even under the most optimistic assumptions, both because opioids are addictive and because long-term pain sufferers have ongoing need.

![Death Rate per 100,000 if No New Opioid Patients after 2011](image)

**Figure 27:** The most optimistic extrapolation of the epidemic

If I add the assumption that 30% of these heavy users switch to heroin, then the number of new heroin users exceeds a million before the end of the decade. Consistent with the assumption of tighter prescription practices, the number of long-term pain patients experiencing under-treatment of their pain also grows rapidly. Mandatory PDMP implementation is no more successful, but necessarily produces similar outcomes, because its intent is to curtail the number of opioid initiates, but cannot logically do so to a greater degree than the radical assumption I made of no new opioid patient after 2011.
6. Discussions

6.1 The Rationale for PDMPs: I described in Section 2.1 how physicians in the nineteenth century, faced with a lethal combination of ignorance and limited alternatives, were seduced by the short-term symptomatic relief delivered by morphine, and often addicted their patients to opioids. The tragic lessons of that time led to stricter prescription laws, and taught twentieth-century physicians to be extremely cautious in using opioids. Warnings about the dangers through popular and professional publications were widespread and, because opioids were understood to be extremely addictive, they became a solution of last resort.

Yet at the end of the twentieth century the use of prescription opioids suddenly and dramatically increased. The number of opioid prescriptions written, and the rate of deaths by opioid poisoning, grew by large factors year over year, as shown in Figure 28.

![Figure 28: Increase in the rate of prescriptions and the rate of opioid deaths](image)

The lessons of the nineteenth century had been forgotten. A change in attitude of the nation’s doctors – a change without which there would be no opioid epidemic -- had been driven by two very strong and very different factors. The first driver was the desire to eliminate pain completely, and the second was aggressive marketing by drug manufacturers (Section 4.2). The nation was awash in prescription drugs, and the government was obliged to take remedial action through the introduction of new policies (Section 2.2).
Because information technology (specifically proliferation of access to the Internet) was growing so very rapidly during the onset of the opioid epidemic it was natural that the idea of PDMPs would arise, in the words of the New York Attorney General,

...to increase detection of prescription fraud and drug diversion [and] establish an on-line, real-time, controlled substance reporting system that requires prescribers and pharmacists to search for and report certain data at the time a controlled substance prescription is issued, and at the time such substance is dispensed (Section 2.3).

The next four sections, 6.2 through 6.5, discuss the four research questions identified for detailed consideration in chapter 3. In each case the question is stated as the header of the section.

6.2 Are Prescription Drug Monitoring Programs an effective tool in curbing opioid abuse? In answer to this first research question I find that the decrease in prescription opioid abuse caused by PDMPs is often offset by a collateral increase in the use of heroin (Section 5.3). Furthermore, the focus of PDMPs on doctor shopping does little to curb abuse for two fundamental reasons. Firstly, a majority of opioid abusers have their first experiences through recreational drug use (Section 5.1) using products supplied free by friends and family, because doctors routinely write prescriptions only a fraction of which is consumed by the patient. My model calculations show that such a prescription, not completely consumed by the patient, will typically be distributed among four friends and family. PDMPs are not able to track this activity, and yet the casual user may go on to become habituated or addicted. Secondly, such a now-habituated user, presenting as a first-time “pain” patient to a doctor, is indistinguishable from a legitimate patient in pain, and so will not trigger the PDMP system either (Section 5.4).

6.3 How does the mandatory use of Prescription Drug Monitoring Programs affect the supply of opioids to long-term pain sufferers, many of whom already contend that their pain is under-treated? In answer to this second research question I find that long-term patients, who are known to develop tolerance over time, may (because of the
regulation of opioids through PDMPs) have the experience that they are insufficiently supplied, and therefore still in pain. I find that the mandatory use of PDMPs does limit the access of long-term pain patients, who are caught in an unfortunate bind as their already-large appetite for opioids grows through habituation. They therefore become the individuals most likely to attract negative attention from PDMPs. Yet such long-term users lobby effectively for relief. Organizations like the APS and the VHA (Section 4.2), drive doctors towards the writing of more prescriptions. A year long comprehensive survey of all opioid deaths in Utah (Section 4.6) is pivotal in demonstrating the outcome of prescription to pain sufferers. This survey finds that 75% of close relatives of the 254 decedents had expressed concern about medication use even though the deceased got their drugs as prescriptions from their doctors; that 52.9% had taken pills more often than their prescription specified; and that 31.6% had obtained prescriptions from more than one doctor during the previous year.

6.4 How large a factor in the opioid epidemic is sharing of drugs with family and friends? In answer to this third research question I find that drug diversion is a major contributor to the opioid death rate. Initial access to opioids for many people is from family or friends. Aggressive lobbying has created a culture in which opioids are represented as no more hazardous than over-the-counter painkillers, and so many people accept a “gift” of opioids without reservation, and use them either for pain relief or recreation. For a significant fraction of such casual users, whose number the pharmaceutical industry has caused to be huge, this is the first step to addiction.

6.5 Does a System Dynamics analysis provide an adequate description for the onset of the opioid epidemic? In answer to this fourth research question I find that a System Dynamics model fits the parameters of the opioid epidemic. The fact that the model provides a satisfactory fit is consistent with the possibility that these six assumptions I made in building my model are valid: (1) A population exposed to opioids exhibits dependency and death at an empirically determinable rate. The original reason for exposure to opioids is not a factor. (2) When the number of pills prescribed exceeds patient needs, exposure of family and friends leads to non-medical use. (3) Initially the
excess of pills is greater than any demand for this diversion of supply. (4) Recreational users supplied by family and friends give pills to their peers. (5) Initially the excess of pills is greater than any demand for this diversion of supply. (6) As tolerance to the drug grows in an individual dependent user, doctor shopping arises in order to meet increasing individual need. For long-term pain sufferers who develop dependency, their supply from a single doctor becomes insufficient to meet their needs. Patients with expectations that this need should be fulfilled within the medical system voice complaints about under-treatment while the world nevertheless sees an ongoing epidemic. The purity and reputable source of pharmaceutical opioids makes them preferable to heroin when they are free and readily available. When cost and scarcity become factors, use of heroin (which is cheaper but riskier) rises.

Variation of the various parameters within the model provides a sensitivity analysis that highlights the huge importance of sharing of pills with family and friends as a driver of the opioid epidemic (Section 5.1). The death rate might plausibly be halved by a major reduction in pill sharing, but the model also shows that the effects of the epidemic would linger even under the most optimistic assumptions, both because opioids are addictive and because long-term pain sufferers have ongoing need (Section 5.5).

6.6 The Tradeoff Between Access and Addiction:

Opioids can relieve terrible suffering. Well-informed patients in pain, aware of the argument of “pain as the 5th vital sign” (section 2.6), visit their doctors in full expectation of relief. They are naturally unwilling to take no for an answer. Indeed they are incredulous whenever they are denied their drug. But opioids are also dangerously addictive. Therefore there is an inherent and unavoidable tension between the potential of opioids, both to do great good through pain relief and to do great harm through the scourge of addiction.

In the literature search (chapter 2) I discovered an unsurprising consensus that

 accesses to healthcare generally, and to dentists and pharmacists in particular, increases the availability of prescription opioids in communities, which, in turn, is
associated with higher rates of opioid abuse” (Wright et al 2014).

The GAO hearing discussed in sections 2.6 and 4.2 recognized that tradeoff in its title: “TO DECREASE ABUSE AND MISUSE … WHILE ASSURING AVAILABILITY FOR PATIENTS”. This difficult and perhaps irreconcilable dilemma is implicit in the task facing pain doctors. It is therefore naturally repugnant to prosecutors and public alike when pill mills are set up to prey upon people in pain.

The problem is further compounded by the recreational use of opioids, recorded in history since the time of the Sumerians (section 2.1). The initial use of “the joy plant” in a search for euphoria can end in addiction. As tolerance to the drug increases, so the amount of drug need to achieve the same degree of effect is collaterally increased.

The best recourse to achieve a proper balance between access and addiction lies in a clear understanding of the risks and benefits. As this thesis has shown, we live in a time when the dangers of opioids have been broadly underestimated for more than a generation. This has been a major contributor to the present epidemic. The introduction of PDMPs is an attempt to regulate the balance. The counter-pressures implicit from addiction, and from those who supply the addicts, work to thwart the regulatory effort.

6.7 Limitations of the Present Study: The modeling software I used is able to add almost unlimited degrees of complexity. It would therefore be possible to extend the present work to include more factors. Indeed there have been a few efforts to build system dynamics models of the opioid epidemic that include factors beyond the scope of my work -- most notably those by Wakeland and his collaborators -- including a paper published 2015 November that

*incorporates use trajectories including development of use disorders, transitions from reliance on informal sharing to paying for drugs, transition from oral administration to tampering to facilitate non-oral routes of administration, and transition to heroin use by some users, as well as movement into and out of the population through quitting and mortality.*
I made a design decision to keep my assumptions and my model as simple as possible. The major advantage of this approach is that it captures the dynamics of the epidemic system in a way that exposes the root issues. This is consistent with the best traditions of the field of System Dynamics (Sterman 2000).

A second and potentially more troublesome limitation of my approach is the possibility that the system dynamics model contains elements of self-fulfilling prophecy. Specifically, when I choose an element to model, for example “homes with oversupply available for extra-medical use”, that topic inevitably becomes a subject for discussion and analysis. Perhaps this is not so bad, because the model may return a value of zero for the contribution of a factor that turns out to be irrelevant. More concerning is the possibility that an important factor has been omitted from the model. For in such a case, there is no mechanism within the scope of my approach for that missing important factor to arise from the exercise of modeling. The only checks for such potentially missing factors lie in the completeness of my literature review and in critique of the thesis itself.

6.8 Future Work: (1) Among the factors that should be considered in future work, the issue of drug interactions is perhaps the greatest. Benzodiazepines and alcohol are both known to increase the risk of mortality for opioid users, and yet doctors often prescribe benzodiazepines to their opioid patients (especially to older patients, for whom they are specifically counter indicated), and many patients drink alcohol. The statistics from emergency room admissions are alarming with regard to the issue of drug interactions -- 23.2% acute benzodiazepine intoxication and 7.6% acute alcohol intoxication in a large sample of 92,209 admissions. (http://archinte.jamanetwork.com/article.aspx?articleid=1918924).

(2) The extremely troublesome finding (section 4.5) that young people are in most jeopardy from diverted drugs while older people are in most jeopardy from their prescribed drugs should be the subject of future study and intervention. The data I presented in support of this conclusion are compelling. Anecdotal reports are fully consistent with this finding. The mindsets and motives for opioid use in these two groups
are widely different. Yet separate interventions tailored to the needs of the two groups have yet to be identified.

6.9 Latest Policy From The White House: Another measure of the plausibility of the ideas presented in this thesis is the extent to which they anticipate emergent national policy, enacted since the completion of my model calculations. In February 2016 President Obama proposed $1.1 Billion in new funding to address prescription opioid abuse and the heroin use epidemic. Several of the tools and interventions identified as effective in the president’s proposal that are fully consistent with the themes of this thesis include “evidence-based prevention programs”, “prescription drug monitoring”, and “prescription drug take-back events”.

https://www.whitehouse.gov/the-press-office/2016/02/02/president-obama-proposes-11-billion-new-funding-address-prescription

Also reported in the president’s proposal:

The federal government is expanding access to prescription drug monitoring program data throughout federal agencies. The Department of Defense’s (DoD) Pharmacy Data Transaction Service automatically screens all new medication orders against a patient’s computerized medication history and permits DoD physicians to monitor for concerning drug usage patterns.

This expansion of the federal program aligns with my policy recommendation (below; section 8.3) to use PDMPs to monitor drug interactions.
7. Conclusions

A review of the literature has shown that the forces driving the current prescription opioid epidemic raging across the United States include aggressive marketing, weak regulation, addiction, freely prescribing doctors, a glut of pills available for sharing, and easy access to illicit drugs including heroin. This thesis has quantitatively analyzed the interactions between these drivers through construction of a System Dynamics model, in order to determine the efficacy of policy intervention through Prescription Drug Monitoring Programs, leading to the following conclusions:

1. PDMPs will not substantially affect the supply of opioids because they will catch only the most egregious of doctor shoppers. Opioids are addictive, people are crafty, and pain is a subjective experience not determinable by any test available to the prescriber. Therefore, as long as the opioids continue to be over-supplied by doctors, their proliferation into the community will continue to spread addiction.

2. Mandatory PDMP use will slow but not stop opioid proliferation, and will cause long term pain patients to be under-treated in larger numbers. Doctors who presently do not choose to use PDMPs will do so when participation is mandatory, and as a result some types of doctor shopping will be curtailed. Collaterally, access to drugs by legitimate long-term pain sufferers will become more difficult. Specifically, because it is not uniformly acknowledged by the medical profession that long-term opioid users have become addicted and habituated (and so require larger doses to obtain pain relief) those long-term patients will be under-treated. There are very large numbers of such patients.

3. PDMPs as presently implemented are poor at addressing the problem for which they were originally designed. They do, however, provide a good framework for dealing with drug interactions in a complicated prescription system. Many patients have a legitimate need for three or more prescribers, who occasionally will prescribe drugs that interact poorly with each other. PDMPs will not stop the flow of opioids but they could be improved by policy to stop an individual from being prescribed, for example, dangerous
amounts of both opioids and benzodiazepines.

4. Drug diversion is a major contributor to the opioid death rate. Initial access to opioids for many people is from family or friends. Aggressive lobbying has created a culture in which opioids are represented as no more hazardous than over-the-counter painkillers, and so many people accept a “gift” of opioids without reservation, and use them either for pain relief or recreation. For a significant fraction of such casual users, whose number the pharmaceutical industry has caused to be huge, this is the first step to addiction.

5. Opioids are addictive and should only be prescribed in cases of extreme need. Serious acute pain and people with terminal diseases should likely be the only people prescribed these drugs. As I was writing this thesis, I was delighted to see that the CDC came to this very conclusion in a guideline published on 3/15/2015.

6. The rate of opioid overdose deaths will remain high. Physiological changes are caused by ingestion of opioids, and the behavior of addicted individuals is driven, often fatally, towards the satisfaction of their need. Opioids are dangerous, and a society plagued by a glut of pills is at risk.

7. A significant number of people addicted to prescription opioids will transition to heroin use for reasons of price and availability. An addicted person will find a way to satisfy the need for drugs. If prescription opioids become less readily available, or if their price compares unfavorably with available alternatives, addicted people will turn to whatever satisfies their need. For many, that will be heroin, as rapidly rising statistics across the nation demonstrate so tragically.

In summary, the opioid epidemic was created by the confluence of greed and good intention: some people wanted to get fabulously rich, and others wanted to banish all pain. Now the country is awash with pills and populated by unwitting addicts. This study helps conclude that the efforts of state governments and the FDA will be insufficient to
stem the flow of opioids, and that there is no simple intervention to thwart drug diversion and sharing of pills. The opioid epidemic will ebb like other epidemics, as much through self-regulation as through policy intervention. When the cultural meme that opioids destroy lives takes hold, replacing the current idea -- that opioids are an accessible, safe painkiller and intoxicant – then, and only then, the epidemic will subside.
8. Policy Recommendations

I have identified the factors that drive the ongoing opioid epidemic (Section 6), and find that there are three specific policy interventions that I would recommend highly.

1. Opioids should be used only as a solution of last resort.

   Nineteenth-century physicians addicted patients—and, not infrequently, themselves—because they had few alternatives to symptomatic treatment. Cures were scarce and the etiology of painful conditions was poorly understood. An injection of morphine almost magically alleviated symptoms, pleasing doctors and patients. Many patients continued to acquire and inject morphine, the sale of which was poorly controlled.

   The revolutions in bacteriology and public health, which reduced diarrheal and other diseases commonly treated with opium; the development of alternative analgesics such as aspirin; stricter prescription laws; and admonitions about morphine in the lay and professional literature stemmed the addiction tide. One important lesson of the first narcotic epidemic is that physicians were educable. Indeed, by 1919, narcotic overprescribing was the hallmark of older, less-competent physicians. The younger, better-trained practitioners who replaced them were more circumspect about administering and prescribing opioids.

   Throughout most of the twentieth century physicians remained “circumspect about administering and prescribing opioids” because they understood that opioids are extremely addictive. Yet towards the end of the twentieth century a deliberate lobbying effort by opioid manufacturers led important sectors of the healthcare community to act as if opioids are safe, resulting in the epidemic described in this thesis.

   Yet parts of our society, influenced by the enormous revenue that opioids generate, continue to act as if there is no epidemic. I have described earlier how the role of education about opioids was ceded to the drug manufacturers, and how the FDA was, and remains, complicit in this dangerous situation. This state of affairs persists despite
public hearings at which extensive public testimony emphasizes that “making opioid training mandatory for doctors [is] important, and that it shouldn’t be controlled by the drug industry”.

http://www.wsj.com/articles/fda-panel-urges-mandatory-opioid-training-for-doctors-1462405146

The headline of the quoted Wall Street Journal article, “FDA Panel Urges Mandatory Opioid Training For Doctors,” fails to reveal that the panel, as is typical, recommended no remedial changes, but rather opted for the status quo. Specifically, the briefing material for the FDA panel, the Joint Meeting of the Drug Safety and Risk Management (DSaRM) Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC), May 3-4, 2016, included the following paragraph:

The Extended Release/Long Acting (ER/LA) Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS) is intended to reduce risks and improve safe use of ER/LA opioid analgesics while continuing to provide access to these medications for patients in pain. The central component of the ER/LA Opioid Analgesics REMS is an education program for prescribers (e.g., physicians, nurse practitioners, physician assistants). Under the REMS, application holders of ER/LA opioid analgesics are required to make education programs available to healthcare providers (HCPs) who are prescribers of ER/LA opioid analgesics. The application holders are meeting this requirement by providing educational grants to accredited continuing education (CE) providers who offer training to prescribers at no or nominal cost. To be considered compliant with the ER/LA Opioid Analgesic REMS, the CE courses are required to include the content and messages of a “blueprint” developed by FDA for this purpose. The FDA Blueprint includes general and product-specific information about the ER/LA opioid analgesics; information on proper patient selection for use of these drugs; guidance for safely initiating therapy, modifying dosing, and discontinuing use of ER/LA opioid analgesics; guidance for monitoring patients; and information for counseling patients and caregivers about the safe use of these drugs. Additionally, prescribers are provided information for how to recognize evidence of and potential for opioid misuse, abuse, and addiction.

http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM497290.pdf
Through these kinds of activities the FDA continues to promote the present practices for the prescription of opioids -- by the use and dissemination of language like “proper patient selection”, “guidance for safely initiating therapy”, and “counseling patients and caregivers about the safe use of these drugs”. Although the existence of the opioid epidemic is increasingly fully acknowledged in some branches of government especially the White House, nowhere in this FDA “oversight” activity is it mentioned that people are dying in epidemic numbers.

Nor is the problem limited to the behavior of the FDA. For example, The New York Times reported:

A pain management specialist, Dr. Nathaniel Katz, was stunned in 2012 when the Food and Drug Administration rejected a recommendation from an expert panel that had urged mandatory training for doctors who prescribed powerful painkillers like OxyContin. That panel had concluded that the training might help stem the epidemic of overdose deaths involving prescription narcotics, or opioids. At first, Dr. Katz, who had been on the panel, thought that drug makers had pressured the F.D.A. to kill the proposal. Then an agency official told him that another group had fought the recommendation: the American Medical Association, the nation’s largest doctors organization.

http://www.nytimes.com/2016/05/03/business/fda-again-reviews-mandatory-training-for-painkiller-prescribers.html?action=click&contentCollection=Business%20Day&module=RelatedCoverage&region=EndOfArticle&pgtype=article&_r=0

This entrenched behavior in the regulatory agencies and among senior doctors is like that seen in the nineteenth century’s epidemic; and so the latter part of the quotation that began this section is pertinent here:

One important lesson of the first narcotic epidemic is that physicians were educable. Indeed, by 1919, narcotic overprescribing was the hallmark of older, less-competent physicians. The younger, better-trained practitioners who replaced them were more circumspect about administering and prescribing opioids.

The lessons of history therefore suggest that an effective policy intervention will be to change the way our society views opioids. Future doctors, concerned by what they
see happening around them now, are already beginning to demand better training to confront the ravages of the opioid epidemic:

Calling their curriculum deficient, students at Harvard Medical School are teaching themselves how to treat opioid addiction — joining the ranks of critics who say medical schools across the country aren’t doing enough to prepare doctors for a deadly crisis.
This spring, students at Harvard have organized their own trainings on how to use new medication to treat opioid addiction. And they’ve launched a campaign to raise awareness about how to buy and use naloxone, the overdose-reversal drug.

https://www.statnews.com/2016/05/17/opioid-addiction-medical-schools/

In March 2016, The White House asked medical schools to sign a pledge to require students to learn new federal guidelines for safe opioid prescribing before they graduate. Of the nation’s 170-plus medical schools, 61 signed on. Harvard Med and others refused. “We don’t agree with the idea of taking pledges with what to put in our curriculum,” Dean Dr. Jeffrey Flier said...

Another important form of education is that our elected officials become able and willing to talk about the epidemic, and so begin to break down the stigma associated with addiction. Governor Chris Christie did so to great effect during his presidential candidacy, saying:

You don’t go to a neighborhood dinner party and say, “Hey, my daughter is addicted to heroin. What’s new with you? But if she had cancer you would tell them.

The desired outcome of my policy recommendation that we use opioids only as a remedy of last resort is that it becomes widely understood that opioids are extremely addictive. For that to happen, it will be necessary for many people to discuss the crisis honestly. One place for such discussion is among family and friends, which leads to my second policy recommendation.
2. Eliminate proliferation of pills to friends and family. The typical prescription for minor injury provides too many pills. These fall into the hands of others, who then also run the risk of addiction. Presently it is not easy to give back unused pills. It should be.

My model calculations have shown that proliferation of opioids to friends and family is a major channel for abuse and addiction, and that curtailing this proliferation would save large numbers of lives presently lost to the opioid epidemic.

Surveys show that more than 20% of people are willing to admit that they share opioids they obtained by prescription (Kennedy-Hendricks et al 2016). Fifty percent of the respondents who were still taking opioids at the time of the survey said that they expect to have drugs left over at the end of their treatment, and most of them also said that they would keep the drugs for future use in ameliorating pain for themselves (or others). Almost half of the survey respondents had received no counseling on storage or disposal of the drugs.

These results confirm that doctors prescribe too many opioids, and that people are unaware of their dangerous addictiveness. My first policy recommendation is to educate doctors about the dangers; my second is to enact policy that limits the flow of pills from doctors via patients to family and friends -- doctors should prescribe fewer pills, and it should be easy for patients to dispose of any excess.

3. Use PDMPs to monitor drug interaction through the tracking of benzodiazepines and carisoprodol in addition to opioids. Post mortem studies show that many who die from opioids have used other drugs too. The rapid PDMP electronic monitoring put in place for opioids should be extended to provide patient advice and protection against drug interactions.

The number of prescription drugs used by Americans increases steeply with age. Seniors are often prescribed five or more drugs at the same time. Under these circumstances the possibility of unintended drug interactions rises steeply. Post mortem
studies (described earlier) show that people dying from opioids often have other drugs in their system.

A particularly dangerous and increasingly common three-part mixture is that of an opioid, a benzodiazepine, and carisoprodol. (Both benzodiazepine and carisoprodol have muscle relaxant, sedating, and anti-anxiety properties; carisoprodol also further potentiates the effect of an opioid).


Pill-mills frequently prescribe this combination. Doctor shoppers treated by a variety of doctors may be prescribed the components separately and ingest the mixture unwittingly. A single doctor may prescribe two or three of these drugs together in ignorance of their potential for interaction. Drug abusers may take the mixture deliberately.

Protection of patients from this potentially lethal drug interaction can be achieved by policy. Since opioids, benzodiazepine, and carisoprodol are each prescription drugs, it would be straightforward to extend the PDMP system to track them (and other prescription drugs), and so monitor the potential for interaction in a patient. Beyond the saving of lives, the potential cost savings in health care costs could offset the cost of the program.

A retrospective cohort analysis (Pergolizzi et al 2014) using claims data from a commercial enterprise showed that among 57,752 chronic, non-cancer pain patients 5.7% (3,302 people) were exposed to a potentially major drug-drug interaction that resulted in a $609 per month increase in health care costs for the exposed patients.

The rationale for my recommendations is simple: each of these policy recommendations – limitation of the use of opioids to cases of last resort, reduction in the proliferation of prescribed pills to family and friends of the patient, and PDMP monitoring of potential drug interactions -- could save a very large number of lives.
I was very pleased to see, as I was completing this thesis, that the White House and the CDC issued provisions very similar to my recommendations, as follows:

In connection with this Federal announcement, more than 60 medical schools are announcing that, beginning in fall 2016, they will require their students to take some form of prescriber education, in line with the newly released Centers for Disease Control and Prevention Guideline for Prescribing Opioids for Chronic Pain.

This CDC guideline was published March 18, 2016. It begins:

*This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to*
improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.
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