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Chapter 1: Introduction

Over the last two and a half decades, an epidemic of prescription opioid abuse has developed in the United States. Legal prescription opioid sales and opioid overdose deaths have risen in parallel, approximately quadrupling over a ten-year time span [1]. By 2010, the volume of prescription opioids sold in the US in 2010 was the equivalent of a month's supply of hydrocodone for every adult in the country [1]. Opioid addiction is costly both in terms of dollars and lives. Opioid-related health insurance spending is approximately $72.5 billion annually [1] and opioids were a contributing factor in 42,000 overdose deaths in 2016 [2]. The Centers for Disease Control and Prevention (CDC) found a significant association between states with high prescription opioid sales and states with high overdose rates [1]. In this context, nearly all states have implemented programs to monitor controlled substance prescription sales [3].

Attempts to limit controlled substance prescribing may result in reduced opioid accessibility for patients who could medically benefit from them [4]. Such trade-offs are consequential considering that opioids are prescribed for pain, and approximately 100 million Americans suffer from chronic pain with a total cost estimated at $560 to $635 billion annually [5]. Acute pain is also widespread, and Americans undergo an average of 9.2 surgical procedures over a lifetime [6]. It is estimated that 10 – 50 percent of patients who experience acute postoperative pain transition to chronic pain [7]. Thus, the challenge for policy makers is to develop policies that simultaneously discourage dangerous prescribing practices while encouraging appropriate medical treatment.

State-level prescription drug monitoring programs (PDMPs) are one tool employed to control the opioid epidemic. Literature has shown that PDMPs successfully reduce opioid prescriptions [8-10]. However, informal reports of increased pain as a result of restrictive opioid policies and guidelines have also surfaced [11-14]. Scientific research on the effect of PDMPs on pain is limited [4]. Given these reported negative effects of PDMPs, it is important to study their existence in order to shape policy that both deters opioid abuse and minimizes unintended consequences for people in pain. The aim of this study is to explore the relationship between PDMP laws and measures of disability (i.e., functional limitations). I hypothesize that disability is associated with the implementation of PDMP laws, as suggested by the popular media reports. In this study I use the National Health Interview Survey from 2006-2015 and quasi-experimental regression methods to examine whether PDMPs affect the number of days spent bedridden and missed work days in the general population and among those who have had a recent surgery or surgery. I examine the heterogeneous effects of policy strength by distinguishing between optional and mandatory PDMP laws. This design can provide strong evidence for policy effect because it exploits the variable timing of policy implementation between states and measures two different strengths of PDMP laws.

Chapter 2: Review of the Literature

Background

Prior to the 1990s, doctors were hesitant to prescribe opioids, given their reputation for being highly addictive [15]. In the 1990s, the attitude toward prescription opioids began to change, driven in part by extrapolations from a brief research letter published in The New England Journal Of Medicine and marketing from the pharmaceutical industry [15]. In the mid-1990s, the American Pain Society created the concept of pain as the fifth vital sign and the prevailing attitude in the medical field began to emphasize doctors' obligation to treat pain [15]. Opioid prescribing grew four-fold in the first decade of the 2000s [1]. By 2011, accidental poisonings had surpassed motor vehicle accidents as the leading cause of accidental death [16]. The recognition of the opioid addiction epidemic then led to another attitude shift, in which both clinicians and policy makers began to shift attention to limiting opioid use [15, 17].

In response to the growing public health problem presented by the opioid epidemic, state governments passed a variety of legislation to reduce over-prescription and misuse of these drugs. One common strategy was the implementation of a PDMP, which typically compiles information on filled prescriptions for controlled substances into a database, allowing clinicians to review a patient's prescription filling history prior to prescribing [18]. Although PDMPs are often discussed as opioid-control measures, they typically monitor all controlled substances included in Drug Enforcement Agency (DEA) Schedules II-V [3]. Reports of low clinician utilization led a number of states to implement regulations requiring prescribers to register for and/or consult the PDMP prior to issuing a controlled substance prescription [19]. The CDC considers mandatory clinician use of a PDMP to be a key policy for ameliorating the prescription opioid epidemic [20]. Typically, PDMPs are intended to flag patients seeking excessive opioid prescriptions, reduce drug diversion, and identify patients in need of addiction treatment. PDMPs also facilitate monitoring clinician behavior [21].Currently, 17 states have formal procedures to identify suspicious prescribing patterns based on PDMP data [22].

Current Empirical Literature

Recent evaluations of the PDMPs' impact on opioid outcomes in the general population have shown reductions across a number of opioid-use metrics. These evaluations have examined a suite of outcomes related to either the implementation of a PDMP alone or the implementation of pain clinic regulations in conjunction with a mandatory PDMP. Following the implementation of these policies, clinicians prescribe fewer Schedule II opioids [23], patients receive lower volumes of opioids [8, 24], and opioid-related overdoses decline [8, 9]. However, some studies specifically focused on Medicare beneficiaries and optional PDMP laws have shown little or no effect of PDMP implementation [10, 18, 25]. These findings suggest that the effect of PDMPs may differ by subpopulation and strength of the law. Although the literature on the effect of PDMPs on opioid outcomes is robust, the literature examining non-opioid controlled substance outcomes is sparse and reports conflicting results [26, 27].

Limited research exists on the possible unintended consequences of PDMPs. Although popular media outlets have suggested that strict opioid policies and guidelines can create barriers to pain treatments [11, 14], these effects have been studied almost exclusively by advocacy organizations [12, 13] using non-scientific methods. One rigorous research study on the topic is Kilby's 2015 working paper, which examines several unintended consequences of PDMPs, including self-reported pain in the hospital setting and missed work. Kilby finds that self-reported pain in the hospital, as measured by Hospital Consumer Assessment of Health Providers and Systems (HCAHPS) survey data, increases following the implementation of a PDMP. Furthermore, workers who have a pain-related diagnosis and are on short-term disability miss more days of work after the implementation of a PDMP when compared with workers prior to the implementation of a PDMP [4]. These findings suggest that PDMPs may have an effect on the population suffering from acute pain. Similarly, if PDMPs result in reduced access to non-opioid controlled substances for legitimate medical users, these users may face increased disability caused by increased anxiety or other conditions. In general, the research on unintended consequences of PDMPs is limited.

Theory and Conceptual Framework

In order to analyze the hypothesized relationship between PDMP presence and disability, I employed Donabedian's approach to measuring quality of care [28]. The structure is the implementation of a PDMP, which is my independent variable of interest. Clinician behaviors related to prescribing controlled substances and other therapies comprise the processes, and the outcome of interest is disability. Figure 1 shows the conceptual framework.

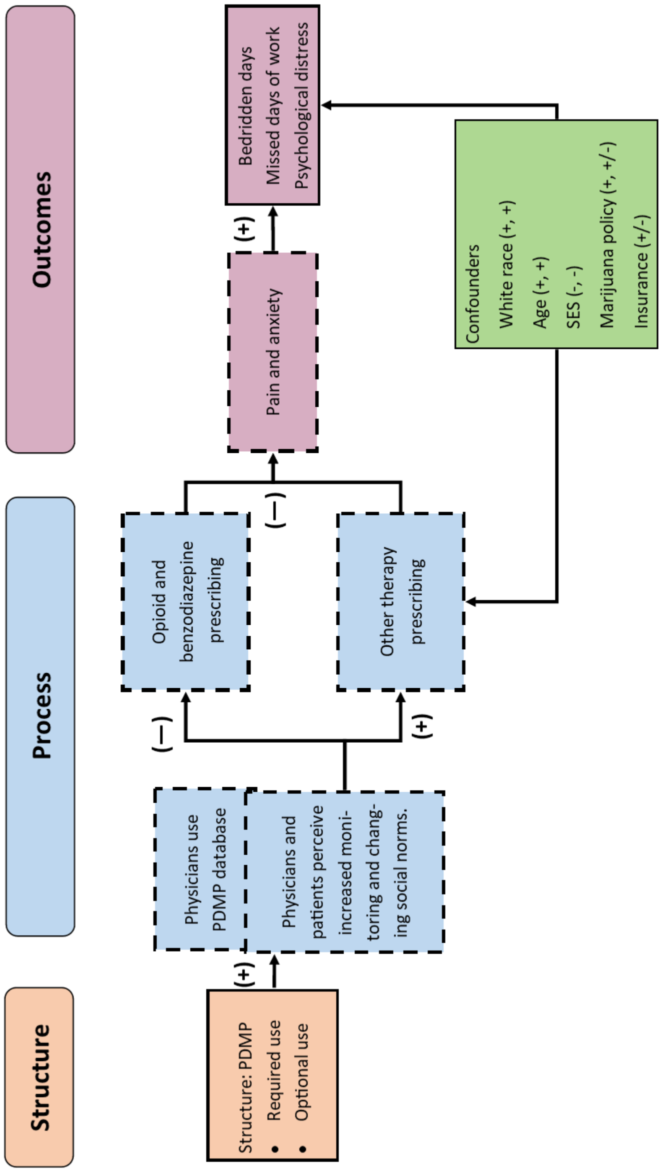

Figure 1: Conceptual Model

Two primary processes serve as the mechanisms through which PDMP implementation may affect patient experience of pain. First, PDMP implementation has been shown to influence opioid prescribing behavior of physicians [8, 23, 24]. The central role of opioid prescribing behavior in this conceptual model aligns with the

PDMP model proposed by Finley et al. [29]. PDMP implementation has been shown to decrease opioid prescribing measured by number of prescriptions and volume[1], particularly among high-prescribing clinicians [24]. This is likely a function of prescribers acquiring new information on their patients from the PDMP, but also may involve other mechanisms, such as increased monitoring of physician prescribing decisions and perceived change in social norms surrounding opioid prescribing. Second, clinicians may change their prescribing patterns of other, non-controlled substance therapy (referred to throughout the remainder of this paper as "other therapy"). For example, clinicians may prescribe non-steroidal anti-inflammatory drugs (NSAIDs) or provide physical therapy referrals. Such a substitution would be in line with the current CDC guidelines on opioid use for chronic pain [30], and probability of having a therapy visit will be measured as a secondary outcome. For patients with anxiety or insomnia, clinicians may provide referrals for cognitive behavioral therapy instead of prescribing benzodiazepines.

Disability is the outcome of interest, following from the processes of controlled substance and other therapy prescribing. According to the World Health Organization (WHO) definitions, disability encompasses "impairments, activity limitations, and participation restrictions" [31]. In the context of this study, "disability" is used to indicate functional impairments of either short or long-term duration. Disability is

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[1] Opioid volume is defined as the total amount of opioids prescribed to a patient over a specified time period, adjusted for quantity and prescription strength.

operationalized with two primary measures that assess broad limitations as a result of health limitations:

1. Missed work days: During the past 12 months…about how many days did you miss work at a job or business because of illness or injury? (do not include maternity leave)
2. Bedridden days: During the past 12 months…about how many days did illness or injury keep you in bed more than half of the day? (Include days while an overnight patient in a hospital)

If controlled substance prescriptions are being restricted for patients who depend on these prescriptions for pain relief, these patients may face an increase in pain-induced disability. Such an increase in pain would represent one pathway through which PDMPs increase disability. Based on Kilby's work regarding opioid restrictions and acute pain [4], I assume that the effect of non-controlled substance therapies would not wholly compensate for the reduction in controlled substance prescribing.

Three additional secondary outcomes were assessed: general psychological functioning, alcohol use, and probability of surgery. General psychological functioning was assessed using the Kessler-6 scale [32]. The Kessler-6 is a validated scale that reliably differentiates individuals with a mental health diagnosis from those without such a diagnosis [32]. Higher scores on the Kessler-6 scale indicate higher levels of psychological distress and are correlated with high intensity, frequent pain [33]. That is, as pain increased, general psychological functioning decreased. However, given the psychoactive properties of opioids and the effects of opioid discontinuation, the direction of the relationship between PDMP laws and general psychological functioning was unclear. Alcohol use was hypothesized to serve as a substitute for opioids, and therefore be positively related to PDMP implementation. Surgery was also hypothesized to be positively related to PDMP implementation, serving as a substitute for ongoing opioid therapy. An increase in spending on surgery has previously been documented for select populations following PDMP implementation [4].

As indicated by the existing literature, this model includes a variety of patient characteristics as potential confounders. First, race is a confounder because research shows pain is undertreated in African American populations as compared with White populations and experience of pain differs by race [7]. Age is another necessary control variable given that reported pain increases with age [7], opioid prescriptions per person increase with age [34], and non-medical opioid use differs across age groups [35]. I controlled for education and home ownership, given that opioid use and reported pain differ by socioeconomic status indicators. Lower education levels are correlated with higher levels of opioid use [36], and lower levels of income and education are associated with higher levels of reported pain across a variety of conditions [7]. Type of disease or injury is intuitively related to pain experience and affects clinicians' treatment decisions. For example, opioid recommendations differ for acute and chronic conditions. Within the chronic pain category, the recommendations differ for cancer, palliative, and end-of-life care versus other forms of chronic pain [30].

Testable Hypothesis

This study explores the potential relationship between prescription drug monitoring program (PDMP) implementation and disability. Specifically, I hypothesized that PDMP implementation is associated with an increase in days of work missed and days spent in bed as a result of illness/injury.

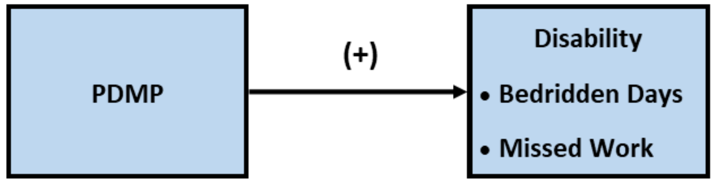


Figure 2: Hypothesis Relationship Diagram

I expected PDMP implementation to be related to disability via the pathway of changing prescriptions in controlled substance medication. Multiple studies have demonstrated a decrease in opioid prescribing following the implementation of a PDMP program [8, 9, 23, 24]. Given that 95 percent of patients who take opioids report “pain control” as their primary reason for using opioids [36], I expected pain to increase as opioid prescriptions decrease. Following from the increase in pain, I anticipate increases in disability measured by bedridden and missed work days.

Chapter 3: Methods

Data Sources and Construct Measurement

I used the National Health Interview Survey (NHIS) data for the time period 2006 – 2015. The NHIS is a cross-sectional survey collected yearly by the CDC [37]. The sample frame for the NHIS is the US civilian noninstitutionalized population and is based on census data [37]. The sample is stratified by geographic clustering to facilitate in-person data collection using computer assisted personal interviewing (CAPI) [37]. Certain racial minorities and age groups are oversampled [37]. The yearly response rate at the household level is approximately 80 percent [38]. The survey includes family-level questions, along with a set of core questions for one sample adult and one sample child per household [38]. Core questions are consistent from year to year, and include a variety of questions about health status, conditions, and medical service use [38]. This data set is well-suited to the study question because the survey questions and methodology were consistent throughout the ten-year period of interest and disability could be measured in terms of functioning. This study was exempt from IRB approval.

Table 1 shows how constructs were mapped to NHIS survey measures.

Table 1: NHIS Construct Mapping

Construct	Role in Model	Measure	Relationship with Dependent Variable
Disability	Dependent Variable	Number of work loss days, past 12 months • Continuous count	N/A
		Number of injury/illness kept you in bed for at least ½ day, past 12 months • Continuous count	N/A
Opioid Prescribing	Mediator	Unmeasured	-

Construct	Role in Model	Measure	Relationship with Dependent Variable
Insurance	Moderator	Covered by Medicaid Covered by Medicare Covered by any private insurance Other coverage Uninsured	+ - - +
Socioeconomic Status	Confounder	*Respondent's Education* – highest level achieved • Less than HS • HS/GED • College graduate • Graduate	Higher education, less disability
		Family Structure One adult with children	+
		Other Owns home	-
Race	Confounder	Race • White • Black • AIAN • Asian • Multiracial or other	+/-
Age	Confounder	Age in years at time of survey	+
Disease Status	Confounder	Health status (Excellent, very good, good, fair, poor)	Better health, less disability
		Ever told you have cancer	+
		Currently pregnant	+/-
		Had a surgical procedure in past 12 months	+
		Unmeasured - Has a condition for which opioids are clinically indicated	+
Rural Location	Confounder	Rural residence	+
General Psychological Functioning	Secondary Outcome	Kessler 6 score [32, 39] calculated from: • How often so sad nothing cheers you up • How often nervous • How often restless/fidgety • How often hopeless • How often felt everything was an effort • How often felt worthless	N/A

Construct	Role in Model	Measure	Relationship with Dependent Variable
Alcohol Use	Secondary Outcome	Average number drinks consumed on days drank • Continuous count	N/A
Therapy Visits	Secondary Outcome	Seen/talked to a therapist (PT/OT/etc.) in past 12 months	N/A
PT – Physical Therapy *OT – Occupational Therapy* *AIAN – American Indian or Alaska Native*			

Non-NHIS data sources were used to identify PDMP policies and state/county-level control variables, as described in Table 2. Following the definition employed by Yarbrough 2017 [10], only PDMPs that allow online access for prescribers and dispensers and require reporting of all prescriptions dispensed by pharmacies were considered operational. These criteria were selected to ensure that the PDMP databases were accessible to prescribers and contained the information prescribers need. Status and implementation dates were determined based on existing literature, the National Alliance for Model State Drug Laws, and personal communication with the Prescription Drug Monitoring Training and Technical Assistance Center [10, 40, 41]. Mandatory PDMPs were defined as those receiving a green or yellow State PDMP Use Requirement rating in the CDC prevention status reports [20]. This means that minimally, prescribers are required to check the PDMP prior to writing the initial opioid prescription and perform a follow-up check within a year [20]. The dates of mandatory implementation in each state were determined based on a review of state web sites, newspaper articles, and prior literature [8]. All policy dates can be found in Appendix A. Additional data sources included per capita income at the state-year level from the US Department of

Commerce Bureau of Economic Analysis [42], county border information from the US Census Bureau [43], and the dates of marijuana law implementation derived from publicly available sources.

Table 2: Non-NHIS Construct Mapping

Construct	Role in Model	Measure	Relationship with Dependent Variable
Mandatory PDMP	Independent Variable	The state had a mandatory, functional PDMP in place during a given quarter	+
Any PDMP	Independent Variable	The state had a functional PDMP in place during a given quarter	+
Economic Climate	Confounder	Average per capita state income on an annual basis	-
Marijuana Availability	Confounder	Whether a state had, during a given quarter, • Legal medical marijuana • Marijuana available in dispensaries	-
Access to Pharmacies in Multiple States	Confounder	Whether the individual lives in a county that borders a different state	-

The dependent variable, disability, was operationalized with two measures: number of work loss days and number of bedridden days. These two outcomes were hypothesized to be associated with PDMP laws via a pathway related to pain. Previous work has explored the relationship between pain questions asked in the 2012 NHIS supplement and certain outcome metrics on the core NHIS questionnaire, and has shown strong correlation between bedridden days and reported pain [33]. Additionally, including missed work days as an outcome builds upon previous work that has shown a relationship between PDMP implementation and missed work days for workers' comp claims [4].

One mediating variable, controlled substance prescribing, was not measured in the NHIS therefore not included in the model. The second hypothesized mediating variable, other therapy, was broadly defined to include both non-pharmacological treatments, such as physical therapy and cognitive behavioral therapy, and pharmacological treatments based on non-controlled substances. One variable in the NHIS can approximate non-pharmacological therapy prescribing: seen/talked to a therapist (PT/OT/etc.) in the past 12 months. This metric was not ideal, given that it included therapies irrelevant to the research question such as audiology and respiratory therapy. However, the therapy variable was examined as a secondary outcome. I hypothesized that the relationship between non-pharmacological pain treatment and disability would be bi-directional, as patients with interfering pain are more likely to seek this form of care than patients without pain, and the therapy should, in turn, reduce the level of disability.

One major group of confounders pertains to disease status, which influences both clinical treatment and disability. Guidelines for pain treatment differ based on whether the pain is acute or chronic [30]. I controlled for surgical procedures within the last 12 months, which would correspond to an acute increase in pain. Similarly, I controlled for general health status, since chronic illness may cause pain that is sometimes treated with opioids [30]. Furthermore, I controlled for cancer diagnosis since the CDC specifically exempts cancer patients from the recommendation to avoid using opioid therapy as a first-line treatment for patients with chronic pain [30]. Given the myriad issues wrapped up with pregnant opioid users [44], I controlled for pregnancy.

As discussed previously, I controlled for a variety of demographic characteristics related to opioid use. Additionally, I controlled for insurance status, which effectively changes the price of prescription opioids that the patient faces. It is important to control for insurance because pattern of opioid use is thought to vary with insurance products. For example, a study in Washington state showed that the age-adjusted opioid overdose death rate among Medicaid members was seven times that of the general population [45]. Furthermore, I included rural residence because the drug overdose rate in rural areas is higher than in metropolitan areas [46].

In addition to the individual-level characteristics, I included several county or state level characteristics that could influence the individual's access to or need for opioid medication. Since PDMP data is generally not shared between states, proximity to a state line means that residents effectively have access to multiple PDMPs. Given that medical marijuana laws have been shown to decrease opioid deaths, I included marijuana laws [47]. Furthermore, since income is related to persistent opioid use, I controlled for state-level per capita income [48].

Sample

The included population was comprised of all sampled adults over the age of 18 in the NHIS between 2006-2015. After removing individuals with incomplete data, the population contained 280,821 adults. The days of missed work model was limited to adults reporting employment within the last year and included 184,132 individuals.

Furthermore, a subpopulation of individuals who reported a recent surgery or injury was identified. Surgery was defined as having reported a surgery in the past year and injury included injuries in the past three months for which the patient sought care. The population derivation is shown below in Figure 3.

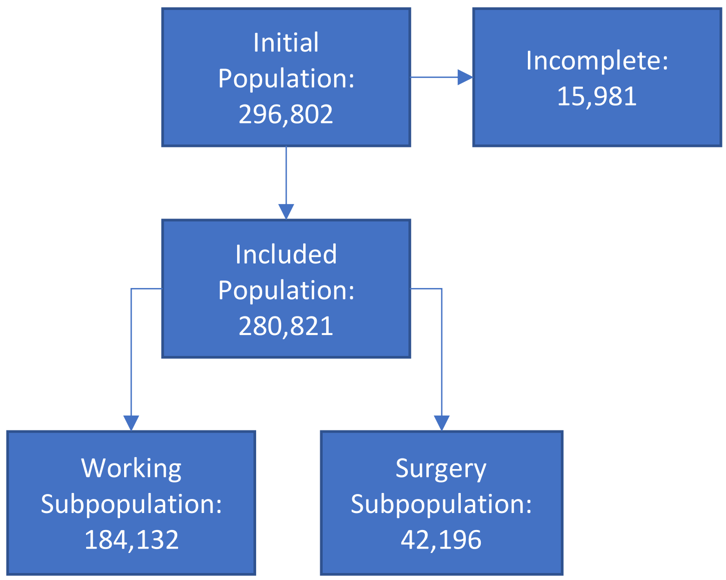


Figure 3: Population Derivation

Data Analysis

Two-way fixed effects were used to control for state and year effects. The state fixed effects controlled for underlying state characteristics, such as baseline opioid abuse levels and attitudes toward medicine, which may affect both the implementation of a PDMP and disability. Optional and mandatory PDMPs were coded as separate binary indicators.

The primary hypothesis was that PDMP implementation would be associated with an increase in disability, measure in missed days of work and bedridden days. Both of these outcome variables were present in the data as integers between 0 and 366 and were modeled as negative binomial variables. The generalized equation is shown below.

Days=f(Optional PDMP, Mandatory PDMP, controls, state fixed effects, year fixed effects)

In this model, optional PDMP indicates that there was a PDMP operating at the time of the interview that was not mandatory. Similarly, mandatory PDMP indicates there was a mandatory PDMP operating at the time of the interview.

Secondary outcomes examined included alcohol use, general psychological functioning, therapy visits, and surgery. Alcohol use (average number drinks consumed on days drank) and general psychological functioning were assessed using negative binomial regression. Logistic regression was used to model the probabilities of having a surgery or a physical/occupational therapy visit.

An important assumption underlies this analysis. As a generalized difference-in-difference model, the treatment and control groups are assumed to have similar trends in the pre-period. This assumption was tested using a series of placebo models for the four years leading up to actual policy implementation.

The alpha level for statistical significance was set as 0.05 prior to conducting the analysis.

Chapter 4: Results

Table 3 provides descriptive characteristics of the included sample by any type of PDMP and non-PDMP. Both groups were approximately 56 percent female with an average age of 48-49 years.

Table 3: Descriptive Characteristics by Policy

Characteristic	No PDMP	Any Type of PDMP
Female	56.08%	55.50%
Age (average [SD])	47.77 (18.08)	48.66 (18.18)
Education		
Less than HS diploma	17.23%	15.83%
GED or HS diploma	26.90%	25.75%
Some college	28.99%	30.91%
Bachelors degree	17.37%	17.66%
Graduate degree	9.51%	9.85%
Family Structure		
One adult, no children	33.02%	32.99%
Multiple adults, no children	34.26%	35.39%
One adult, 1+ child(ren)	6.82%	6.05%
Multiple adults, 1+ child(ren)	25.90%	25.58%
Own home	59.98%	59.88%
Insurance		
Private	60.69%	59.61%
Medicaid	6.92%	7.62%
Medicare	12.12%	13.45%
Other	3.27%	3.47%
Uninsured	17.07%	15.92%
Race		
White only	75.88%	75.80%
Black/African American only	16.58%	14.50%
AIAN only	0.73%	1.16%
Asian only	5.33%	6.59%
Multiple race	1.48%	1.96%
Hispanic	18.03%	16.97%
Alcohol Use		
Lifetime abstainer	22.21%	22.03%
Former infrequent	8.98%	9.21%
Former regular	6.22%	6.65%
Current infrequent	12.87%	13.27%

Characteristic	No PDMP	Any Type of PDMP
Current light	29.53%	29.12%
Current moderate	14.66%	14.35%
Current heavy	5.53%	5.37%
Ever diagnosed with arthritis	23.81%	24.77%
Surgery/surgical procedure, past 12 m	12.78%	12.58%
Health Status		
Excellent	26.68%	26.15%
Very good	31.26%	31.42%
Good	27.34%	27.47%
Fair	11.22%	11.34%
Poor	3.50%	3.61%
Ever told by a doctor you had cancer	8.34%	9.03%
Currently pregnant	1.08%	1.00%
Resides in border county	38.05%	35.88%
Urban/Rural Residence	81.99%	79.70%
Joint symptoms, past 30 days	32.20%	34.43%
Neck pain, past 3 months	15.15%	15.97%
Lower back pain, past 3 months	28.57%	29.95%
Moderate exercise		
1-2 times per week	15.43%	16.04%
3-4 times per week	13.73%	13.81%
5 times per week	23.61%	25.69%
Less than weekly	1.94%	1.93%
Never	45.29%	42.52%
Vigorous exercise		
1-2 times per week	11.76%	12.68%
3-4 times per week	13.32%	14.06%
5 times per week	11.94%	13.46%
Less than weekly	2.64%	2.71%
Never	60.34%	57.09%
SD – standard deviation, AIAN – American Indian or Alaska Native		

Table 4 shows the distribution of outcomes in the overall and surgery/injury population. In the general population, missed days of work averaged 3.9 and bedridden days averaged 5.0. In contrast, the surgery/injury subpopulation had an average of 13.4

missed work days and 12.2 and bedridden days. In both populations there was wide variation in both missed work days and bedridden days.

Table 4: Outcomes By Population

Measure	General Population Mean (SD)	Surgery/Injury Subpopulation Mean(SD)
Missed Work Days	3.93 (17.37)	13.38 (34.39)
Bedridden Days	4.95 (26.21)	12.17 (38.61)
Kessler 6 Score	2.55 (3.97)	3.4 (4.6)
Number Drinks	2.45 (2.45)	2.29 (2.33)
Therapy visit in last year (%)	9.35%	24.32%

The marginal effects for the primary outcomes of interest are shown in Table 5. Optional PDMPs were significantly associated with an increase in bedridden days for both the general and surgery/injury populations, with marginal effects of 0.3 and 1.6 respectively. Furthermore, mandatory PDMPs were associated with 2.4 additional bedridden days on average in the surgery/injury subpopulation. Effects for missed work days in the full working population were positive, but insignificant. For the surgery/injury employed subpopulation, mandatory PDMPs were associated with an average increase of 3.5 missed work days. Full regression results are provided in Appendix B.

Table 5: Marginal Effects for Bed and Missed Work Days

PDMP Type	Bedridden days		Missed Work Days	
	Complete Population	Surgery/ Injury Population	Employed Population	Surgery/Injury Population
Optional PDMP	0.319^{**} (0.148)	1.572^{***} (0.583)	0.156 (0.0953)	1.122 (0.736)
Mandatory PDMP	0.549 (0.470)	2.353^{**} (0.973)	0.301 (0.251)	3.540^{***} (1.365)
Standard errors in parenthesis are clustered at the state level *p≤ *** 1%, ** 5%, * 10%*				

Effects for the secondary outcomes of therapy visits, general psychological distress, surgery, and alcohol use were generally insignificant. General psychological distress in the surgery/injury subpopulation under a mandatory PDMP decreased by 0.308 points on the Kessler-6 scale; the effect was only significant at the alpha < 0.10 level, but in sensitivity analyses, the effect was significant at the alpha < 0.01 level. Table 6 presents the marginal effects for therapy and general psychological distress.

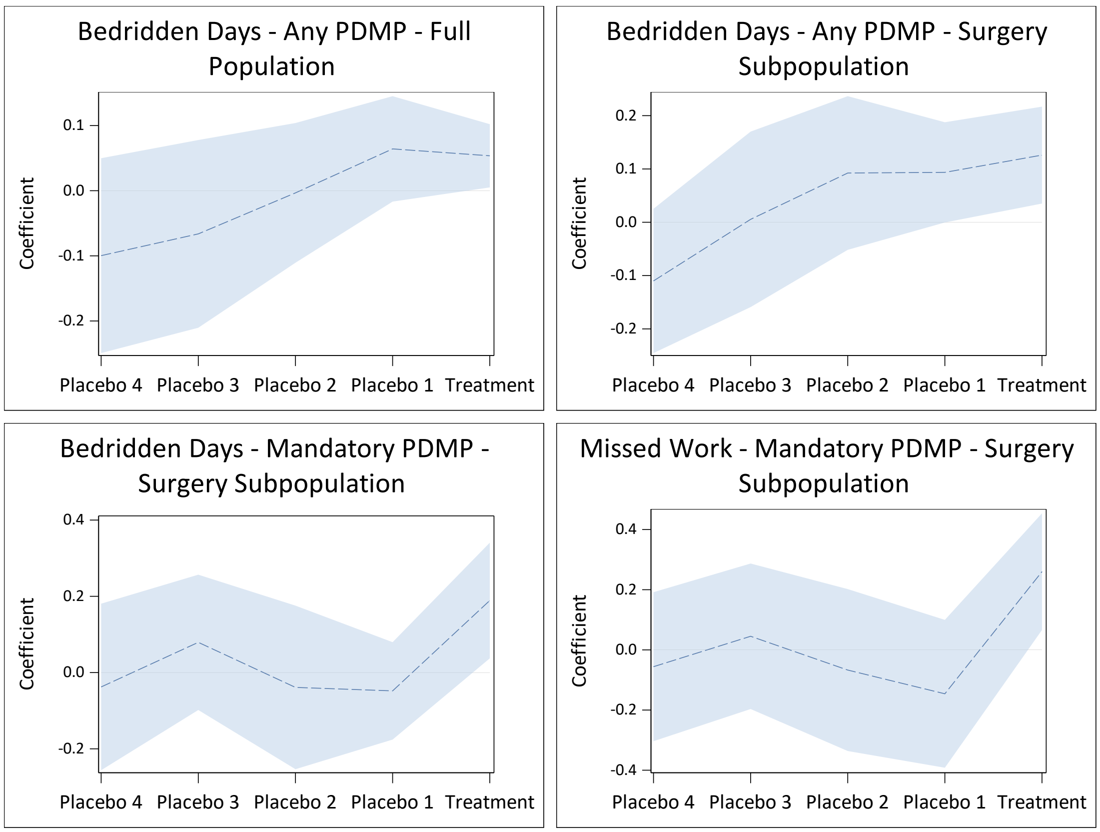
Table 6: Marginal Effects for Select Secondary Outcomes

PDMP Type	Therapy		Kessler-6	
	Full Population	Surgery/ Injury Population	Full Working Population	Surgery/ Injury Population
Optional PDMP	0.00240 (0.00231)	0.0105 (0.00813)	0.0474 (0.91)	0.0406 (0.53)
Mandatory PDMP	0.00126 (0.00450)	0.00979 (0.0168)	-0.0819 (-1.01)	-0.308* (-1.96)
Standard errors in parenthesis are clustered at the state level *p≤ *** 1%, ** 5%, * 10%*				

Sensitivity Analyses

In order to exclude the possibility of policy endogeneity as a result of reverse causation where states with differing patterns of opioid related missed work and bedridden days, I used a series of models employing an indicator for one, two, three, and four years prior to policy implementation as placebo tests. If the states implemented PDMPs in response to pre-existing trends related to opioids and disability in the state, these placebo tests would indicate changes in outcomes in the years leading up PDMP deployment even though a policy had yet to be implemented. In the surgical population under the mandatory PDMP, the placebo policy tests were insignificant, showing no evidence of trends diverging from non-policy states prior to policy implementation. For the optional PDMPs, the placebo models showed weak evidence of non-parallel trends for bedridden days.

Figure 4 presents the placebo test analysis for the outcomes in Table 5 that were statistically significant.



Note: 95% Confidence Intervals shown in light blue

Figure 4: Placebo Tests for Select Models

The NHIS is administered using a complex sampling methodology that employs geographical clustering and oversampling [38]. Incorporating survey weights into the regression estimation process precludes clustering the standard errors at the state level. Because this study did not seek to create population-level prevalence estimates and policies varied at the state level, the primary analysis employed clustered standard errors at the state level. As a sensitivity analysis, the regressions for the primary outcomes were run with the survey weights. Minor differences in the estimates between the two methods were observed, but the overall results are qualitatively similar. For the bedridden days outcome, the most substantial change associated with using survey weights was that the effect of a mandatory PDMP in the surgery/injury subpopulation is not statistically distinguishable from zero. Conversely, for the missed days of work outcome, the marginal effects increased by approximately a day in the surgery/injury population. Finally, the marginal effect for generalized psychological distress increased in magnitude to -0.56.

Chapter 5: Discussion

Summary

This study analyzed the impact of both optional and mandatory PDMPs on two primary outcomes, bedridden days and missed days of work. PDMPs were associated with a significant increase in bedridden days and missed work days, with the most notable effects occurring in the subpopulation of people who had either a surgery or an injury. Furthermore, a dose-response effect was observed with the optional PDMPs being associated with a smaller effect than the mandatory PDMPs in the surgery/injury subpopulation. An average increase of 2.4 bedridden days was associated with mandatory PDMP policies in the surgery/injury population. Mandatory PDMPs were also associated with significant increases in missed days of work in the surgery/injury subpopulation. Although optional PDMPs were associated with an increase in bedridden days in both the general and surgery/injury populations, placebo models indicated possible endogeneity. Further research is necessary to understand the relationship between bedridden days and optional PDMPs.

One positive affect associated with PDMP implementation was the decrease in psychological distress among the surgery/injury population as measured by the Kessler-6 scale. A decrease of 1 point on the Kessler-6 scale is the equivalent of a change in one of the questions (e.g., during the past 30 days, how often did you feel so sad nothing could cheer you up?) from the answer “some of the time” to “none of the time.” Thus, the marginal effect of -0.301 indicates approximately a one-point decrease for a third of the population.

Conclusions

In addition to the human suffering costs of pain, there are economic costs associated with diminished functional capacity. On a societal level, bed and missed work days are productivity losses. Twenty-eight percent of workers in private industry lacked paid sick leave in 2017 [49]. Loss of income as a result of longer post-surgical recovery time effectively adds to the medical cost of surgery.

These results align with unpublished research [4] and claims made by the popular media and advocacy groups [11-14]. However, from a clinical perspective on the efficacy of opioids, these results are somewhat surprising. Randomized controlled trials have shown no significant difference between opioid and non-opioid pain management protocols in terms of patient pain scores for common chronic pain conditions and some types of surgery [50, 51]. The observed increases in bedridden and missed work days suggest a possible gap between non-opioid pain management protocols used in formal clinical trials and actual clinical practice. Similarly, guidelines recommending alternative treatments to opioids may only be partially implemented. For example, the CDC opioid guidelines recommend the use of physical therapy to address ongoing pain [30]. Despite this recommendation, PDMPs were not associated with a change in the probability of receiving at least one physical/occupational therapy visit. The lack of change in therapy may be indicative of a reduction in opioid use unaccompanied by other treatment changes, and future research should explore the practices being substituted for opioid prescriptions. Furthermore, research on the diversity of patient responses to pain treatments may provide additional insight that reconciles the clinical findings on average opioid responses and these findings that provide evidence of increasing disability following PDMPs.

Strengths and Limitations

This study has several limitations. First, the hypothesized causal pathway centers on changes in prescribing practice and pain. Neither of these constructs were possible to operationalize with the NHIS data. Casual pathways other than pain (e.g., increased withdrawal symptoms following a sharp reduction in prescription opioid availability) are possible. Although prior work has shown reduced opioid prescribing as a result of PDMPs, little is known about corresponding practice changes that may accompany reduced opioid prescribing. Future research on these clinical changes under PDMPs will be necessary to identify potential areas for clinical quality improvement.

Second, a number of states implemented pain clinic laws at approximately the same time as mandatory PDMP requirements. In the current study, it was not possible to distinguish between the effects of mandatory PDMPs alone versus mandatory PDMPs implemented in conjunction with pain clinic laws. In the surgery/injury subpopulation, the effects of the pain clinic regulations are likely to be muted since pain medication is traditionally prescribed by the surgeon. However, pain clinic regulations may have contributed to the observed effects.

Due to data constraints, it was not possible to create a general indicator for chronically ill patients. Much of the concern around unintended consequences from PDMPs centers around this subpopulation [12, 13]. Future research that distinguishes between effects on the general population and the chronically ill population is necessary for a more nuanced understanding of PDMP consequences.

This study's strengths included using a quasi-experimental design to establish an effect of the implementation of PDMP laws on two measures of disability, bedridden days and missed work days. The measurement period of 2006 – 2015 was a time period of intense PDMP implementation activity during which 44 states implemented a functioning optional or mandatory PDMP. The conclusions of this study are strengthened by analyses demonstrating 1) a dose-response effect with optional/mandatory laws and 2) increases in bedridden and missed work days under mandatory PDMPs did not precede law implementation. To date, published literature on PDMPs has focused exclusively on opioid-specific outcomes. Furthermore, the literature on PDMPs has generally used shorter time spans and drawn conclusions about mandatory PDMPs based on the first few mandatory PDMPs implemented. This study presents a more complete picture of PDMPs by examining downstream effects related to the prescribing changes spurred by the laws.

Implications

These findings show that PDMPs appear to have some negative consequences, particularly for surgical patients. From a policy perspective, states that have regulations that require prescribers to review the PDMP prior to any controlled substance prescription may want to create limited exceptions for surgeons writing short-term (e.g., 3-day) opioid prescriptions. From a clinical perspective, providers implementing practice changes related to opioids can implement proactive follow-up with patients to ensure that pain is appropriately managed. For example, Luk et al. 2016 documents success with employing a nurse follow-up call after implementation of a protocol to avoid prescribing opioids to young patients undergoing tonsillectomy [52]. Misuse and overuse of prescription opioids led to serious harm in the United States, and policy has begun to address this issue. However, certain people may incur unnecessary harm as a result of these policies, and efforts should be made to adjust policy and clinical practice in a manner that continues to decrease opioid overdoses while also limiting pain-induced disability.

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Appendix A: Policy Dates

Table A-1 presents the policy dates used in the models. Policy dates that occurred after the end of the measurement period are omitted.

Table A-1: Policy Dates

State	Optional PDMP	Mandatory PDMP	Medical Marijuana Legal	Marijuana Dispensary Available	Medicaid Expansion
AL	01-Aug-07				
AK	01-Jan-12		01-Mar-99		01-Sep-15
AZ	01-Dec-08		01-Nov-10	01-Dec-12	01-Jan-14
AR	01-Mar-13		01-Nov-16		01-Jan-14
CA	02-Jul-09		01-Nov-96	01-Jan-06	01-Jan-14
CO	04-Feb-08		01-Jun-01	01-Jul-05	01-Jan-14
CT	01-Nov-08	01-Oct-15	01-May-12	01-Aug-14	01-Jan-14
DE	12-Aug-12		01-Jul-11	01-Jun-15	01-Jan-14
DC					01-Jan-14
FL	14-Oct-11				
GA	01-Jul-13				
HI	01-Jan-08		01-Dec-00		01-Jan-14
ID	01-Jan-08				
IL	01-Jan-08		01-Jan-14	01-Oct-15	01-Jan-14
IN	01-Jan-07				01-Feb-15
IA	19-Mar-09				01-Jan-14
KS	01-Apr-11				
KY	01-Mar-05	20-Jul-12			01-Jan-14
LA	01-Jan-09				01-Jul-16
ME	01-Jan-05		01-Dec-99	01-Mar-11	
MD	01-Jan-14		01-Jun-14		01-Jan-14
MA	01-Dec-10		01-Jan-13	01-Jun-15	01-Jan-14
MI	01-Apr-07		01-Dec-08		01-Apr-14
MN	15-Apr-10		01-May-14	01-Jul-15	01-Jan-14
MS	01-Jan-08				
MO					
MT	15-Oct-12		01-Nov-04		01-Jan-16
NE					
NV	01-Jan-07		01-Oct-01	01-Mar-15	01-Jan-14
NH	16-Oct-14		01-Jul-13		15-Aug-14
NJ	01-Jan-12	01-Sep-15	01-Jun-10	01-Dec-12	01-Jan-14
NM	01-Jan-12		01-Jul-07	01-Mar-09	01-Jan-14

State	Optional PDMP	Mandatory PDMP	Medical Marijuana Legal	Marijuana Dispensary Available	Medicaid Expansion
NY	01-Feb-10	27-Aug-13	01-Jul-14		01-Jan-14
NC	01-Oct-07				
ND	01-Feb-08		01-Nov-16		01-Jan-14
OH	02-Oct-06	01-Oct-11	01-Sep-16		01-Jan-14
OK	01-May-06	15-Nov-15			
OR	01-Sep-11		01-Dec-98	01-Mar-14	01-Jan-14
PA	30-Jun-15		01-May-16	01-Dec-16	01-Jan-15
RI	01-Jul-12	01-Mar-15	01-Jan-06	01-Apr-13	01-Jan-14
SC	01-Jun-08				
SD	01-Mar-12				
TN	01-Jan-07	01-Apr-13			
TX	01-Aug-12				
UT	01-Jan-05				
VT	01-Apr-09		01-Jul-04	01-Jun-13	01-Jan-14
VA	01-Jun-06				
WA	04-Jan-12		01-Dec-98	01-Dec-98	01-Jan-14
WV	01-Jan-05				01-Jan-14
WI	01-May-13				
WY	01-Jul-13				

Appendix B: Regression Output

Table B1: Regression Coefficients Bedridden Days and Missed Work Days Models

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
Optional PDMP – Post Implementation	0.0536**	0.126***	0.0373	0.0825
	(0.0249)	(0.0466)	(0.0227)	(0.0540)
Mandatory PDMP - Post Implementation	0.0923	0.189**	0.0717	0.260***
	(0.0792)	(0.0778)	(0.0601)	(0.0994)
Private insurance	0	0	0	0
	(.)	(.)	(.)	(.)
Medicare	0.474***	0.267***	-0.196**	-0.425***
	(0.0425)	(0.0458)	(0.0867)	(0.114)
Medicaid	0.494***	0.260***	-0.00410	-0.108
	(0.0544)	(0.0415)	(0.0500)	(0.0663)
Other insurance	0.223***	0.100*	-0.0830*	-0.0936
	(0.0506)	(0.0545)	(0.0489)	(0.0889)
Uninsured	0.0523	0.216***	-0.118***	0.0553
	(0.0376)	(0.0549)	(0.0400)	(0.0398)
Age (years)	-0.0119***	-0.0125***	-0.00830***	0.00206
	(0.000966)	(0.00144)	(0.000792)	(0.00158)
Female	0.292***	0.121***	0.0921***	-0.123***
	(0.0214)	(0.0257)	(0.0219)	(0.0343)

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
Surgery/surgical procedure, past 12 m	1.177***	0.655***	1.613***	0.809***
	(0.0210)	(0.0360)	(0.0247)	(0.0357)
Ever told by a doctor you had cancer	0.182***	0.169***	0.189***	0.183***
	(0.0372)	(0.0373)	(0.0359)	(0.0413)
Own home	-0.0839***	0.0103	-0.0290	-0.0142
	(0.0203)	(0.0300)	(0.0191)	(0.0411)
Family: Multiple adults, no children	-0.0208	0.0153	-0.148***	-0.0733**
	(0.0280)	(0.0330)	(0.0224)	(0.0347)
Family: One adult, 1+ child(ren)	-0.126***	-0.0915**	0.000884	-0.00218
	(0.0301)	(0.0414)	(0.0367)	(0.0553)
Family: Multiple adults, 1+ child(ren)	-0.135***	-0.0776**	-0.114***	-0.149***
	(0.0294)	(0.0390)	(0.0245)	(0.0430)
White only	0	0	0	0
	(.)	(.)	(.)	(.)
Black/African American only	-0.0715***	0.100*	0.0781***	0.235***
	(0.0263)	(0.0528)	(0.0296)	(0.0459)
AIAN only	0.0747	0.0963	0.106*	0.213
	(0.0808)	(0.114)	(0.0565)	(0.159)
Asian only	-0.306***	-0.176***	-0.255***	-0.0556
	(0.0456)	(0.0626)	(0.0387)	(0.0908)
Multiple race	0.165***	0.247***	0.131*	0.208*

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
	(0.0561)	(0.0781)	(0.0720)	(0.119)
Education: GED or HS diploma	0.0805**	0.0482	0.0648	0.0160
	(0.0393)	(0.0566)	(0.0414)	(0.0521)
Education: Some college	0.174***	0.109*	0.0805*	-0.0956
	(0.0268)	(0.0579)	(0.0469)	(0.0606)
Education: Bachelors degree	0.120***	0.0656	-0.00413	-0.274***
	(0.0407)	(0.0597)	(0.0428)	(0.0643)
Education: Graduate degree	0.150***	0.0331	-0.00373	-0.407***
	(0.0449)	(0.0664)	(0.0565)	(0.0812)
Hispanic	-0.359***	-0.109**	-0.146***	0.191***
	(0.0311)	(0.0430)	(0.0286)	(0.0559)
Currently pregnant	0.205***	-0.321**	0.187***	-0.294*
	(0.0746)	(0.160)	(0.0476)	(0.173)
Joint symptoms, past 30 days	0.352***	0.261***	0.307***	0.283***
	(0.0252)	(0.0269)	(0.0315)	(0.0335)
Ever diagnosed with arthritis	0.165***	0.171***	0.271***	0.162***
	(0.0238)	(0.0352)	(0.0305)	(0.0391)
Lower back pain, past 3 months	0.460***	0.292***	0.380***	0.188***
	(0.0204)	(0.0390)	(0.0270)	(0.0404)
Neck pain, past 3 months	0.499***	0.274***	0.360***	0.149***
	(0.0284)	(0.0284)	(0.0252)	(0.0385)

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
Health: Excellent	0	0	0	0
	(.)	(.)	(.)	(.)
Health: Very good	0.226***	0.326***	0.241***	0.282***
	(0.0179)	(0.0455)	(0.0229)	(0.0408)
Health: Good	0.762***	0.763***	0.581***	0.573***
	(0.0228)	(0.0571)	(0.0257)	(0.0482)
Health: Fair	1.715***	1.482***	1.222***	0.964***
	(0.0533)	(0.0803)	(0.0639)	(0.0848)
Health: Poor	2.848***	2.250***	1.818***	1.331***
	(0.0420)	(0.0724)	(0.0923)	(0.144)
Vigorous exercise: Never	0.242***	0.290***	0.167***	0.189***
	(0.0326)	(0.0435)	(0.0314)	(0.0389)
Vigorous exercise: Less than weekly	0.106*	-0.00731	0.0568	-0.150*
	(0.0543)	(0.135)	(0.0468)	(0.0846)
Vigorous exercise: 1-2 times per week	0.0622	-0.0214	0.0403	-0.0970
	(0.0393)	(0.0581)	(0.0285)	(0.0611)
Vigorous exercise: 3-4 times per week	0.0634**	0.0480	0.00693	-0.0323
	(0.0314)	(0.0522)	(0.0263)	(0.0501)
Vigorous exercise: 5 times per week	0	0	0	0
	(.)	(.)	(.)	(.)
Moderate exercise: Never	0.162***	0.209***	-0.00816	-0.0260
	(0.0255)	(0.0351)	(0.0223)	(0.0359)

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
Moderate exercise: Less than weekly	-0.0600	-0.322***	-0.0147	-0.194
	(0.0583)	(0.0986)	(0.0495)	(0.118)
Moderate exercise: 1-2 times per week	-0.0320	-0.119***	-0.00567	-0.112**
	(0.0257)	(0.0382)	(0.0288)	(0.0445)
Moderate exercise: 3-4 times per week	-0.0471**	-0.0917**	-0.0206	-0.0647**
	(0.0193)	(0.0443)	(0.0277)	(0.0328)
Moderate exercise: 5 times per week	0	0	0	0
	(.)	(.)	(.)	(.)
Rural residence	-0.0840***	-0.0180	-0.0883***	0.0445
	(0.0260)	(0.0361)	(0.0236)	(0.0394)
Resides in border county	-0.0361*	-0.0213	-0.0223	0.0256
	(0.0214)	(0.0336)	(0.0268)	(0.0354)
Per capita income	-0.00000880	-0.00000431	0.0000110	0.0000246*
	(0.0000105)	(0.0000126)	(0.0000117)	(0.0000144)
Marijuana dispensary available	0.119	-0.00570	0.0292	-0.160
	(0.0962)	(0.0989)	(0.0370)	(0.158)
Marijuana legally available	-0.0943	0.0277	-0.0552	0.0356
	(0.0820)	(0.0728)	(0.0394)	(0.0781)
Processing year=2006	0	0	0	0
	(.)	(.)	(.)	(.)

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
Processing year=2007	0.0463	-0.0177	0.0463	-0.0858
	(0.0544)	(0.0894)	(0.0479)	(0.0891)
Processing year=2008	0.0722	-0.0923	0.0196	-0.222***
	(0.0673)	(0.0772)	(0.0460)	(0.0749)
Processing year=2009	0.0978*	-0.0565	-0.0673	-0.225***
	(0.0587)	(0.0560)	(0.0420)	(0.0781)
Processing year=2010	0.0339	-0.111	-0.111**	-0.207***
	(0.0686)	(0.0826)	(0.0489)	(0.0782)
Processing year=2011	0.0309	-0.119	-0.161**	-0.215**
	(0.0694)	(0.0795)	(0.0640)	(0.0855)
Processing year=2012	-0.0170	-0.208*	-0.0935	-0.320***
	(0.0954)	(0.107)	(0.0791)	(0.0948)
Processing year=2013	0.0785	-0.157	-0.135*	-0.275***
	(0.0963)	(0.111)	(0.0723)	(0.102)
Processing year=2014	0.0340	-0.256*	-0.138	-0.405***
	(0.119)	(0.134)	(0.0970)	(0.128)
Processing year=2015	0.0947	-0.111	-0.196*	-0.476***
	(0.133)	(0.163)	(0.108)	(0.148)
Constant	0.650	1.023	0.155	-0.0554
	(0.610)	(0.715)	(0.714)	(0.841)
/ lnalpha	1.734***	1.384***	1.473***	1.298***

	Bedridden Days - Complete Population	Bedridden Days - Surgery/Injury Subpopulation	Missed Work Days – Complete Population	Missed Work Days – Surgery/Injury Subpopulation
	(0.0223)	(0.0157)	(0.0291)	(0.0196)
Observations	278717	41690	183422	23740

*** 1% ** 5% * 10%

Note: Coefficients for state fixed effects omitted per agreement with the Centers for Disease Control

AIAN – American Indian or Alaska Native

Table B2: Regression Coefficients for Therapy and Surgery Models

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
Optional PDMP – Post Implementation	0.0321	0.0620	0.0122
	(0.0310)	(0.0483)	(0.0264)
Mandatory PDMP - Post Implementation	0.0169	0.0581	0.0246
	(0.0603)	(0.0995)	(0.0472)
Private insurance	0	0	0
	(.)	(.)	(.)
Medicare	0.0229	-0.0927**	0.0377
	(0.0221)	(0.0368)	(0.0242)
Medicaid	0.0159	-0.232***	0.155***
	(0.0362)	(0.0514)	(0.0352)
Other insurance	0.242***	-0.0667	-0.00156
	(0.0372)	(0.0637)	(0.0354)
Uninsured	-0.684***	-0.448***	-0.720***
	(0.0313)	(0.0526)	(0.0252)
Age (years)	0.00795***	0.00547***	0.00220***
	(0.000779)	(0.00111)	(0.000570)
Female	0.0347**	-0.0515**	0.175***
	(0.0137)	(0.0231)	(0.0152)
Surgery/surgical procedure, past 12 m	1.140***	0.293***	
	(0.0224)	(0.0369)	
Ever told by a doctor you had cancer	0.0565***	-0.0863***	0.772***

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
	(0.0194)	(0.0299)	(0.0215)
Own home	-0.00593	0.0284	0.0464**
	(0.0205)	(0.0344)	(0.0192)
Family: Multiple adults, no children	-0.0120	-0.00987	0.101***
	(0.0180)	(0.0280)	(0.0150)
Family: One adult, 1+ child(ren)	-0.254***	-0.233***	0.178***
	(0.0351)	(0.0505)	(0.0282)
Family: Multiple adults, 1+ child(ren)	-0.201***	-0.220***	0.119***
	(0.0270)	(0.0379)	(0.0176)
White only	0	0	0
	(.)	(.)	(.)
Black/African American only	-0.00405	-0.0175	-0.229***
	(0.0401)	(0.0493)	(0.0195)
AIAN only	0.0546	0.0114	-0.00264
	(0.0745)	(0.136)	(0.0696)
Asian only	-0.288***	0.0187	-0.544***
	(0.0397)	(0.0610)	(0.0341)
Multiple race	0.0176	0.0142	0.00245
	(0.0781)	(0.0867)	(0.0524)
Education: GED or HS diploma	0.224***	0.280***	0.127***
	(0.0307)	(0.0374)	(0.0204)
Education: Some college	0.439***	0.417***	0.265***
	(0.0292)	(0.0441)	(0.0206)

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
Education: Bachelors degree	0.563***	0.515***	0.254***
	(0.0356)	(0.0493)	(0.0217)
Education: Graduate degree	0.720***	0.622***	0.394***
	(0.0376)	(0.0543)	(0.0277)
Hispanic	-0.172***	-0.150***	-0.188***
	(0.0290)	(0.0419)	(0.0242)
Currently pregnant	-0.203**	-0.287	-0.267***
	(0.0887)	(0.233)	(0.0704)
Joint symptoms, past 30 days	0.486***	0.502***	0.218***
	(0.0191)	(0.0242)	(0.0123)
Ever diagnosed with arthritis	0.465***	0.448***	0.318***
	(0.0215)	(0.0325)	(0.0181)
Lower back pain, past 3 months	0.410***	0.204***	0.188***
	(0.0188)	(0.0313)	(0.0126)
Neck pain, past 3 months	0.350***	0.177***	0.0609***
	(0.0226)	(0.0367)	(0.0155)
Health: Excellent	0	0	0
	(.)	(.)	(.)
Health: Very good	0.164***	0.111***	0.155***
	(0.0240)	(0.0380)	(0.0206)
Health: Good	0.332***	0.233***	0.336***
	(0.0300)	(0.0440)	(0.0270)
Health: Fair	0.602***	0.452***	0.536***

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
	(0.0275)	(0.0366)	(0.0267)
Health: Poor	0.949***	0.695***	0.775***
	(0.0424)	(0.0610)	(0.0317)
Vigorous exercise: Never	-0.0980***	-0.0180	-0.000250
	(0.0236)	(0.0399)	(0.0198)
Vigorous exercise: Less than weekly	-0.184***	-0.181**	-0.0626
	(0.0585)	(0.0824)	(0.0422)
Vigorous exercise: 1-2 times per week	-0.123***	-0.178***	-0.115***
	(0.0337)	(0.0554)	(0.0246)
Vigorous exercise: 3-4 times per week	-0.0112	-0.0290	0.00883
	(0.0362)	(0.0490)	(0.0281)
Vigorous exercise: 5 times per week	0	0	0
	(.)	(.)	(.)
Moderate exercise: Never	-0.113***	-0.0685**	-0.113***
	(0.0243)	(0.0293)	(0.0172)
Moderate exercise: Less than weekly	-0.296***	-0.399***	-0.136***
	(0.0600)	(0.0974)	(0.0356)
Moderate exercise: 1-2 times per week	-0.0663**	-0.0865*	-0.0705***
	(0.0294)	(0.0457)	(0.0185)
Moderate exercise: 3-4 times per week	0.00988	-0.0290	-0.0688***
	(0.0255)	(0.0368)	(0.0192)

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
Moderate exercise: 5 times per week	0	0	0
	(.)	(.)	(.)
Rural residence	-0.153***	-0.119***	0.0151
	(0.0238)	(0.0342)	(0.0196)
Resides in border county	-0.0714***	-0.0436	-0.0369*
	(0.0231)	(0.0314)	(0.0199)
Per capita income	-0.00000558	0.000000136	-0.000000390
	(0.00000729)	(0.00000917)	(0.00000884)
Marijuana dispensary available	-0.0804	-0.0976	0.0488
	(0.0525)	(0.0890)	(0.0594)
Marijuana legally available	0.118***	0.130***	-0.0226
	(0.0283)	(0.0432)	(0.0475)
Processing year=2006	0	0	0
	(.)	(.)	(.)
Processing year=2007	0.0170	-0.00463	0.0241
	(0.0372)	(0.0609)	(0.0306)
Processing year=2008	0.00552	-0.0271	-0.0141
	(0.0435)	(0.0798)	(0.0436)
Processing year=2009	-0.000498	0.0195	-0.0269
	(0.0396)	(0.0631)	(0.0351)

	Therapy – Complete Population	Therapy, Surgery/Injury Subpopulation	Surgery – Complete Population
Processing year=2010	0.00273	-0.0782	0.0202
	(0.0394)	(0.0802)	(0.0375)
Processing year=2011	0.0123	-0.0272	-0.0441
	(0.0474)	(0.0749)	(0.0523)
Processing year=2012	-0.0295	-0.0729	-0.0617
	(0.0589)	(0.0889)	(0.0692)
Processing year=2013	0.0304	0.0107	-0.124*
	(0.0595)	(0.0954)	(0.0702)
Processing year=2014	0.112	0.0356	-0.147
	(0.0687)	(0.106)	(0.0897)
Processing year=2015	0.0890	-0.0166	-0.173*
	(0.0754)	(0.109)	(0.102)
Constant	-3.208***	-2.263***	-2.761***
	(0.435)	(0.551)	(0.501)
Observations	280464	42116	280464

*** 1% ** 5% * 10%

Note: Coefficients for state fixed effects omitted per agreement with the Centers for Disease Control
AIAN – American Indian or Alaska Native

Table B3: Regression Coefficients for Therapy and Surgery Models

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Optional PDMP – Post Implementation	-0.00815	-0.00808	0.0181	0.0117
	(0.0111)	(0.0203)	(0.91)	(0.53)
Mandatory PDMP - Post Implementation	0.0124	-0.00886	-0.0314	-0.0892*
	(0.0185)	(0.0418)	(-1.01)	(-1.96)
Suspected incorrect value[1]	3.476***	3.400***		
	(0.0516)	(0.127)		
Private Insurance	0	0	0	0
	(.)	(.)	(.)	(.)
Medicare	0.0137*	0.0523**	0.156***	0.133***
	(0.00797)	(0.0238)	(13.56)	(5.99)
Medicaid	0.0500***	0.0699***	0.260***	0.211***
	(0.0113)	(0.0204)	(12.88)	(10.22)
Other insurance	0.0250***	0.0350	0.167***	0.192***
	(0.00894)	(0.0214)	(9.98)	(6.65)
Uninsured	0.0862***	0.119***	0.224***	0.251***
	(0.00620)	(0.0194)	(16.59)	(11.30)
Age (years)	-0.0129***	-0.0144***	-0.0151***	-0.0160***
	(0.000351)	(0.000492)	(-55.52)	(-27.47)
Female	-0.337***	-0.358***	0.194***	0.153***
	(0.00749)	(0.0118)	(25.61)	(9.92)
Surgery/surgical procedure, past 12 m	-0.0153***	-0.0359**	0.0981***	-0.0719***
	(0.00521)	(0.0141)	(12.23)	(-5.19)

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Ever told by a doctor you had cancer	-0.0138**	-0.00256	0.0467***	0.0188
	(0.00645)	(0.0156)	(4.50)	(0.92)
Own home	-0.0400***	-0.0415***	-0.112***	-0.108***
	(0.00549)	(0.0127)	(-13.25)	(-6.97)
Family: Multiple adults, no children	-0.102***	-0.0991***	-0.133***	-0.100***
	(0.00744)	(0.0116)	(-15.35)	(-5.99)
Family: One adult, 1+ child(ren)	-0.0749***	-0.0632***	-0.0200	-0.0390
	(0.00768)	(0.0208)	(-1.40)	(-1.15)
Family: Multiple adults, 1+ child(ren)	-0.142***	-0.161***	-0.199***	-0.194***
	(0.00879)	(0.0171)	(-15.32)	(-6.82)
White only	0	0	0	0
	(.)	(.)	(.)	(.)
Black/African American only	-0.156***	-0.141***	-0.144***	-0.154***
	(0.0109)	(0.0188)	(-6.63)	(-6.42)
AIAN only	0.172***	0.235***	-0.00259	0.0789
	(0.0621)	(0.0866)	(-0.06)	(1.05)
Asian only	-0.185***	-0.136***	-0.140***	-0.0881**
	(0.0165)	(0.0341)	(-5.61)	(-2.46)
Multiple race	-0.0172	-0.0111	0.107***	0.0678
	(0.0146)	(0.0266)	(4.92)	(1.47)
Education: GED or HS diploma	-0.0804***	-0.0574***	-0.0877***	-0.0873***
	(0.00952)	(0.0211)	(-6.17)	(-4.21)

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Education: Some college	-0.163***	-0.133***	-0.102***	-0.121***
	(0.00981)	(0.0191)	(-4.98)	(-5.16)
Education: Bachelors degree	-0.284***	-0.245***	-0.165***	-0.196***
	(0.0129)	(0.0260)	(-6.98)	(-7.03)
Education: Graduate degree	-0.381***	-0.323***	-0.155***	-0.195***
	(0.0122)	(0.0244)	(-6.04)	(-6.61)
Hispanic	0.0605**	0.0523*	-0.134***	-0.0604**
	(0.0253)	(0.0277)	(-8.99)	(-2.38)
Currently pregnant	-0.0497**	0.0636	-0.0926***	-0.0647
	(0.0220)	(0.0530)	(-2.82)	(-0.79)
Joint symptoms, past 30 days	0.0323***	0.0206*	0.374***	0.295***
	(0.00446)	(0.0109)	(42.14)	(20.10)
Ever diagnosed with arthritis	0.00144	-0.00536	0.0431***	0.0620***
	(0.00553)	(0.0123)	(6.14)	(3.56)
Lower back pain, past 3 months	0.0371***	0.0310**	0.359***	0.282***
	(0.00426)	(0.0134)	(33.08)	(20.24)
Neck pain, past 3 months	-0.00464	-0.0237*	0.325***	0.287***
	(0.00688)	(0.0127)	(37.28)	(25.44)
Health: Excellent	0	0	0	0
	(.)	(.)	(.)	(.)
Health: Very good	0.0262***	0.00859	0.221***	0.200***
	(0.00458)	(0.00794)	(27.29)	(8.31)

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Health: Good	0.0673***	0.0306***	0.507***	0.467***
	(0.00476)	(0.0105)	(33.34)	(15.76)
Health: Fair	0.0911***	0.0735***	0.947***	0.882***
	(0.00973)	(0.0234)	(45.96)	(26.17)
Health: Poor	0.0985***	0.0364	1.369***	1.292***
	(0.0179)	(0.0349)	(64.74)	(43.47)
Vigorous exercise: Never	-0.0314***	-0.0125	0.0255	0.0444
	(0.00725)	(0.0153)	(1.49)	(1.53)
Vigorous exercise: Less than weekly	-0.0192*	0.0302	0.163***	0.120***
	(0.0101)	(0.0340)	(8.95)	(2.92)
Vigorous exercise: 1-2 times per week	-0.0237***	-0.0208	0.0725***	0.0204
	(0.00632)	(0.0142)	(5.99)	(0.51)
Vigorous exercise: 3-4 times per week	-0.0219***	-0.0259*	-0.0142	-0.0536
	(0.00692)	(0.0154)	(-0.91)	(-1.60)
Vigorous exercise: 5 times per week	0	0	0	0
	(.)	(.)	(.)	(.)
Moderate exercise: Never	0.0192***	-0.0204*	-0.0721***	-0.00872
	(0.00568)	(0.0107)	(-6.23)	(-0.57)
Moderate exercise: Less than weekly	0.0761***	0.0303	0.105***	0.0481
	(0.0151)	(0.0462)	(5.03)	(1.07)
Moderate exercise: 1-2 times per week	0.00954*	-0.0238*	0.0101	-0.0128
	(0.00553)	(0.0125)	(0.98)	(-0.58)

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Moderate exercise: 3-4 times per week	-0.00759	-0.0187	-0.0440***	-0.0448*
	(0.00518)	(0.0127)	(-3.98)	(-1.84)
Moderate exercise: 5 times per week	0	0	0	0
	(.)	(.)	(.)	(.)
Rural residence	0.0225***	0.0274*	-0.0603***	-0.0335*
	(0.00569)	(0.0144)	(-4.18)	(-1.88)
Resides in border county	0.00570	0.0126	-0.00546	0.0225
	(0.0101)	(0.0119)	(-0.25)	(0.93)
Per capita income	-0.00000379*	-0.00000378	0.00000105	-0.00000292
	(0.00000229)	(0.00000429)	(0.20)	(-0.37)
Marijuana dispensary available	0.0271	0.0501**	-0.00219	0.00647
	(0.0186)	(0.0247)	(-0.05)	(0.13)
Marijuana legally available	-0.0213**	0.00816	-0.0238	-0.0297
	(0.0103)	(0.0228)	(-0.86)	(-0.73)
Processing year=2006	0	0	0	0
	(.)	(.)	(.)	(.)
Processing year=2007	0.0223**	0.0141	-0.0365*	-0.0206
	(0.00910)	(0.0256)	(-1.93)	(-0.51)
Processing year=2008	0.0442***	0.00652	0.0870***	0.0779*
	(0.0143)	(0.0285)	(2.96)	(1.78)

	Alcohol – Complete Population	Alcohol - Surgery/Injury Subpopulation	Kessler 6 – Complete Population	Kessler 6 - Surgery/Injury Subpopulation
Processing year=2009	0.0461***	0.0149	0.0797***	-0.000378
	(0.0161)	(0.0266)	(2.83)	(-0.01)
Processing year=2010	0.0540***	0.0402	0.126***	0.0373
	(0.0170)	(0.0335)	(3.51)	(1.02)
Processing year=2011	0.0391*	0.0350	0.0532	-0.00608
	(0.0234)	(0.0331)	(1.38)	(-0.14)
Processing year=2012	0.0563**	0.0373	-0.0585	-0.0523
	(0.0238)	(0.0368)	(-1.19)	(-0.84)
Processing year=2013	0.0486**	0.0635*	0.156***	0.123**
	(0.0236)	(0.0379)	(3.07)	(2.08)
Processing year=2014	0.0590**	0.0461	0.0704	0.0651
	(0.0278)	(0.0416)	(1.18)	(0.96)
Processing year=2015	0.0473	0.0213	0.147**	0.147*
	(0.0319)	(0.0480)	(2.14)	(1.70)
Constant	1.953***	2.057***	0.825***	1.391***
	(0.131)	(0.256)	(2.65)	(2.98)
/ lnalpha	-2.526***	-2.766***	0.613***	0.315***
	(0.0913)	(0.140)	(16.35)	(9.33)
Observations	174000	25770	277038	41565

[1] *In the alcohol regressions, values greater than 50 were flagged as outliers.*

*** 1% ** 5% * 10%

Note: Coefficients for state fixed effects omitted per agreement with the Centers for Disease Control

AIAN – American Indian or Alaska Native