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The Association between Pain Clinic Laws and Prescription Opioid Exposures: New Evidence from Multi-state Comparisons

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Abstract

Objectives: States in the US are controlling opioid prescribing to combat the opioid epidemic. Prescription Drug Monitoring Programs (PDMPs) were widely adopted, whereas less attention was given to pain clinic laws. This study examined the associations of mandatory use of PDMPs and pain clinic laws with prescription opioid exposures.

Methods: State-level quarterly prescription opioid exposures reported to the National Poison Data System during 2010-2017 were analyzed. The primary outcome was age-adjusted rates of prescription opioid exposures per 1,000,000 population. The primary policy variables included the implementation of mandatory use of PDMPs alone, the implementation of pain clinic laws alone, and the implementation of both mandatory use of PDMPs and pain clinic laws. Linear regressions were used to examine the associations, controlling for other opioid policies, marijuana policies, socioeconomic factors, state fixed effects, time fixed effects, and state-specific time trends.

Results: Requiring mandatory use of PDMPs alone was not associated with significant changes in prescription opioid exposures. The implementation of pain clinic laws with or without concurrent mandatory use of PDMPs was associated with 5 fewer prescription opioid exposures per 1,000,000 population or a 9% reduction compared to the pre-policy period (p<0.01). Further analysis revealed that the reduction associated with pain clinic laws was pronounced in exposures reported by healthcare facilities.

Conclusions: This multi-state study provided new evidence that the implementation of pain clinic laws was associated with a significant reduction in prescription opioid exposures. Pain clinic laws may deserve further evaluation and consideration.

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Keywords

pain clinic laws; Prescription Drug Monitoring Programs; prescription opioid; poisoning exposures

1. Introduction

The opioid epidemic has been one of the major public health challenges in the US. In 2017, 11.1 million people aged 12 or older misused prescription opioids, and 1.7 million had prescription opioid use disorders (SAMHSA, 2018). Drug overdose deaths involving prescription opioids rose from 3,442 in 1999 to 17,029 in 2017 (NIDA, 2019). The misuse and abuse of prescription opioids also contributed to the increased use of heroin and synthetic opioids (e.g., fentanyl), which has further fueled the spike in opioid overdose deaths (Ciccarone, 2017; Compton et al., 2016; Kolodny et al., 2015). To address the opioid crisis, states have considered and adopted a variety of policy actions, among which Prescription Drug Monitoring Programs (PDMPs) and pain clinic laws aim at reducing inappropriate prescription of opioids.

PDMPs provide electronic databases to track the dispensing of controlled drugs and make the data available to prescribers, pharmacists, and many other entities (e.g., boards of licensure, law enforcement). As of 2019, all 50 states and Washington DC implemented PDMPS with the only exception of Missouri. The success of PDMPs in large part depends on whether prescribers use PDMPs frequently enough to identify patients with excessive use of drugs or inappropriate co-use of drugs. The actual utilization of PDMPs by prescribers was low at the early stage of PDMPs (Irvine et al., 2014; Rutkow et al., 2015b). In recent years, states improved the utilization of PDMPs by mandating prescribers to query PDMP data in certain clinical conditions and time intervals (PDMPexcellence, 2016). Most states required that the prescribers query the PDMP data for initial prescriptions of opioids. Some states further required subsequent checks at certain time intervals, such as three months or twelve months, for continuing prescriptions. In contrast, some other states allowed prescribers to use their subjective judgment to determine the use of PDMPs. Whether the mandates applied to all prescribers regardless of practice settings and specialties also varied across states (Wen et al., 2019). Existing evidence suggested that mandatory use of PDMPs was associated with reduced opioid prescribing, drug treatment admissions, and overdose and deaths (Brown et al., 2017; Buchmueller and Carey, 2018; Dowell et al., 2016; Grecu et al., 2019; Meinhofer, 2018; Pauly et al., 2018; Suffoletto et al., 2018; Wen et al., 2019; Wen et al., 2017).

Less attention has been given to pain clinic laws. Pain clinics provide pain management services and prescribe pain medicines including opioids. Some pain clinics overprescribed opioids for profit without legitimate medical needs and became sources of large quantities of prescription opioids (DEA, 2013). In order to reduce inappropriate prescribing, pain clinic laws usually require pain clinics to register with the state, have physician ownership, comply with prescribing restrictions, and keep patient records. By 2019, only ten states have implemented pain clinic laws (Andraka-Christou et al., 2018).

Pain clinic laws were suggested effective in reducing opioid prescribing and opioid-related deaths. But the evidence is still limited overall, and most studies did evaluations in a single state with or without a comparison state. For instance, Florida saw considerable reductions in opioid prescribing and overdose deaths after pain clinic laws, PDMP, and other drug policies and enforcements were implemented almost simultaneously around 2010 and 2011 (Chang et al., 2016; Delcher et al., 2015; Johnson et al., 2014; Kennedy-Hendricks et al., 2016; Rutkow et al., 2015a). Texas saw a significant reduction in opioid prescribing following the implementation of pain clinic laws in the absence of an operational PDMP (Lyapustina et al., 2016). The only study utilizing data from multiple states found that mandatory use of PDMPs and pain clinic laws were jointly associated with reduced opioid prescribing and opioid-related mortality (Dowell et al., 2016). Because of data limitations, previous research was not able to disentangle the effects of pain clinic laws from those of mandatory use of PDMPs.

This study aimed at providing new evidence about the associations of mandatory use of PDMPs and pain clinic laws with opioid-related outcomes. We extended the previous research by including all the states with pain clinic laws and more data points after policy implementation. We focused on prescription opioid exposures reported to the National Poison Data System (NPDS), an indicator of problem prescription opioid use that has been rarely studied. We estimated the separate associations of mandatory use of PDMPs and pain clinic laws with prescription opioid exposures.

2. Methods

This is a population-based ecological study analyzing secondary data on state-quarter aggregate records of prescription opioid exposures reported to the NPDS.

2.1 Data

The data source of prescription opioid exposures was the NPDS administered by the American Association of Poison Control Centers. A total of 55 regional poison centers in the US provide immediate expert treatment advice and referral to healthcare facilities to residents who call the poison help hotlines. They also use follow-up calls to monitor case progress and medical consequences. Standardized and consistent protocols are used to obtain and record information on each poison exposure case, including caller and patient characteristics such as basic demographics and geographic location, information on exposure such as reason, route, acuity, and substance involved, and information on case management and medical consequences. The Information is submitted to the NPDS automatically in near real-time (Wolkin et al., 2012). The NPDS data include not only exposures treated in healthcare facilities but also those managed outside of healthcare facilities. Each year, the NPDS record nearly 3.5 million encounters (Gummin et al., 2018), accounting for half of the total poison exposures in the US (InstituteOfMedicine, 2004). Specifically, the opioid exposures recorded by the NPDS are complementary to and consistent with emergency department visits involving opioids in the Drug Abuse Warning Network and opioid-related mortality data in the National Vital Statistics Systems (Dasgupta et al., 2012; Davis et al., 2014; Iwanicki et al., 2018). In this study, prescription opioid exposure data from all the 50 states and DC between January 1st, 2010 and December 31st, 2017 were analyzed. Most PDMP mandatory use policies and pain clinic laws were implemented during this study period.

2.2 Measures

The outcome was the age-adjusted rates of prescription opioid exposures per 1,000,000 population per quarter per state. A prescription opioid exposure was defined as any human contact (e.g., ingestion, inhalation) with prescription opioids. Because the exposure cases were reported to the NPDS for expert treatment advice, they can be considered to be indicators of problem use of prescription opioids. The detailed list of prescription opioids included in the analysis is presented in Table S1. To facilitate comparisons across states and over time, the quarterly count of prescription opioid exposures in a state was standardized to age-adjusted rate in 1,000,000 population.

The two policy variables of interest included 1) the implementation of PDMP mandates on data use, and 2) the implementation of pain clinic laws. We first created two dichotomous indicators to represent the status of PDMP mandatory use and pain clinic laws, respectively, which took the value of 1 if a policy was implemented in that quarter and 0 otherwise. Because a state may have both policies in place simultaneously, we further created three mutually exclusive dichotomous indicators for 1) the presence of PDMP mandatory use policies alone in the absence of pain clinic laws, 2) the presence of pain clinic laws alone in the absence of PDMP mandatory use policies, and 3) the presence of both PDMP mandatory use policies and pain clinic laws, respectively. The policy dates were obtained from multiple sources, including National Alliance for Model State Drug Laws, Pew Research Center, Prescription Drug Abuse Policy System, and Center for Disease Control and Prevention (Table S2). When different dates were reported from these sources, we cross-validated them with state laws/regulations to identify the effective dates. During the study period of 2010-2017, there were considerable variations in policy implementation (Figure 1). At the beginning of 2010 (Figure 1a), only Nevada required mandatory use of its PDMP, and only Texas and Louisiana implemented pain clinic laws. By the end of 2017 (Figure 1b), 34 states required mandatory use of PDMPs, and ten states implemented pain clinic laws. Among them, nine states implemented both PDMP mandatory use policies and pain clinic laws.

The following covariates were included to account for time-variant state policies and socioeconomic factors that might impact prescription opioid exposures. Detailed definitions of covariates are described in Technical Note S1. Other opioid-related policy variables included a dichotomous indicator for PDMPs with accessible data, a dichotomous indicator for quantity/time limits on opioid prescriptions, a dichotomous indicator for naloxone access laws which expanded public access to naloxone, a dichotomous indicator for Good Samaritan laws that provided legal protections for people who call for medical assistance in the event of an overdose, a continuous variable for buprenorphine treatment capacity per 1,000 population, and Medicaid expansion that might expand treatment for opioid use disorder and opioid overdose. Because marijuana laws were associated with opioid prescribing and dispensing (Bradford and Bradford, 2016, 2017; Bradford et al., 2018; Liang et al., 2018; Shi et al., 2019; Wen and Hockenberry, 2018), we included four dichotomous indicators for medical marijuana legalization, presence of active medical marijuana dispensaries, recreational marijuana legalization, and presence of active recreational marijuana dispensaries, respectively. Socioeconomic variables included a continuous variable for annual poverty rate and a continuous variable for annual unemployment rate. Finally, a continuous variable for total human exposures reported to the NPDS per 1,000,000 population was used to represent residents' overall awareness and willingness to call the poison help hotlines in a state.

2.3 Statistical Analysis

The observations were analyzed at state-quarter level. Two-way fixed effects models were used to examine the associations of PDMP mandatory use polices and pain clinic laws with prescription opioid exposures. Specifically, four linear regressions were estimated. Model 1 included mandatory use of PDMPs as the primary policy variable. Model 2 included pain clinic laws as the primary policy variable. Model 3 included both mandatory use of PDMPs and pain clinic laws. Notably, the two indicators in Model 3 for mandatory use of PDMPs and pain clinic laws could both take the value of 1 in the same quarter and the state, as states might have these two policies in place simultaneously. Model 4 included the three mutually exclusive policy indicators for the presence of PDMP mandatory use alone, the presence of pain clinic laws alone, and the presence of both PDMP mandatory use and pain clinic laws. The reference category was the absence of both PDMP mandatory use and pain clinic laws. Model 4 was the preferred model in this study because it separated the association of mandatory use of PDMPs from that of pain clinic laws.

All models also controlled for policy and socioeconomic covariates, state fixed effects, time fixed effects, and state-specific linear time trends. Specified as a series of state indicators, state fixed effects accounted for time-invariant state-level unobserved heterogeneities. Specified as a series of year and quarter indicators, time fixed effects accounted for time-specific heterogeneities common to all the states at the same time, such as the reclassification of hydrocodone combination products from schedule III to schedule II by the Drug Enforcement Administration in 2014. State-specific linear time trends accounted for state-level natural trends in the outcome. Standard errors in the regression were clustered at state level. More details on model specifications can be found in Technical Note S1.

To explore the associations among subpopulations, we conducted separate regressions among exposures stratified by age (under 21 years and 21 years or older), gender (males and females), and source of reporting (reported by healthcare facilities and reported by patients or others).

2.4 Projection in Hypothetical Policy Scenarios

We projected prescription opioid exposures in 2017 under three hypothetical scenarios based on Model 4 estimates. We assumed that, by the end of 2017, all the 50 states and DC 1) : implemented PDMPs and required mandatory use but kept pain clinic law status as the status quo; 2) implemented pain clinic laws but kept PDMP mandates as the status quo, and 3) implemented both PDMP mandatory use policies and pain clinic laws. For each scenario, the projected total number of prescription opioid exposures were annualized at national level.

2.5 Sensitivity Analysis

We conducted two sensitivity tests. First, we excluded West Virginia and Kentucky, because these two states implemented pain clinic laws at the same time of requiring mandatory use of PDMPs. The associations with prescription opioid exposures could not be differentiated between the two polices. Second, we excluded Florida, which took multiple law enforcement and public health actions along with pain clinic laws around 2010 and 2011 in response to its escalating opioid overdose deaths (Delcher et al., 2015; Delcher et al., 2016). The changes in prescription opioid exposures therefore could not be solely attributed to pain clinic laws.

3. Results

3.1 Descriptive Statistics

During 2010-2017, states in the US on average had 57.78 age-adjusted prescription opioid exposures per 1,000,000 population per quarter per state (Table S3). The exposure rate began to level off around 2011 (Figure S1), in accordance with opioid-related mortality trend recorded in the National Vital Statistics Systems (Seth et al., 2018). In total, 497 (30%) and 232 (14%) out of the 1632 state-quarter observations had mandatory use of PDMPs and pain clinic laws implemented during the study period, respectively (Table S3). The average exposure rates in this period did not differ significantly between states did and did not require PDMP mandatory use or between states did and did not implement pain clinic laws (Table S3).

3.2 Regression Results

Table 1 report detailed regression results from Models 1-4 in full sample. In Model 1 where only the indicator for mandatory use of PDMPs entered the regression, mandatory use of PDMPs was not associated with changes in prescription opioid exposures. In Model 2 where only the indicator of pain clinic laws entered the regression, the implementation of pain clinic laws was associated with 5.16 (95% CI: −8.34, −1.97) fewer prescription opioid exposures per 1,000,000 population per quarter ($p<0.01$). This was roughly a 9% reduction compared to the pre-policy period.

In Model 3 where both indicators for mandatory use of PDMPs and pain clinic laws entered the regression, mandatory use of PDMPs was again not associated with changes in prescription opioid exposures. Yet the implementation of pain clinic laws was associated with 4.99 (95% CI: −8.47, −1.52) fewer prescription opioid exposures per 1,000,000 population per quarter or a 9% reduction ($p<0.01$).

Figure 2 summarizes the regression results from Model 4 where the three mutually exclusive indicators for the two policies (mandatory use of PDMPs and pain clinic laws) entered the regressions simultaneously. In full sample, requiring mandatory use of PDMPs alone was not associated with changes in prescription opioid exposures. Implementing pain clinic laws without or with concurrent mandatory use of PDMPs was respectively associated with 5.07 (95% CI: −8.49, −1.65) and 5.25 (95% CI: −8.41, −2.08) fewer prescription opioid exposures per 1,000,000 population per quarter ($ps<0.01$). These reductions could be also roughly converted to a 9% reduction relative to the pre-policy period. Similar results were found in subsamples stratified by age and gender. When the sample was stratified by source of reporting, the reduction associated with pain clinic laws was only seen in exposures reported by healthcare facilities. Exposures reported by patients or other sources were not associated with pain clinic laws. Detailed results of Model 4 in full sample as well as in stratified samples are presented in Table 1 and Tables S4–S6.

3.3 Projection in Hypothetical Scenarios

Figure 3 shows the projected annual number of prescription opioid exposures based on Model 4 estimations. In 2017, the actual total number of prescription opioid exposures in all the states was 54,794 (status quo scenario). If we assumed that all the 50 states and DC implemented PDMP mandatory use policies while keeping the pain clinic law status unchanged, the projected prescription opioid exposures were 54,559 (difference with status quo: −234, (95% CI: −827, 756)). Similarly, if all the states implemented pain clinic laws while keeping the PDMP mandates unchanged, the projected prescription opioid exposures were 50,270 (difference with status quo: −4,523, (95% CI: −7,358, −2,255)). Finally, had all the states implemented both PDMP mandatory use polices and pain clinic laws in 2017, the total number of prescription opioid exposures would have been reduced to 50,036, or roughly a 9% reduction (difference with status quo: −4,757, (95% CI: −7,743, −2,405)).

3.4 Sensitivity Analyses

The coefficient estimates and significance levels were similar to the main analyses when West Virginia and Kentucky were removed (Table S7) or when Florida was removed (Table S8).

4. Discussion

Using multiple-state data during 2010-2017, this study added new evidence that pain clinic laws were associated with a significant reduction in prescription opioid exposures reported to the NPDS. This association held regardless of whether PDMP mandatory use policies were concurrently implemented. Had all the US states implemented pain clinic laws by 2017, the total number of prescription opioid exposures would have been decreased by approximately 9%.

Our findings supported previous studies that found association between reduced opioid prescribing and the implementation of pain clinic laws in a single state that had no concurrent implementation of PDMP mandatory use policies (Chang et al., 2016; Johnson et al., 2014; Lyapustina et al., 2016; Rutkow et al., 2015a). The estimated 9% reduction in prescription opioid exposures in our study was also comparable to the only multi-state study that reported the associations between joint implementation of mandatory use of PDMPs and pain clinic laws and reductions in opioid prescribing by 8% and overdose death rates by 12% (Dowell et al., 2016).

We found no evidence that mandatory use of PDMPs alone was associated with changes in prescription opioid exposures. This appears to contradict the findings in most previous research that suggest effectiveness of PDMP mandates in reducing opioid-related prescribing, treatment, and deaths (Brown et al., 2017; Buchmueller and Carey, 2018; Dowell et al., 2016; Grecu et al., 2019; Meinhofer, 2018; Pauly et al., 2018; Suffoletto et al., 2018; Wen et al., 2019; Wen et al., 2017). This discrepancy may have two possible explanations. First, prescription opioid exposures reported to the NPDS were never examined in previous research. They likely represent an opioid outcome that was more responsive to pain clinic laws or less responsive to PDMPs. Unfortunately, this is a speculation and cannot be directly tested in the data. Second, depending on the study period and the states included in the study samples, some previous studies may have captured the combined effects of PDMPs and pain clinic laws even though they only evaluated PDMPs. Further, it should be noted that the states adopting pain clinic laws generally had weaker PDMP mandates. The PDMP mandates were considered comprehensive in only two out of the ten states with pain clinic laws, which required that all prescribers, regardless of practice settings, specialties, and subjective judgement, check PDMPs upon initial prescribing and at least every twelve months subsequently (Wen et al., 2019). PDMP mandates in states with pain clinic laws thus might have smaller impacts on opioid prescribing compared to states that did not implement pain clinic laws but had comprehensive PDMP mandates. This might explain why pain clinic laws were associated with significant reductions in the exposures regardless of whether PDMP mandatory use policies were implemented. Future research should validate our findings in other opioid-related outcomes and explore the policy interactions between PDMPs and pain clinic laws.

Pain clinic laws received much less attention from policymakers. Compared to nearly nation-wide adoption of PDMPs, pain clinic laws have been only implemented in ten states. While PDMPs and pain clinic laws both aim at reducing excessive opioid prescribing, pain clinic laws could be particularly effective in jurisdictions where substantial proportions of opioids are prescribed and dispensed in pain clinics (Chang et al., 2016; Johnson et al., 2014; Kennedy-Hendricks et al., 2016; Rutkow et al., 2015a). Pain clinic laws were also effective in reducing opioid prescriptions among high-risk opioid prescribers yet had little impacts among low-risk opioid prescribers (Chang et al., 2016). High-risk opioid prescribers consistently prescribe higher volumes of opioids than their peers. They are responsible for a disproportionately large fraction of opioid prescriptions. Evidence in Florida suggested that opioid prescribing remained highly concentrated among high-risk prescribers even after the implementation of PDMP (Chang et al., 2016). There are continued opportunities to reduce opioid prescribing through strategies targeting this group of prescribers. Furthermore, mandatory use of PDMPs could sometimes be burdensome to clinical practice (Haffajee et al., 2015). Restricting the legitimate source of prescription opioids via PDMPs might also unintentionally distress patients with chronic pain or opioid use disorders (Islam and McRae, 2014). Pain clinic laws have little effects on the majority of the prescribers who have low risks of excessive opioid prescribing. Given the evidence in previous literature and the new evidence in this study, states may reconsider the role of pain clinic laws in the opioid epidemic and use them as complements of PDMPs.

As a passive surveillance system (Wang et al., 2018), the NPDS relies upon voluntary reporting from healthcare facilities, patients, and other sources. Thus, NPDS data are not free of reporting bias commonly seen in any other self-reported data. The estimated association in this study could be biased if people were less willing to call poison centers after pain clinic laws were implemented for reasons such as stigma. We argue that, however, the reporting bias could not be a major explanation of the estimated relationship between prescription opioid exposures and pain clinic laws. In this study, the reduction in prescription opioid exposures following the implementation of pain clinic laws was only seen among exposures reported by healthcare facilities, which represent real needs for immediate medical treatments. Healthcare facilities were also less likely to be influenced by stigma compared to patients. If the reporting by healthcare facilities was indeed entirely biased, we should have observed the same level or even a greater level of reduction in exposures reported by patients. Yet we did not find significant changes in exposures reported by patients or other sources. Future studies are encouraged to explicitly investigate the magnitude of reporting bias and its impacts on association estimations.

This study has limitations. First, as in other ecological studies on aggregate data, the findings cannot be interpreted as individual-level associations or as causal even after we controlled for a rich set of covariates and fixed effects. We were also not able to directly explore the causal mechanisms underlying the differential associations of prescription opioid exposures with PDMP mandatory use policies and pain clinic laws. Second, exposures reported to NPDS were estimated to represent approximately half of the total exposures in the US. The findings may not be generalizable to exposure data from other sources such as self-report population surveys, drug prescriptions, or hospital records. Third, information provided via the poison help hotlines do not necessarily represent poisonings or overdoses because exposure cases in the NPDS are generally not verified by laboratory testing. Fourth, the findings may not be generalizable to exposures to illicit opioids, such as fentanyl which has been a major driver in the most recent opioid epidemic (Ciccarone, 2017). Fifth, we used binary indicators of PDMP mandatory use policies and pain clinic laws in the regressions without modeling the detailed variations across states due to collinearity problem. We were not able to examine particular characteristics of PDMPs other than mandatory data use such as data update frequency and number of drug schedules monitored for the same reason, either. Further, we were not able to attribute the observed associations to pain clinic laws alone in states where PDMP mandates and pain clinic laws were implemented simultaneously (e.g., Kentucky, West Virginia). Lastly, we cannot rule out the possibility that the estimated reduction in prescription opioid exposures was partially influenced by variations in reporting bias and reporting rates across states.

Conclusion

In this multi-state study, implementing pain clinic laws with or without concurrent mandates on PDMP data use was associated with reduced rates of prescription opioid exposures in the US. While further studies are warranted to validate the findings with data on other opioid-related outcomes, this study indicated that pain clinic laws may deserve more attention from researchers and policymakers than they currently receive.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Andraka-Christou B, Rager JB, Brown-Podgorski B, Silverman RD, Watson DP, 2018 Pain clinic definitions in the medical literature and U.S. state laws: an integrative systematic review and comparison. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5964673/ Subst. Abuse Treat. Prev. Policy 13, 17. [PubMed: 29789018]

Bradford AC, Bradford WD, 2016 Medical marijuana laws reduce prescription medication use in medicare part D. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2015.1661?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed Health Aff. (Millwood) 35, 1230–1236. [PubMed: 27385238]

Bradford AC, Bradford WD, 2017 Medical marijuana laws may be associated with a decline in the number of prescriptions for medicaid enrollees. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2016.1135 Health Aff. (Millwood) 36, 945–951. [PubMed: 28424215]

Bradford AC, Bradford WD, Abraham A, Adams GB, 2018 Association between us state medical cannabis laws and opioid prescribing in the medicare part D population. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2676999 JAMA Intern. Med 178, 667–672. [PubMed: 29610897]

Brown R, Riley MR, Ulrich L, Kraly EP, Jenkins P, Krupa NL, Gadomski A, 2017 Impact of New York prescription drug monitoring program, I-STOP, on statewide overdose morbidity. https://www.sciencedirect.com/science/article/pii/S0376871617302971?via%3Dihub Drug Alcohol Depend. 178, 348–354. [PubMed: 28692945]

Buchmueller TC, Carey C, 2018 The effect of prescription drug monitoring programs on opioid utilization in medicare. https://www.aeaweb.org/articles?id=10.1257/pol.20160094 Am. Econ. J. Econ. Policy 10, 77–112.

Chang HY, Lyapustina T, Rutkow L, Daubresse M, Richey M, Faul M, Stuart EA, Alexander GC, 2016 Impact of prescription drug monitoring programs and pill mill laws on high-risk opioid prescribers: A comparative interrupted time series analysis. https://www.sciencedirect.com/science/article/pii/S0376871616300722?via%3Dihub Drug Alcohol Depend. 165, 1–8. [PubMed: 27264166]

Ciccarone D, 2017 Fentanyl in the US heroin supply: A rapidly changing risk environment. https://www.sciencedirect.com/science/article/pii/S0955395917301810?via%3Dihub Int. J. Drug Policy 46, 107–111. [PubMed: 28735776]

Compton WM, Jones CM, Baldwin GT, 2016 Relationship between nonmedical prescription-opioid use and heroin use. https://www.nejm.org/doi/full/10.1056/NEJMra1508490 New Engl. J. Med 374, 154–163. [PubMed: 26760086]

Dasgupta N, Davis J, Funk MJ, Dart R, 2012 Using poison center exposure calls to predict methadone poisoning deaths. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0041181 Plos One 7.

Davis JM, Severtson SG, Bucher-Bartelson B, Dart RC, 2014 Using poison center exposure calls to predict prescription opioid abuse and misuse-related emergency department visits. https://onlinelibrary.wiley.com/doi/full/10.1002/pds.3533 Pharmacoepidemiol. Drug Saf 23, 18–25. [PubMed: 24130046]

DEA, 2013 2013 national drug threat assessment summary. Available at https://www.hsdl.org/?abstract&did=747046 Office of Intelligence Warning, Plans and Programs, Drug Enforcement Administration.

Delcher C, Wagenaar AC, Goldberger BA, Cook RL, Maldonado-Molina MM, 2015 Abrupt decline in oxycodone-caused mortality after implementation of Florida's prescription drug monitoring program. https://www.sciencedirect.com/science/article/pii/S0376871615000939?via%3Dihub Drug Alcohol Depend. 150, 63–68. [PubMed: 25746236]

Delcher C, Wang Y, Wagenaar AC, Goldberger BA, Cook RL, Maldonado-Molina MM, 2016 Prescription and illicit opioid deaths and the prescription drug monitoring program in florida. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4880260/ Am. J. Public Health 106, e10–11.

Dowell D, Zhang K, Noonan RK, Hockenberry JM, 2016 Mandatory provider review and pain clinic laws reduce the amounts of opioids prescribed and overdose death rates. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6583870/ Health Aff. (Millwood) 35, 1876–1883. [PubMed: 27702962]

Grecu AM, Dave DM, Saffer H, 2019 Mandatory access prescription drug monitoring programs and prescription drug abuse. https://www.ncbi.nlm.nih.gov/pubmed/30572414 J. Policy Anal. Manage 38, 181–209. [PubMed: 30572414]

Gummin DD, Mowry JB, Spyker DA, Brooks DE, Osterthaler KM, Banner W, 2018 2017 annual report of the american association of poison control centers' national poison data system (NPDS): 35th annual report. https://www.tandfonline.com/doi/abs/10.1080/15563650.2018.1533727 Clin. Toxicol. (Phila) 56, 1213–1415. [PubMed: 30576252]

Haffajee RL, Jena AB, Weiner SG, 2015 Mandatory use of prescription drug monitoring programs. https://jamanetwork.com/journals/jama/fullarticle/2107540 JAMA 313, 891–892. [PubMed: 25622279]

InstituteOfMedicine, 2004 Forging a poison prevention and control system. Institute of Medicine, The National Academies Press, Washington, DC.

Irvine JM, Hallvik SE, Hildebran C, Marino M, Beran T, Deyo RA, 2014 Who uses a prescription drug monitoring program and how? Insights from a statewide survey of Oregon clinicians. https://www.sciencedirect.com/science/article/pii/S1526590014006944?via%3Dihub J. Pain 15, 747–755. [PubMed: 24787089]

Islam MM, McRae IS, 2014 An inevitable wave of prescription drug monitoring programs in the context of prescription opioids: pros, cons and tensions. https://bmcpharmacoltoxicol.biomedcentral.com/articles/10.1186/2050-6511-15-46 BMC Pharmacol. Toxicol 15, 46. [PubMed: 25127880]

Iwanicki JL, Severtson SG, Margolin Z, Dasgupta N, Green JL, Dart RC, 2018 Consistency between opioid-related mortality trends derived from poison center and national vital statistics system, United States, 2006-2016. https://ajph.aphapublications.org/doi/full/10.2105/AJPH.2018.304728?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed Am. J. Public Health 108, 1639–1645. [PubMed: 30403501]

Johnson H, Paulozzi L, Porucznik C, Mack K, Herter B, 2014 Decline in drug overdose deaths after state policy changes - Florida, 2010-2012. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6326a3.htm MMWR Morb. Mortal. Wkly. Rep 63, 569–574. [PubMed: 24990490]

Kennedy-Hendricks A, Richey M, McGinty EE, Stuart EA, Barry CL, Webster DW, 2016 Opioid overdose deaths and Florida's crackdown on pill mills. https://ajph.aphapublications.org/doi/full/10.2105/AJPH.2015.302953?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed Am. J. Public Health 106, 291–297. [PubMed: 26691121]

Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC, 2015 The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. https://www.annualreviews.org/doi/full/10.1146/annurev-publhealth-031914-122957?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed Annu. Rev. Public Health 36, 559–574. [PubMed: 25581144]

Liang D, Bao Y, Wallace M, Grant I, Shi Y, 2018 Medical cannabis legalization and opioid prescriptions: evidence on US Medicaid enrollees during 1993-2014. https://onlinelibrary.wiley.com/doi/full/10.1111/add.14382 Addiction 113, 2060–2070. [PubMed: 29989239]

Lyapustina T, Rutkow L, Chang HY, Daubresse M, Ramji AF, Faul M, Stuart EA, Alexander GC, 2016 Effect of a "pill mill" law on opioid prescribing and utilization: The case of Texas. https://

www.ncbi.nlm.nih.gov/pmc/articles/PMC4976392/ Drug Alcohol Depend. 159, 190–197. [PubMed: 26778760]

Meinhofer A, 2018 Prescription drug monitoring programs: The role of asymmetric information on drug availability and abuse. https://www.mitpressjournals.org/doi/abs/10.1162/ajhe_a_00101 Am. J. Health Econ 4, 504–526.

NIDA, 2019 Overdose death rates. Available at https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates (Accessed August 22 2019).

Pauly NJ, Slavova S, Delcher C, Freeman PR, Talbert J, 2018 Features of prescription drug monitoring programs associated with reduced rates of prescription opioid-related poisonings. https://www.sciencedirect.com/science/article/pii/S0376871618300103?via%3Dihub Drug Alcohol Depend. 184, 26–32. [PubMed: 29402676]

PDMPexcellence, 2016 PDMP prescriber use mandates: characteristics, current status, and outcomes in selected states. Available at http://www.pdmpassist.org/pdf/COE_documents/Add_to_TTAC/COE%20briefing%20on%20mandates%203rd%20revision.pdf Prescription Drug Monitoring Program Center of Excellence at Brandeis University.

Rutkow L, Chang HY, Daubresse M, Webster DW, Stuart EA, Alexander GC, 2015a Effect of Florida's prescription drug monitoring program and pill mill laws on opioid prescribing and use. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2429105 JAMA Intern. Med 175, 1642–1649. [PubMed: 26280092]

Rutkow L, Turner L, Lucas E, Hwang C, Alexander GC, 2015b Most primary care physicians are aware of prescription drug monitoring programs, but many find the data difficult to access. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1085 Health Aff (Millwood) 34, 484–492. [PubMed: 25732500]

SAMHSA, 2018 Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSDUH Series H-53). Available at https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.htm Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Seth P, Rudd RA, Noonan RK, Haegerich TM, 2018 Quantifying the epidemic of prescription opioid overdose deaths. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5844400/ Am. J. Public Health 108, 500–502. [PubMed: 29513577]

Shi Y, Liang D, Bao Y, An R, Wallace MS, Grant I, 2019 Recreational marijuana legalization and prescription opioids received by Medicaid enrollees. https://www.sciencedirect.com/science/article/pii/S0376871618307567?via%3Dihub Drug Alcohol Depend. 194, 13–19. [PubMed: 30390550]

Suffoletto B, Lynch M, Pacella CB, Yealy DM, Callaway CW, 2018 The effect of a statewide mandatory prescription drug monitoring program on opioid prescribing by emergency medicine providers across 15 hospitals in a single health system. https://www.sciencedirect.com/science/article/pii/S1526590017307873?via%3Dihub J. Pain 19, 430–438. [PubMed: 29241835]

Wang A, Law R, Lyons R, Choudhary E, Wolkin A, Schier J, 2018 Assessing the public health impact of using poison center data for public health surveillance. https://www.tandfonline.com/doi/full/10.1080/15563650.2017.1413194 Clin. Toxicol. (Phila) 56, 646–652. [PubMed: 29235366]

Wen H, Hockenberry JM, 2018 Association of medical and adult-use marijuana laws with opioid prescribing for medicaid enrollees. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2677000 JAMA Intern. Med 178, 673–679. [PubMed: 29610827]

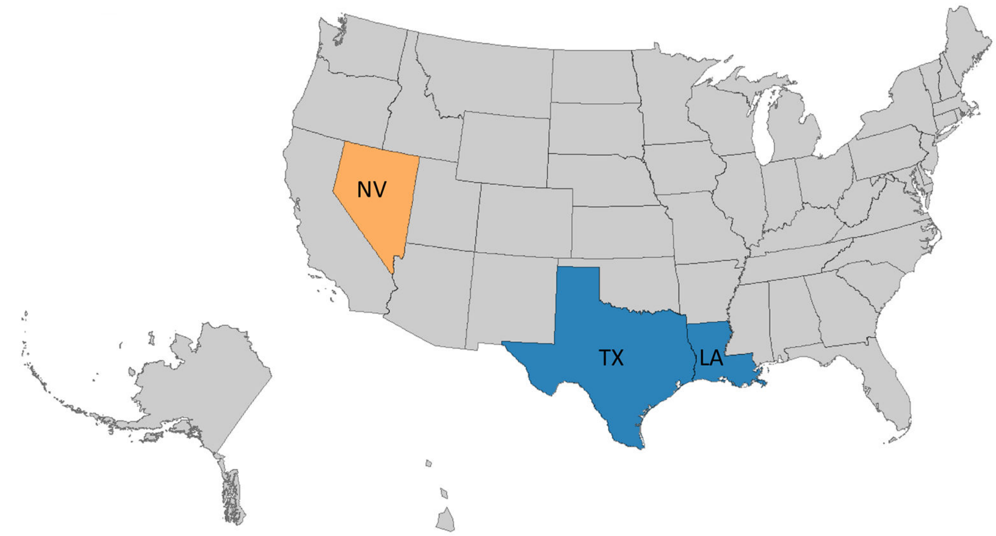
Wen H, Hockenberry JM, Jeng PJ, Bao Y, 2019 Prescription drug monitoring program mandates: Impact on opioid prescribing and related hospital use. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2019.00103 Health Aff. (Millwood) 38, 1550–1556. [PubMed: 31479368]

Wen H, Schackman BR, Aden B, Bao Y, 2017 States with prescription drug monitoring mandates saw a reduction in opioids prescribed to medicaid enrollees. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2016.1141 Health Aff. (Millwood) 36, 733–741. [PubMed: 28373340]

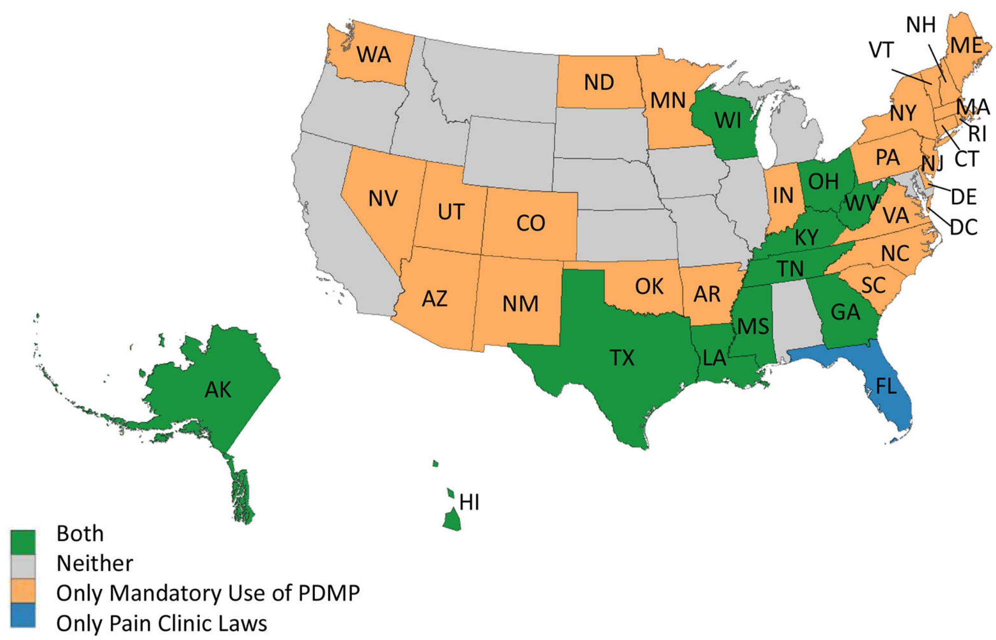
Wolkin AF, Martin CA, Law RK, Schier JG, Bronstein AC, 2012 Using poison center data for national public health surveillance for chemical and poison exposure and associated illness. https://www.sciencedirect.com/science/article/pii/S019606441101417X?via%3Dihub Ann. Emerg. Med 59, 56–61. [PubMed: 21937144]

Highlights

- Mandatory use of PDMPs alone was not associated with prescription opioid exposures.
- Pain clinic laws were associated with reduced prescription opioid exposures.
- Reduction was pronounced in exposures reported by healthcare facilities.



a.



b.

Figure 1.

States Requiring Mandatory Use of PDMPs and States Implementing Pain Clinic Laws in 2010 and 2017

a. January 1, 2010

b. December 31, 2017

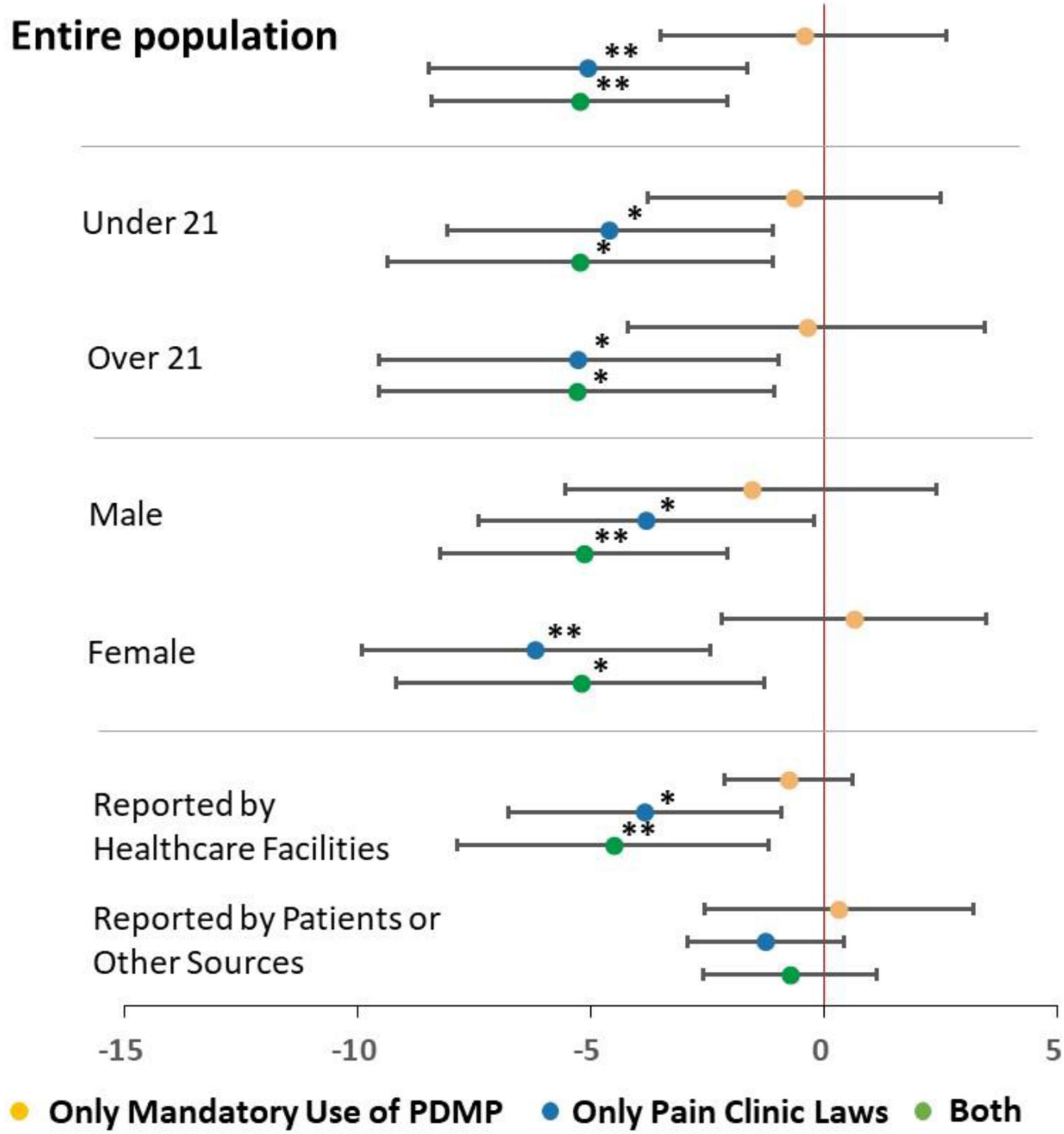


Figure 2. Estimated Changes in Prescription Opioid Exposures per 1,000,000 Population per Quarter per State Associated with PDMP Mandatory Use Policies and Pain Clinic Laws.

Coefficient estimates with 95% CI from Model 4 are presented. All regressions also controlled for other opioid-related policies (PDMP data access, quantity/time limits on opioid prescriptions, naloxone access laws, Good Samaritan laws, buprenorphine treatment capacity, Medicaid expansion), marijuana policies (medical marijuana legalization, presence of active medical marijuana dispensaries, recreational marijuana legalization, presence of active recreational marijuana dispensaries), socioeconomic factors (poverty rate, unemployment rate, and total number of exposures), state fixed effects, time fixed effects, and state-specific time trends. *p<0.05, **p<0.01, ***p<0.001

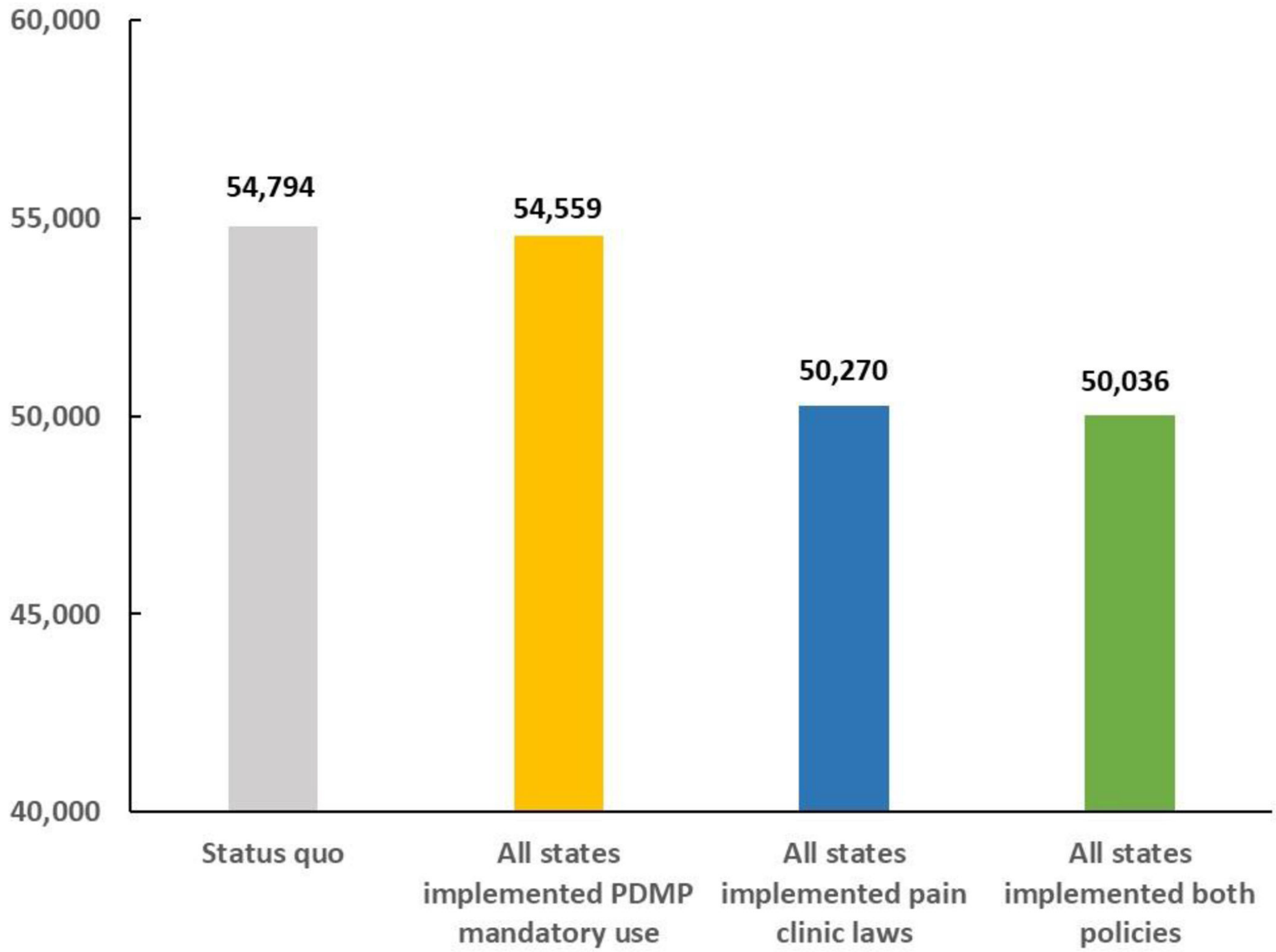


Figure 3. Projected Annual Number of Prescription Opioid Exposures in Hypothetical Scenarios.

The projections were based on Model 4 estimations, assuming that all the states in the US adopted the policy(ies) in 2017.

Table 1.

Full Regression Results: Full Sample.

	Model 1	Model 2	Model 3	Model 4
	Coefficients (95% CI)			
Mandatory Use of PDMPs	−0.95 (−3.35, 1.46)		−0.37 (−2.84, 2.09)	
Pain Clinic Laws		**−5.16** ** **(−8.34, −1.97)**	**−4.99** ** **(−8.47, −1.52)**	
Mutually Exclusive Policy Status				
Mandatory Use of PDMPs Alone, No Pain Clinic Laws				−0.44 (−3.50, 2.63)
Pain Clinic Laws Alone, No Mandatory Use of PDMPs				**−5.07** ** **(−8.49, −1.65)**
Mandatory Use of PDMPs AND Pain Clinic Laws				**−5.25** ** **(−8.41, −2.08)**
PDMP Data Access	−2.64 (−5.76, 0.48)	−2.63 (−5.71, 0.45)	−2.61 (−5.69, 0.48)	−2.59 (−5.71, 0.53)
Quantity/Time Limits on Opioid Prescriptions	−0.79 (−3.34, 1.75)	−0.88 (−3.40, 1.64)	−0.83 (−3.41, 1.75)	−0.82 (−3.43, 1.78)
Naloxone Access Laws	−1.23 (−3.22, 0.77)	−1.27 (−3.20, 0.66)	−1.25 (−3.24, 0.75)	−1.26 (−3.23, 0.72)
Good Samaritan Laws	0.37 (−1.44, 2.19)	0.057 (−1.79, 1.90)	0.086 (−1.73, 1.90)	0.10 (−1.71, 1.91)
Buprenorphine Treatment Capacity per 1,000 Population	**−0.90** * **(−1.58, −0.22)**	**−0.96** ** **(−1.66, −0.27)**	**−0.95** ** **(−1.65, −0.26)**	**−0.95** ** **(−1.65, −0.25)**
Medicaid Expansion	1.27 (−1.26, 3.79)	1.19 (−1.36, 3.74)	1.23 (−1.26, 3.72)	1.26 (−1.24, 3.76)
Medical Marijuana Legalization	0.052 (−2.52, 2.63)	−0.31 (−2.80, 2.18)	−0.26 (−2.82, 2.30)	−0.25 (−2.86, 2.37)
Active Medical Marijuana Dispensaries	−1.36 (−4.62, 1.90)	−1.42 (−4.72, 1.87)	−1.42 (−4.69, 1.84)	−1.42 (−4.68, 1.84)
Recreational Marijuana Legalization	−0.66 (−3.71, 2.39)	−0.62 (−3.71, 2.46)	−0.60 (−3.68, 2.47)	−0.60 (−3.68, 2.47)
Active Recreational Marijuana Dispensaries	0.65 (−2.37, 3.66)	0.68 (−2.32, 3.68)	0.75 (−2.25, 3.74)	0.76 (−2.26, 3.78)
Poverty Rate	−0.35 (−0.79, 0.085)	−0.33 (−0.76, 0.094)	−0.33 (−0.77, 0.10)	−0.33 (−0.77, 0.10)
Unemployment Rate	−0.92 (−2.10, 0.26)	−0.97 (−2.12, 0.18)	−0.98 (−1.21, 0.15)	−0.99 (−2.12, 0.14)
Total Human Exposures per 1,000,000 Population	**0.018** *** **(0.010, 0.025)**	**0.018** *** **(0.010, 0.025)**	**0.018** *** **(0.010, 0.025)**	**0.018** *** **(0.010, 0.025)**
Constant	**62.86** *** **(41.64, 84.07)**	**62.84** *** **(42.11, 83.57)**	**62.95** *** **(42.35, 83.54)**	**62.99** *** **(42.36, 83.63)**
Number of State-Quarter Observations	1,632	1,632	1,632	1,632
Overall R^2	0.88	0.88	0.88	0.88

* $p<0.05$,

** $p<0.01$,

*** $p<0.001$.

Data were analysed at state-quarter level. All regressions also controlled for state indicators, year indicators, quarter indicators, and state-specific time trends. Standard errors were clustered at state level.