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EVALUATING STATE POLICY INTERVENTIONS FOR OPIOID ABUSE AND DIVERSION: THE IMPACT ON CONSUMERS, HEALTHCARE PROVIDERS, AND THE U.S. MARKET FOR PRESCRIPTION OPIOIDS

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DISSERTATION

A dissertation submitted in partial fulfillment of the
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By

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ABSTRACT OF DISSERTATION

EVALUATING STATE POLICY INTERVENTIONS FOR OPIOID ABUSE AND DIVERSION: THE IMPACT ON CONSUMERS, HEALTHCARE PROVIDERS, AND THE U.S. MARKET FOR PRESCRIPTION OPIOIDS

Prescription opioid pain reliever utilization has been increasing since the 1990s, due in part to changes in recommendations for the treatment of chronic pain, but also to abuse and diversion. One innovative policy solution to the abuse and diversion of prescription opioids is state prescription drug monitoring programs (PDMPs), which provide prescribers and other selected parties with patient controlled substance dispensation history; thereby, correcting an information asymmetry problem between prescribers and patients.

The widespread implementation of state PDMPs, which vary in program design and requirements, has resulted in a variety of intended and unintended consequences. Previous PDMP evaluations have suggested such outcomes as the reduction of consumer access to opioids, the influencing of healthcare provider prescribing behaviors for opioids, and the re-shaping of the United States market for prescription opioids. PDMPs may also be associated with unintended outcomes: namely, the restriction of pharmaceutical opioids could be associated with an increase in heroin use, as evidenced by increases in heroin substance abuse treatment facility discharges. The analyses in this project examine the influence of PDMPs on healthcare providers and the market for prescription drugs by comparing trends in opioid utilization in states with varying PDMP features using Medicaid prescription utilization data and commercial insurance claims. The effect of PDMPs on consumers is explored with an analysis comparing substance abuse treatment facility discharge data for heroin abuse with pharmaceutical opioid prescriptions before and after PDMP regulatory change. Finally, the impact of other related opioid policy interventions, opioid overdose medication access laws, are analyzed by comparing opioid overdose mortality across states with differing overdose medication access policies over time. Contributions to the understanding about the impacts of these state-level opioid abuse and diversion policies can be used to improve or amplify intended outcomes and ameliorate unintended consequences.

KEYWORDS: opioid abuse and diversion, drug policy, prescription drug monitoring program

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July 1, 2015

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INTRODUCTION

Professional healthcare organizations, government agencies, and law enforcement entities have decried the abuse and diversion of prescription opioid pain-relievers in the United States as an epidemic.[1-3] Prescription drugs in general, and opioids in particular, are now the second-most abused substance, after marijuana.[4] The consequences of opioid abuse and diversion for both public safety and public health have lead to novel collaborations and conflicts between healthcare providers and law enforcement on the policy front.

The spread of prescription opioid abuse and diversion has been attributed to a host of factors that converged beginning in the late 1990s. The most widely blamed of these factors includes the methods in which the medical community addresses and manages chronic pain, the introduction of multiple high-strength prescription opioid products with aggressive marketing campaigns by pharmaceutical manufacturers, and the changing preferences of consumers who are more likely to view nonmedical use of prescription medications as “safer” alternatives to illicit substance abuse.[5] Figure 1.1 illustrates this trend of simultaneous increases of visits to primary care providers for non-cancer pain and the increasing proportion of those visits resulting in an opioid prescription.[6] An unfortunate side effect of the improvement in access to chronic pain treatment has arisen, with reports of nonmedical use of licit prescription opioids and illicit heroin substitutes increasing (Figure 1.2),[7] particularly in certain populations.

Figure 1.1 United States Opioid Prescriptions Resulting from Care for Pain*

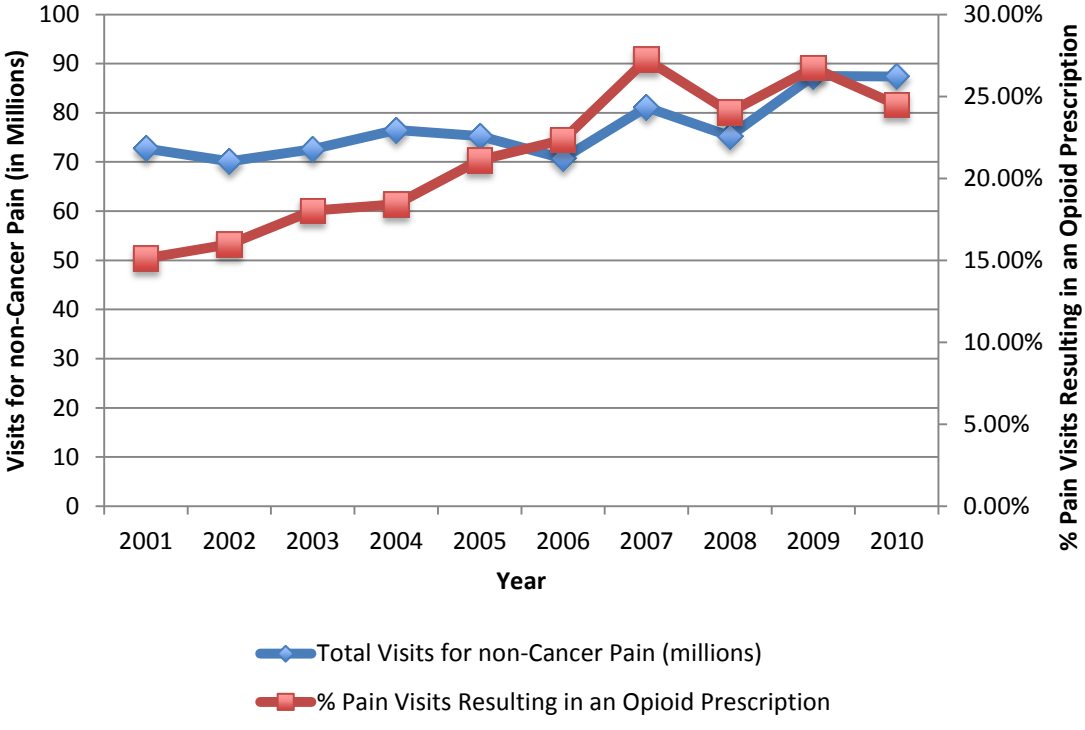


Figure 1.2 Past Month Nonmedical Use in United States Adults Aged 18 and Over†

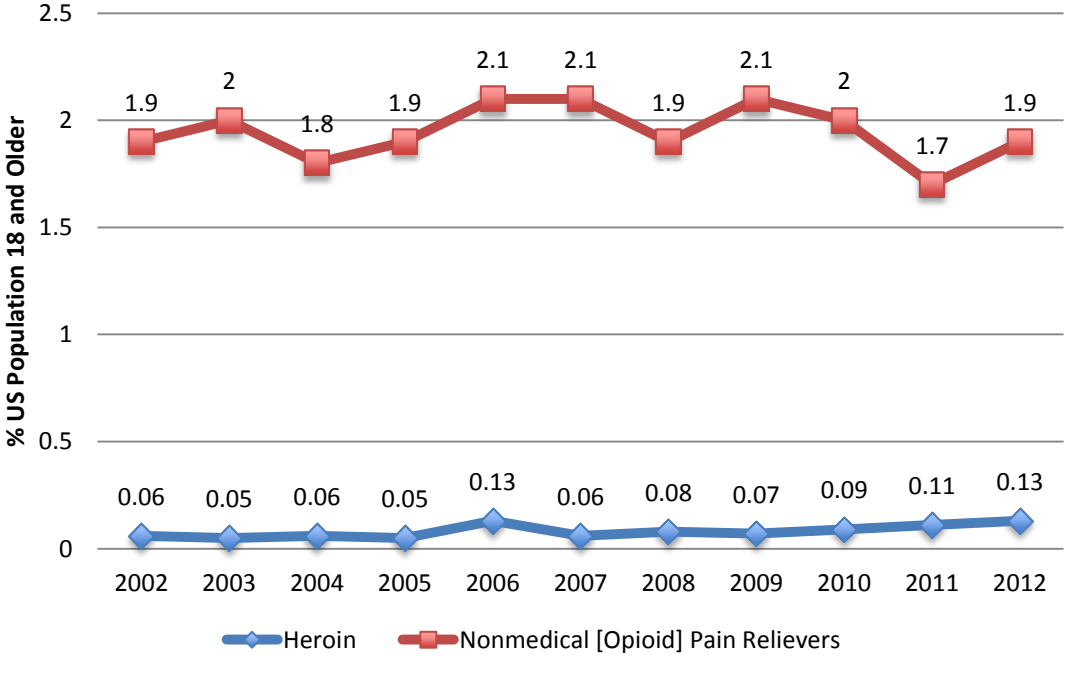


*Figure 1.1 created using data tables published by: Daubresse, Chang, et al. (2013) via the National Ambulatory Medical Care Survey.
†Data source used to create Figure 1.2: National Survey on Drug Use and Health, SAMHSA, 2013.

The most encompassing state-level policy innovation to address the problems associated with prescription drug abuse and diversion are prescription drug monitoring programs (PDMPs), which are state programs that track the prescribing and dispensing of controlled prescription substances, such as opioids, to individual consumers. The information on consumer controlled substance prescription history is made available to authorized users, such as healthcare providers or law enforcement officials, through reports generated by the PDMP at request and/or through unsolicited automation to the relevant parties. State PDMPs have proliferated throughout the nation; as of 2015, all states but Missouri and the District of Columbia have operational programs (Appendix A contains a list of the current legislative and operational status of all state PDMPs).

The controlled substance prescription data managed by PDMPs mitigates a multi-directional problem of information asymmetry: first, between healthcare providers and their patients; second, between healthcare providers and law enforcement (or regulatory agents such as medical licensure boards); and finally, between law enforcement and consumers. This information asymmetry problem, however, may not be overcome if relevant parties do not utilize PDMPs. States report low PDMP utilization rates by prescribers of controlled substances in particular, where states that have conducted evaluations found prescriber PDMP utilization below 60 percent when not mandated by law or regulation.[8-10]

PDMPs have been accompanied by various supplemental legislation and regulations at the state level to boost efforts to combat opioid abuse and diversion problems; however, resulting evaluations of PDMPs and these related

policy interventions have not reached definitive conclusions.[10-15] The scope of policy interventions in regards to opioid abuse and diversion is limited throughout this dissertation to state PDMPs and state naloxone access laws. Naloxone access laws are intended to ease access to the pharmaceutical opioid and/or heroin overdose reversal medication named naloxone. Currently, 27 states have some type of policy expanding access to naloxone, and 21 of these states adopted their policies within the past 3 years.[16] Naloxone access policies are discussed in greater detail in Chapter 6.

For this dissertation a series of analyses was designed to examine the impact of state PDMP policy interventions on consumers, the market for prescription drugs, and healthcare providers in the United States. The "real-world" approach undertaken in this dissertation is conducted using policy variable definitions that reflect the actual implementation rather than the presence of PDMP features, while the data sources for the empirical analyses have been employed to measure PDMP policy intervention outcomes using unique and sometimes novel applications.

Chapters 1 and 2 provide background and rationale for PDMPs as an innovative policy solution to the problem of prescription opioid abuse and diversion, while orienting variations in state PDMP features in terms of a policy theoretical framework. Chapters 3 and 4 examine the effect of PDMP policies on state Medicaid beneficiaries (Chapter 3) and claims data from commercially insured patients (Chapter 4) by comparing trends in opioid utilization in all fifty states and the District of Columbia, which have varying PDMP implementation dates and program features. Chapter 5 moves away from analysis of the

marketplace for prescription opioids and tackles an unintended consequence for restrictions to access and supply of pharmaceutical opioids for consumers: that is, a possible relationship between PDMP policy implementation and substance abuse treatment discharge rates for heroin. Chapter 6 delves further into the possible relationship between PDMPs, pharmaceutical opioid, and heroin consumption by examining the impact of another opioid abuse policy intervention, state-level naloxone access policies, on opioid overdose mortality in all fifty states from 1999 through 2011. Illicit opioids such as heroin will be included in the definition of opioid overdose, along with licit prescription opioids. The final chapter, Chapter 7, synthesizes the analysis results from the previous chapters to inform construction of policy recommendations for PDMPs and naloxone access.

CHAPTER ONE

State Policy Interventions for Opioid Abuse and Diversion: A Review of the Literature on Prescription Drug Monitoring Programs

Chapter Summary: This chapter contains an in-depth accounting of the public health and public safety problems associated with prescription controlled substance abuse and diversion. Focus is narrowed to prescription opioids and the origins of state PDMPs, which were implemented in reaction to abuse and diversion problems. The review process informed the development of three emergent themes from the PDMP literature: the influence of PDMPs on consumer health outcomes, the impact of PDMPs on the market for controlled substances, and the influence of PDMPs on healthcare provider behaviors. Gaps in the literature were identified and several of these gaps are addressed in the empirical analyses within following chapters.

The United States faces two intertwined public health crises: the persistent under-treatment of chronic pain conditions,[17-19] and the abuse and diversion of the controlled substances used to treat chronic pain.[1,20] The categorization of some prescription drugs, including those used to treat chronic pain, as controlled substances began with the 1970 Controlled Substances Act. The Controlled Substances Act created a classification system that divided licit and illicit drugs with abuse potential into five levels, called Schedules, and charged the Food and Drug Administration and the Drug Enforcement Administration with joint responsibility for designating substances to this Schedule classification system.[21] Criteria for controlled substance classification and example substances can be seen in Table 1.1 below.

Table 1.1 Controlled Substance Scheduling

Schedule	Classification Criteria	Examples
I	High abuse potential, no medically acceptable use	Heroin, LSD
II	High abuse potential, potential for psychological or physical dependence	Morphine, Oxycodone
III	Some abuse potential, less potential for dependence than II	Hydrocodone
IV	Low abuse potential relative to III	Diazepam, Alprazolam
V	Low abuse potential relative to IV	Cough medicines containing Codeine

Advocates for improved pain treatment practices urge caution against the adoption of state regulatory actions that influence prescriber practices through

fear of scrutiny by pointing out that undertreated chronic pain tends to disproportionately affect the economically disadvantaged, women, and minorities.[19] In response to these public health crises, the Wisconsin Pain and Policy Studies Group developed the "Central Principle of Balance", which calls for drug policies and regulations to be evaluated in regards to a dual mission: to reduce abuse and diversion while simultaneously supporting medically appropriate treatment for pain.[22]

One of the major policy innovations proposed to address the problem of the abuse and diversion of prescription medications is Prescription Drug Monitoring Programs (PDMPs), which are state programs that track the prescribing and dispensing of controlled substances to individual consumers. The information on consumer controlled substance use history is made available to certain health providers or law enforcement officials, depending upon individual state program regulations, to serve the dual purpose of addressing the crisis of chronically undertreated pain as well as reducing abuse and diversion.[23] Though states have adopted PDMPs to reduce abuse and diversion within their own populations, controlled substance abuse and diversion represents an epidemic that is costly to the nation as a whole. A 2009 Government Accountability Office (GAO) investigative report into Medicaid fraud and abuse found that Medicaid had funded approximately $63 million worth of direct payments for prescriptions that were likely due to doctor shopping in 2006 and 2007, including about $2 million in payments to health care providers that had already been banned from prescribing controlled substances.[24]

The GAO estimate does not reflect indirect costs such as medical bills for treatment, rehabilitative services, or law enforcement investigations. It was recommended that states that had not yet done so adopt PDMPs to combat the problem and states that already had implemented PDMPs should encourage increased participation by health care professionals. A similar Government Accountability Office investigation into Medicare Part D fraud and abuse attributed an estimated $148 million in costs due to payments from doctor shopping in 2008 alone.[25]

Nonmedical use of prescription drugs is most prevalent in rural or suburban areas with limited access to cheap illicit drugs, and prescription drugs are the second-most class of abused substance, after marijuana.[1] Most providers perceive “doctor shopping,” which is loosely defined as the process of visiting multiple providers with the explicit purpose of obtaining controlled substances, to be the primary cause of drug diversion but also express concerns about diversion from online retailers.[26] This perception is not borne out in reality because 55 percent of prescription substance abusers report that they obtain prescription drugs for free from family and friends and not from doctor shopping or online retailers.[27] It is important to note, however, that doctor shopping behaviors occur for opioid pain relievers more so than for any other class of controlled substance, according to prescription tracking patterns observed in California’s PDMP.[28] This is cause for concern because it is estimated that as many as 90 percent of patients undergoing treatment for long-term chronic pain conditions will receive prescriptions for the class of controlled substances known as opioids.[5]

PDMPs and related policies address the legal and public health crises of abuse and diversion by combining government authorities and medical practice in a novel, and at times controversial, way. The specific aims for this literature review are to:

- *describe the origin of PDMPs and related policies;*
- *examine the controversial policy issues surrounding PDMPs;*
- *evaluate the available evidence for PDMP efficacy; and,*
- *analyze the unintended consequences associated with PDMP implementation.*

Methods

PubMed, JSTOR, and Google Scholar were used to search for combinations of the following keywords and phrases: prescription drug monitoring program, PDMP, PMP, controlled substance, opioids, monitoring, and health policy. Literature was excluded if the topic lay outside of the scope of the specific aims addressed, was published as a "letter to the editor" or opinion piece, or was authored before 1999.

The Origins of PDMPs

In 1914 New York state passed a law that required physicians to use duplicate, numbered forms to write prescriptions for certain prescription medications, which were collected and stored by the prescribing physician and were to be presented on demand to state authorities for inspections.[23] It was California, however, that instituted the first official PDMP in 1939, which predated the federal Controlled Substances Act by over 30 years. The California PDMP required physicians to collect records of state-defined controlled substance

prescribing using triplicate copies of prescriptions and forward those records to public health and law enforcement agencies. Most other states did not adopt PDMPs until the 1990s and 2000s and a variety of monitoring strategies have since been attempted. As of 2015, 49 states have enacted legislation to create PDMPs and 43 of those states have operational programs.[29] See Appendix A for more information on state PDMP enactment and operation status.

In a typical, contemporary PDMP, states require dispensers of controlled substances (usually pharmacies) to submit electronic or paper reports for each substance dispensed within one day to two weeks of dispensing. This data transmission process varies across states, but each PDMP grants access to data on an individual's dispensing history to authorized PDMP users only.[30] Most states with PDMPs grant access to controlled substance user data to prescribers, dispensers of controlled substances, licensing authorities, and law enforcement officials conducting investigations of potential illicit activities. Every state with a PDMP monitors Schedule II controlled substances, but some choose not to monitor controlled substances categorized as Schedules III, IV, and V due to less perceived risk for abuse potential. Departmental authority varies from state to state, but most PDMPs are housed within law enforcement departments, departments of public health, boards of pharmacy, or other medical licensure boards.[31] The variability in state PDMP organization, management, and monitoring activities due to competing public health and law enforcement missions will be discussed in greater detail in the following chapter.

Controversial PDMP Policy Issues

PDMP policies frequently blur the boundaries between law enforcement investigation and medical privacy because all state PDMPs rely on information collected about individual patient dispensing and prescribing history. There is a potential conflict between patient privacy as mandated by the Health Insurance Portability and Accountability Act of 1996 due to the possibility of law enforcement officials or providers who are not treating the patient accessing private patient prescription data.[32] The Office of National Drug Control Policy dismisses these privacy concerns by maintaining that PDMP records are protected similarly to other medical records: "Law enforcement may not access patient- specific PDMP data unless they have an active investigation, and healthcare providers can access only the PDMP data relevant to their patients."[33] Surveys collected from Virginia physicians, however, revealed that physicians in that state mistrust law enforcement with patient data and remain skeptical of the level of confidentiality being practiced for patient records and for physician prescribing behaviors.[8]

State PDMPs have varying regulations for the access to and usage of PDMP data. Proactive systems generate reports without solicitation for relevant PDMP users when certain thresholds are met, whereas reactive systems require PDMP users to request reports about prescribing or dispensing for an individual patient's records. Less than half of state programs currently have both the technological capability and legal authority to generate unsolicited reports.[34]

Two federal initiatives have been undertaken to promote the implementation of state PDMPs: first, the Harold Rogers Prescription Monitoring Program grants that were offered through the Department of Justice and second,

the National All Schedules Prescription Electronic Reporting (NASPER) Act of 2005, which offers grants through the Department of Health and Human Services.[35] The NASPER and Harold Rogers grant programs promote slightly different missions. The NASPER program initiative originally intended to promote uniform security requirements, state interoperability, and nationwide database access to approved users, but has since restructured funding incentives to de-emphasize the original initiatives.[5,26] NASPER grants for state PDMPs to start-up or expand existing programs now operate alongside the earlier federal program, the Harold Rogers Prescription Monitoring Program, which offers grant funding for state PDMPs with fewer requirements.[32] NASPER was extended through 2015 and states continue to receive NASPER grants ranging from about $50K-$350K to either implement or upgrade state PDMPs, but variations in program design are now permitted. This relaxation of NASPER requirements has resulted in the implementation of state programs that have few mechanisms for interstate information exchange, though the earlier Harold Rogers grant-funded programs rarely built-in these mechanisms either.[35]

Evidence for PDMP Efficacy

Kentucky's PDMP, the Kentucky All Schedule Prescription Electronic Reporting Program (KASPER), was implemented in 1999 and converted to an electronically based reporting system in 2005. KASPER is widely regarded as the prime example of a successful PDMP and health agencies and health professionals continue to advocate for KASPER to remain the national model program.[31] Comprehensive evaluations of PDMPs have been rare and so a

variety of methods have been used to approximate different facets of PDMP effectiveness and success.

The GAO chose to examine KASPER as a case study to measure the effectiveness of PDMPs in a 2002 evaluation report by counting the average number of days it took law enforcement officials in Kentucky to complete investigations of doctor shopping before and after the implementation of KASPER. The reduction in days to investigation completion dropped from 156 days before KASPER was implemented to 16 days after KASPER implementation. These findings were used as evidence to support the claim that states with PDMPs are successful at reducing drug diversion.[32,36]

Though a wide variety of methods have been used to evaluate PDMP effectiveness, most fall into a few broad categories: tracking prescribing trends, health outcomes and mortality studies, and perceptions of efficacy studies. These categories of PDMP studies will be examined in detail in the sections that follow.

Tracking Prescribing Trends

PDMP data can be used to track prescribing and dispensing patterns across a state. Massachusetts PDMP data collected between the years of 1996 through 2006 was used to monitor trends in dispensing patterns and doctor shopping. Though less than 1 percent of individuals were found to be engaging in doctor shopping, defined here as using services from 4 or more prescribers and 4 or more pharmacies over the course of one year, those individuals accounted for 3.1 percent of all prescriptions for Schedule II opioids.[37] Studies that track

trends in prescribing to identify doctor shopping have the significant limitation of not having a standard definition of doctor shopping to refer to, and so the differences in definitions will influence prevalence estimates.

Evidence from a 2007 study of California PDMP data found that 12.8 percent of patients prescribed opioid controlled substances were potentially engaging in doctor shopping, which is defined in this study as receiving the same prescription from two or more prescribers and filling them at two or more pharmacies within a 30 day period.[28] Again, this piece highlights the need for a standardized definition of doctor shopping because these trend estimates are not comparable with those of other studies using different measurement parameters. Neither doctor shopping trend study measured prescriber or dispenser use of the PDMP nor did they attempt to measure a relationship between PDMP usage and doctor shopping trends. Continued tracking of California PDMP data after minor regulatory changes (moving from triplicate prescription forms to security prescription forms in 2005) revealed that the policy change was correlated with an increase in doctor shopping behaviors for opioid Schedule II controlled substances over time.[38] These trends conflict with evidence from other PDMPs about possible substitution effects that would have predicted a decrease in Schedule II opioid controlled substance prescriptions and an increase in Schedule III opioid controlled substance prescriptions. Schedule III opioid controlled substances were not tracked in this particular analysis and so speculation about substitution effects is not possible. The California study also points out that variability in program design may have significant impacts on the behavior of prescribers.

A study by Han et al. (2012) sought to explore what characteristics of a consumer and county could be related to doctor shopping in an analysis that loosely defined doctor shopping as receiving an opioid prescription from multiple prescribers and pharmacies during 2006.[39] Younger, female patients who obtained prescriptions for Schedule III opioids in counties with high prescriber availability and lower median income were found to be the most likely candidates for obtaining opioid prescriptions from multiple providers. It should be noted that this study fails to rule out the low likelihood of "malicious" intent doctor shopping incidents because all patients with more than one prescription from a second provider are assumed doctor shoppers, when in reality this may reflect the disjointed care provided by specialists and primary providers in our healthcare system rather than an intention to seek opioids for abuse.

A 2010 study measured the impact of Ohio's PDMP using a combination of physician surveys and observations as well as medical record review. The primary outcome of this study was to determine if emergency department physicians changed their initial treatment plan after viewing a patient's controlled substance history report. It was found that 41 percent of treatment management plans were changed after the prescriber saw a report and 61 percent of those changed resulted in fewer or no opioid medications being prescribed to the patient being treated.[40] Unfortunately, this study examined a small group of patients (n=179) treated by an even smaller group of physicians (n~4) and restricted the observations to exclude acute pain conditions. Physicians being prompted via survey about their anticipated use of a patient PDMP report may have unduly influenced their decision to order a report, particularly since the lead

author of the piece himself treated approximately one-third of the sample patients included in the study.

A simple comparison of trends in nationwide prescription claims data revealed that counties located in states with PDMPs have lower overall insurance claims for opioid analgesics, though it is unclear if the PDMP is the cause of lowered claims or if that is even a desirable outcome.[41] It is also unknown whether the observed reduction in claims for opioids reflects a reduction in treatments for legitimate medical need or reduction in illicit use. Tracking prescription trends provides useful information about patterns of prescription drug use over time, but these studies do not offer much in the way of determining PDMP effectiveness.

Health Outcomes Studies

An intuitive approach for measuring the efficacy of PDMPs is to look at health outcomes data in states with and without the programs. Because state PDMP data is limited to prescribing history and not complete medical history, other means of measuring health outcomes have been used to estimate PDMP influence. Two health outcomes that are tracked at the national level with publicly available data sources are substance abuse treatment admissions and drug overdose mortality. Researchers have taken advantage of this data availability and most PDMP evaluations that take a health outcomes approach define either overdose mortality or substance abuse treatment data to be the primary indicator of PDMP effectiveness.

A comparison between states with and without PDMPs found that substance abuse patients in states with PDMPs were less likely to seek substance abuse treatment for prescription opioid abuse than patients seeking substance abuse treatment in states without PDMPs (OR=0.775, 95% CI 0.764-0.785).[42] Another study examining substance abuse treatment admissions yielded similar results, finding that the presence of proactive state PDMPs led to a reduced supply of Schedule II controlled substances and a lower likelihood of substance abuse treatment admission due to prescription drug abuse.[11] Both of these pieces surmise that the reduction in Schedule II controlled substance availability was the likely reason for the decreased odds of opioid treatment admissions.

Prescription drug overdoses disproportionately affect men, middle-aged adults, and persons who identify as white/Caucasian and American Indian or Native American.[43] Residents of rural counties are nearly twice as likely to overdose on prescription drugs as urban residents.[43] Several studies have been conducted using mortality from prescription drug overdose as the determinant of PDMP efficacy. For example, an in-depth examination of West Virginia prescription drug overdose deaths in 2006 found that 93.2 percent of fatalities were caused in total or in part by opioid analgesics.[44] This study used a combination of PDMP data, law enforcement data, and records of death to determine that men who died as a result of overdose were more likely to have obtained prescription opioids via diversion whereas women were more likely to have obtained prescription opioids via doctor shopping, which they defined as receiving prescriptions for controlled substances from five or more health care

practitioners in a year. Though this study does not claim to evaluate PDMPs directly, this was one of the first uses of PDMP data to track and measure doctor shopping outside of the context of law enforcement.

More recent analyses of mortality data have taken different approaches. A 2010 study provided an in-depth case study comparison between Pennsylvania and New York drug overdose mortality rates between the years of 1994 and 2006.[45] The authors offered the differences in the state PDMP characteristics as a plausible explanation for Pennsylvania's much larger opioid consumption and drug overdose mortality rates. New York uses tamper-resistant prescription pads and has a dedicated staff for monitoring suspicious activity, whereas Pennsylvania does not have these PDMP program features. Though the differences in population distribution between urban and rural residents are noted, this is not offered as a possible explanation for the disparities between the two states' overdose mortalities. Pennsylvania's population is substantially more rural (50 percent) than New York's (25 percent) and according to the Centers for Disease Control and Prevention, rural residents are statistically significantly more likely to die of prescription drug overdoses than urban residents.[43] Future research comparing mortality data across states should factor in this key difference in state characteristics or should construct a model of state fixed effects.

Paulozzi and colleagues expanded upon the methods for investigating prescription overdose mortality by developing a research design that allowed for empirical comparisons between all states. Specifically, the effects of PDMPs on opioid overdose-related mortality and overall opioid consumption were measured

using a combination of data from PDMPs, mortality data from all 50 states and the District of Columbia, and publicly available data on prescription drug sales for 1999 through 2005.[34] It was found that states with PDMPs did not have significantly lower rates of opioid overdose mortality, even when controlling for states with proactive PDMP reports versus retroactive PDMP reports. Despite carefully controlling for geographic proximity between states with and without PDMPs, this study failed to control for the variability in other program design features.

Green and colleagues take issue with Paulozzi and colleagues' analysis of one element in program variability across states; specifically, they point out that differences in health care practitioner *access* to PDMP reports are not addressed.[46] Green and colleagues contend that five of the nineteen state PDMPs examined by Paulozzi and colleagues prohibit health care practitioner access to PDMP reports and another six states do not require any health care practitioner participation. Several of the remaining states in the original analysis report low utilization of PDMPs from health care practitioners, so the evidence presented that established a link between PDMPs and overdoses is weak. Kerlikowskie echoes criticisms of the lack of provider utilization data in Paulozzi and colleagues' analysis, but also points out that NASPER funding and electronic system upgrades represent major improvements in PDMP capabilities as tools for clinicians.[47]

Neither criticism offers suggestions for alternative model specifications, but a natural next step for improving Paulozzi's research design could be to compare the overdose mortality rates at smaller units of analysis. An analysis of

PDMP use by practitioners at the county level may help tease out the effects on overdose mortality rates in counties where the practitioner PDMP utilization is high versus counties with similar demographic and socioeconomic characteristics where practitioner PDMP use is low, assuming it is possible to convince state PDMPs to share practitioner utilization data.

An innovative approach to identifying PDMP effect on opioid overdose was taken by Reifler et al. (2012) by utilizing Poison Control Center call data that identified intentional and unintentional opioid exposures by consumers, rather than mortality data.[15] Reifler attempted to analyze differences in PDMP regulatory features by constructing indicators for "superior" and "standard" PDMPs, where superior PDMPs were defined as monitoring Schedule II-IV substances and duration of implementation since 2002. She concluded that PDMPs effectively reduced intentional opioid exposures (0.2 percent versus 1.9 percent total exposures by quarter for states with/without PDMP, p=0.036); however, the characterization of PDMPs as superior or standard failed to generate evidence of an influence of these programmatic features on Poison Control Center call volume or on substance abuse treatment admissions.

Survey Studies: Perceptions of Efficacy

Some states do not require prescriber participation in PDMPs and therefor many physicians may be unaware of the programs or how to use them, according to surveys conducted in Virginia, Kentucky, and Ohio.[8-10] Feldman and colleague's survey study of Ohio physicians found that 84 percent of physicians were aware of Ohio's PDMP, but only 58.8 percent of physicians had ever used the database five years after the program had been implemented.[9] Of those

physicians who reported using Ohio's PDMP, 93.6 percent had altered their prescribing behavior as a result of viewing a patient report. This study only looks at physicians working in a single academic medical center in Ohio, so the results reflect the perceptions and opinions of physicians in a narrow context.

Ohio pharmacists expressed usage similar to that of physicians for their state PDMP. About 62 percent of Ohio community pharmacists who participated in a survey in 2010 reported that they used their state PDMP (n=1,434).[48] Among those who did not use the PDMP, their primary reasons for not doing so included a lack of Internet access, slow reporting times, and time to register for the PDMP. Pharmacists that had received information about the PDMP from continuing education training were more likely to be registered users of the PDMP than pharmacists who had not received information. The Ohio studies point to an important lesson for states implementing PDMPs: it is difficult (and perhaps not worthwhile) to measure PDMP effectiveness if the intended primary users, physicians and pharmacists, are not using the program.

The evaluation of Kentucky's PDMP included an analysis of prescriber, pharmacist, and law enforcement perceptions of PDMP effectiveness.[10] All three groups report overwhelming agreement that Kentucky's PDMP is effective at reducing prescription drug abuse and diversion: prescribers-95.8 percent, pharmacists-92.8 percent, and law enforcement officials- 93.1 percent. While law enforcement officials and pharmacists report a high degree of usage of the PDMP, 64.0 percent of controlled substance prescribers in Kentucky did not have a registered KASPER account at the time of program evaluation. A related study has examined the perception of KASPER from the Medicaid consumer/patient

perspective.[49] It was found that Medicaid patients are generally unaware of KASPER, but patients diagnosed with chronic pain conditions are more likely to report that a physician discussed their KASPER report with them than patients that have not been diagnosed with chronic pain conditions. Chronic pain patients were also more likely to report trouble getting a prescription for controlled substances, but not significantly more likely to experience problems filling a prescription at a pharmacy.

The Wisconsin Pain and Policy Studies Group developed a state PDMP and pain treatment evaluation method that grades individual state programs from A to F based solely upon the language contained in state regulations.[22] Report cards are released every three years, beginning in 2000, and states are assigned grades based upon how well their regulations adhere to the Principle of Balance by providing medically current definitions for treatments and disease states, while avoiding prohibitive limits on medical practitioners' discretion to write prescriptions for controlled substances. This report card approach addresses potential conflicts in the language of state regulations, but does not serve to evaluate the performance of the PDMPs in a direct, empirical way.

Gaps in the Research

Fishman recommends aggregating data from multiple state PDMPs to analyze health outcomes, but cautions that the variability in program regulations and operations would make any analysis of current program data unlikely to pick up on the successful attributes of a program.[12] This incompatibility between state program measures could be ameliorated if states were to agree on a nationwide list of controlled substances to monitor via their PDMPs and move towards

adopting more similar program features. The failure of NASPER to require state interoperability is quite the hindrance to measuring national PDMP effectiveness.

A significant proportion of the studies examined in this paper use the Department of Justice's Automation of Reports and Consolidated Order System (ARCOS) data to track controlled substance sales and the Substance Abuse and Mental Health Services Administration's Treatment Episode Datasets (TEDS) to track substance abuse treatment. These two data sources present researchers with several limitations. For example, ARCOS data does not provide any evidence of illicit drug purchasing or licit interstate purchasing that individuals transport across borders. The ARCOS data is also unable to capture the specific intended indication for each dispensed drug.[50] Substance abuse treatment admissions data (TEDS) is limited in capturing only those individuals who choose to seek inpatient treatment for substance abuse in facilities that receive at least some public funding.[51] States with higher poverty rates may not have their substance abuse populations adequately represented if a smaller proportion of individuals with substance abuse problems from those states seek inpatient treatment. Variation in state drug court policies may also impact court-ordered substance abuse treatment admissions.

Brushwood points out that previous methods of determining PDMP efficacy largely focus on reducing drug diversion and pay little heed to determining whether PDMPs have an impact on reducing drug abuse.[13] Drug abuse, in itself a concept difficult to measure, has often been operationalized as drug overdose deaths or treatment sought for overdose. Limitations associated with using these particular outcomes as the indicator for effectiveness have

already been discussed and it is clear that researchers are in need of more comprehensively defined, standard indicators of health outcomes in order to evaluate PDMPs using these methods.

Healthcare providers and the public have expressed skepticism that PDMPs are effective tools for reducing drug abuse and diversion due to perceived doctor shopping in areas bordering states that do not have PDMPs.[23] Law enforcement agencies, however, cite evidence of increased prosecutions for criminal offenses of diversion and doctor shopping in states that have PDMPs to argue that state border trafficking is not a significant weakness of PDMPs.[52] Law enforcement agencies have more resources to build cases when using PDMP data, but interstate exchange of PDMP data is still limited. The capability to exchange information with other state health providers should be incorporated into future evaluations of PDMP efficacy.

Unintended Consequences

The implementation of PDMPs may lead to unintended consequences. The unintended consequence that has drawn the most concern from communities of health professionals is the phenomenon known as the “chilling effect”, which is the change in prescriber treatment practices as a response to a perceived threat of prosecution or investigation.[10] Another unintended consequence, the possibility of a substitution effect of lower Scheduled controlled substances for higher Scheduled controlled substances, was unanticipated before program implementation but may be related to the chilling effect. What follows is a discussion of the evidence collected thus far about both of these consequences of PDMP implementation.

Chilling Effect Evidence

Physicians and physician interest groups in states that implement PDMPs have sometimes expressed concerns that their medically legitimate treatment of patients with chronic pain conditions will be flagged in electronic systems that monitor prescribing patterns.[53] Some academicians and health care providers have criticized law enforcement organizations like the Drug Enforcement Agency (DEA) of being overtly dismissive of the possibility that PDMPs cause a barrier to access. One paper accuses the DEA as responding "…with sarcasm to the suggestion of a chilling effect...referring with disbelief to what it describes as the 'alleged' chilling effect."[13]

The majority of research conducted with the explicit intent of measuring a chilling effect associated with PDMP implementation has been survey studies. Physicians in several states have been asked about their actual prescribing habits as well as their perceptions of PDMP influence on those habits. Survey questions about regulatory pressures reveal that physicians in various specialties from across the United States are fairly unconcerned with pressure to prescribe fewer opioids for chronic pain treatment, though physicians in states with PDMP-like programs expressed greater comfort with prescribing opioids long term.[54] A survey of Ohio physicians is in agreement with these national survey results, as 30 percent report feeling less concerned about prescribing controlled substances as a result of viewing patient reports, and a few of these physicians (14 percent)

expressed feeling more comfortable increasing the quantity prescribed after viewing a patient's report.[9]

A survey of physician attitudes of Virginia's PDMP found that a small minority of physicians (about 5 percent) reported a decreased ability to treat chronic pain due to the implementation of a PDMP. However, more physicians (about 36 percent) reported a general decrease in prescribing of controlled substances for other reasons, such as media attention and increased law enforcement actions.[8] This piece surveyed a small group of Virginia physicians about initial perceptions of the PDMP and because more than half of the survey sample (52 percent) had never heard of the PDMP before receiving the survey, a follow-up study to report any changes in perception or use would be useful. Interestingly, while the consensus from these prescriber survey studies is that prescribers like having access to the PDMP data about their patients, there is not much enthusiasm reported by prescribers for *confronting* a patient when the data indicates cause for concern.[55]

Fass and Hardigan contend that pharmacists are the health care providers most affected by the implementation of PDMPs, due to the required reporting of controlled substance dispensing by pharmacists. Their survey of Florida pharmacists conducted in the months immediately prior to the implementation of Florida's much-anticipated PDMP found that pharmacists across all practice settings (hospital, independent, chain, or other type of pharmacy) generally disagree with the notion that a PDMP will discourage or prevent them from dispensing controlled substances (total n=836, 59.0 percent).[56] In this survey study, pharmacists also expressed strong support of PDMP implementation (78.6

percent) and, on average, disagreed with statements expressing concerns that a PDMP is an invasion of patient privacy (73.6 percent).

Substitution Effect

There is some evidence that physicians in states with PDMPs have opted to substitute the prescribing of Schedule II controlled substances (like oxycodone) with Schedule III drugs such as hydrocodone. Analysis of prescription drug shipments using the Automation of Reports and Consolidated Order Systems (ARCOS) database, revealed that states with PDMPs received fewer shipments of oxycodone but received shipments of hydrocodone at an increasing rate from 1997 to 2003.[42] ARCOS data also indicates that states without PDMPs experienced the opposite trend during this time- an increasing rate of oxycodone shipments and a decreasing rate of hydrocodone shipments. Substitution of a higher Scheduled drug for a lower Scheduled drug has not been put forward as evidence for the chilling effect, but it certainly represents a change in prescriber behavior. Further analysis of ARCOS data through 2006 indicates a continuation in the trend that the substitution effect between Scheduled II controlled substances for Schedule II controlled substances of opioid pain relievers continues to occur in states with PDMPs.[57]

Other types of controlled substances have been shown to experience similar decreases in use in states with PDMPs. A study comparing New York and New Jersey's Medicaid utilization of benzodiazepines after New York implemented a triplicate prescription program indicated that the program implementation was correlated with a significant decrease in benzodiazepine use.[58] In this particular study, possible benzodiazepine substitutes did not

experience statistically significant increases in utilization, but benzodiazepine substitutes were narrowly defined.

Conclusion

In 2006, Manchikanti described state PDMPs as failures for over-emphasizing law enforcement goals while neglecting to include more proactive tools that would give health providers the information necessary to make clinical decisions to reduce doctor shopping and diversion.[5] He also points out that the highly variable program design across states has slowed the already flagging NASPER initiative, whose budget restrictions and reprioritizations have contributed to the sluggish development of an interoperable system across states.[5,31] These allegations of over-emphasis on law enforcement activities may ring true: chronic pain conditions continue to be under-treated. Estimates of the annual cost of chronic pain conditions in the United States range from $100 billion to $635 billion in treatments and lost productivity, due to the persistent under-treatment of these conditions.[17,18]

A visual comparison of opioid substance abuse treatment admission trends by state, between the year 2000 and 2010 can be found in Appendix B. These trends map national TEDS data and show that, despite the implementation of PDMPs, the abuse of controlled substances (and opioids in particular) is still on the rise, but PDMPs may have slowed the rate of these increasing opioid abuse and diversion trends. The available literature is currently unable to provide a definitive answer, but emerging program evaluations are providing states with evidence that will be useful in making program design decisions.

CHAPTER TWO

Policy Variation in Prescription Drug Monitoring Programs Across States: A Policy Solution to an Information Asymmetry Problem

Chapter Summary: The objective of this chapter is to identify an appropriate theoretical framework to operationalize PDMP policy variation across states. The research design included an analysis of state-level regulatory and PDMP program variation, and exploration of a theoretical framework using evidence from policy implementation and economics literature to explain the process of PDMP feature diffusion across states and their projected variable outcome on PDMP effectiveness. This process informed the operationalization of independent variables and covariates employed throughout the following empirical chapters, which are defined and justified here. It is hypothesized that certain PDMP program features and regulations (e.g., mandatory prescriber registration, required inclusion of Schedule III and Schedule IV controlled substance reporting) have greater impact on the efficacy of PDMPs than other program features and regulations.

The public health and public safety crises associated with the abuse and diversion of certain prescription drugs, known as controlled substances, may best be framed as a problem of information asymmetry. State Prescription Drug Monitoring Programs (PDMPs) have been implemented by most states to correct the information asymmetry problem by maintaining databases of consumer controlled substance prescribing and dispensing information. PDMPs as a policy solution address asymmetric information across multiple parties: between the consumers and prescribers/dispensers of controlled substances, between the regulatory agents (such as licensing boards) and prescribers/dispensers of controlled substances, and between the consumers and law enforcement agents.

The official objectives of state PDMPs are stated similarly: to reduce drug abuse and diversion while maintaining access to controlled substances in the case of legitimate medical need. The means to those ends, however, varies across states in terms of policy structure as well as in implementation strategy.

PDMP Adoption Varies Due to Funding Streams and Focusing Events

The two federal funding sources that incentivize state PDMP adoption are the Harold Rogers grant and the National Association for State Prescription Electronic Reporting (NASPER). Both of these grant programs require states to adopt certain PDMP program characteristics in exchange for funding, but the scope and stated mission for these grant programs differ. NASPER, which was adopted as federal law in 2005 and modeled after Kentucky's state PDMP, initially required state PDMPs to adopt programs that would be interoperable and standardized to promote interstate exchange of PDMP information.[26]

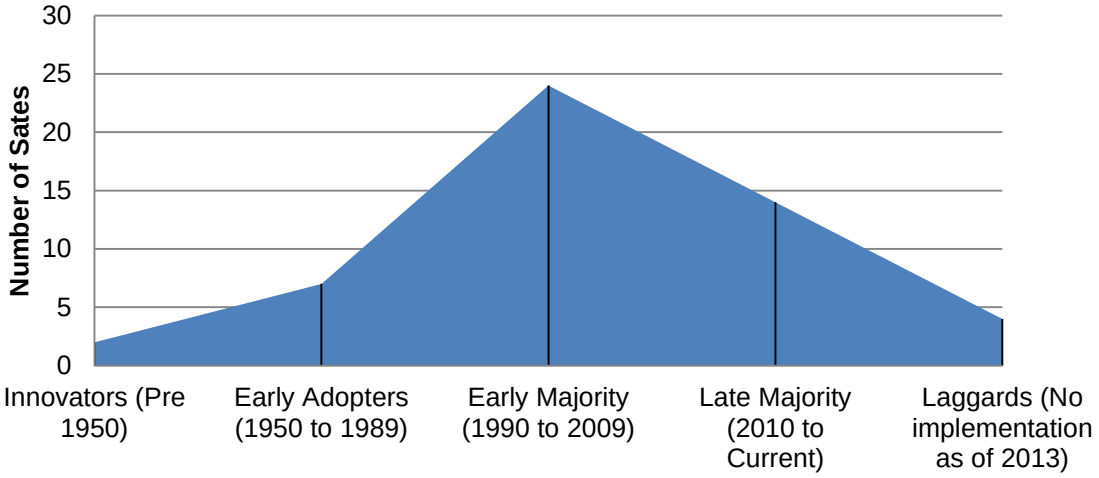
The NASPER program's mission is to identify patients at risk for abuse and is administered via the Department of Health and Human Services, whereas the older (2002) Harold Rogers program offers smaller "no strings attached" grants in order to encourage states to address drug abuse and diversion problems at the first warning signs of prescription drug abuse epidemics.[32] The NASPER program characteristic requirements are slightly less restrictive than the Department of Justice-operated Harold Rogers program, whose stated requirements include contingencies upon grant acceptance that permit law enforcement agents and officials at the local, state, and the federal government level access to state PDMP data during investigations.[35]

California's 1939 PDMP was the policy innovator, but most states did not adopt PDMP-type monitoring policies until the 1990s/2000s. The sudden spike in policy adoption likely occurred as a response to public attention and concern about the rise in public health and legal problems related to prescription drug

abuse. A singular “focusing event”, which can be described as a dramatic and sudden issue (e.g., a natural disaster) that captivates immediate public attention,[59,60] is unlikely to be pinpointed for drawing public attention to prescription drug abuse problems. However, a surge of abuse resulting in deaths, addiction, and incarcerations that arose in rural areas in the late 1990s and early 2000s and quickly spread throughout the United States was the likely impetus for the opening of a policy window. It is also possible that high-profile celebrity deaths due to prescription drug overdose during this time contributed to this sustained wave of focus that captured the attention of the public.

The flood of policy adopters in the 1990s/2000s was followed by a handful of “laggards” who have mostly adopted, but have yet to implement, a PDMP. This implementation pattern illustrates the 5-stage model of diffusion as described by Rogers (1995) very well.[61] Figure 2.1 below shows the bell-curve implementation by each wave, classified by time of implementation.

Figure 2.1 The Diffusion of State PDMP Policies, 1939-2013



Variations in PDMP Policy Features

One policy variation often invoked in PDMP evaluations across states is the authorities in which state PDMPs are housed. Several states house PDMP programs within Departments of Health and Human Services or health provider licensing agencies that focus on a public health mission, whereas other states house PDMP programs within law enforcement agencies, which tend to emphasize the goal of reducing prescription drug diversion. PDMP evaluations and studies have failed to produce evidence that this particular attribute has lead to differences in outcomes and program effectiveness. For this reason, a variable for housing authority was not operationalized.

Another policy variation is the classification of controlled substances into Schedules by some state authorities that compete with the federal drug Schedule classification system. Conflicting state and federal Scheduling classifications may be a regulatory challenge for developing a national model for PDMP regulations in regards to a handful of substances. For example, Mississippi classifies pseudoephedrine, which is a precursor substance in the illicit production of methamphetamine, as a Schedule III controlled substance[62] but pseudoephedrine is not Scheduled as a controlled substance at the federal level.

Most PDMPs require the dispenser of controlled substances, typically a pharmacist, to submit a record of that activity to the PDMP within a defined timeframe. In early PDMPs the timeframe was established as monthly, biweekly, or weekly, but current trends in PDMP regulatory change have shifted data transmission times closer to the time of transaction between pharmacy and

consumer. Significant policy variation then occurs with what state programs choose to do with the data that had been transmitted from pharmacies (dispensers) to the PDMP database. Some states, for example, have enacted compulsory program registration of dispensers and prescribers of controlled substances. Others require participation on the part of the dispenser, but not the prescriber, and the latest trend diffusing across state PDMPs is mandating PDMP use by prescribers for defined circumstances before a controlled substance prescription can be written.

States with proactive PDMPs send unsolicited reports of controlled substance use histories to prescribers, dispensers, and/or law enforcement officials, while other states require all or some of these users to request a report for each individual patient.[29] The proactive reports, however, vary considerably in content by state as well as which PDMP user (or groups of PDMP users) receive the reports. There is some evidence to suggest that pharmacists are more likely to view their PDMP user role as limited to the providers of data, leaving the treatment decisions involving data found in a patient's PDMP report to prescribers.

Most states that have adopted PDMPs grant law enforcement agencies access to PDMP data, but the extent of that access varies substantially across states. Registered law enforcement officials in most states with PDMPs have access to trend analysis of controlled substance prescribing and dispensing. The variation occurs in how a state handles access to an individual's controlled substance prescription history. Some states require warrants, court orders, or

subpoenas before law enforcement is granted access to an individual's controlled substance history,[29] while other states allow more permissive access by law enforcement. Federal agencies, namely the DEA, cite precedent of related health data regulations that permit them to access data if pursuing an active investigation. These regulations have recently caused legal conflicts between state PDMPs with more restrictive patient privacy protections and the DEA.[63]

Table 2.1 provides a summary of the key policy variations in state PDMPs discussed above. Data was acquired from state statutes or codified laws and represents the frequency of PDMP characteristics as they were in December 2013.

Table 2.1 Summary of Variations in State PDMP Policies* as of 2013

Policy	Policy Characteristics (n = number of states)			
Housing Agency	Public Health Agency (38)	Law Enforcement Agency (6)	Other Agency (5)	No legislation (1)
Proactive Reporting	Yes, to medical providers and law agencies (27)	Yes, to medical providers only (7)	Yes, to law and regulatory agencies only (8)	No, no proactive reporting or no legislation (8)
Law Enforcement Access to Reports	Yes, with search warrant or active investigation (46)	Yes, under restricted circumstances (2)	No access (1)	No legislation (1)
Compulsory Registration	Prescribers and Dispensers (13)	Prescribers Only (2)	Not Compulsory (34)	No legislation (1)
Dispenser Reporting Frequency	Daily or more frequently (8)	From 2 to 7 days (33)	Bi-weekly or less frequently (7)	Not specified or no legislation (2)
Interstate Data Sharing	Sharing with other PDMPs and users in other states (18)	Sharing with users in other states only (8)	Sharing with other PDMPs only (18)	No sharing or no legislation (6)
Compulsory Prescriber Use	Required access under certain circumstances (14)	Access never required (35)	No legislation (1)	
Schedules Monitored	II only, or II and III only (4)	II through IV only (16)	II through V (29)	No legislation (1)

*Data obtained from each state's PDMP statutes and regulations.

Operationalizing and Defining PDMP Independent Variables

Table 2.2 provides the list of PDMP features operationalized as indicator variables that will be employed throughout the empirical analyses in the following chapters as independent variables. The presence of an operational PDMP has been defined in previous literature as the year or date of implementation. The simplicity of that definition, though appealing, was found to be lacking an important caveat: PDMPs that have been categorized in previous literature as operational were in many instances collecting data but were unable to provide their authorized users access to that data. In one state, there was found to be a gap of six years between the traditionally defined 'operational' time (where the PDMP was receiving data transmissions and had developed storage architecture) but was not providing reports to users. This change in variable definition represents a substantial departure from previous PDMP evaluations.

Next, it was determined that the two primary user groups of PDMP reports should receive their own indicator variables for the presence of proactive reporting. States that transmit patient controlled substance history records to prescribers and/or law enforcement officials are classified as proactive states. Previous PDMP studies have required that both of these groups or other groups (such as licensing boards and pharmacists) also receive unsolicited reporting to qualify as proactive. This new definition allows for more specificity of report use because prescribers and law enforcement officials utilize the PDMP data with different missions in mind. This definition is more permissive of variation in state policy, which can be seen in the exclusion of several states in previous

definitions of proactive in the literature because those states only send proactive reports to law enforcement officials.

The law enforcement access variable is defined in this series of projects as states that provide records to law enforcement agencies and officials pursuant to any active investigation. This means that states that require warrants, court orders, or subpoenas before PDMP report transmission are not classified as having open law enforcement access by this definition. This topic is a recent point of concern and so has not been explored in other PDMP studies.

States have only recently begun moving towards compulsory registration with the PDMP and compulsory prescriber use of PDMP data and so other PDMP studies have not incorporated these definitions into their PDMP descriptor variables. Eventually, further expansion of this variable definition will be necessary because enough states will have passed compulsory prescriber use mandates. Expansions of the definition will need to distinguish between states that require use in all primary care controlled substance prescription writing situations, states that limit required use to timed intervals, and states that further limit required use to specialist care. At the time of this project, few states had any compulsory prescriber use mandates so all variations of this policy were defined as meeting the criteria for compulsory prescriber use when coding variables.

Previous PDMP studies that control for a state's ability to share data with other PDMPs have generously defined interoperability as states that have the authority and willingness to share interstate data, but this project narrows the scope of the variable definition to those states that actively transmit across state

lines. It should be noted that functional interstate sharing will likely increase now that formal efforts have been undertaken to centralize data-sharing.[64]

The variable for frequent data transmission from pharmacies to PDMPs is defined as states that require the uploading of dispensing data in less than one week after the dispensing event. Data transmission frequency has not been used as a variable in many PDMP evaluations. The Schedules monitored by the state PDMP are often used in PDMP evaluations and so are included as individual indicator variables in these analyses. It should be noted that federal Scheduling is assumed in these variable definitions of "Schedules monitored."

Table 2.2 PDMP Features Variables, Derived from Review of PDMP Documentation

PDMP Variable	Description
Operational PDMP	The state has implemented a PDMP AND its data are accessible to approved users (prescribers, pharmacists, or law enforcement agents)
Proactive PDMP: Prescribers	Unsolicited patient controlled substance history reports are generated and transmitted to prescribers
Proactive PDMP: Law Enforcement	Unsolicited patient controlled substance history reports OR prescriber/dispensing history are generated and transmitted to law enforcement agents
Law Enforcement Access	The state PDMP records are accessible to registered law enforcement agents without a warrant, court order, or subpoena
Compulsory Registration	The state requires that prescribers and pharmacists register with the PDMP
Compulsory Prescriber Use	The state requires that prescribers access patient PDMP records at some defined interval or at the point-of-care
Interstate Data Sharing	The state has the authority to AND actively transmits data to other state PDMPs and/or authorized users in other states
Pharmacy Transmission Frequency: <1 Week	The state requires all pharmacies to transmit controlled substance dispensing records to the PDMP at least once per week or more frequently
Schedule II Monitored	The state uses the PDMP to monitor the prescribing and dispensing of Schedule II controlled substances
Schedule III Monitored	The state uses the PDMP to monitor the prescribing and dispensing of Schedule III controlled substances

Table 2.2 continued, PDMP Features Variables, Derived from Review of PDMP Documentation

PDMP Variable	Description
Schedule IV Monitored	The state uses the PDMP to monitor the prescribing and dispensing of Schedule IV controlled substances
Schedule V Monitored	The state uses the PDMP to monitor the prescribing and dispensing of Schedule V controlled substances
Unscheduled Substances Monitored	The state uses the PDMP to monitor the prescribing and dispensing of non-controlled substances (e.g., pseudoephedrine)

Implications of PDMP Regulatory Variation

While several states currently require certain groups (typically prescribers and dispensers) to register with the PDMP, very few states currently require use of the PDMP data in prescribing or for treatment decisions.[65] Compulsory use of the PDMP may force non-governmental actors, such as healthcare providers, to take on the role of a street-level administrator of policy (i.e., substitute "policing" of abuse and diversion in the absence of a law enforcement investigation). This new role of the provider may be uncomfortable for both providers and consumers and may decrease consumer confidence and trust in providers, which could result in worsened health outcomes for consumers who reluctantly share information with their provider.

The variation in state PDMP housing authority also has interesting implications about the tacit approval to grant power to non-elected bureaucratic agencies that, in effect, *create* policy. These implications are particularly noticeable when PDMPs are housed by auxiliary government agencies, such as professional licensing boards, which have limited public input and operational transparency but have the ability to impose binding regulations on licensees that influence the availability of treatment options to the public. The phenomenon of

policy-making bureaucratic agencies has been referred to as the "4th branch of government"[66] and it is unclear whether this policy-making role is appropriate for these agencies due to limited opportunities to incorporate the checks and balances built in to the primary branches of government.

State level agencies that operate PDMPs may also be susceptible to external political influences. Brudney and Herbert (1987) examined external political influence on a collection of agencies at the state level and found that unlike federal agencies, clientele groups and professional associations were found to have (overall) less significant influence on state agencies than the governor and the state legislature.[67] Influence on state agencies was measured by surveying agency heads directly and the self-report nature of this measure is potentially problematic. It may behoove agency heads to under-report influence from external interest groups, by intention or by genuine inability to estimate their influence. This is particularly concerning in the case of PDMPs because Congressional staff self-report that the pharmaceutical industry's most prominent lobbying force, PhRMA, is the most influential interest group in health policy.[68]

Later analyses of political actor influence on agencies conceptualized influence in a more objective fashion, by measuring quantifiable federal agency outputs. Congress, the president, and other political actors may exert political influence on the bureaucracy using more indirect means. Balla and Wright (2001) explored one of these other avenues of political control: congressionally appointed advisory committees.[69] The control exerted in this case refers specifically to the flow of information from legislation to institutions by selecting

members to advisory committees that represent legislative interests. The case study examined here was a prominent advisory committee to the EPA, the National Drinking Water Advisory Council (NDWAC). They found that agency decisions were impacted by advisory committee membership and representation from interests. It is possible that these political influences work via similar mechanisms at the state level. Kentucky's PDMP Advisory Council is appointed by the Kentucky Governor and other state PDMP advisory council's or committee's are appointed by each respective state's Governor or by a member(s) of state legislature.[70]

Policy-makers have been criticized for avoiding evidence-based decision making approaches similar to those that health care practitioners advocate when evaluating new policies,[71] but these criticisms ignore the myriad constraints of political influences operating on policy-makers as well as the process by which problems demand attention through policy intervention. Balla points out that professional organizations have an important role to play in the diffusion of health-related policies[72] and the deferral of state PDMP requirements to regulation by licensing boards rather than by statute speak to the importance of this role (e.g., compulsory use of Kentucky's PDMP by prescribers in certain circumstances is regulated and enforced by professional licensing boards and is not explicitly mentioned in statute). These professional organizations, which are interest groups better poised to influence policy development with licensing boards for their respective professions[68] than the state level PDMP, should not

be overlooked as likely having significant influence in the development of state PDMP regulations.

Conclusion

State PDMPs present a policy solution to the asymmetric information problem grappled with by prescribers and dispensers of controlled substances, but the blurring of realms between law enforcement and health care raises questions about the implications of further policy interventions in medical practice. The variation that arose in state PDMP policies may be attributed to a variety of factors, many of which are described in this piece, and can partially explain the observed differences in the impacts of these policies on several key program outcomes such as,

1) Prescriber and dispenser behaviors;
2) Law enforcement activities;
3) Consumer behaviors and outcomes related to controlled substance consumption; and,
4) Reimbursement policies of controlled substances by publicly funded health insurance programs (e.g., Medicaid, Medicare).

Several of these outcomes will be examined empirically in the following chapters, the next of which utilizes state Medicaid prescription drug data to measure changes in quantities dispensed of selected controlled substances across states with and without PDMPs to Medicaid beneficiaries.

CHAPTER THREE

Prescription Drug Monitoring Programs and Opioid Dispensing to Medicaid Beneficiaries

Chapter Summary: This chapter examines the relationship of PDMP presence and program features with the marketplace for prescription drugs, particularly opioids, among state Medicaid beneficiaries. A hypothesized "substitution effect" following the implementation of state PDMPs is also explored in this chapter. Data for this chapter was acquired from the Medicaid Drug Rebate Program for the years 1991-2011. The research design consists of aggregating all opioids utilized by Medicaid patients to the state-year level, where the specific method employed was a time series, random effects generalized least squares (GLS) random effects regression analysis. The dependent variable is quantity of opioid substances, standardized to morphine milligram equivalents in order to account for variation in substance quantity, dosage, and strength. The independent variables include PDMP features as defined in Chapter 2 and year is also included as a covariate. Supplementary analyses of benzodiazepines are also conducted.

Consumption of prescription medications for nonmedical use has increased substantially in the last two decades and prescription medications are now the second-most class of abused substance, after marijuana.[1] Drug overdoses overtook traffic accidents in 2009 as the number one cause of accidental death for adults aged 25 to 64 in the United States and are the second leading cause of accidental death among people of all ages.[73] The majority of these drug overdose deaths (75 percent in 2010) involve the class of pain-relieving medications known as opioids.[74] In addition to elevated mortality risks when compared to other drugs, opioids tend to have a high potential for abuse. Substance abuse treatment admissions for opioids have increased substantially in the last two decades: from less than 1 percent of total national treatment admissions in 1993 to approximately 9 percent total national treatment admissions in 2011 and approximately 32 percent of total treatment admissions in Kentucky.[51]

The negative economic, social, and public health consequences associated with the abuse and diversion of prescription drugs, and opioids in

particular, have sparked the innovation and diffusion of policy solutions that mitigate the information asymmetry problem that health providers face when providing access to controlled substances to consumers. These policy solutions, in the form of Prescription Drug Monitoring Programs (PDMPs), track the prescribing and dispensing of controlled substances with the purpose of reducing abuse and diversion[23] by allowing health providers to access information about the history of controlled substance use by individual consumers. As of 2015, 49 states and the District of Columbia have enacted PDMP legislation. Currently, 43 states have implemented this legislation and are administering operational programs.[29]

Prescription medications and illicit substances that have the potential for abuse are classified as controlled substances by the Food and Drug Administration and the Drug Enforcement Administration.[21] Controlled substances are classified according to the level of risk for abuse potential and these classifications are called “Schedules,” as defined in Chapter 1. This piece will isolate the impact of state PDMPs on the dispensing of two classes of controlled substances in particular, opioids and benzodiazepines. Opioids and benzodiazepines are two large families of drugs with several individual forms and dosages that are categorized as controlled substances. Opioids, which are pain-relieving drugs derived naturally or synthetically from chemical components of opium, are of particular interest due to the high potential for abuse and overdose as well as the most likely class of drug to be sought in instances of “doctor shopping.”[28] Opioids, when Scheduled, can be classified as Schedule II,

Schedule III, Schedule V, or in rare cases are Unscheduled (typically cough syrups). Benzodiazepines are a class of drugs that act as sedatives (anxiolytics) and formulations tend to be Scheduled lower than opioid drug formulations due to less overall abuse potential.[75] All benzodiazepines are Schedule IV controlled substances.

As discussed in Chapter 1, there is some evidence that PDMP implementation has caused the unintended consequence of a "substitution effect" where prescribers substitute the prescribing of Schedule II controlled substances with prescribing of lower Scheduled substances in order to decrease abuse potential or to decrease prescriber liability. However, these previous analyses rely on data from the Department of Justice's Automation of Reports and Consolidated Order System (ARCOS), which does not have the ability to monitor interstate purchasing or to capture the intended indication for each dispensed drug.[50]

This study uses Medicaid Drug Rebate Program data as an alternative data source to track the total quantity dispensed of certain controlled substances. Medicaid drug rebate data compensates for the limitations of ARCOS data because Medicaid beneficiaries must reside in the state in which the reimbursement claim for the prescription drug is dispensed, which significantly reduces the potential for interstate purchasing. The characteristics of this data source will be discussed further in the Methods section.

The purpose of this study is to test the following three hypotheses:

- Hypothesis 1: States with operational PDMPs will have total fewer opioids and benzodiazepines dispensed as compared to states with no operational PDMP.
- Hypothesis 2: Proactive prescriber reporting, proactive law enforcement reporting, unfettered law enforcement access, compulsory prescriber registration, compulsory prescriber use, and monitoring of lower Scheduled substances are program characteristics that are associated with decreased total opioid and benzodiazepine units dispensed.
- Hypothesis 3: A "substitution effect" between higher Scheduled substances and lowered Scheduled substances occurs in states with a PDMP.

Methods

The Omnibus Budget Reconciliation Act of 1990 (OBRA) called for drug manufacturers to agree to the creation of prescription drug rebates in exchange for federal matching funds for state Medicaid prescription drug spending.[76] Beginning in 1990, agreements are annually negotiated for each covered drug. The reimbursement rate is typically calculated as a percentage discount from the drug's average retail price or as the difference between the drug's average retail price and the lowest wholesale price offered in a transaction in the previous year.

Medicaid Drug Rebate Program data is publicly available from the time since the program's inception to two years before the present and includes the following data for each state: each drug covered in every state, the total number

of prescriptions dispensed, the total quantity of units of each drug dispensed (e.g., number of pills, number of liquid doses, etc.), the total dollar amount of Medicaid reimbursement for each drug dispensed, and the total dollar amount of reimbursement for drugs that were not eligible for Medicaid matching funds.[77] (Note: data is not available for Arizona before 2010 due to nonparticipation.) This rebate data has been validated in the literature and is typically used to perform state-level trend analysis of prescription drug utilization and expenditures in Medicaid.[78-82]

Data files from all 50 states and the District of Columbia were web-scraped and merged into a single database after being tagged with state, year, and quarter identifiers for the years 1991 through 2011. Drugs were uniquely identified in the data using the National Drug Code (NDC), which assigns each drug an 11-digit number that is coded to identify the manufacturer, product, strength, package size, and distributer of the drug.[83] The total quantity of units of each drug dispensed by state was selected as the primary outcome of interest rather than the total number of prescriptions dispensed so that changes in the actual quantity of each drug supplied to states could be measured. Number of prescriptions varies by the days supply provided in the prescription (e.g., 7 days, 30 days, 60 days, etc.). Without knowing the days supply, it is difficult to accurately count the units of the drug dispensed.

Two classes of drugs, opioids and benzodiazepines, were isolated for this analysis due to the availability of conversion factors for these classes of drugs. Also, benzodiazepines are often implicated in adverse events when prescribed or

used in conjunction with opioids.[84] The conversion factor for opioids, known as morphine milligram equivalents, allows for the comparison of the units of each opioid to occur in a standardized fashion.[9] Morphine milligram equivalents (MMEs) were derived from a peer-reviewed conversion of each specific opioid based on factors such as the route of administration, dosage form, quantity, and strength of drug.[85,86] A total of 12,050 unique opioid formulations were converted to MMEs based upon these procedures and Table 3.1 contains a sample of these MME conversions for selected prescription opioids.

Table 3.1 Conversion Factors for Selected Opioids to Standardized MMEs

Generic Medication Name	National Drug Code (NDC)	Dosage Form	Strength	Unit of Dosage Measurement	MME Conversion Factor
Buprenorphine	35356060504	Patch, extended release	10	MCG/HR	42
Hydromorphone Hydrochloride	23635040801	Tablet, extended release	8	MG	4
Methadone Hydrochloride	00054454725	Tablet	40	MG	3
Morphine Sulfate	00034051310	Tablet, extended release	200	MG	1
Oxycodone Hydrochloride	00093002401	Tablet, extended release	10	MG	1.5
Acetaminophen/Codeine Phosphate	00005313123	Tablet	16	MG	0.15
Hydrocodone Bitartrate/Ibuprofen	68115035260	Tablet	7.5	MG	1

The conversion factors for standardizing benzodiazepines are not as universally agreed upon. For this analysis, the peer-reviewed conversion factors reported by Shader et al. (1994) that converts all benzodiazepines into a standardized diazepam milligram equivalent (DME) were selected, but there are some disagreements in the literature about the appropriate scale of conversion factors for some benzodiazepine drugs and the difference in conversion magnitude for parenteral versus oral dosage forms.[87,88] Table 3.2 contains a

sample of these diazepam-equivalent conversions for selected prescription benzodiazepines.

Table 3.2 Conversion Factors for Selected Benzodiazepines to Standardized Diazepam Milligram Equivalents

Generic Medication Name	National Drug Code (NDC)	Dosage Form	Strength	Unit of Dosage Measurement	Diazepam Conversion Factor
Clorazepate Dipotassium	00003086250	Capsule	3.75	MG	15
Chlordiazepoxide Hydrochloride	00074264853	Capsule	5	MG	50
Temazepam	00078009913	Capsule	30	MG	30
Estazolam	00093013001	Tablet	2	MG	2
Clonazepam	00185006310	Tablet	0.5	MG	0.5
Triazolam	00364259833	Tablet	0.125	MG	0.25

The unit of analysis for this retrospective study was NDC-State-Year level observations. The standardized quantities of dispensed opioid and benzodiazepines were set as the dependent variables (four specifications: Schedule II opioids, Schedule III opioids, Schedule IV benzodiazepines, and Unscheduled opioids) and data on the characteristics of state PDMPs, defined and operationalized in Chapter 2, were the explanatory variables of interest. State PDMP characteristics of interest were coded as dummy variables where “1” represented the presence of the PDMP characteristic within the state during the time period of the observation and “0” represented the absence of the PDMP characteristic within the state during the time period of the observation. Summary frequencies of each PDMP characteristic of interest as well as frequency of NDC observations per state-year within the dataset can be found in Table 3.3.

All statistical analysis was performed in Stata v13. A correlation matrix that tested the relationship between the explanatory variables and the dependent variables was constructed before regression analysis to test for unexpected relationships between the explanatory variables. There were several strong correlations between certain PDMP characteristics as expected; for instance, all states with operational PDMPs monitor Schedule II controlled substances so this variable is not included in the analysis.

The longitudinal nature of the observations called for setting up the analysis as panel data. Fixed and random effects models were run and a Hausman test was performed to compare within and between estimators. The Hausman test indicated that the random effects model was a more appropriate fit, but it should be noted that the "within" effects estimators were small (within estimators <0.001 in all specifications) due to the limited variation in PDMP characteristics over time. Coefficients were estimated via Greater Least Squares (GLS) regression and Stata's "robust" option was utilized to correct for heteroscedasticity. The summary of the regression results can be seen in Table 3.5.

There was significant variation in the number of controlled substance Schedules monitored by state PDMPs. Controls for Schedule monitoring were used but there were too few observations to conduct the Schedule V opioid specification, due to the rarity of Schedule V opioids.

Results

Table 3.3 below provides a summary of the PDMP characteristic frequencies observed in the data. All states with a PDMP monitor Schedule II controlled substances and most monitored Schedules III and IV controlled substances by 2011, the end of the study period. Few states require registration and compulsory prescriber use was relatively rare during the study period.

Table 3.3 State PDMP Characteristics (Total NDC-State-Years=180,578)

PDMP Variable	States with Characteristic (in 2011)	Total NDC-State-Year Observations
Operational PDMP	43	45,891
Proactive PDMP: Prescribers	38	35,065
Proactive PDMP: Law Enforcement	25	50,429
Law Enforcement Access	13	25,978
Compulsory Registration	14	12,892
Compulsory Prescriber Use	5	1,532
Interstate Data Sharing	22	12,097
Data Transmission <1 Week	7	2,314
Schedule III Monitored	37	42,042
Schedule IV Monitored	36	41,870
Schedule V Monitored	22	30,505
Unscheduled Substances Monitored	37	13,780

Table 3.4 illustrates the Schedule classification of the prescription opioids and benzodiazepines in the data and how they are distributed. There were very few observations of Schedule V drugs and Unscheduled substances.

Table 3.4 NDC-State-Year Observations of Opioids and Benzodiazepines, by Schedule

Schedule	Frequency (% of Total)
Schedule II	266,411 (23.91%)
Schedule III	226,481 (20.33%)
Schedule IV	596,274 (53.52%)
Schedule V	18 (<0.01%)
Unscheduled Substances	24,904 (2.24%)

Figure 3.1 shows the log of opioid and benzodiazepine prescriptions dispensed over time by Schedule, as measured in standardized units of MMEs (opioids) and DMEs (benzodiazepines). Only Unscheduled prescription

medications experienced a downward trend in dispensing over time. Schedule V was excluded due to there being too few Schedule V opioids.

Figure 3.1 Opioid (Schedule II, II, Unscheduled) and Benzodiazepine (Schedule 4) Controlled Substance Dispensing, 1999-2011

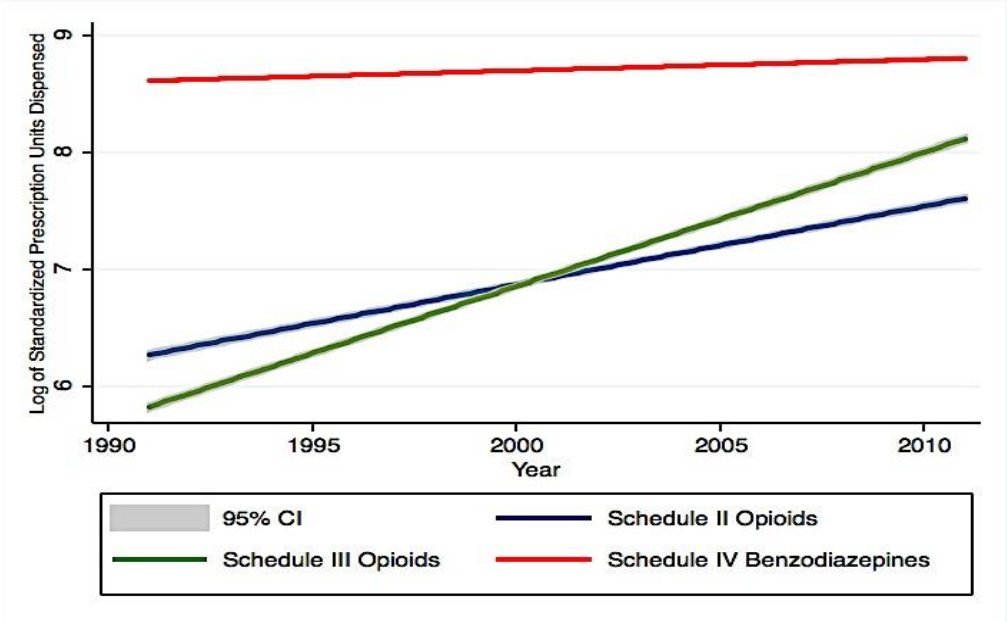


Figure 3.2 below shows the (log) dollar amount of Medicaid reimbursement for all opioids and benzodiazepine prescription medications over time for each Schedule of controlled substances. Total Medicaid reimbursement increased for each Schedule, but at a lower rate for Schedule IV substances. Schedule V substances were excluded due to a lack of observations.

Figure 3.2 Medicaid Reimbursement for Opioids and Benzodiazepines, by Schedule for 1999-2011

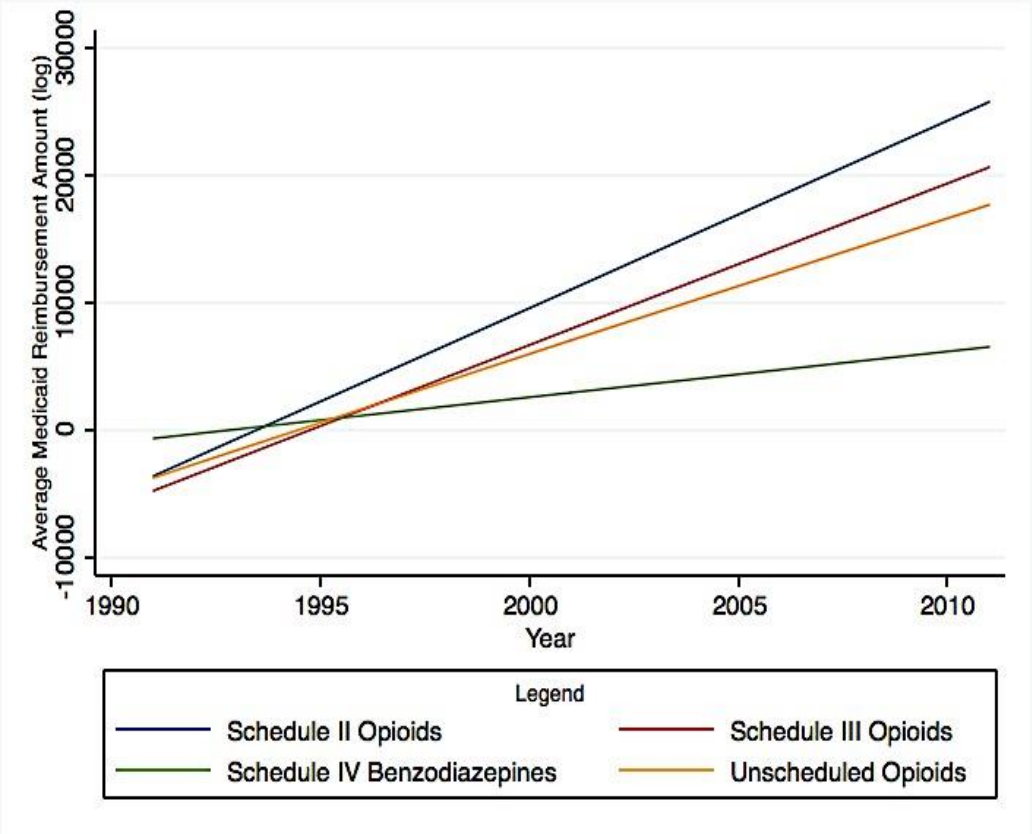


Table 3.5 includes the results of the regression analysis for Schedule II and Schedule III opioid MMEs, and Table 3.6 includes regression results for Unscheduled opioid MMEs and Schedule IV benzodiazepine DMEs. The presence of an operational PDMP was associated with 26 percent decrease in Schedule II opioid MMEs dispensed ($p<0.05$) and a 24 percent increase in Schedule IV benzodiazepine DMEs ($p<0.05$) dispensed to Medicaid beneficiaries, but had no significant impact in dispensed opioid MMEs from lower Schedules.

Schedule III opioid MME dispensing increased in states that had compulsory registration and prescriber use of the PDMP by 28 percent and 27

percent, respectively ($p<0.05$). While interstate data sharing was associated with an 18 percent decrease in Schedule II opioid MME dispensing, there was no statistically significant impact on Schedule III opioid MME dispensing. Conversely, frequent pharmacy data transmission was associated with decreased Schedule III opioid MME dispensing (29 percent, $p<0.05$), but not with Schedule II opioid MME dispensing.

Proactive reports to prescribers were associated with increases in MMEs and DMEs dispensed in every Schedule, with the exception of Schedule III. Open law enforcement access to PDMP data was associated with decreases in Unscheduled MME and Schedule IV DME dispensing, but had no significant relationship with MME dispensing of higher Scheduled opioids. Frequent data transmission was associated with a 36 percent decrease in Unscheduled opioid MME dispensing and a 34 percent decrease in benzodiazepine DME dispensing ($p<0.05$) as well.

Table 3.5 The Impact of PDMP State Characteristics on (logged) Total Units of Schedule II and Schedule III Opioid MMEs Dispensed

	Schedule II Opioid MMEs		Schedule III Opioid MMEs	
Independent Variables	**Coefficient**	**Robust SE†**	**Coefficient**	**Robust SE**
PDMP Variables				
Operational PDMP	-0.26*	0.09	-0.06	0.08
Proactive PDMP: Prescribers	0.12*	0.05	0.12	0.07
Proactive PDMP: Law Enforcement	0.08*	0.02	-0.03	0.03
Law Enforcement Access	-0.03	0.04	0.04	0.04
Compulsory Registration	0.08	0.05	0.28*	0.06
Compulsory Prescriber Use	-0.08	0.10	0.27*	0.13
Interstate Data Sharing	-0.18*	0.04	-0.01	0.06
Data Transmission <1 Week	-0.08	0.07	-0.29*	0.10
Monitors Schedule III	-0.57*	0.24	-1.06*	0.31
Monitors Schedule IV	0.85*	0.23	1.12*	0.31
Monitors Schedule V	-0.04	0.05	-0.13*	0.06
Monitors Unscheduled Substances	-0.18*	0.05	0.11	0.06
Year Covariates (1991 is reference)				
1992	0.04	0.06	0.55*	0.06
1993	0.06	0.06	0.31*	0.06
1994	0.12*	0.06	0.52*	0.06
1995	0.07	0.06	0.81*	0.06
1996	0.02	0.06	0.88*	0.06
1997	0.11	0.06	0.83*	0.06
1998	-0.03	0.06	0.91*	0.06
1999	0.12*	0.06	0.95*	0.06
2000	-0.06	0.06	0.77*	0.06
2001	-0.01	0.06	0.90*	0.06
2002	-0.13*	0.06	0.66*	0.06
2003	0.02	0.06	0.63*	0.06
2004	0.03	0.06	0.69*	0.06
2005	0.11	0.06	0.51*	0.06
2006	0.01	0.06	0.43*	0.06
2007	-0.01	0.06	0.52*	0.06
2008	0.06	0.06	0.68*	0.07
2009	0.15*	0.06	0.79*	0.07
2010	0.09	0.06	0.99*	0.07
2011	0.03	0.06	1.13*	0.08

†Abbreviation for Standard Error

**Indicates statistical significance: p<0.05*

Table 3.6 The Impact of PDMP State Characteristics on (logged) Total Units of Unscheduled Opioid MMEs and Schedule IV Benzodiazepine DMEs Dispensed

	Unscheduled Opioid MMEs		Schedule IV Benzodiazepine DMEs	
Independent Variables	**Coefficient**	**Robust SE**	**Coefficient**	**Robust SE**
PDMP Variables				
Operational PDMP	-0.12	0.25	0.24*	0.07
Proactive PDMP: Prescribers	0.47*	0.13	0.40*	0.06
Proactive PDMP: Law Enforcement	-0.10	0.09	-0.05	0.03
Law Enforcement Access	-0.21*	0.10	-0.06*	0.03
Compulsory Registration	-0.00	0.11	0.11*	0.05
Compulsory Prescriber Use	0.05	0.24	-0.24*	0.13
Interstate Data Sharing	-0.01	0.10	-0.03	0.05
Data Transmission <1 Week	-0.36*	0.16	-0.34*	0.09
Monitors Schedule III	-0.74	0.58	-1.21*	0.39
Monitors Schedule IV	0.83	0.54	0.99*	0.39
Monitors Schedule V	0.15	0.11	-0.17*	0.05
Monitors Unscheduled Substances	0.04	0.12	0.22*	0.05
Year Covariates (1991 is reference)				
1992	0.10	0.29	0.01	0.03
1993	-0.54	0.35	0.05	0.05
1994	-0.30	0.34	-0.17*	0.04
1995	0.21	0.35	-0.33*	0.04
1996	0.24	0.29	-0.28*	0.04
1997	0.65*	0.32	-0.37*	0.04
1998	0.45	0.31	-0.36*	0.04
1999	0.44	0.31	-0.29*	0.04
2000	-0.29	0.32	-0.71*	0.04
2001	1.54*	0.33	-0.79*	0.04
2002	0.60*	0.27	-0.93*	0.04
2003	-0.43	0.28	-0.91*	0.04
2004	-0.60*	0.28	-0.85*	0.05
2005	-0.82*	0.27	-1.16*	0.05
2006	-0.98*	0.26	-1.27*	0.05
2007	-0.85*	0.27	-1.52*	0.05
2008	-1.19*	0.27	-1.38*	0.05
2009	-1.60*	0.26	-1.59*	0.05
2010	-1.53*	0.26	-1.28*	0.06
2011	-1.37*	0.27	-1.29*	0.06

**Indicates statistical significance: p<0.05*

Discussion

States dispense an increasing number of opioids and benzodiazepines each year to Medicaid beneficiaries, but states with operational PDMPs tend to dispense fewer total units of Schedule II opioids and Schedule IV benzodiazepines to Medicaid beneficiaries when compared to states without operational PDMPs. This suggests a possible substitution effect or shift from

Schedule II opioids to alternative pain-relief treatments; though, an increase in Schedule III opioids was not observed in states with operational PDMPs. PDMP features also appear to have differential impacts on the Schedule of controlled substance being examined; for example, states that share PDMP data with other states had lower Schedule II opioid dispensations, but not lower Schedule III opioid dispensations.

Interestingly, states with compulsory PDMP registration appear to dispense more units of Scheduled II opioids and Schedule IV benzodiazepines than states without compulsory PDMP registration. This seems to contradict the notion that PDMPs decrease controlled substance prescribing/dispensing; however, it is possible that prescribers who are required to use the PDMP are more confident in their prescribing decisions when compared to prescribers that only use the PDMP in circumstances where they already suspect a patient's problematic controlled substance history. Compulsory use of the PDMP suggests that the prescriber must incorporate PDMP data into the assessment and treatment of the patient's conditions; whereas, the availability of PDMP data in a state where the prescriber may use the PDMP only at their discretion suggests that the PDMP serves as one of many tools by which assessment and treatment decisions are justified.

The Schedules monitored by state PDMPs also have an influence on the amount of opioids and benzodiazepines dispensed within states. Most notably, there was reduced dispensing of both Schedule II and Schedule III opioids in states that enacted Schedule III opioid monitoring by the PDMP; however, the

magnitude of the reduction in Schedule III opioids was much larger. What remains unclear, however, is if decreases in the amount of opioids and benzodiazepines dispensed is the "desirable" outcome of PDMPs.[41]

This research design has several limitations. First, the analysis was limited to two classes of prescription medications, though opioids and benzodiazepines do make up a significant portion of controlled substance dispensing in the United States. Further study with this data should include an expanded selection of drugs, both Scheduled and Unscheduled. A second limitation of this design is the possibility that PDMPs cause a shift in dispensing of Scheduled substances that is unobserved due to the use of conversion factors. For example, lower Scheduled substances tend to be converted to smaller unit sizes than higher Scheduled substances. This could lead to an underrepresentation of lower Scheduled substances, or overrepresentation of higher Scheduled substances, in the standardized count of units dispensed. Repeating the analysis without the use of conversions to standardized units and comparing the results to the current analysis could test this possibility.

Finally, total quantities of opioids and benzodiazepines dispensed to Medicaid beneficiaries may not be representative of trends of opioid and benzodiazepine dispensing to the population as a whole. There is some evidence to suggest that Medicaid patients tend to use more opioid controlled substances and for longer periods of time than patients with private pay or commercial insurance and this increased usage has been documented for non-cancer pain conditions[89] as well as all pain conditions.[90]

Several characteristics of state PDMPs are associated with changes in the total amount of opioids and benzodiazepines dispensed to Medicaid beneficiaries in a state, but it is unclear whether changes in the dispensing of these substances has a clinical impact on treatment accessibility for legitimate medical need or an impact on the reduction of abuse and diversion. The evidence presented above supports hypothesis 1 (states with PDMPs have decreased dispensing of opioids and benzodiazepines) and partially supports hypothesis 2 (some PDMP characteristics are associated with decreased dispensing of opioids and benzodiazepines).

The evidence does not definitely support the hypothesis that a "substitution effect" between higher Scheduled substances and lower Scheduled substances is occurring between opioids, and the possibility of unobserved factors not accounted for in this analysis should encourage caution with the conclusions that have been drawn. Future versions of this study should attempt to include measurements of prescriber, pharmacist, and law enforcement *participation* in the PDMP rather than the indicator variables for compulsory registration and compulsory prescriber use of the PDMP. Information about the frequency of use and the change in prescriber or dispenser behavior resulting from PDMP use would provide a more complete measurement tool of PDMP impact on dispensing.

CHAPTER FOUR

Trends in Opioid Prescribing Associated with Prescription Drug Monitoring Programs: Claims from a Commercially Insured Population

Chapter Summary: A retrospective analysis of commercial insurance prescription claims data is undertaken to examine the impact of PDMPs on the healthcare system by analyzing patterns in opioid prescription claims. Utilization estimates of selected opioids dispensed over time are calculated to characterize prescribing trends, then the relationship between opioid prescribing and the PDMP features and regulations operationalized in Chapter 2 is quantified. The 2007-2009 time period for this analysis allows for a "natural" policy experiment, due to the heavy uptake in state PDMP implementation within this time frame.

This empirical chapter continues with the exploration of state prescription drug monitoring program (PDMPs) effects on the marketplace for prescription drugs and touches upon effects on the healthcare system resulting from PDMPs by analyzing patterns in opioid prescription claims from a commercially insured United States patient population. At this time, commercial insurance prescription claims have rarely been used as a data source in published evaluations of PDMPs or in conceptualizing opioid consumption with regards to PDMP implementation. A pharmacy benefit manager database for commercial claims was used to calculate state-level opioid prescription prevalence estimates for the year 2000, and this estimate did include an analysis of the relationship between PDMP presence and opioid prescription rate (finding decreased opioid utilization in states that monitored Schedule II controlled substances), but did not control for other PDMP characteristics or pharmaceutical opioid control policies.[41]

In contrast with Medicaid populations, commercially insured populations tend to be older, wealthier, and report different frequencies of diseases and injuries associated with chronic pain.[91] This suggests that PDMPs may have a differential impact on commercially insured patient prescription opioid

consumption as compared to the trends observed from Medicaid in the previous chapter. The purpose of this study is to quantify overall opioid consumption and consumption by opioid type in this population, then explore a possible relationship between PDMP presence and features of the quantity and type of opioids prescribed and consumed.

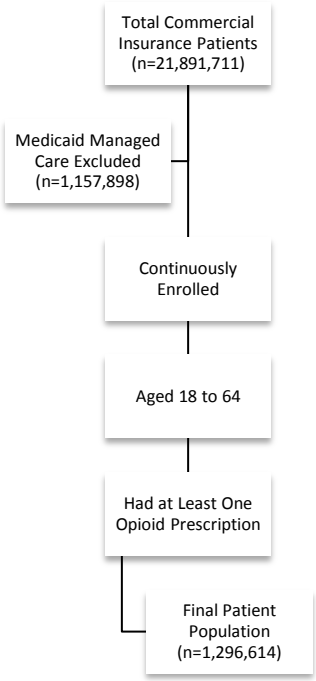
Methods

The research design for this chapter is a retrospective analysis of commercial insurance claims data, with calculated utilization estimates of selected opioids (hydrocodone, oxycodone, buprenorphine, methadone, and hydromorphone) dispensed over time to examine prescribing trends as correlated with the PDMP features and regulations operationalized in the prior two chapters. The highlighted opioids (hydrocodone, oxycodone, buprenorphine, methadone, hydromorphone) are isolated as dependent variables to determine if there are differential impacts of PDMPs on the dispensation of these substances to commercial insurance beneficiaries. These opioids were chosen based on the review of the literature, where evidence suggests that these opioids are the most susceptible to abuse and diversion.[92-94]

The 2007-2009 time period for this analysis allows for a "natural" policy experiment, due to the heavy uptake in state PDMP implementation within this time frame (i.e., 23 states had established PDMPs for the whole research period, 17 states and the District of Columbia had no PDMP during the research period, and 10 states implemented their PDMP at some point *during* this period).

The patient population is defined as those who were continuously enrolled in the commercial insurer's health plans from January 1, 2007 through December 31, 2009. The commercial insurance claims database, the i3 InVision Data Mart, contains de-identified medical and prescription claims records from a representative sample of every state totaling 22 million covered lives. This database does contain a small number of records for Medicaid Managed Care patients but these patients were excluded from analysis. Figure 4.1 outlines exclusion and inclusion procedure. Patients were included if they were over 18 years of age and under 64 years of age to avoid un-captured prescriptions due to potential overlapping coverage from the Children's Health Insurance Program if under 18 or Medicare if older than 64. Patients were required to have at least one prescription opioid for inclusion in the study population.

Figure 4.1 Patient Population Inclusion and Exclusion Procedure



Opioid prescriptions were identified in claims using national drug code identification numbers as outlined in the previous chapter. For clarity, opioid prescriptions were summed as whole prescriptions per patient rather than quantity of dosages to patient per prescription. The database contained pre-coded flags for opioid prescriptions, and individual opioid prescription types (e.g., products containing hydrocodone, products containing oxycodone, products containing hydromorphone) were flagged using regular expressions of partial or full text matches within the field for active ingredient drug name. Descriptive statistics were calculated for prescription frequencies as well as patient and patient state of residence characteristics. Next, a count regression model was employed to examine predictors of the count of opioid prescriptions per patient, the dependent variable, on patient-level and state-level independent variables. Patient-level predictors and covariates include age, gender, and race, and state-

level predictors include PDMP presence in the state of patient residence and PDMP program features.

Clustering was conducted by state and estimated coefficients were converted to incidence rate ratios. The first specification included all opioid prescriptions, while additional specifications were isolated to selected opioid types. Negative binomial distributions were fitted to each specification of the dependent variable, which was appropriate due to over-dispersed counts of opioid prescriptions per patient. All analysis was conducted in Stata v13.[95]

Results

Total opioid prescriptions increased during the study period, with oxycodone and hydrocodone products representing the most substantial increases in opioid prescriptions from 2007 to 2009 (Table 4.1). Prescriptions for "other" opioids decreased during the study period. Overall, 6,310,730 opioid prescriptions were dispensed to the commercially insured patients in this population during the study period.

Table 4.1 Commercial Insurance Patient Utilization of Opioid Prescriptions by Year and Type, All States and District of Columbia

Opioid Type	Year 2007 n (%)	Year 2008 n (%)	Year 2009 n (%)
Hydrocodone	942,639 (49.85%)	1,066,857 (49.54%)	1,118,978 (49.37%)
Oxycodone	354,747 (18.76%)	415,018 (19.27%)	463,809 (20.46%)
Buprenorphine	11,535 (0.61%)	16,905 (0.79%)	23,022 (1.02%)
Methadone	19,250 (1.02%)	21,729 (1.01%)	23,167 (1.02%)
Hydromorphone	13,168 (0.70%)	16,918 (0.80%)	21,161 (0.93%)
Other Opioids	549,668 (29.07%)	515,871 (23.96%)	516,288 (22.78%)
Total Opioid Prescriptions*	**1,891,007**	**2,153,298**	**2,266,425**

** An individual patient may have multiple prescriptions in the dataset.*

There were 1,296,614 unique patients represented in the data and a patient could potentially have multiple opioid prescriptions. More females (56.53 percent) than males (43.47 percent) received an opioid prescription at least once

during the study period (Table 4.2). The majority of patients who received at least one opioid prescription identified as white race (75.84 percent) and 8.01 percent identified as Hispanic. More than half of patients had either some college education or a college degree and mean age was 44 years. Hydrocodone prescriptions (mean 12.34 prescriptions) were the most common type of opioid prescriptions in the patient population, but it should be noted that the distribution of opioid prescriptions in each opioid type was skewed such that mean was greater than the median.

Patients resided in all 50 states and the District of Columbia. In 2007, 40.33 percent of patients were residing in states that had an operational PDMP and by 2009 that proportion increased to 55.47 percent due to the uptake in state PDMP implementation. Proactive prescriber reporting by state PDMPs also experienced a substantial increase in implementation, with 28.66 percent of patients residing in proactive states in 2007 and 41.49 percent by 2009. Few states engaged in compulsory prescriber PDMP use or pharmacy prescription record data transmissions of less than one week during the study period. There was no variation in state PDMP monitoring of Schedule III and Schedule IV substances during this period.

Table 4.2 Commercial Insurance Patient Population and State of Residence Characteristics by Year, All States and District of Columbia

Characteristics	Year 2007	Year 2008	Year 2009	All Years
Patient	*n (%)*	*n (%)*	*n (%)*	*n (%)*
Gender				
Female	359,965 (58.03%)	221,907 (55.95%)	151,168 (54.04%)	733,040 (56.53%)
Male	260,320 (41.97%)	174,698 (44.05%)	128,556 (45.96%)	563,574 (43.47%)
Race				
White	475,795 (76.71%)	298,645 (75.30%)	208,856 (74.67%)	983,296 (75.84%)
Black	31,579 (5.09%)	23,844 (6.01%)	16,011 (5.72%)	71,434 (5.51%)
Other and Multiple Races	60,744 (9.79%)	39,868 (10.05%)	29,701 (10.62%)	130,313 (10.05%)
Missing Race Data	52,167 (8.41%)	34,248 (8.64%)	25,156 (8.99%)	111,571 (8.6%)
Hispanic Ethnicity	48,505 (7.82%)	31,836 (8.03%)	23,501 (8.40%)	103,842 (8.01%)
Education Level				
Less than High School	9,857 (1.59%)	6,633 (1.67%)	4,722 (1.69%)	21,212 (1.64%)
High School	213,206 (34.37%)	137,902 (34.77%)	93,438 (33.40%)	444,546 (34.29%)
Some College	284,750 (45.91%)	177,282 (44.70%)	126,691 (45.29%)	588,723 (45.40%)
College and Beyond	95,108 (15.33%)	63,481 (16.01%)	47,086 (16.83%)	205,675 (15.86%)
Missing Education Data	17,364 (2.8%)	11,307 (2.85%)	7,787 (2.79%)	36,458 (2.81%)
	Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Age in Years	43.77 (11.18)	44.48 (11.37)	45.34 (11.36)	44.32 (11.29)
Hydrocodone Prescriptions	12.23 (19.27)	12.57 (19.22)	12.21 (18.53)	12.34 (18.99)
Oxycodone Prescriptions	7.40 (18.38)	7.34 (17.99)	7.08 (17.42)	7.27 (17.91)
Buprenorphine Prescriptions	0.40 (3.65)	0.37 (3.52)	0.34 (3.37)	0.37 (3.51)
Methadone Prescriptions	0.66 (4.49)	0.62 (4.38)	0.58 (4.23)	0.62 (4.36)
Hydromorphone Prescriptions	0.41 (3.22)	0.40 (3.16)	0.38 (2.96)	0.39 (3.11)
Other Opioid Prescriptions	9.50 (19.56)	9.42 (18.98)	8.82 (18.05)	9.23 (18.83)
All Opioid Prescriptions	30.60 (36.05)	30.73 (35.14)	29.41 (33.82)	30.22 (34.96)
Patient State of Residence[*]	*n (%)*	*n (%)*	*n (%)*	*n (%)*
PDMP Operational	268,761 (43.33%)	188,817 (47.61%)	155,165 (55.47%)	612,743 (47.26%)
Proactive Prescribers	177,778 (28.66%)	136,584 (34.44%)	116,057 (41.49%)	430,419 (33.20%)
Proactive Law Enforcement	254,319 (41.00%)	175,055 (44.14%)	126,095 (45.08%)	555,469 (42.84%)
Law Enforcement Access	152,762 (24.63%)	98,837 (24.92%)	71,486 (25.56%)	323,085 (24.92%)
Compulsory Registration	83,820 (13.51%)	75,045 (18.92%)	65,834 (23.54%)	224,699 (17.33%)
Compulsory Prescriber Use	23,477 (3.78%)	13,601 (3.43%)	9,438 (3.37%)	46,516 (3.59%)
Interstate Data Sharing	111,994 (18.06%)	82,378 (20.77%)	72,114 (25.78%)	266,486 (20.55%)
Data Transmission <1 Week	0 (0.00%)	12,419 (3.13%)	10,503 (3.75%)	22,922 (1.77%)
Schedule III Monitored	262,998 (42.40%)	185,097 (46.67%)	152,311 (54.45%)	600,406 (46.31%)
Schedule IV Monitored[†]	262,998 (42.40%)	185,097 (46.67%)	152,311 (54.45%)	600,406 (46.31%)
Schedule V Monitored	241,446 (38.93%)	157,475 (39.71%)	118,174 (67.27%)	517,095 (39.88%)
Unscheduled Substances Monitored	71,329 (11.50%)	45,344 (11.43%)	38,422 (13.74%)	155,095 (11.96%)
Total Unique Patients[‡]	**620,285**	**396,605**	**279,724**	**1,296,614**

[*] *Indicates the number of unique patients residing in states with the highlighted program characteristics.*
[†] *Omitted in multivariate modeling due to lack of state-level variation between Schedule III and Schedule IV monitoring during the study period.*
[‡] *Unique patients represent the number of unduplicated individual patients identified in the dataset (i.e., an individual may appear in the dataset multiple times if they have more than one prescription, but here they are only counted on their first appearance).*

Table 4.3 contains regression results for each model specification. Females were less likely than males to receive prescriptions for oxycodone (IRR:

0.87; 95% CI: 0.80-0.95), methadone (IRR: 0.82; 95% CI: 0.71-0.95), and buprenorphine (IRR: 0.50; 95% CI: 0.41-0.61); however, females were more likely than males to receive hydrocodone (IRR: 1.09; 95% CI: 1.04-1.14), and prescriptions for all other types of opioids (IRR: 1.41; 95% CI: 1.33-1.49). Patients who identified as black race were less likely to receive prescriptions for any type of opioid when compared to their white race counterparts and patients who are Hispanic were less likely to receive prescriptions for any type of opioid when compared to patients who are not Hispanic.

Lower educational attainment (high school degree or some college) was associated with a greater number of hydrocodone prescriptions when compared to patients with a college degree. Interestingly, lower educational attainment was associated with significantly *fewer* buprenorphine prescriptions when compared to patients with a college degree. Older age was associated with a greater number of opioid prescriptions for every type of opioid with the exception of buprenorphine, where younger age was associated with a higher number of buprenorphine prescriptions.

The presence of an operational PDMP was associated with fewer prescriptions for hydrocodone (IRR: 0.73; 95% CI: 0.62-0.86) and methadone (IRR: 0.65; 95% CI: 0.53-0.80), but greater prescriptions for oxycodone (IRR: 1.58; 95% CI: 1.20-2.09). Proactive reporting of patient prescription records to prescribers was associated with greater prescriptions for buprenorphine (IRR: 1.61; 95% CI: 1.16-2.25) and hydromorphone (IRR: 1.85; 95% CI: 1.34-2.55). Proactive reporting of prescription records to law enforcement officials was also

associated with greater buprenorphine prescriptions (IRR: 1.39; 95% CI: 1.14-1.69).

States that permitted law enforcement access to PDMP records without requiring a warrant, court order, or subpoena had an interesting relationship with opioid prescribing; hydrocodone prescriptions, which were Scheduled III during the study period, were higher in these states (IRR: 1.27; 95% CI: 1.06-1.52) while prescriptions for the Schedule II oxycodone products were lower in these states (IRR: 0.62; 95% CI: 0.46-0.85).

Compulsory prescriber registration was associated with a greater number of prescriptions for oxycodone (IRR: 1.83; 95% CI: 1.20-2.78), methadone (IRR: 1.34; 95% CI: 1.09-1.64), and hydromorphone (IRR: 1.58; 95% CI: 1.04-2.38), as was compulsory prescriber use of the PDMP; oxycodone (IRR: 2.08 (1.17-3.70), methadone (IRR: 1.82; 95% CI: 1.21-2.73), and hydromorphone (IRR: 2.16; 95% CI: 1.42-3.27). Participation in interstate data sharing between state PMDPs was also associated with greater oxycodone prescriptions (IRR: 1.22; 95% CI: 1.03-1.46), but was not significantly associated with other types of opioid prescriptions.

Frequent (<1 week) pharmacy data transmission to the PDMP was associated with fewer opioid prescriptions overall (IRR: 0.85; 95% CI: 0.75-0.95), and specifically with oxycodone (IRR: 0.63; 95% CI: 0.45-0.89), methadone (IRR: 0.73; 95% CI: 0.58-0.93), and hydromorphone (IRR: 0.54; 95% CI: 0.32-0.89).

All prescription opioids were classified as Schedule II, III, or V during the study period. The monitoring of lower (III and V) Scheduled substances had

varying relationships with the number of opioid prescriptions in the population, while the monitoring of non-controlled substances, also known as un-Scheduled substances, were not associated with changes in the number of opioid prescriptions in this commercially insured population.

Table 4.3 Negative Binomial Regression Results (n=6,310,730 prescriptions)

	All Opioid Prescriptions	Hydrocodone Prescriptions	Oxycodone Prescriptions	Buprenorphine Prescriptions	Methadone Prescriptions	Hydromorphone Prescriptions
	IRR† (95% CI‡)	*IRR (95% CI)*	*IRR (95% CI)*	*IRR (95% CI)*	*IRR (95% CI)*	*IRR (95% CI)*
Female	1.09 (1.04-1.13)*	1.09 (1.04-1.14)*	0.87 (0.80-0.95)*	0.50 (0.41-0.61)*	0.82 (0.71-0.95)*	1.04 (0.91-1.19)
Race (Reference White)						
Black	0.73 (0.69-0.78)*	0.76 (0.70-0.81)*	0.73 (0.62-0.86)*	0.71 (0.53-0.96)*	0.62 (0.48-0.82)*	0.68 (0.50-0.93)*
Other and Multiple Races	0.90 (0.85-0.94)*	0.88 (0.82-0.95)*	0.87 (0.81-0.94)*	1.22 (0.93-1.60)	0.85 (0.71-1.01)	0.90 (0.69-1.17)
Hispanic Ethnicity	0.71 (0.65-0.77)*	0.68 (0.61-0.75)*	0.75 (0.59-0.96)*	0.76 (0.50-1.15)	0.53 (0.44-0.65)*	0.74 (0.55-1.00)*
Education Level						
Less than High School	0.96 (0.87-1.05)	1.12 (0.98-1.28)	0.88 (0.71-1.08)	0.28 (0.12-0.63)*	0.44 (0.29-0.66)*	0.58 (0.35-0.95)*
High School	1.15 (1.10-1.20)*	1.25 (1.18-1.32)*	1.11 (0.99-1.24)	0.68 (0.48-0.95)*	1.16 (0.99-1.35)	0.67 (0.53-0.85)*
Some College	1.14 (1.11-1.18)*	1.15 (1.10-1.21)*	1.17 (1.07-1.26)*	0.72 (0.57-0.92)*	1.18 (1.05-1.33)*	1.01 (0.83-1.23)
College and Beyond	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Age	1.01 (1.01-1.01)*	1.01 (1.00-1.01)*	1.01 (1.00-1.01)*	0.94 (0.93-0.95)*	1.01 (1.00-1.02)*	1.00 (1.00-1.01)
Year (Reference 2007)						
2008	0.99 (0.95-1.02)	1.01 (0.98-1.04)	0.97 (0.90-1.04)	0.92 (0.83-1.01)	0.93 (0.87-0.98)*	0.98 (0.88-1.10)
2009	0.93 (0.90-0.97)*	0.98 (0.95-1.00)	0.91 (0.83-1.00)	0.88 (0.78-1.00)*	0.86 (0.80-0.92)*	0.93 (0.81-1.06)
State of Residence Characteristics						
PDMP Operational	1.03 (0.95-1.12)	0.73 (0.62-0.86)*	1.58 (1.20-2.09)*	1.14 (0.85-1.53)	0.65 (0.53-0.80)*	1.29 (0.91-1.83)
Proactive Prescribers	1.14 (1.04-1.26)*	1.10 (0.94-1.29)	1.25 (0.80-1.97)	1.61 (1.16-2.25)*	1.29 (0.88-1.90)	1.85 (1.34-2.55)*
Proactive Law Enforcement	0.99 (0.94-1.06)	1.09 (0.95-1.24)	0.90 (0.71-1.14)	1.39 (1.14-1.69)*	1.07 (0.88-1.31)	0.88 (0.69-1.14)
Law Enforcement Access	1.01 (0.92-1.11)	1.27 (1.06-1.52)*	0.62 (0.46-0.85)*	0.98 (0.66-1.45)	0.89 (0.74-1.07)	1.02 (0.71-1.46)
Compulsory Registration	1.16 (1.06-1.27)*	1.06 (0.90-1.24)	1.83 (1.20-2.78)*	1.40 (0.83-2.36)	1.34 (1.09-1.64)*	1.58 (1.04-2.38)*
Compulsory Prescriber Use	1.15 (1.01-1.31)*	0.92 (0.72-1.17)	2.08 (1.17-3.70)*	1.47 (0.86-2.53)	1.82 (1.21-2.73)*	2.16 (1.42-3.27)*
Interstate Data Sharing	1.08 (0.99-1.17)	1.01 (0.90-1.12)	1.22 (1.03-1.46)*	0.79 (0.60-1.04)	1.06 (0.92-1.22)	1.32 (0.87-2.00)
Data Transmission <1 Week	0.85 (0.75-0.95)*	0.89 (0.79-1.01)	0.63 (0.45-0.89)*	0.62 (0.34-1.13)	0.73 (0.58-0.93)*	0.54 (0.32-0.89)*
Schedule III Monitored	0.87 (0.74-1.01)	1.27 (0.95-1.69)	0.57 (0.29-1.12)	0.76 (0.26-2.14)	0.97 (0.60-1.58)	0.33 (0.19-0.56)*
Schedule V Monitored	0.95 (0.86-1.05)	1.06 (0.93-1.21)	0.57 (0.38-0.86)*	0.72 (0.35-1.49)	1.00 (0.83-1.21)	0.93 (0.61-1.40)
Unscheduled Substances Monitored	0.98 (0.91-1.06)	0.96 (0.84-1.10)	0.99 (0.73-1.34)	0.86 (0.62-1.18)	1.03 (0.76-1.40)	1.30 (0.98-1.72)

†IRR refers to Incidence Rate Ratio, abbreviated throughout the remaining chapters.

‡CI refers to Confidence Interval, abbreviated throughout the remaining chapters.

**Indicates statistically significant: p<0.05.*

Discussion

Commercially insured patients are likely impacted by PDMP regulations differentially than those insured by Medicaid. In fact, several results in this analysis suggest that access to certain opioids increased to this population after PDMP regulations were strengthened or implemented as compared to the overall decrease in Schedule II opioid utilization by Medicaid patients found in the previous chapter.

This increase in access to certain opioids suggests that compulsory prescriber PDMP use may have increased prescriber confidence in treatment decisions when prescribing certain opioids and opioids in general to their patients for pain, but just having an operational PDMP (and not necessarily a PDMP with compulsory use) would seem to decrease access to opioids such as hydrocodone and methadone while increasing access to oxycodone in this population.

There are several limitations associated with this analysis. First, the exogenous impacts of changes in other policies, regulations, and clinical recommendations related to opioid prescribing are not controlled for in this analysis. Second, the definition of this population was limited to individuals who were continuously enrolled in the same, albeit large, insurer for the duration of the study period. This means that the prescription records of patients lost to plan switches or changes in eligibility status were not captured in this analysis, nor were patients under age 18 or over age 65, both of which age groups are included in the aggregate Medicaid data analysis in the previous chapter.

CHAPTER FIVE

Heroin Abuse Treatment Discharges and Opioid Prescriptions Dispensed in Kentucky

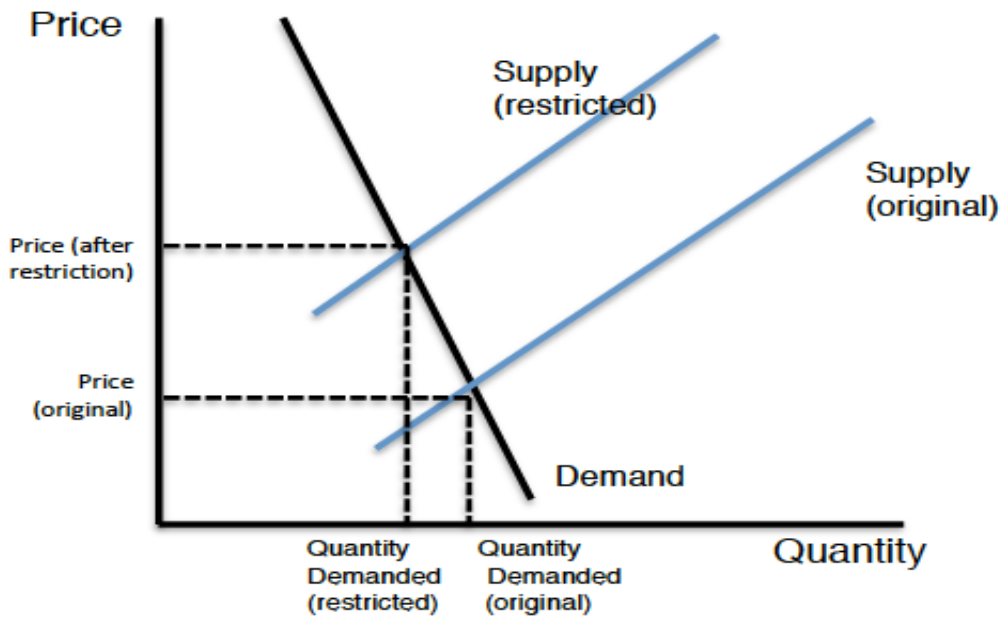
Chapter Summary: This chapter delves into one of the more controversial relationships between state policy interventions for opioid abuse and the resulting possible unintended consequences by focusing on data collected from Kentucky. House Bill 1, a statute enacted by Kentucky legislature in 2012, called for tightening PDMP regulations to combat prescription opioid abuse. A potential relationship between the presumed restriction in prescription opioid supply and heroin abuse, by proxy of heroin abuse treatment discharge records, is explored using linked data between Kentucky's PDMP records and substance abuse treatment facility discharges for fiscal years 2009-2013. Prescriptions for opioids for patients with and without heroin abuse treatment discharges are compared before and after the implementation of the policy.

The Commonwealth of Kentucky enacted House Bill 1 in 2012,[96] which required prescribers of controlled substances to register with and utilize Kentucky's prescription drug monitoring program, known as the Kentucky All-Schedule Prescription Electronic Reporting program (KASPER). House Bill 1 was intended to quell prescription opioid abuse; however, surveillance indicators suggest heroin abuse is on the rise while prescription opioid abuse has decreased in Kentucky.[7,51]

Prescription opioid abuse deterrents have included changes to KASPER such as those mentioned above, reformulation of certain prescription opioids, tightening of pain clinic regulations, and changes in treatment guidelines for both pain management and opioid dependence. Heroin, an illicit opioid, may serve as a substitute for licit pharmaceutical opioids when persons with prescription opioid substance use disorders have difficulty obtaining their substance of preference. Research has established the co-occurrence of prescription opioid and heroin use for individuals receiving substance abuse treatment.[97,98] However, prescription opioid access via licit channels has not been previously characterized for individuals discharged from substance abuse treatment

facilities. This missing piece represents a critical component for evaluating the unintended consequences associated with PDMP regulation changes such as HB1 that are primarily intended as “supply side” policies. Supply side policies are policies that cause a shift in supply (in this case, a downward shift in pharmaceutical opioid supply), that ultimately result in an excess of quantity of opioids demanded. Figure 5.1 provides an illustration of this theory.

Figure 5.1 Supply Shift in the Market for Prescription Opioids



Researchers who study the marketplace for prescription and “street” drugs have heatedly criticized supply-side policies, due to the lack of accompanying policy to address the excess demand once supply restrictions are enacted.[99-101] The process of continuously updating supply restrictions can be likened to a game of policy “whack-a-mole,” where new drug abuse and diversion problems pop up because substitutes are sought when the substance of preference becomes more difficult to obtain; a new policy is then required to control the

supply of the new substance or distribution channel, followed by another surge in new problematic substitutes or distribution channels, and so on, ad infinitum. The latest move in the prescription drug policy arms race may well be the illicit pharmaceutical opioid substitute heroin. This chapter explores the relationship between opioid prescriptions and heroin abuse by comparing prescription dispensation records to heroin abuse treatment facility discharges before and after the implementation of Kentucky's House Bill 1.

Methods

Data was acquired from two sources: the Kentucky All-Schedule Prescription Electronic Record (KASPER) database, Kentucky's PDMP that contains patient-level controlled substance prescription dispensing data, and patient-level substance abuse treatment facility discharge data from the Treatment Episodes Data Set (TEDS). A linkage of these two datasets was conducted on patient identifiers by a third party honest broker from the Center for Clinical and Translational Sciences Enterprise Data Trust at the University of Kentucky. Linked data included all controlled substance prescriptions and substance abuse treatment facility discharges for the years 2009 through 2013. Please note the researcher did not have access to identifying patient information at any point in this process and worked with de-identified data transferred after the linkage was completed. University of Kentucky and Cabinet for Health and Family Services (CHFS) guidelines exempt this project from standalone Institutional Review Board review because the human subjects data is de-identified,[102] and use of this de-identified data for analysis was granted

permission by CHFS on June 24, 2014 with decision document CHFS-IRB-OATS-FY14-38 (documentation available upon request).

Prescriptions dispensed for pharmaceutical opioids were calculated by select opioid type and summed to the fiscal year at the patient level for fiscal years 2010-2013, where the pre-House Bill 1 period was defined as fiscal years 2010-2012 and the post-House Bill 1 period was defined as fiscal year 2013. Fiscal years were selected as the unit of time for this analysis rather than calendar years due to the July 2012 implementation date of House Bill 1.

The analysis contained several components. Patient characteristics and prescription history for dispensed opioids for patients with treatment discharges for heroin, opioid or other substances were compared to patients who did not experience a treatment discharge. Additionally, trends in treatment discharges over time for heroin, pharmaceutical opioids and other substances were compared.

An individual patient may have multiple treatment discharge events during the study period and may also report poly-abuse of substances within each episode of treatment. In the case of poly-abuse, the first three substances for which treatment is sought are included in counts of treatment discharges but the patient's demographic characteristics are only counted once per treatment event. This convention was utilized to due its presence throughout TEDS record systems, where "primary" substance of abuse, "secondary" substance of abuse, and "tertiary" substance of abuse are listed by ranking of the patient as well as his/her treatment providers upon admission.

Mean total opioid prescriptions for substance abuse treatment facility patients discharged for heroin abuse versus treatment facility patients discharged for the abuse of other non-opioid substances before and after House Bill 1 were compared using two-tailed t tests. Logistic regression models estimated the likelihood of treatment discharge for heroin relative to the discharge for other non-opioid substances, where the predictors were number of each type of opioid prescription with controls for age, gender, number of pharmacies dispensing to the patient, and number of providers prescribing to the patient.

An alternative specification was constructed that included controls for previous discharges as well as an interaction term between year of discharge and number of previous discharges. A supplementary analysis with pharmaceutical opioid treatment discharges rather than heroin treatment discharges as the dependent variable was also conducted using the alternative specification. All analysis was conducted in Stata v13.[95]

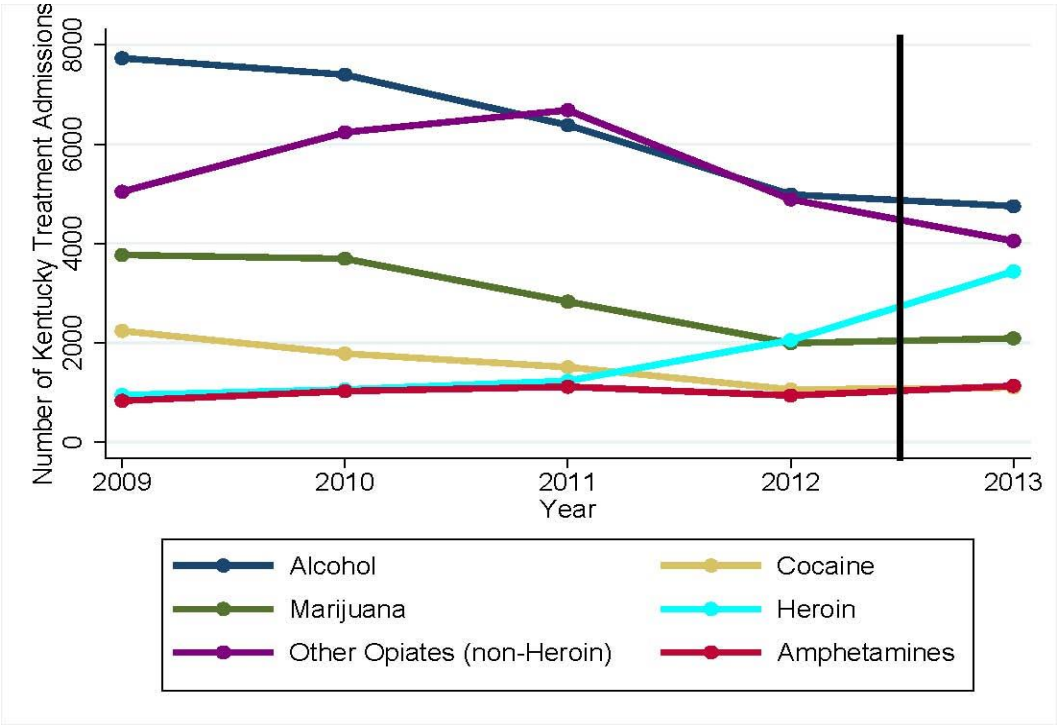
Results

Alcohol represents the most widely used substance for which treatment is sought in Kentucky in every year examined, with the exception of 2011 when it was briefly overtaken by demand for treatment of non-heroin pharmaceutical opioid abuse.[‡] Substance abuse treatment for pharmaceutical opioids has declined since peaking in 2011, while heroin treatment has increased in this time (Figure 5.2). Poly-abuse of substances was most frequently reported in combination with alcohol (e.g., treatment sought for alcohol + pharmaceutical

[‡] *TEDS data uses the terminology 'other opiates' when classifying pharmaceutical opioids as a category of substances of abuse.*

opioids, or treatment sought for alcohol + cocaine + amphetamines). The maximum number of treatment discharges for both heroin and pharmaceutical opioids by an individual patient was 15 discharges in the study period. Heroin treatment discharges represented 10.25 percent of all treatment discharges before the implementation of House Bill 1 and 21.81 percent post-House Bill 1 ($p<0.001$).

Figure 5.2 Substance Abuse Treatment Facility Admissions in Kentucky, by Substance and Year



Patients discharged from treatment facilities were a mean of 35.51 years old as compared to a mean of 45.93 years old for Kentuckians with controlled substance prescriptions but no treatment discharges ($p<0.001$). Patients with treatment discharges were 46.90 percent female and patients with no treatment discharges 54.84 percent were female ($p<0.001$). Those with discharges visited a mean of 6.56 pharmacies (3.27 pharmacies if no treatment discharges, $p<0.001$),

and had a mean of 6.96 prescribers (3.45 prescribers if no treatment discharges, $p<0.001$).

In Table 5.1, opioid prescriptions dispensed to patients with treatment discharges for heroin, pharmaceutical opioids, and other substances are compared for the period leading up to HB1 (fiscal year 2010-2012) and following HB1 implementation (fiscal year 2013). Pre-House Bill 1 heroin discharge patients had greater mean opioid prescriptions compared to patients with other substance discharges, even when including opioid discharge patients (7.38 vs. 7.29, p=NS). Heroin discharge patients, however, had fewer opioid prescriptions post-House Bill 1 (7.32 vs. 7.38, p=NS) when opioid discharge patients were included in the comparison group.

Table 5.1 Characteristics and Prescriptions Dispensed to Kentucky Patients Discharged from Substance Abuse Treatment

	Pre-House Bill 1 (FY2010-2012)			*Post-House Bill 1 (FY2013)*		
	Heroin Treatment Discharges (n=5,755)	**Opioid** Treatment Discharges (n=20,090)	**Other Substance** Treatment Discharges (n=48,116)	**Heroin** Treatment Discharges (n=3,148)	**Opioid** Treatment Discharges (n=5,085)	**Other Substance** Treatment Discharges (n=11,720)
Females	47.97%	51.16%	45.89%	46.07%	52.79%	46.35%
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Age at Discharge	32.25 (10.19)	33.71 (10.67)	35.62 (11.88)	31.76 (9.68)	34.17 (10.65)	34.46 (11.96)
Prescribers	6.59 (6.67)	7.42 (7.13)	6.71 (6.66)	6.39 (6.68)	7.21 (6.66)	6.72 (6.51)
Pharmacies	6.30 (6.28)	7.09 (6.60)	6.30 (6.05)	6.10 (6.29)	6.89 (6.25)	6.32 (5.94)
Oxycodone Scripts	1.25 (3.50)	1.26 (3.52)	0.95 (2.90)	1.23 (3.58)	1.33 (3.66)	0.96 (2.87)
Hydrocodone Scripts	3.46 (5.66)	3.75 (5.75)	3.64 (5.64)	3.63 (5.82)	3.95 (5.70)	3.77 (5.69)
Hydromorphone Scripts	0.01 (0.26)	0.01 (0.22)	0.01 (0.25)	0.04 (0.54)	0.02 (0.39)	0.01 (0.32)
Buprenorphine Scripts	1.50 (6.16)	2.28 (8.08)	1.12 (6.07)	1.43 (8.68)	1.93 (9.37)	1.17 (7.84)
All Other Opioid Scripts	0.50 (2.37)	0.46 (2.16)	0.39 (1.95)	0.42 (1.79)	0.47 (2.34)	0.41 (2.01)
TOTAL Opioid Scripts	**7.38 (9.85)**	**8.70 (10.79)**	**6.93 (9.48)**	**7.32 (11.43)**	**8.53 (11.76)**	**7.08 (10.64)**

Interestingly, patients who sought treatment for the abuse of *any* substance had higher mean opioid prescriptions than Kentuckians receiving controlled substance prescriptions but who did not seek substance abuse treatment (Table 5.2). Hydrocodone prescriptions were the most frequent opioid prescriptions amongst patients with treatment discharges as well as patients with controlled substance prescriptions but no treatment discharges ($p<0.001$). Patients with any treatment discharges had been dispensed significantly more hydrocodone than other types of opioids.

Table 5.2 Mean Prescriptions for Kentucky Patients with and without Substance Abuse Treatment Discharges

Mean Prescriptions	**Patients with ANY treatment discharges**	**Patients with NO treatment discharges**	**P-value**
Total Opioids	**7.31**	**2.68**	**<0.001**
Oxycodone	1.02	0.39	<0.001
Hydrocodone	3.69	1.52	<0.001
Hydromorphone	0.01	0.01	0.031
Buprenorphine	1.34	0.07	<0.001
Other Opioids	0.41	0.29	<0.001

Oxycodone prescriptions were significant predictors of heroin treatment discharge in each regression specification (Table 5.3, Table 5.4). Hydromorphone prescriptions were the most strongly correlated opioid with heroin treatment discharges (OR: 1.14, 95% CI: 1.05-1.24). Hydrocodone, buprenorphine, and other opioid prescriptions were also significant predictors of heroin treatment discharge (Table 5.3, Figure 5.3). Females were 9 percent less likely than males to have a heroin treatment discharge (OR: 0.91; 95% CI: 0.86-0.96) and every year increase in age was associated with a 4 percent decrease in the odds of having a heroin treatment discharge.

Table 5.3 Patient Characteristics and Number of Opioid Prescriptions Associated with Heroin Treatment Discharges

	Odds Ratio	95% Confidence Interval
Fiscal Year		
2010	Reference year	---
2011	1.30**	1.20 to 1.42
2012	1.86**	1.71 to 2.03
2013	3.27**	3.03 to 3.54
Female	0.91**	0.86 to 0.96
Age	0.96**	0.96 to 0.96
Number of Prescribers	0.98**	0.96 to 0.99
Number of Pharmacies	1.01	0.99 to 1.02
Oxycodone Prescriptions	1.04**	1.03 to 1.05
Hydrocodone Prescriptions	1.01**	1.00 to 1.02
Hydromorphone Prescriptions	1.14**	1.05 to 1.24
Buprenorphine Prescriptions	1.01**	1.00 to 1.01
All Other Opioid Prescriptions	1.03**	1.02 to 1.04

**Indicates statistically significant: p<0.05*

Figure 5.3 Patient Characteristics and Number of Opioid Prescriptions Associated with Heroin Treatment Discharges

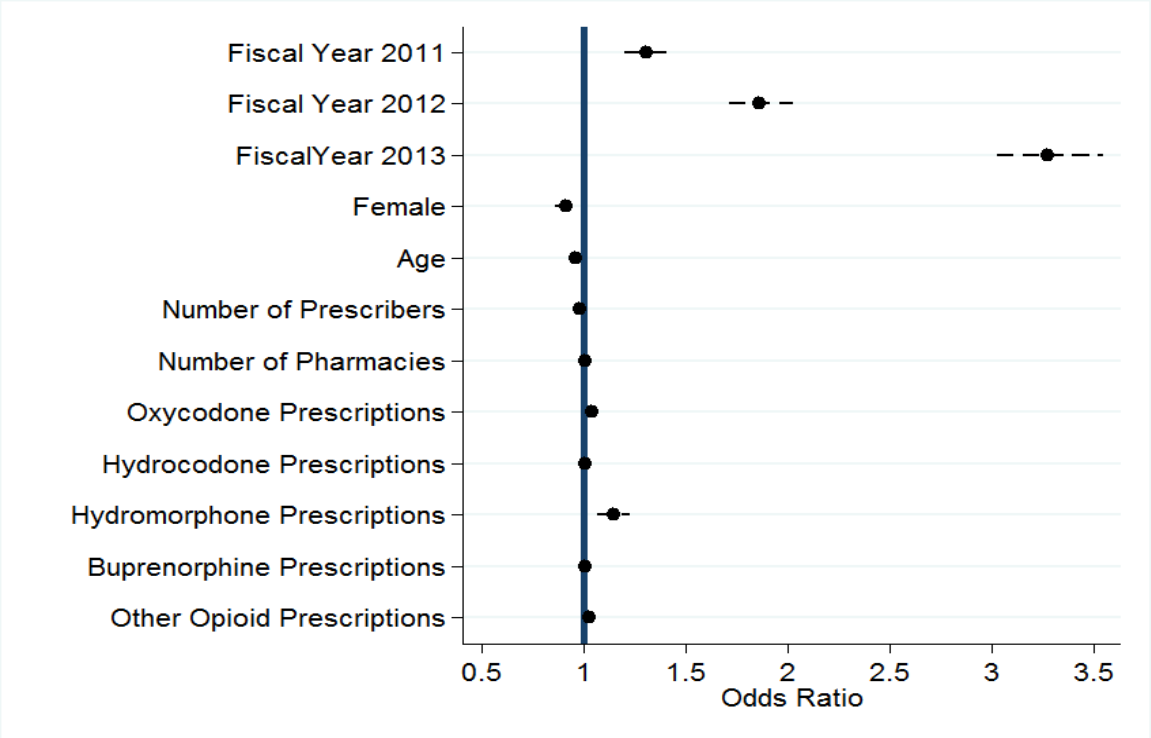


Table 5.4 includes results with controls for previous discharges and interactions between year of discharge and number of previous discharges. Females were 14 percent less likely to have a discharge for heroin than males

(95% CI: 0.82-0.92), but were 1.29 times *more* likely to have a treatment discharge for pharmaceutical opioids than males (95% CI: 1.24-1.34). Buprenorphine prescriptions were associated with an increased likelihood of treatment discharges for pharmaceutical opioids (OR: 1.08; 95% CI: 1.07-1.08).

Table 5.4 Alternative Specification: Patient Characteristics and Number of Opioid Prescriptions associated with Heroin and Opioid Discharges

	Heroin Discharges		Opioid Discharges	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**
Fiscal Year				
2010	Reference year	---	Reference year	---
2011	1.33**	1.14 to 1.54	1.25**	1.15 to 1.35
2012	1.80**	1.55 to 2.10	1.58**	1.45 to 1.73
2013	4.31**	3.74 to 4.96	1.24**	1.14 to 1.36
Female	0.86**	0.82 to 0.92	1.29**	1.24 to 1.34
Age	0.96**	0.96 to 0.96	0.97**	0.97 to 0.97
Number of Prescribers	0.98**	0.97 to 0.99	0.97**	0.96 to 0.98
Number of Pharmacies	1.01	0.99 to 1.02	1.05**	1.04 to 1.06
Oxycodone Prescriptions	1.04**	1.03 to 1.05	1.08**	1.07 to 1.09
Hydrocodone Prescriptions	1.01**	1.01 to 1.02	1.02**	1.01 to 1.02
Hydromorphone Prescriptions	1.14**	1.05 to 1.24	0.94	0.88 to 1.02
Buprenorphine Prescriptions	1.00	1.00 to 1.01	1.08**	1.07 to 1.08
All Other Opioid Prescriptions	1.03**	1.02 to 1.04	1.03**	1.02 to 1.04
Number of Previous Discharges				
0	Reference	---	Reference	---
1	1.84**	1.69 to 2.00	1.51**	1.43 to 1.59
2	2.56**	2.31 to 2.84	1.75**	1.64 to 1.87
3	2.69**	2.34 to 3.06	1.97**	1.81 to 2.15
4	3.40**	2.92 to 3.96	2.34**	2.11 to 2.60
5	4.05**	3.36 to 4.87	2.07**	1.81 to 2.35
6	3.30**	2.62 to 3.96	2.06**	1.76 to 2.42
7	3.52**	2.68 to 4.62	1.42**	1.18 to 1.71
8	6.08**	4.53 to 8.15	4.31**	3.41 to 5.45
9	7.71**	5.57 to 10.66	1.87**	1.45 to 2.40
10	3.16**	1.83 to 5.45	2.75**	1.82 to 4.15
11	1 (single case)	---	2.75**	1.92 to 3.95
12	4.95**	2.83 to 8.64	1.10	0.73 to 1.67
13	1 (single case)	---	3.76**	2.22 to 6.35
14	1 (single case)	---	1 (single case)	---
Interaction: Previous Discharges and Year				
n discharges X 2011	0.98	0.95 to 1.02	0.97*	0.95 to 0.99
n discharges X 2012	1.08**	1.03 to 1.12	0.99	0.97 to 1.02
n discharges X 2013	0.98	0.95 to 1.02	1.05**	1.11 to 1.30

**Indicates statistically significant: p<0.05.*

Discussion

Although opioid prescribing decreased overall during the study period among all persons in Kentucky receiving controlled substance prescriptions, hydrocodone and hydromorphone prescriptions increased among heroin treatment discharge patients following the implementation of House Bill 1. This finding suggests that the PDMP and prescribing provisions in House Bill 1 may have influenced which substances were preferred in opioid-seeking behaviors. Alternatively, HB1 may have influenced shifts in prescribing behaviors.

The findings of this analysis also indicate that prescription opioid consumption amongst individuals with substance abuse treatment stays for any substance, even non-opioid substances, is higher than prescription opioid consumption in the Kentucky population as a whole. This lends further support to the theory that substance use disorders tend to develop into poly-abuse when the supply of the preferred substance becomes limited or sporadic. PDMPs and other prescription opioid abuse deterrent policies and regulations have been enacted with almost exclusive supply-side restrictions of prescription opioids, while few policies have attempted to curb demand via the expansion of treatment opportunities or increased public insurance coverage of rigorous treatment options. The implementation of the Patient Protection and Affordable Care Act of 2010 enabled participating states to expand their Medicaid eligibility and coverage to include “essential” treatments for substance use disorders;[103] however, the substance use disorder treatments recommended for reimbursement and classified as “essential” are typically behavioral and

counseling-based treatments and place substantial barriers on evidence-based medication assisted therapies.[104]

There are several limitations in this study. First, substance abuse treatment data from private-pay only facilities was not available in the TEDS dataset, which means that it is difficult to generalize prescription opioid trends amongst patients enrolled in these mixed public and private pay treatment facilities to the patient population who enrolled in private-pay only facilities. Next, prescription data from KASPER was not available for opioid prescriptions that were dispensed during inpatient hospital stays or to patients that were dispensed opioids as part of a medication-assisted substance abuse treatment regimen (i.e., buprenorphine prescribed by a Primary Care Physician would appear in KASPER data, but buprenorphine dispensed by an outpatient clinic in conjunction with a medication-assisted treatment program would not appear in KASPER data). Lastly, treatment discharge records and prescription data for patients that received treatment and prescriptions across state lines were not available from either data source. It is possible that some Kentuckians sought health care services involving controlled substances or treatment from providers in other states following the tightening of pain clinic regulations and PDMP usage as outlined in HB1. Despite these limitations, there appears to be a relationship between prescription opioid utilization and heroin abuse that merits further exploration.

CHAPTER SIX

The Impact of Naloxone Access Policies on Opioid Overdose Deaths

Chapter Summary: This final empirical chapter explores other state-level policy interventions in opioid abuse and diversion by widening the focus from PDMP programs to include broader opioid intervention policies, namely naloxone access laws. Naloxone is a medication used to reverse heroin and/or pharmaceutical opioid overdose, which some states have made more widely available to consumers at risk of overdose. This analysis examines the relationship between naloxone access policies and PDMPs with opioid overdose mortality using data from the CDC for 1999-2012.

Pharmaceutical opioid and/or heroin overdoses, largely reversible with timely administration of a medication called naloxone,[105] have risen substantially since 1999. In fact, unintentional opioid overdose poisoning deaths have now surpassed vehicle accidents as the number one cause of injury death in adult citizens of the United States.[73] Naloxone is not a controlled substance, but has been traditionally administered by medical professionals in an emergency department environment. The time-sensitive nature of administration for successful overdose reversal, coupled with a low potential for abuse, has prompted several states to implement policies that increase access to naloxone for individuals at risk of opioid and/or heroin overdose.

Naloxone distribution programs have been declared successes by cities and states that have implemented them. Between 1996-2010, naloxone was distributed by these programs to 53,032 persons nationwide, which resulted in 10,171 overdose reversals.[106] The majority of injectable users report willingness to administer naloxone to others during an overdose (88.5 percent), particularly if they have used heroin, or have witnessed or have had an overdose themselves.[107] This street-level treatment option for overdose has been hailed as a lifesaver where authorized, due to the relatively high prevalence of overdose

experiences in self-reported users of injected substances such as heroin. In a survey of 329 people using injected drugs, Lagu et al. (2006) found that 34.6 percent had experienced an overdose themselves and 64.6 percent had witnessed an overdose.[107]

In addition to naloxone distribution programs, which are typically implemented by city or local health departments, states have implemented policies to increase access to naloxone where outright distribution is not available. Three of these naloxone access policies are examined in this analysis: the authority of prescribers to write prescriptions for third parties (e.g., a parent could receive a naloxone prescription for their child if they felt he/she was at risk for overdose), standing order prescriptions (e.g., a state director of public health or similar official may "write" a prescription for all persons in the state, meaning that naloxone would be available for purchase at pharmacies without an explicit prescription, or non-prescribers such as pharmacists may dispense without a prescription), and prescriber immunity policies that protect prescribers from liability in case the party receiving naloxone on their behalf experiences overdose mortality or morbidity. Pilot studies evaluating these naloxone access policies have found evidence for the effectiveness of third party prescribing, in particular, for reducing heroin overdose deaths in communities where the practice is permitted.[108] The purpose of this piece is to determine whether these state naloxone access policies may have contributed to changes in state opioid overdose mortality rates.

Methods

Data for the dependent variable, pharmaceutical opioid and heroin overdose deaths per state-year from 1999-2012, were obtained from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiological Research (WONDER) database. Deaths were identified using the following International Classification of Disease version 10 codes for opioid poisoning: X40-44 for accidental poisoning deaths, X60-64 for intentional poisoning deaths, and Y10-14 for poisoning deaths of undetermined intent. These codes were coupled with underlying substance codes of T40.0-40.4, representing opium, heroin, "other" opioids, methadone, synthetic opioids, or T40.6, representing unspecified opioids. Diagnosis codes and underlying substance codes were identified based on reviews of the literature as well as a line-item review of the International Classification of Disease billing code diagnoses listings.[109-112] A state-year death total was not included in WONDER if there were fewer than 10 overdose deaths attributed to a particular substance in a given state and year, for decedent privacy protection.

The presence of state naloxone access policies, including third party naloxone prescribing authorization, standing order prescriptions and prescriber immunity laws, were operationalized as independent dummy variables at the month-year of implementation. Implementation dates and formal definitions of state statutes meeting the criteria to be classified as one of these three policies were derived from the National Institute on Drug Abuse's and Legal Science Partner's 2012 report on Naloxone Overdose Prevention Laws.[113] The

distribution of count of overdose deaths were found to be over-dispersed (variance>mean); therefore, a negative binomial, time series regression model with state and year fixed effects was constructed to estimate the relationship between naloxone access policy implementation and opioid overdose deaths. Lag years of the dependent variable (deaths) were used to address potential endogeneity problems. State-level control variables included: state population, operational PDMP, PDMP characteristics as defined in Chapter 2, and state average annual unemployment rate.

Results

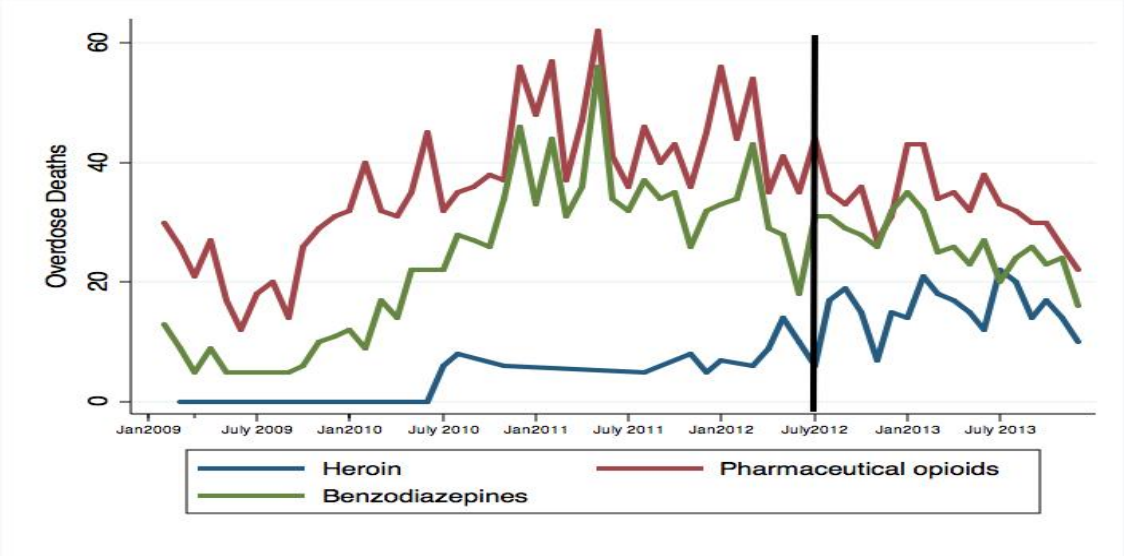
During the study period, eight states implemented at least one of the three naloxone access policies examined: New Mexico, New York, California, Colorado, Connecticut, Illinois, Massachusetts, and Washington state. Nationally, mean state pharmaceutical opioid overdoses increased 4 fold during the study period, while mean heroin overdoses also increased but at a much slower rate (Table 6.1).

Table 6.1 State Mean and Median Opioid Overdose Deaths, 1999-2012

Year	Pharmaceutical Opioid Overdoses		Heroin Overdoses	
	Mean (SD)	Median	Mean (SD)	Median
1999	72.63 (152.15)	32	88.61 (151.58)	23
2000	81.49 (117.37)	50	85.02 (127.43)	30
2001	102.53 (116.51)	92	83.84 (123.28)	31
2002	141.57 (188.50)	116	94.98 (143.04)	33
2003	162.86 (194.08)	120	95.08 (137.78)	33
2004	189.12 (215.79)	140	83.29 (114.31)	35
2005	209.80 (210.33)	164	87.84 (117.14)	41
2006	264.94 (261.29)	214	90.78 (124.07)	34
2007	279.18 (281.34)	231	92.27 (121.05)	44
2008	286.39 (295.40)	224	108.51 (135.56)	61
2009	302.47 (327.72)	216	107.98 (136.23)	53
2010	322.04 (340.28)	229	98.02 (129.75)	48
2011	328.53 (336.84)	256	130.80 (159.39)	84
2012	319.54 (292.92)	260	182.22 (202.39)	117

For a glimpse into recent overdose mortality trends specific to Kentucky, Figure 6.1 was created with data from Kentucky Office of Vital Statistics.[114] The black vertical line represents the implementation of House Bill 1 in Kentucky in July 2012, which was discussed in the previous chapter. Kentucky, specifically, experienced an upward trend in heroin overdose mortality from 2011 through 2013, while pharmaceutical opioid overdose mortality trended downwards.

Figure 6.1 Overdose Deaths in Kentucky, by Substance for 2009-2013



States authorizing third party naloxone prescriptions experienced 35% fewer pharmaceutical opioid overdose deaths per year after policy implementation (95% CI: 0.46-0.95), but no statistically significant change in pharmaceutical opioid overdose deaths were observed in states that implemented standing order prescriptions and prescriber immunity. No significant change in heroin overdose deaths was observed in states authorizing third party prescriptions, standing order prescriptions, or prescriber immunity (Table 6.2). Operational PDMP presence was associated with 10.55 times greater heroin overdoses (95% CI: 4.75-23.44), and there were also relationships between

increased heroin overdoses with PDMP interstate data sharing (IRR: 1.37; 95% CI: 1.12-1.68), data transmission occurring more frequently than once per week (IRR: 1.89; 95% CI: 1.53-2.34), as well as the monitoring of Schedule V substances (IRR: 1.77; 95% CI 1.35-2.32). The monitoring of Schedule III substances was associated with a 90 percent decrease in heroin overdoses (95% CI: 0.04-0.24) and controls for time accounted for minor relationships with heroin overdose.

Table 6.2 The Association between Pharmaceutical Opioid and Heroin Overdose Deaths with Naloxone Access Policy Implementation

Variable Description	Opioid Overdose IRR (95% CI)	Heroin Overdose IRR (95% CI)
Naloxone Policy Variables		
Prescriber Immunity	1.14 (0.93-1.40)	0.93 (0.78-1.11)
Standing Order Prescriptions	1.22 (0.81-1.84)	0.98 (0.56-1.72)
Third Party Naloxone Prescriptions	0.65 (0.46-0.95)*	0.89 (0.53-1.49)
PDMP Covariates		
PDMP Operational	1.66 (1.04-2.67)*	10.55 (4.75-23.44)*
Proactive Prescriber	0.81 (0.68-0.97)*	0.73 (0.53-1.01)
Proactive Law Enforcement	1.00 (0.85-1.17)	0.95 (0.74-1.21)
Law Access	1.08 (0.89-1.32)	1.21 (0.88-1.66)
Compulsory Registration	0.95 (0.82-1.11)	0.99 (0.78-1.26)
Compulsory Prescriber Use	0.88 (0.73-1.05)	0.81 (0.60-1.09)
Interstate Data Sharing	1.02 (0.91-1.05)	1.37 (1.12-1.68)*
Data Transmission <1 Week	1.26 (1.11-1.44)*	1.89 (1.53-2.34)*
Schedule III Monitored	0.69 (0.42-1.15)	0.10 (0.04-0.24)*
Schedule V Monitored	1.22 (1.04-1.43)*	1.77 (1.35-2.32)*
Unscheduled Substances Monitored	0.79 (0.67-0.94)*	0.80 (0.60-1.07)
Other Covariates		
State Population	1.00 (1.00-1.00)*	1.00 (1.00-1.00)*
Average Annual Unemployment Rate	0.99 (0.96-1.02)	0.97 (0.92-1.03)
Year (reference 2000)		
2001	1.36 (1.07-1.75)*	0.92 (0.75-1.11)
2002	2.03 (1.60-2.58)*	0.80 (0.62-1.02)
2003	2.75 (2.19-3.46)*	0.99 (0.80-1.23)
2004	3.24 (2.59-4.05)*	0.97 (0.78-1.20)
2005	3.99 (3.20-4.96)*	0.85 (0.69-1.04)
2006	4.40 (3.54-5.46)*	0.83 (0.67-1.03)
2007	5.48 (4.42-6.79)*	0.81 (0.65-0.99)*
2008	5.77 (4.62-7.20)*	0.88 (0.68-1.10)
2009	6.40 (4.90-8.37)*	1.22 (0.86-1.72)
2010	6.42 (4.88-8.46)*	1.24 (0.86-1.78)
2011	6.88 (5.29-8.95)*	1.02 (0.73-1.42)
2012	6.94 (5.39-8.93)*	1.30 (0.96-1.75)
Total State-Years (n)	663	598

**Indicates statistically significant: p<0.05.*

The magnitude of the relationship between opioid overdose deaths in states with operational PDMPs (IRR: 1.66; 95% CI: 1.04-2.67) is overshadowed substantially by the magnitude of the relationship with heroin overdose deaths, though both are positively associated.

Pharmaceutical opioid overdoses have similar relationships to PDMP features as heroin overdoses, with observed increases in opioid overdoses

among states with Schedule V monitoring (IRR: 1.22; 95% CI: 1.04-1.43) and increases in opioid overdoses among states with data transmission more frequently than once per week (IRR: 1.26; 95% CI: 1.11-1.44). Proactive or unsolicited reports to prescribers from PDMPs, however, appear to be significantly associated with decreases in pharmaceutical opioid overdose deaths (IRR: 0.81; 95% CI: 0.68-0.97), but not with heroin overdose deaths. The passage of time is also more significantly associated with increases in pharmaceutical opioid deaths, whereas heroin overdose deaths have increased slowly throughout the study period.

Discussion

Findings from this analysis demonstrate that decreases in heroin overdose death rates observed in states with expanded implementation of naloxone access policies were not statistically significant. However, pharmaceutical opioid death rates have slowed in states with third party naloxone prescriptions. It is possible that the naloxone access policies examined in this chapter were enacted in states with particularly severe heroin epidemics, so the *rate* of heroin overdose deaths may have been slowed by these policies in a manner unable to be captured by this type of analysis.

Research on optimal naloxone access laws and their implementation is needed as naloxone has few documented negative health effects and has been determined to be a cost-effective method of saving lives.[115] It should be noted that this analysis has several limitations. Most significantly, there is no control for the extent of naloxone access policy enforcement in the states that implemented

the examined policies. Also, there is no control for exogenous events and trends that possibly contributed to changes in opioid overdose mortality beyond PDMP features. Other contributing factors to the observed downward mortality trends in some states could include the “methadone migration” (a term I use to describe changing prescribing preferences for buprenorphine/naloxone combination products over the traditional, but overdose-prone, methadone in medication-assisted substance abuse treatment programs), the implementation of needle exchange programs, or states that enhanced substance abuse treatment availability during the study period. Lastly, this analysis does not capture overdoses that did not result in deaths. Future expansions of this analysis should include emergency department discharge data for non-fatal opioid overdose treatment.

CHAPTER SEVEN

Policy Implications and Recommendations

Chapter Summary: The final chapter concludes the dissertation by re-iterating themes observed throughout the empirical analyses and synthesizing these findings to expand the existing policy implementation and evaluation literature on state-level interventions in opioid abuse and diversion. Recommendations for future PDMP policy are presented and discussed.

The law enforcement and medical communities have expressed markedly different perspectives for the most effective methods of defining and solving the problem of prescription drug abuse and diversion. Some of these differences are most apparent in the language used to describe their respective goals and policy recommendations. For example, law enforcement communities tend to define prescription drug abuse and diversion in terms of a problem to be met with by force (e.g., the war on drugs, the drug threat), whereas the medical community tends to define the problem using terminology such as “epidemic” or “crisis of abuse.” This difference in perspective has become even more apparent as policy efforts to combat the problem from both law enforcement and medical communities have been met with few measureable successes. Reports and statements about PDMPs issued by health agencies tend to make references to the Principle of Balance, which is the effort to reduce abuse and diversion while providing access to controlled substances for legitimate medical need, and reports and statements issued by law enforcement agencies typically neglect to include this language.

The Department of Justice releases an annual publication titled “The National Drug Threat Assessment”, which features an analysis on nationwide drug crime and reports from lower level regional and district officials. An annual

survey of local law enforcement conducted from 2005 to 2009 found that officials have steadily increased their perceptions of prescription drugs, particularly opioids, as the greatest “drug threat” to their region (3.9 percent in 2005 to 9.8 percent in 2009).[20] The nomenclature used to describe the drugs themselves in these types of publications is noticeably different between law enforcement agencies and health agencies. For example, law enforcement agencies and the court systems tend to use the ill-defined term “narcotic” when describing certain controlled substances, whereas health agencies and clinicians often use more clinically-specific drug class terms, such as “opioid”, “sedative”, or “stimulant;”[1] however, it is interesting to note that law enforcement and health agencies seem equally likely to use the terms “opiate” and “opioid” interchangeably despite the problems of using the oft too-specific “opiate.” On an even more fundamental level, substances are more likely to be referred to by one of several clinically oriented terms (e.g. medications, drug therapy, prescription drugs, and nonmedical versus medical use of prescription drugs) by health agencies and health professionals, whereas law enforcement agencies tend to avoid these qualifiers by using the catch-all term “drugs” to describe almost any type of ingested, injected, or inhaled substance for medical or nonmedical use.

Additionally, the law enforcement communities and medical communities have both developed the problematic tendency to refer to persons with substance use disorders using reductive, and sometimes hostile, language. Terms like “addict” are commonplace in law enforcement documentation whereas the clinically equivalent version “abuser” crops up equally as often in

medical literature written by health professionals whose specialties lay outside the treatment of substance use disorder. If an effort was made to agree upon the language used in the reporting and research of controlled substance trends, then there may be increased potential for more productive collaboration between law enforcement, health agencies, and the communities who face the brunt of prescription opioid abuse and diversion problems with fewer tensions.

Policy Implications

Changes in the marketplace for prescription opioids, one of the most widely prescribed classes of controlled substances, could have implications throughout the health care system for insurers who reimburse for opioids, for providers who treat patients with opioids and for opioid use-related disorders, and for patient-consumers who may face barriers to access for opioids or barriers to access for treatment of opioid use disorders. Any changes in the quantity of prescription medications reimbursed by Medicaid, in particular, represent significant shifts in the marketplace for prescription drugs, as Medicaid is the largest health insurer in the United States.[116]

State Medicaid programs are dispensing (or, more accurately, reimbursing) an increasing amount of controlled substances each year, but states that have implemented PDMPs tend to dispense fewer total units of controlled substances to their respective Medicaid beneficiaries. The presence of a PDMP would appear to be influencing changes in prescriber and dispenser behavior, but specific PDMP policy characteristics, such as the ability to share data with other state PDMPs, shape the nature of that behavior change. The

decrease in both higher and lower Scheduled controlled substance dispensing in states with operational PDMPs would suggest that prescribers and dispensers may possibly be suffering from a “chilling effect” (a reduction in prescribing/dispensing due to fears of investigation), but the increase of units of all Scheduled substances dispensed in states with law enforcement-housed PDMPs would seem to contradict this notion. Perhaps providers are more confident in making prescribing and dispensing decisions in states that encourage access to consumer use history information when endorsed by law enforcement agencies.

PDMP policies were intended to reduce abuse and diversion, but the observed national increases in overdose mortality as well as substance abuse treatment admissions since widespread state PDMP implementation implies that these policies have not achieved this goal; however, it is possible that PDMP policies have tempered the upward abuse trend. The coordination of state program information sharing and the implementation of more-uniform PDMP policies could intensify the intended impact of PDMPs, particularly if the intended user groups are afforded adequate access to program data and the training to use that data appropriately.

Recommendations and Conclusion

It is recommended that state-level PDMP programs reconcile statutes with agency regulations (e.g., clarify professional licensure board requirements versus “guidelines” for registration and participation), in cases where these bodies experience conflicting language or when agencies have limited ability or

resources to implement the regulations they have been charged with enacting. For example, it is widely cited by state PDMPs and PDMP advocacy groups that “most” states have interstate data-sharing capabilities, and while it is true that most states have approved agreements to transmit interstate data, the reality is that as of 2015 only 27 states have been able to successfully transmit data across state lines and the majority of these transmissions are limited to border states.

It is also recommended that states expand monitoring to lower Scheduled substances if they are currently exempt from the PDMP, and to petition the FDA and DEA to reconcile state-level Scheduling with the federal Schedule. Several states have re-Scheduled upward substances such as hydrocodone and tramadol due to perceived uptake in abuse and it is apparent that these states respond to changes in problematic substance use more quickly than the federal agencies.

Reconciliation between federal agency regulations and state PDMP policies on law enforcement access is also recommended. The DEA, FBI, and other federal investigative bodies are permitted to access state PDMP data pursuant to active investigations, but this conflicts with some state laws that restrict law enforcement access to PDMP data to cases where the investigative body has a warrant, court order, or subpoena issued by a court within the state. This conflict has come to a head recently in the state of Oregon, where Oregon’s PDMP in conjunction with the American Civil Liberties Union filed suit against the DEA for unwarranted requests to access Oregon’s PDMP data. While a U.S.

Circuit Court ruled in Oregon's favor in 2014, the DEA has since issued an appeal.[63]

It is also recommended that evaluations of PDMPs should continue to be conducted so that states can process relevant outcomes data regarding the effectiveness of such PDMP features as pharmacy data reporting frequency and compulsory prescriber use. A crucial missing component in the formulation of variables for PDMP features was the *participation* rates of prescribers, pharmacists, and law enforcement officials in states that do not mandate usage. Information about the frequency of use and the change in prescriber or dispenser behavior resulting from PDMP use would provide a more complete measurement tool of PDMP impact on dispensing and so it is recommended that state PDMPs publish these data when available. Policy recommendations for related opioid interventions, primarily naloxone access, are more difficult to formulate. It is still unclear whether the observed trends in decreased opioid deaths in some states were due to the changes in state-level naloxone access laws or to exogenous factors. The results from the analyses conducted in the Chapters 5 and 6 suggest that there is an association between PDMPs, naloxone policy interventions, substance abuse treatment enrollment, and overdose mortality, but causality and the direction of this relationship has not been established with certainty.

The use of "real world" data sources in this project included: aggregate reimbursement claims from Medicaid, patient-level prescription data from commercial health insurance, a novel data linkage between substance abuse

facility records with individual controlled substance prescription histories from a state PDMP, and publicly available policy and epidemiological data. The analyses conducted throughout this project suggest the conclusion that the state interventions in prescription opioid abuse in diversion known as PDMPs have influenced far-reaching facets of the United States population's health and safety, such as; as consumer health outcomes by way of changes in substance abuse treatment prevalence and changes in access to pain management care, the market for prescription opioids and possibly illicit heroin substitutes, and health care provider behaviors related to the treatment of pain and substance use disorders.

APPENDIX A

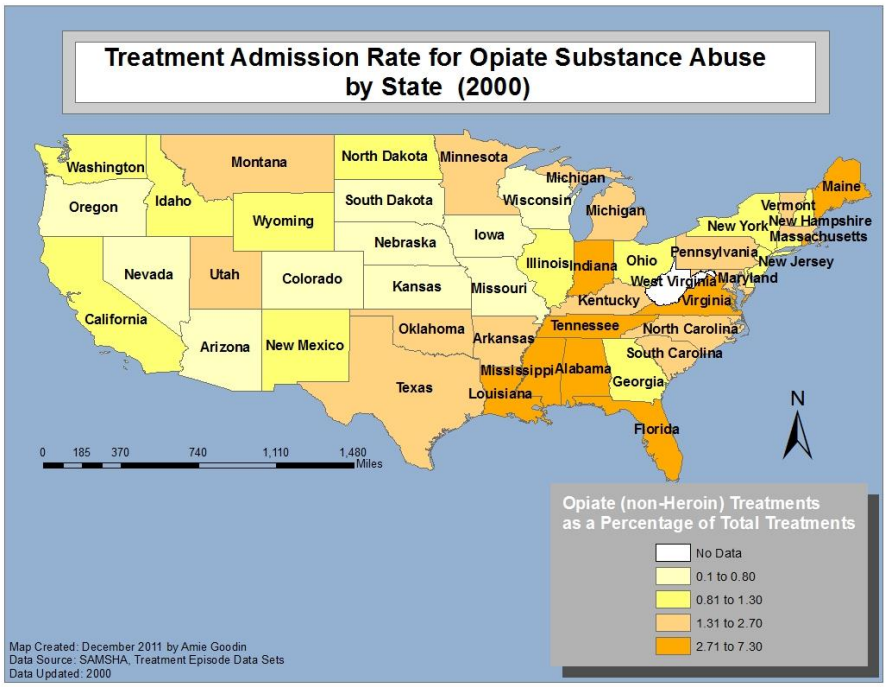
PDMP Year Enacted and Year Operational, as of 2015

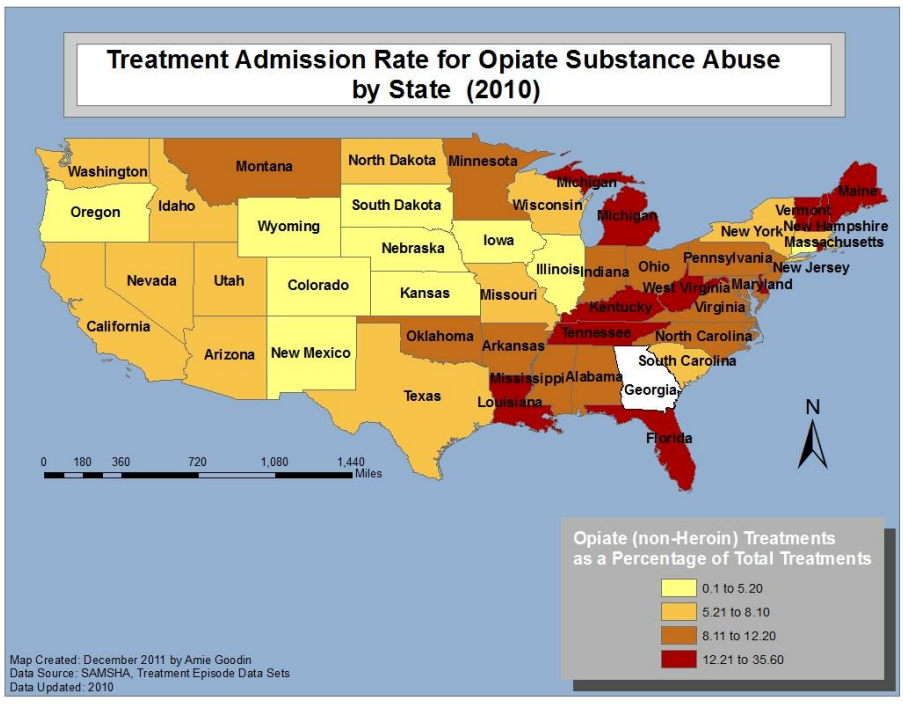
State	Year Enacted	Year Operational	State	Year Enacted	Year Operational
Alabama	2004	2007	Nebraska	2011	2011
Alaska	2008	2012	Nevada	1995	1997
Arizona	2007	2008	New Hampshire	2012	2014
Arkansas	2011	2013	New Jersey	2008	2012
California	1939	2009	New Mexico	2004	2005
Colorado	2005	2008	New York	1972	1973
Connecticut	2006	2008	North Carolina	2005	2007
Delaware	2010	2012	North Dakota	2005	2008
Florida	2009	2011	Ohio	2005	2006
Georgia	2011	2013	Oklahoma	1990	2006
Hawaii	1943	1996	Oregon	2009	2011
Idaho	1986	1998	Pennsylvania	1972	1973
Illinois	1961	1999	Rhode Island	1978	2001
Indiana	1997	2007	South Carolina	2006	2008
Iowa	2006	2009	South Dakota	2010	2012
Kansas	2008	2011	Tennessee	2003	2007
Kentucky	1998	1999	Texas	1981	1989
Louisiana	2006	2009	Utah	1995	1997
Maine	2003	2005	Vermont	2006	2009
Maryland	2011	2014	Virginia	2002	2006
Massachusetts	1992	2010	Washington	2007	2012
Michigan	1988	2003	West Virginia*	2002	2002
Minnesota	2007	2010	Wisconsin	2010	2013
Mississippi	2005	2005	Wyoming	2004	2005
Missouri	---	---	District of Columbia	2014	2015
Montana	2011	2012			

**Note: West Virginia originally adopted PDMP legislation in 1995; it was repealed soon after, and then replaced with the contemporary version in 2002.*

APPENDIX B

Substance Abuse Treatment Admissions for 2000 and 2010





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Amie J. Goodin
Curriculum Vitae

EDUCATION

Certificate in Informatics **May 2012**
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Master of Public Policy **May 2009**
Martin School of Public Policy and Administration, University of Kentucky, Lexington, KY

Bachelor of Science **May 2007**
University of Kentucky, Lexington, KY
Majors: Biology, Sociology

RESEARCH AND PROFESSIONAL EXPERIENCE

Statistics and Research Design Consultant **2014-Present**

Research Scientist **2011-Present**
Institute for Pharmaceutical Outcomes and Policy, University of Kentucky.

Academic Appointment, Instructor **2012-2014**
Gatton College of Business and Economics, University of Kentucky.

Research Assistant **2008-2011**
Institute for Pharmaceutical Outcomes and Policy, University of Kentucky.

Internship **2008-2010**
Money Follows the Person Program, Department of Medicaid Services, Frankfort, Kentucky.

Teaching Assistant **2007-2008**
College of Pharmacy, University of Kentucky.

PUBLICATIONS

Wixson S, Blumenschein K, **Goodin AJ**, Talbert J, and PR Freeman. (2015). *Prescription Drug Monitoring Program Utilization in Kentucky Community Pharmacies.* Pharmacy Practice 13(**2**): 540-552.

Fallin A, **Goodin AJ**, Lee YO, and K Bennett. (2015). *Smoking Cessation Awareness and Utilization among Lesbian, Gay, Bisexual, and Transgender Adults: An Analysis of the 2009-2010 National Adult Tobacco Survey.* Nicotine &

Tobacco Research. E-pub ahead of print on May 25, 2015. doi: 10.1093/ntr/ntv103.

Hickson R, Perin N, Talbert J, Thornbury W, and **AJ Goodin.** (2015). *Online Medical Care: The Current State of eVisits in Primary Care Delivery.* Telemedicine and e-Health 21(**2**): 1-7.

Fallin A, **Goodin AJ**, and B King. (2015). *Menthol Cigarette Smoking among Lesbian, Gay, Bisexual, and Transgender Adults in the U.S.* American Journal of Preventive Medicine 48 (**1**): 93-97.

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Goodin AJ Blumenschein K, Freeman P, and J Talbert. (2012). *Consumer/Patient Encounters with Prescription Drug Monitoring Programs: Evidence from a Medicaid Population.* Pain Physician 15(**3S**): 169-175.

AWARDS AND HONORS

Date	*Activity*
2014	Best Poster Award (first author Sarah Wixson), International Society of Pharmacoeconomics and Outcomes Research.
2014	University of Kentucky Graduate School Travel and Research Funding Grant: $800.
2014	Thomas D. Clark Medallion awarded to *Kentucky Government, Politics, and Public Policy*, by Thomas D. Clark Foundation.
2013	Best Student Podium Presentation Award, International Society of Pharmacoeconomics and Outcomes Research.
2013	University of Kentucky Graduate School Travel and Research Funding Grant: $400.
2013	Second Place Poster Award: Rho Chi Society Research Day, University of Kentucky College of Pharmacy.
2007	Graduated Cum Laude Biology, University of Kentucky.
2007	Graduated Cum Laude Sociology, University of Kentucky.
2002-2007	Governor's Scholars Presidential Award and Scholarship.