Behavioral Responses to Supply-Side Drug Policy During the Opioid Epidemic*

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Abstract

We investigate behavioral responses to a staggered disruption in the supply of prescription opioids across U.S. states: the introduction of electronic Prescription Drug Monitoring Programs (PDMPs). Using administrative datasets, we find PDMPs curtail the proliferation of prescription opioids. Physicians respond to monitoring on the extensive margin, limiting the number of patients to whom they prescribe opioids without adjusting dosage or duration. This decreases supply to long-term opioid users, who evade the restrictions by acquiring prescriptions from out-of-state prescribers and by substituting to heroin. This causes a surge in heroin overdoses, which offsets reductions in hospitalizations and deaths from prescription opioids.

Keywords: Prescription drugs, opioid crisis, heroin, prescription drug monitoring programs.

JEL Classification: H75, I11, I12, I18.

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1 Introduction

In the last 20 years, use of prescription opioids has grown dramatically in the United States. Since 1999, the number of opioid prescriptions increased by 300%, surpassing 255 million prescriptions in 2012 (81.3 prescriptions per 100 people) before declining to 153 million prescriptions by 2019 (46.7 per 100 people) (CDC, 2020; U.S. Department of Health & Human Services, 2016). Opioids may be an effective analgesic for acute pain but are also associated with high risks of addiction and overdose (Fields, 2011). Death rates from opioid poisoning tripled between 2000 and 2014 (Rudd et al., 2016), contributing to a stunning reversal in the long-running decline in midlife mortality since 1999 (Case and Deaton, 2015). The increase in overdose deaths was initially driven by prescription opioid poisonings, but the more recent surge in deaths has been attributed to illicit opioids such as heroin and fentanyl (Rudd et al., 2016).

In efforts to abate the opioid epidemic, federal, state and local governments have implemented an array of policies aimed at curbing harms related to prescription opioid misuse. These policies typically follow one of three lines of attack: prevention of opioid misuse, treatment of opioid use disorder (OUD), and reducing drug availability (Office of National Drug Control Policy, 2020). While prevention and treatment are demand-side interventions, reducing drug availability targets the opioid supply. Throughout the epidemic, policymakers have relied heavily on supply-side interventions. Half of all federal drug control funding ($17 billion) for fiscal year 2020 was assigned to supply reduction, 44 percent was allocated to treatment ($15 billion) and only six percent to prevention ($2 billion).[1] Although supply-side interventions dominate drug policy, evidence of their effectiveness is mixed (e.g., Alpert, Powell, and Pacula, 2018; Buchmueller and Carey, 2018; Dobkin and Nicosia, 2009; Evans, Lieber, and Power, 2019; Haegerich et al., 2014; Mauri, Townsend, and Haffajee, 2020).

At the state level, Prescription Drug Monitoring Programs (PDMPs) are the primary tool used to control the supply of prescription opioids.[2] PDMPs record patients' prescription histories, with the purpose of facilitating detection of suspicious fill patterns, "doctor shopping," or other behaviors indicative of prescription drug misuse. By raising awareness among physicians of the risks of opioid prescribing, and facilitating detection of inappropriate prescribing, PDMPs are intended to discourage excess or high-risk opioid prescribing, thereby limiting exposure of consumers to opioids and preventing addiction. But,

[1] In the last decade, the budget allocated to supply reduction has been stable at $15-17 billion per year, while that allocated to demand reduction has been steadily increasing from $9 billion in 2011 to $17 billion in 2020 (Office of National Drug Control Policy, 2019).

[2] Other common supply-side interventions (both state and federal) include Medicaid "lock-ins" that limit patients to a single, designated opioid prescriber, the development of abuse-deterrent drug formulations, "black box" warnings on drug packaging, regulations targeting pain clinics, and limits on the duration and potency of initial prescriptions.

in creating access barriers, PDMPs may inadvertently increase the likelihood that individuals who are already addicted to prescription opioids switch to illicit opioids – primarily heroin and fentanyl traded on the black market. This is known as the "balloon effect" (Mora, 1996): when the government closes down a source of drug supply, individuals dependent on these substances resort to other sources instead of reducing drug use. Indeed, deaths from heroin and synthetic opioids have surged to record numbers nationwide, increasing seven-fold since 2012 and now surpassing deaths from firearms and car crashes combined (CDC, 2021).

In this paper, we conduct a comprehensive investigation of the direct and indirect effects of PDMPs. Our research design leverages the staggered implementation of electronic PDMPs across U.S. states between 1993-2018. We have assembled a comprehensive suite of large administrative and survey datasets not used in previous studies to examine the effects of prescription drug regulation across a broad range of outcomes and actors, revealing the chain of events that unfolds after an opioid supply disruption limits access to prescription drugs.

We first test whether PDMPs are effective at limiting the proliferation of prescription opioids. Using the nation's largest database of commercial insurance claims, Blue Cross Blue Shield (BCBS) Axis®, we find that electronic PDMPs reduce the overall number of opioid prescriptions by 14% and the number of people receiving opioid analgesics by 13%. We corroborate this finding in data from the Drug Enforcement Administration (DEA), which track shipments of oxycodone and hydrocodone (the two most commonly prescribed opioid analgesics) from manufacturers to dispensers. These data confirm that PDMPs reduce the volume of dispensing by both pharmacies and practitioners.

We then focus on the behavioral responses of prescribers across a heterogeneous set of patients. Our analysis reveals that providers respond entirely on the extensive margin; reducing the number of prescriptions they issue but not their daily dosage or duration. While physicians limit opioid prescriptions across a diverse set of patients, first-time prescriptions to opioid-naive patients are reduced the most. However, the majority of the reduction arises from limiting prescriptions to long-term opioid users – a smaller set of users that nevertheless accounts for the majority of prescription volume. This extensive margin response cuts off patients with a history of chronic opioid use – and therefore a higher risk of opioid dependence – from a steady supply of legal prescription drugs.

Patients respond by seeking other sources of opioids. Using BCBS Axis® and the National Survey on Drug Use and Health, we document an increase in the number of prescriptions obtained from out-of-state prescribers. At the same time, patients are also more likely to rely on diverted prescription drugs or other illicit drugs, primarily heroin. The number of individuals who report using heroin increases by

9%. We then compute bounds for the rate of substitution between prescription opioids and heroin. Our preferred estimate suggests that for every six prescription drug users who lose legal access to opioids after PDMP introduction, one person initiates heroin consumption.

Probing further, we investigate whether these PDMP-induced reductions in prescribing translate into health improvements. Our results suggest that aggregate mortality estimates hide meaningful and opposing health effects arising from changes in the consumption patterns of people dependent on opioids. Although mortality due to semi-synthetic prescription opioids decreases, aggregate mortality remains unaffected by PDMPs. This is because mortality due to heroin and fully synthetic opioids (e.g., fentanyl) increases sharply, by about 14%, reflecting the substitution towards illicit drugs. Our results suggest that although prescription drug mortality is reduced permanently, heroin mortality spikes sharply following the introduction of a PDMP and remains at an elevated level.

Having established the existence and magnitude of substitution effects for mortality, we focus on hospitalizations as a non-terminal health outcome and assess the costs imposed on the health care system. Using the National Inpatient Sample, we find that hospitalizations due to prescription opioid poisoning decrease, while those caused by heroin poisoning increase. As in the case of mortality, overall opioid hospitalizations remain stable. Although average effects are similar to those for mortality, the time pattern of hospitalization effects differs. In the years following PDMP introduction, hospitalizations for both prescription opioid and heroin poisonings steadily decrease and increase, respectively. This suggests that as heroin consumption spreads, harm reduction practices become more established and the risk of fatal overdose decreases while hospitalization becomes more likely.

These changes in the composition of hospital cases are costly: total hospital costs associated with opioid poisonings increase by 3%. Most of the additional costs are borne by commercial insurers and not by Medicaid or Medicare. Excess hospitalizations occur mostly among middle-aged, white and commercially insured individuals. While both men and women are affected, incidence among men is higher compared to women. In the final part of the paper, we present a case study of pain clinics in Florida ("pill mills"), where providers engaged in excessive prescribing practices, to highlight their unique role in sustaining widespread opioid addiction.

Our paper contributes novel findings to four distinct strands of literature. First, we advance the growing literature on prescription monitoring. This literature has largely focused on elderly and disabled Medicare beneficiaries (e.g., Buchmueller and Carey, 2018; Meara et al., 2016), even though evidence suggests middle-aged, commercially insured individuals have been most affected by the opioid epidemic (see Case and Deaton, 2015; Ruhm, 2019). Understanding outcomes for the general population is of

widespread interest. Krueger (2017) argued that the proliferation of prescription opioids could account for up to 43% of the decline in men's labor force participation between 1999 and 2015. We show that a large part of the policy incidence falls on commercial insurance enrollees, while broadly confirming previous results for Medicare beneficiaries (Buchmueller and Carey, 2018).

Most studies in this literature investigate effects on opioid prescriptions and misuse outcomes (e.g., Brady et al., 2014; Buchmueller and Carey, 2018; Grecu, Dave, and Saffer, 2019; Mauri, Townsend, and Haffajee, 2020; Meara et al., 2016; Simoni-Wastila and Qian, 2012). Among studies of the most restrictive type of electronic PDMP, which *requires* physicians and pharmacies to check patients' prescription records prior to dispensing, there is consensus that "must-access" laws cause moderate reductions in prescriptions and opioid misuse. But studies of PDMPs more broadly or of their effects on other outcomes present mixed results. For example, the few studies focusing on mortality offer conflicting results: Pardo (2017) finds that PDMPs are associated with a reduction in opioid overdoses, whereas Grecu, Dave, and Saffer (2019) and Meinhofer (2018) do not find any relation between PDMPs and mortality. Results for other health outcomes, which could help resolve these conflicting findings are scarce.[3] Our analysis incorporates the full class of electronic PDMPs and looks beyond prescriptions patterns to a broad array of health outcomes, health care use and costs in the general population, adding to the limited evidence on mortality.

In addition, few studies have assessed downstream outcomes, such as heroin use.[4] Individuals who lose access to opioids may turn to illicit markets to obtain substitute drugs in the form of diverted prescription opioids, heroin, or fentanyl. Theoretical work by Strulik (2021) suggests out that discontinuing a prescription induces fully rational individuals to quit using opioids, while imperfectly rational individuals experiencing addiction switch to heroin. We advance the literature by quantifying these indirect effects, tracing how PDMPs affect drug consumption, hospitalizations, and mortality associated with illicit opioids.

Our paper also informs the broader literature on supply-side drug policies by illustrating how consumers react to supply contractions. Limited effectiveness and evasion of supply-side restrictions have been documented for a wide range of drugs. For example, Dobkin and Nicosia (2009) analyze the effects

[3] Another potential explanation for the divergent findings in the literature is the heterogeneity of the particular PDMP legislation under study and related measurement error (Griffin et al., 2020; Horwitz et al., 2018; Schuler et al., 2020, see also). Buchmueller and Carey (2018) focus on must-access PDMP laws. They find that must-access PDMPs reduce excessive quantity prescriptions and doctor shopping behavior in the Medicare Part D prescription drug program. Grecu, Dave, and Saffer (2019) add that must-access PDMPs decrease treatment admissions for substance abuse and reduce opioid mortality for younger adults, while Kim (2021) show that the introduction of must-access PDMPs caused an increase in heroin mortality.

[4] Notable exceptions are Grecu, Dave, and Saffer (2019), who study treatment admissions for drug misuse, Gihleb, Giuntella, and Zhang (2019), who study the effect of must-access PDMPs on foster care admissions, and Evans, Harris, and Kessler (2020), who examine how child abuse and neglect change after must-access PDMP implementation and OxyContin reformulation.

of supply disruptions in the market for methamphetamine across a range of outcomes, and find that the impact is largely temporary.[5] Closely related to our paper, Cicero and Ellis (2015), Alpert, Powell, and Pacula (2018) and Evans, Lieber, and Power (2019) analyze the 2010 abuse-deterrent reformulation of OxyContin and its effects on drug consumption. They find that while the reformulation has reduced illicit use of OxyContin, it has also caused individuals to switch to other opioid drugs, primarily heroin. Building on this evidence, we show that evasion and drug substitution also occur on a large scale in response to prescription monitoring. We pin down the physician and consumer behaviors that drive this result and link these behaviors to health outcomes and health care costs. Our analysis highlights the gatekeeper role and special responsibility of physicians in prescription drug markets.[6]

Lastly, our paper informs the recent discourse about the causes of the opioid epidemic and the interpretation of recent trends in mortality. Case and Deaton (2015) documented the reversal in mortality trends in the United States, pointing out the historic increase in rates of mortality by drug poisoning among middle-aged, white non-Hispanics compared to other demographic groups, and also a pronounced increase in suicides and deaths from chronic liver disease and cirrhosis. They tie these "deaths of despair" to economic insecurity, interpreting the changes in mortality in the context of a broader deterioration in economic conditions for people without a college degree (Case and Deaton, 2020). Others have explored alternative explanations, arguing that supply-side factors related to public health and the availability of drugs are the major driving forces of the aggregate trend in mortality (e.g., Ruhm, 2016, 2018). These demand and supply-side explanations are complementary and not mutually exclusive (see also Case and Deaton 2017, 2018, 2020; Currie and Schwandt 2020; Meara and Skinner 2015). Grossmann and Strulik (2021) emphasize that both socio-economic decline and falling opioid prices need to coincide to explain the rise in illicit drug use. Institutions also matter: in a recent paper on the origins of the opioid crisis, Alpert et al. (2019) highlight how initial differences in state laws governing the ease with which prescriptions for controlled substances could be issued led to targeted marketing efforts by pharmaceutical companies, which influenced the proliferation of OxyContin. We complement these papers by showing how institutions shape prescribing behavior and access to prescriptions; and how prescribing laws can induce drug substitution in the presence of illicit substitutes.

[5] Evaluations of supply-side drug policy interventions are available for methamphetamine (Dobkin and Nicosia, 2009; Dobkin, Nicosia, and Weinberg, 2014), cocaine (Caulkins, 2001), heroin (Smithson, McFadden, and Mwesigye, 2005), and marijuana (DiNardo and Lemieux, 2001). For a general discussion on drug policy, see Murphy, Grossman, and Becker (2006).

[6] For a broader discussion on the key role of physician behavior during the opioid epidemic, see Schnell (2017) and Schnell and Currie (2018).

2 Background

Opioids are a class of natural and synthetic substances that act by binding to opioid receptors, which are found principally in the central and peripheral nervous system and the gastrointestinal tract. These receptors mediate both the psychoactive and the somatic effects of opioids, relieving pain and creating a feeling of relaxation and sometimes euphoria. However, because of their effect on the part of the brain that regulates breathing, opioids can lead to respiratory depression during overdoses.

Beginning in the mid-1990s, the medical community began treating pain more aggressively, easing access to prescription painkillers. Following this paradigm shift, opioid prescribing increased significantly over the next two decades. Previously, opioids had been utilized almost exclusively for the treatment of severe acute pain, pain due to cancer or in palliative care, or were administered in hospital settings and rarely prescribed as self-administered medication. In the mid-1990s, however, physicians began prescribing opioids for people experiencing chronic pain or episodes of minor acute pain, which were previously treated with non-steroidal anti-inflammatory drugs. Today, opioid analgesics – in particular, oxycodone or hydrocodone – are commonly prescribed for conditions like back pain or following dental treatments. The increase in opioid prescriptions has been accompanied by rising rates of opioid misuse, addiction, and overdoses.

In response to growing misuse of prescription medication, U.S. states have introduced prescription drug monitoring programs (PDMPs). A PDMP is an electronic database that tracks prescriptions of controlled substances in a state. The goal of PDMPs is to support the legitimate medical use of controlled substances while limiting their misuse and diversion. Pharmacies and prescribers register with their state PDMP and pharmacies report prescriptions and dispensations of controlled substances to the electronic online database. By providing prescribers and health authorities with information about patient and provider behaviors, they may enable rapid identification of high-risk prescribing or fill patterns indicating potential misuse (e.g., overlapping prescriptions, multiple prescribers, etc.), thereby facilitating targeted enforcement. PDMPs are thus designed to help prevent adverse drug-related events such as opioid overdoses, drug diversion, and substance misuse by decreasing unsafe or potentially inappropriate opioid prescribing. As of 2020, 49 states have active PDMPs that track patients' prescription histories of controlled substances.

The primary goal of PDMPs is to limit access to opioid medication to legitimate users only. This type of supply-side restriction is similar in spirit to other drug policies like abuse-deterrent drug formulations, lock-in programs used in Medicaid, or box warnings. From an economic perspective, theory predicts

that policies which reduce the supply of a specific drug should lead to an increase in the price of the drug, in turn lowering its quantity demanded (e.g., Reuter and Kleiman, 1986). However, with health insurance as the primary payer, this price mechanism only holds for diverted opioids on the secondary market. Moreover, substitution responses by consumers may partially undo the benefits of these policies. By increasing the cost of prescription opioid misuse, the introduction of a PDMP likely decreases consumption of opioid medication, but could induce a proportion of existing consumers to substitute toward illicit opioids like heroin, fentanyl, or other related substances.

The health risks associated with these black market opioids are large: they are more potent, more addictive, typically cheaper than prescription painkillers, are often used with non-sterile injecting equipment that can lead to infectious complications, and may vary in their concentration or in the presence of dangerous contaminants that together can substantially increase the risk of overdose. In contrast, prescription opioids are of known strength and purity and free from contaminants or adulterants. Overdose risks have also increased tremendously with the increased availability of fentanyl and the established practice of cutting heroin with cheaper fentanyl. Fentanyl is about 100 times as potent as morphine (from which heroin is derived). Due to its higher potency, fentanyl is easier to smuggle across borders and has become progressively more popular on illicit drug markets. Compared to heroin, which is typically manufactured from morphine obtained from poppy seeds, fentanyl can be synthesized from precursor chemicals with relative ease. However, since illicit drug suppliers do not have access to the same technology as professional labs, the concentration of fentanyl can vary substantially, and improper mixing techniques by drug suppliers leave "hot-spots" of fentanyl in the final product that are often lethal, especially for intravenous drug users.

The secondary goal of PDMPs is to limit potential supplier-induced demand for prescription opioids and to curb the pill mill phenomenon. Physicians can use the PDMP to query patients' treatment histories. Prescription information is automatically registered when prescriptions are dispensed. The automatic record taking and easy access to these records can potentially affect prescriber behavior. PDMPs can typically also be accessed by law enforcement, which can use the database to identify and prosecute physicians or clinics that prescribe opioids freely to patients with minimal checks. There is widespread anecdotal evidence that PDMPs lead to the closure of pill mill-type pain clinics. With a PDMP, prescribers are more likely to face professional consequences for excessive prescribing. Hence, they may be reluctant to start new patients on opioids (turning to non-opioid pain medication instead), more likely to decrease the duration/potency among current opioid patients, or perhaps both. It is a priori unclear which behavioral response will prevail. We answer this question empirically by examining prescrip-

tions at the extensive margin (new prescriptions) and intensive margin (potency and duration of existing prescriptions).

PDMP legislation and programs exhibit some degree of heterogeneity. In this paper, we examine electronic PDMPs. Electronic PDMPs are now the most common type of program (see Horwitz et al., 2018) and consist of real-time, easy-to-access query systems. We discard PDMPs that were introduced early as a registration system when real-time queries were still technically impossible (for example, the first PDMP in New York dates back to 1972). Within the class of electronic PDMPs, some states adopted "mandated" or "must-access" PDMPs, which legally require prescribers to query them under certain circumstances. We refrain from looking exclusively at must-access PDMPs, as these are only introduced in a small number of states, mostly during a limited time period (2011-2013), directly following the abuse-deterrent reformulation of OxyContin in August 2010 (Evans, Lieber, and Power, 2019). Since we have assembled a comprehensive range of data not used in previous studies, we choose to examine the effects of electronic PDMPs more generally and over a longer time period.

3 Data

For the present study, we combine information on states' laws and regulations from multiple sources, prescription claims from Blue Cross Blue Shield Axis®, drug shipment records from the DEA's Automation of Reports and Consolidated Orders System, drug consumption data from the National Survey on Drug Use and Health, street prices for prescription drugs from StreetRx, individual-level mortality data from the Centers for Disease Control and Prevention, and case-level hospitalization data from the National Inpatient Sample. Appendix Table A.1 gives a complete overview of all the state-level variables.

3.1 PDMP Implementation Data

The focus of the present paper is to examine the effect of modern (electronic) PDMPs. Modern PDMPs are electronic systems that provide direct web-based access to prescribers and dispensers. We count a program as operational if the end user (e.g., physician, pharmacist, or member of law enforcement) can query a database directly, rather than through a phone call or fax because the latter are unlikely to allow the user to access patient histories. This is a major difference from the literature, which either uses legislated start dates for any PDMP or is unspecific about their protocol in choosing a definition of a PDMP and the relative enactment date (for a general discussion on this topic, see Horwitz et al., 2018).

Our primary source of information about state laws is the detailed database collected by the Pre-

scription Drug Abuse Policy System (PDAPS). This database was created by trained legal researchers who independently reviewed – and are perpetually reviewing – state laws on PDMP operations. The database contains information about each state's PDMP regulation, the exact contents of the law and dates of enactment or modification (Davis, Pierce, and Dasgupta, 2014). We utilize the PDAPS data as a starting point and complement it with records from the states' statutes, the National Alliance for Model State Drug Laws (NAMSDL), and the Prescription Drug Monitoring Program Training and Technical Assistance Center (TTAC).

While identifying which PDMPs are electronic is relatively easy, determining exactly when these PDMPs became operational is more challenging. Complications arise because reported dates often differ and original sources for databases like PDAPS or NAMSDL are sometimes missing.[7] For the few cases where we were not able to find a reliable source for the operational date, we rely on the dates provided by Horwitz et al. (2018), who apply a research protocol similar to ours for electronic PDMPs. Our final PDMP database is consistent with the dates identified by Schuler et al. (2020) in the RAND PDMP policy data and Horwitz et al. (2018), who started working on PDMP operational dates around the same times as we did. Appendix Table A.2 provides a comprehensive overview of each state's PDMP, from legislative enactment (column 1) to active operational status of a modern electronic PDMP (column 2).

Appendix Figure A.1 illustrates the staggered introduction of PDMPs by plotting the cumulative number of operational PDMPs over time. At the beginning of our observation period, no state has an electronic PDMP, whereas towards the end of our time frame nearly all states have one. In contrast to most previous studies, we focus on a longer time frame, both before and after the introduction of a PDMP. This allows us to better assess the internal validity of the identification strategy and, at the same time, examine potential delayed and longer-term effects.

3.2 Blue Cross Blue Shield Axis®Claims Data

To analyze prescription use patterns, we access data from Blue Cross Blue Shield (BCBS) Association. Blue Cross Blue Shield affiliated insurers offer health insurance plans in all U.S. states. Together, the BCBS Association and its licensees are the largest commercial insurance group in the U.S., and the BCBS Axis® database is the largest source of commercial insurance claims. The BCBS Axis®data represent prescribing by three-quarters of active, non-federal physicians. In 2018, more than 106 million people – one in three Americans – were covered by BCBS health insurance plans.

Our sample consists of 210,051,436 observations of unique commercial enrollee-plan combina-

[7]Moreover, some states also operated pilot programs, but we take the date at which the full program became operational.

tions between 2012 to 2018 and a total of 133,042,732 opioid prescription claims.[8] Over this time period, BCBS records a total of 109.7 billion Morphine Milligram Equivalent (MME) units dispensed by providers, amounting to over 520 milligrams per enrollee-plan combination.[9]

Our data are based on the full sample of members without imposing further restrictions. To account for the fact that BCBS insurance coverage varies by state, we control for the lagged number of enrollees in all empirical models. Based on the individual claims data, we construct measures of the total number of opioid prescriptions, the total number of long-duration or high-dose prescriptions, and the total MME amount prescribed for each state per year. In the claims data, the prescription duration is recorded as number of days' supply. We compute prescription strength as the MME-per-day dose based on the recorded drug strength per dose unit, the number of units per day and the drug-specific MME conversion factor. To measure the average strength of an opioid prescription and to disentangle extensive and intensive margin effects of PDMPs on prescriber behavior, we also calculate the total number of days supplied and the average MME amount/day per claim.

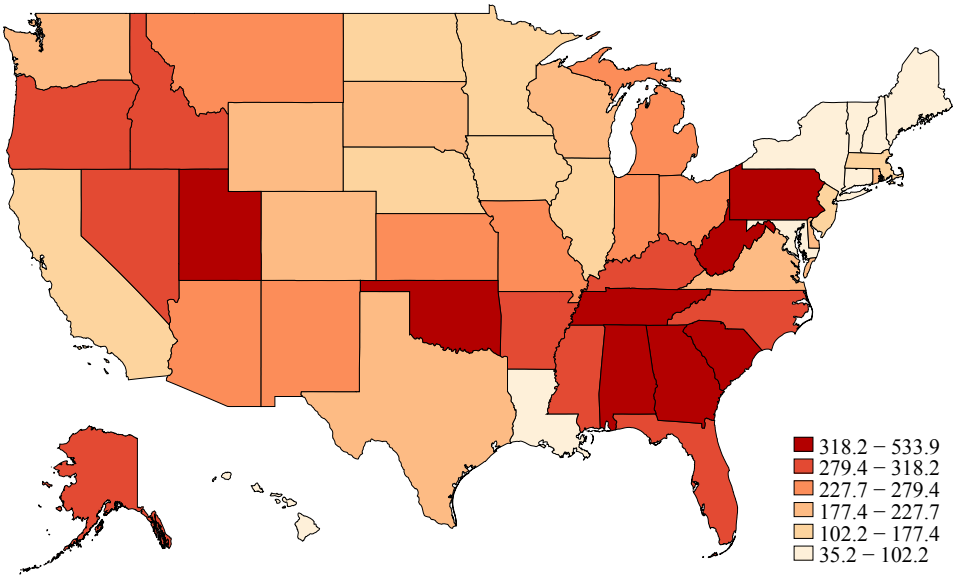
For acute pain, the Centers for Disease Control and Prevention (CDC) recommends prescribers start patients on the lowest effective dose of opioids, and opioid prescriptions above 50 MME per day should be carefully considered (CDC, 2016; Dowell, Haegerich, and Chou, 2016). Prescriptions above 50 MME/day are associated with a twofold increased overdose risk compared to a lower dose sufficient for pain relief. Prescriptions should only be issued for the expected duration of pain severe enough to require opioids, and rarely for longer than seven days. Following the CDC's guidelines, we define problematic prescriptions as either long-duration (days' supply ≥ 7) or high-dose (daily MME amount ≥ 50 mg).

To examine prescriber behavior in more detail, we distinguish between prescriptions to chronic opioid users and initial prescriptions to opioid-naive patients. We define chronicity as at least 90 days of consecutive use following established practice (e.g., Brummett et al., 2017; Martin et al., 2011). Since consecutive prescriptions are difficult to disentangle in the claims, we identify chronic use as receiving at least a 90 days' supply in a given year. To further identify chronic long-term users, we also consider higher durations (at least 180/360 days' supply) and additional potency thresholds. Following Zhu et al. (2019), we define opioid-naive patients as enrollees without any history of opioid prescribing in the last six months. Again, we differentiate between high-dose and long-duration prescriptions to examine prescriber responses in detail.

[8]Enrollees are identified through a member ID. If an individual changes insurance plan, he or she will receive a new member ID.

[9]This estimate is lower than corresponding per-individual estimates based on ARCOS data as we only observe unique individual-plan combinations, and consider a younger, commercially-enrolled population.

Figure 1: Average MME Amount Prescribed per BCBS Enrollee-Plan Combination Across the United States in 2012



Note: The map plots the average total MME amount per enrolled member-plan combination of all opioid prescriptions in the Blue Cross Blue Shield claims data for 2012. The categories are based on sextiles of the MME amount per member. Data are from the Blue Cross Blue Shield Axis® database.

To investigate patient responses to the supply restrictions, we also develop measures of doctor shopping. Similar to Rose et al. (2018), we define doctor shopping as individuals who receive prescriptions from at least three different prescribers within a 3-month window. To examine whether consumers attempt to evade detection by the PDMP in response to the policy, we differentiate between in-state and out-of-state doctor shopping. Out-of-state doctor shopping occurs when individuals who engage in doctor shopping acquire one or more of their prescriptions from out-of-state prescribers.

We find that in 2018, 21% of all opioid prescriptions exceeded the CDC's recommendation for initial prescriptions of 50 MME per day. These high-strength prescriptions are not restricted to a small number of chronic-use individuals: Across the U.S., 21% of enrollees who received an opioid prescription received a prescription strength above 50 MME at least once, and 20% of initial prescriptions to opioid-naive patients exceeded the 50 MME limit. The problem of excessive opioid prescribing is widespread across the United States: In 33 states, more than one in five prescriptions exceeded the CDC's guideline, and in no state was the rate lower than one in ten. Figure 1 shows that prescription strength, while excessive in some states, is universally high across the U.S.

Patterns of opioid usage are highly skewed. We find that about 1% of enrollees are chronic opioid users. These users account for a disproportionate share of opioid consumption. Consistently, about 50% of all opioid prescriptions are filled by chronic users, and they account for 85% of the total MME-amount consumed.

3.3 DEA Automation of Reports and Consolidated Orders System

To further investigate the effectiveness of PDMPs in reducing opioid misuse and prescriptions, we utilize data from the DEA's Automation of Reports and Consolidated Orders System (ARCOS). ARCOS is a drug reporting system which monitors shipments of controlled substances from the manufacturer to the dispenser – retailers, practitioners and hospitals. Under federal law, manufacturers and distributors must report all transactions of controlled substances to the DEA. The ARCOS database tracks these transactions. The database was partially published by the Washington Post after a protective order was lifted following legal action. The database is available from 2006 and 2014 and covers nearly 500 million transactions. We focus on shipments of two of the most prominent opioid medications, oxycodone and hydrocodone, and distinguish between shipments to pharmacies and to practitioners.

3.4 National Survey on Drug Use and Health

To investigate drug consumption and user behavior, we utilize data from the National Survey on Drug Use and Health (NSDUH), conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA). The NSDUH is a nationally representative, biannual household survey and the largest source of information on drug use patterns and user health available in the United States. The survey is available in two-year waves from 2002-2003 to 2017-2018, with a structural break in some questions in 2014. The data contain detailed information on the use of pain medication, heroin and other drugs. Respondents are asked whether they ever used a specific drug. This facilitates analysis of incidence, since changes in the rate of "ever use" come about only from first-time use. The outcomes we focus on are the overall use of pain relievers, non-medical use of pain relievers ("not directed by a doctor"), overall and non-medical use of sedatives or tranquilizers, and use of heroin and benzodiazepines specifically. Benzodiazepines are frequently misused and one of the most common drugs associated with polysubstance use of opioids (Jones, Mogali, and Comer, 2012; Sun et al., 2017). We also investigate whether respondents received treatment for substance misuse at a facility. For the substance use outcomes, we are focusing on first-time use ('ever used'), because data on past-year use is not consistently available for all outcomes over the analysis time frame. This implies that we are picking up effects on incidence (new users initiating drug use) rather than prevalence.

Regrettably, access to the restricted individual-level NSDUH data is currently not possible. We obtain the state-level data from the online data portal, which restricts access to variables that have low case counts in some states. The NSDUH data is representative of persons aged 12 and over in the civilian noninstitutionalized population in each state. State estimates are obtained using a survey-weighted hi-

erarchical Bayes methodology. We only rely on data for which a balanced state-year panel is available. This prevents us from studying outcomes for other specific substances, drug dependence and treatment admissions in more detail.[10]

Since the NSDUH relies on self-reported information on drug use, underreporting of drug use is a potential issue. The NSDUH assures survey participants of a confidential environment and safety from criminal prosecution. A small-sample validation study by Harrell (1997) shows that reporting of illicit drug use was accurate in 68-96% of cases, depending on drug type. As noted by Alpert, Powell, and Pacula (2018) who also use the NSDUH data, unless underreporting is systematically related to state geography, it will not confound the treatment effect estimates.

3.5 StreetRx: Street prices for Illicit and Prescription Drugs

We obtain data on street prices for prescription drugs using crowd-sourced data from streetrx.com. StreetRx is a review site that aggregates prices and ratings for illicit street purchases of prescription drugs. Users enter the specific drug they purchased, where they bought it and how much they paid for it. The site also lists the prices for a specific substance and dosage paid within the last two weeks so users can get a reference price for their area. We exclude all prices associated with bulk purchases from the data. We then measure both the number of purchases registered, the prices paid, and the price per mg for commonly prescribed opioids. Since PDMPs potentially affect both the demand for opioids and the supply of legal prescription opioids diverted to black markets, we use the StreetRx data to investigate whether PDMPs ultimately affect the equilibrium prices paid for opioids on the street.

3.6 National Vital Statistics System Individual Mortality Data

Mortality data are made available by the CDC through the National Vital Statistics System (NVSS). Death certificates are coded by the states and provided to the National Center for Health Statistics, the data center of the CDC. Each death certificate records the main cause of death, additional contributing causes, and demographic information. Causes of death are coded according to the ninth revision of the World Health Organization's (WHO) International Classification of Diseases (ICD-9) until 1998 and according to the tenth revision since 1999 (ICD-10). This transition complicates our analysis because,

[10] Access to the individual-level has been restricted by SAMHSA. A new, restricted-use data portal was under construction since 2016 and became available in 2019. The new portal provides aggregated location-specific information, but requests for many variables are prohibited due to a limited number of respondents in some data cells. SAMHSA migrated the restricted-use microdata to the National Center for Health Statistics for use at their Federal Statistical Research Data Centers. The NSDUH microdata was unavailable for our study, both due to the ongoing migration and the subsequent access restriction due to the COVID-19 pandemic. Other researchers have been facing the same issue with the NSDUH data and use the limited available state-level information in lieu of alternatives (Alpert, Powell, and Pacula, 2018).

while we can disentangle the cause of death by opioid type in the ICD-10 data, this is not possible with the ICD-9 version. For this reason, we analyze opioid-related mortality in aggregate for the 1993-2017 period while we examine mortality by opioid type from 1999 onward.

Identifying opioid deaths with ICD-9 classification is straightforward, because only two dedicated categories exist: "opiates and related narcotics" for poisonings and "opioid type dependence" for drug misuse. Our focus in this paper is primarily on poisonings, which refer to overdose deaths. To identify opioid-related deaths in the ICD-10 data, we proceed as follows. First, we select the underlying cause of death, which in our case is drug induced (ICD-10 X40-44, X60-64, X85, Y10-14).[11] Second, among deaths with drug overdose as the underlying cause, the type of opioid is indicated by the following ICD-10 multiple cause-of-death codes: opium (T40.0), heroin (T40.1), natural and semi-synthetic opioids (T40.2), methadone (T40.3), synthetic opioids other than methadone (T40.4), other and unspecified narcotics (T40.6). In addition to mortality related to opioid poisonings, we also analyze mortality associated with opioid dependence syndrome caused by repeated substance use (F11.2).

The disambiguation by drug category beginning in 1999 allows us to separate mortality due to common prescription opioids and illicit drugs. Popular prescription painkillers like oxycodone (e.g., OxyContin, Percocet), hydrocodone (Vicodin) and hydromorphon (Dilaudid) are all semi-synthetic. Similarly, heroin is listed in its own category. Fentanyl, often illicitly sold as heroin, is the most common fully synthetic opioid. Since different causes of death are not mutually exclusive and some deaths may involve more than one type of drug, our estimates reflect the presence of a drug. Although we cannot attribute mortality to a single cause if multiple drugs are mentioned on the death certificate, the data allow analysis of substitution patterns across different substances.

Since we rely on drug-specific mortality information from the NVSS, it is important that reports for causes of death based on individual death certificates are reliable. Reporting of multiple drugs and causes of death has improved over time (Ruhm, 2016). Concerns about the use of drug-specific mortality data have emerged mostly regarding the reliability of the county-level data (Jones et al., 2019; McClellan, 2019), which we do not use. Although variations in reporting of multiple causes may lead us to understate the effect of supply-side restrictions, it is unlikely that improvements in reporting are directly associated with PDMP introduction.

We aggregate the data at the state level and calculate mortality rates as deaths per 100,000 population. The dependent variables measuring opioid-related mortality are divided in two groups. First, we consider the entire time period (1993-2017) and mix ICD-9 and ICD-10 classifications if, for a given ICD-9 code,

[11] For robustness, we also perform the analysis for all-cause mortality, with no tangible impact on the results.

an ICD-10 analogue exists. Second, we consider the shorter – yet more disaggregated by drug type – ICD-10 period (1999-2017).

3.7 National Inpatient Sample

The National Inpatient Sample (NIS) is a database developed for the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality. The NIS is the largest publicly available all-payer inpatient health care database in the United States, yielding national estimates of hospital inpatient stays. The NIS is the only nationwide hospital database with information on all types of patients, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. This broad inclusion criteria is a major advantage of our study compared to the prior literature, which focuses on Medicare patients (Buchmueller and Carey, 2018), patients admitted in treatment facilities for substance misuse (Grecu, Dave, and Saffer, 2019), or disabled adults in Medicare (Meara et al., 2016), because it increases the external validity of our results.

NIS data are available from 1988 through 2015, and the number of states participating in the NIS has grown from 8 in the first year to 46, plus the District of Columbia, at present. Designed to approximate a 20% sample of U.S. community hospitals each year, the NIS contains data from more than 7 million hospital stays each year. Although the NIS data are available until 2015, all geographical identifiers have been removed since 2012. We also drop the first five years of data, because the NIS was re-designed and improved in 1993. The only sample restriction we impose on the NIS data is to exclude hospitals that appear in the data only twice or less. In sum, the estimation sample covers the years 1993-2011 and comprises 16,369 hospital-year observations from 2,973 hospitals.

For each sampled hospital, we observe the universe of hospitalizations in a given year. For each patient admitted, we know the admission type (emergency, urgent, or elective), the primary diagnosis, and all medical and surgical procedures administered. Diagnoses and procedures are coded according to the ICD-9-CM classification, which allows disambiguation of hospitalizations by drug class.[12] The NIS also registers patient characteristics (gender, age, and race), the length of stay (in days), total hospital charges, and the expected primary payer (Medicare, Medicaid, private insurance, self-pay, or other).

Given that the dataset is a hospital panel, the dependent variables are expressed in counts per hospital. For example, for a given hospital we observe how many opioid poisonings occur in a certain year, using information extracted directly from the primary diagnosis. For each poisoning by opiates and re-

[12]The International Classification of Diseases, Ninth Revision, *Clinical Modification* (ICD-9-CM) is the official classification system of diagnoses and procedures associated with hospital utilization in the United States and based on the World Health Organization's ICD-9 system.

lated narcotics, we know the opioid type according to the following categories: opium alkaloids, heroin, methadone, or other. The category "opium alkaloids" includes all derivatives of thebaine, the main alkaloid extracted from *Papaver bracteatum* (Iranian poppy) and converted industrially into a variety of narcotics, including hydrocodone, hydromorphone, oxycodone, oxymorphone, nalbuphine, naloxone, naltrexone, buprenorphine, and etorphine. In the category "other" we find the following opiates: codeine, meperidine, and morphine. For the analyses, we focus on total opioid poisonings, along with the following three sub-categories: opioid medication, heroin, and all others. While opioid medication includes all prescription opioids used as analgesics, heroin consists exclusively of heroin poisonings. The third category is a residual category, which includes methadone, codeine and other narcotic analgesics.

Our main outcomes are opioid-related hospitalizations, total charges and length of stay, for all admissions and the subset of emergency admissions. For heterogeneity analyses we further stratify by gender and race.

4 Empirical Strategy

The principal analysis tests the impact of the introduction of electronic PDMPs on opioid prescriptions, opioid shipments, opioid consumption, opioid-related mortality, and hospitalizations due to opioid poisonings. We specify the following regression model:

$$y_{it} = \exp\left(\alpha_i + \mu_t + \beta\,\text{PDMP}_{it} + X_{it}'\gamma + \varepsilon_{it}\right)\ , \tag{1}$$

where y_{it} is the outcome of interest in unit i (state or hospital) in year t, α_i are unit fixed effects, μ_t are time fixed effects, and PDMP_{it} is an indicator of whether a state has an operational electronic PDMP in a given year. In some models, we include a set of time-varying characteristics (state census population, unemployment rate, per-capita real personal income, per capita real GDP, and hospital size). Throughout the analysis, standard errors are clustered at the state (hospital) level (Griffin et al., 2020). We apply randomization inference to obtain valid p-values whenever we observe the full population, because in such cases the remaining uncertainty is design-based and not sampling-based. Because this inferential method relies on nonparametric tests, no assumptions about the distribution of the error terms are needed and the distribution of the test statistic may be unknown (Fisher, 1935; Hess, 2017; Young, 2019).

We choose the exponential specification because of the non-negative nature of the dependent variables and the (potentially) multiplicative structure of the error terms (α_i, μ_t, and ε_{it}). We estimate equation (1) using the Poisson fixed-effect estimator, which has been shown to perform better than a linear

model when the dependent variable is non-negative (Santos Silva and Tenreyro, 2006), has many zeros (Santos Silva and Tenreyro, 2011), or has multiplicative unobserved components (Wooldridge, 1999). Note that the Poisson fixed-effect estimator does not require the dependent variable to be an integer and is also consistent in the presence of over-dispersion; no additional distributional assumption is required for consistency (Fally, 2015). The estimator is a quasi-maximum likelihood estimator; i.e., it is consistent if the mean is correctly specified (like OLS) and does not require the error term to be Poisson-distributed. Another attractive feature of the Poisson estimator is that, even though non-linear, it features constant relative effects that can be intuitively interpreted as semi-elasticities. Finally, we follow Ciani and Fisher (2019) who suggest using the non-transformed outcome in difference-in-difference models and estimate an exponential model by Poisson Pseudo Maximum Likelihood, which does not require statistical independence of the error term.[13]

The main identifying assumption is that the treated and the control states exhibit parallel time trends in outcomes before the introduction of an electronic PDMP. In the current setting this assumption requires that prescriptions, mortality rates, and hospitalizations in states with a PDMP would have evolved in the same way as the control states in the absence of a PDMP. Although the parallel-trend assumption cannot be tested directly, we perform three validity checks.

First, we examine the evolution of all outcomes under analysis before the introduction of PDMPs. To do so, we regress the lagged outcomes on the adoption of a PDMP. This exercise will reveal any policy endogeneity or diverging trends in the years leading to a PDMP introduction. The results are shown in the Appendix (tables A.3, A.4, A.5, A.6, A.7 and A.8) where we gradually include up to three lagged years for all outcomes under analysis. Out of 91 models estimated, three F-tests on the lags are statistically significant at conventional levels (one at the 10% level and two at the 5% level), no more than what is expected by chance. We thus conclude that pre-PDMP trends in outcomes did not cause the introduction of a PDMP.

Second, to further analyze potential violations of the parallel trends assumption, we conduct an event study. Event-study approaches essentially estimate the treatment effect for each year before, during, and after the introduction of an electronic PDMP. While we do not discuss the results from the event-study approach here (this is done extensively in the results section), we find no significant effect of a PDMP before its actual introduction for all outcomes under analysis.

Third, we employ a series of methodological extensions for difference-indifference models with

[13] We have tested the sensitivity of the results to the model choice (linear vs. log-linear Poisson), weighting and other modeling parameters (see Griffin et al., 2020) and verified that our results are qualitatively unchanged by variations. Results for all main specifications in the paper using a conventional linear model are reported in Appendix B.

multiple time periods proposed by Callaway and Sant'Anna (2020). These extensions consist of both robustness checks using a doubly-robust estimand for the aggregate treatment effect on the treated and decomposition of the average treatment effect on the treated by group (where groups are defined by the timing of PDMP adoption). Since this third approach is based on a linear model, we log-transform the outcome (or use the inverse hyperbolic sine transformation in the presence of zeros). We defer the full discussion of these extensions to the results section, but preview here that the Callaway and Sant'Anna (2020) approach yields similar results as our main estimation strategy.

To address potential confounding by alternative state policies implemented during our analysis period, we also test the robustness of our main estimates to controlling for other state prescription drug policies (prescription duration limits, pill mill regulations, good samaritan and naloxone access laws) as well as laws governing access to medical and recreational marijuana through dispensaries. Our estimates are unchanged when adding controls for these time-varying state policies.

Overall, the tests indicate that our identification strategy is valid. Note, however, that not finding any anticipation effects or diverging trends before a PDMP becomes operational is not completely surprising. The exact date of first user access to a PDMP is difficult to anticipate, because user access likely depends on many factors (e.g., funding, pilot programs, system architecture) that are hidden from patients and people dependent on opioids, and interact in complex ways that are difficult to predict.

5 Results

This section presents our results in three parts. The first part investigates prescriber behavior by focusing on prescriptions and drug shipments to pharmacies. The second part examines patient behavior from doctor shopping to illicit opioid consumption and drug substitution. The third part deals with the health consequences following the introduction of electronic PDMPs. The core of the analysis revolves around mortality and hospital admissions, along with a brief case study of Florida's pills mills and an investigation of the dynamic health effects.

5.1 Prescriber Responses

5.1.1 Prescriptions and Proliferation of Opioids

In the first step, we investigate whether PDMPs are effective in achieving their desired aim: reducing the proliferation of opioid prescription drugs by changing providers' prescribing behavior. The results are shown in Table 1, panel A. We first look at the number of all opioid prescription claims registered in the

BCBS data. We find that introducing a PDMP reduces the number of enrollees who receive an opioid prescription by 13.5%. Similarly, the total number of opioid prescriptions (any type) is reduced by about 13.7%. Next, we look at the number of high-dosage (MME/day $\geq$ 50) and long-duration (days' supply $\geq$ 7) opioid prescriptions. These prescriptions are associated with high risks of addiction and overdose. We find that the number of enrollees with high-dosage prescriptions is reduced by about 13.7%, and the number of prescriptions itself by 12.7%. In the last two columns, we look at very high-dosage prescriptions (MME/day $\geq$ 90) and long-duration prescriptions. These prescriptions are associated with extremely high risks of addiction and overdose, and the CDC recommends increasing the daily dosage above 90 MME/day only in exceptional cases. Again, we find that the number of enrollees with such high prescriptions is reduced by 12.6% and the number of prescriptions by 12.4%.

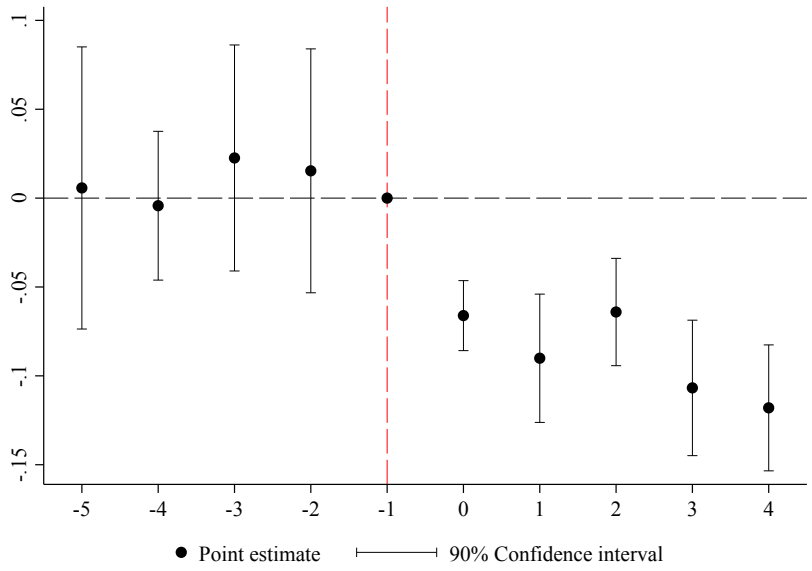
These results differ from those by Buchmueller and Carey (2018), who find no effect of PDMPs on prescriptions. The most likely explanation for this difference in findings is the difference in study population: we analyze claims from non-elderly enrollees in private health insurance plans, whereas Buchmueller and Carey (2018) analyze claims from enrollees in Medicare Part D. Supply-side restrictions may simply have more bite among the non-elderly, possibly because of more elastic demand among the non-elderly, differential provider responses to monitoring, or a mixture of both.

Table 1: The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions

	(1)	(2)	(3)	(4)	(5)	(6)
	(A) PRESCRIPTIONS					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
	Enrollees	Prescriptions	Enrollees	Prescriptions	Enrollees	Prescriptions
PDMP	–0.135	–0.137	–0.137	–0.127	–0.126	–0.124
	(0.035)	(0.032)	(0.039)	(0.033)	(0.043)	(0.034)
	[0.000]	[0.000]	[0.001]	[0.000]	[0.004]	[0.000]
	(B) DOSAGE					
	Total amount			Per-claim average		
	Dosage in MME	Duration in days	Strength in MME/day	Dosage in MME	Duration in days	Strength in MME/day
PDMP	–0.108	–0.128	–0.167	–0.031	0.009	–0.031
	(0.057)	(0.032)	(0.064)	(0.064)	(0.009)	(0.044)
	[0.058]	[0.000]	[0.009]	[0.628]	[0.335]	[0.491]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51
Observations	306	306	306	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Data are from the Blue Cross Blue Shield Axis® database.

Figure 2: Event Study: Opioid User Rate



Note: Results from Poisson regression, with standard errors clustered at the state level. Data are from the Blue Cross Blue Shield Axis® database.

Next, we study how prescribers adjust prescriptions by looking at different dosage measures and how they are affected by the introduction of a PDMP (Table 1, panel B). We find a large 10.8% reduction in the total MME amount prescribed (column 1), and similarly large reductions for total days' supply prescribed and total prescription strength (12.8% and 16.7%, respectively).

In columns 4-6, we study the MME dosage amount prescribed per claim, the average length of days' supply and the daily MME amount prescribed per claim. These outcomes can be seen as measures of the potency of an individual prescription and allow further insights into how practitioners adjust their prescribing behavior in response to PDMPs. For all three measures, the estimates are indistinguishable from zero. This suggests that practitioners do not adjust the total amount of opioids prescribed, nor the duration of their prescriptions. Together, this implies that practitioners respond only on the extensive margin, reducing the number of prescriptions, but not adjusting the strength of individual prescriptions if they decide to prescribe opioids. This finding is also confirmed by the fact that high-dose/long-duration prescriptions are reduced by about the same relative amount as overall prescriptions. A recent study by (Alpert, Dykstra, and Jacobson, 2020) for Kentucky reports the same type of prescriber response.

We also analyze the change in prescriptions using an event study. In Figure 2, we confirm our finding that prescriptions are permanently lowered following PDMP introduction. The number of opioid users decreases substantially immediately following the operationalizing of a PDMP, and remains permanently lowered. Note that the absence of any pre-trend effects in Figure 2 supports the internal validity of our identification strategy.

When we distinguish by type of medication (see Appendix Table A.9), we find that reductions are particularly large for oxycodone and hydrocodone. We study these substances in more detail in the next section. In comparison, effects are smaller for medications that are less potent (codeine and tramadol), less commonly prescribed (oxymorphone, morphine, and fentanyl), or for medication treatment of OUD or severe chronic pain only (buprenorphine and methadone).[14]

Before proceeding with the remainder of the results, we discuss alternative estimation methods and the robustness of our results to recent methodological extensions in the difference-in-differences literature (e.g., Callaway and Sant'Anna, 2020; De Chaisemartin and d'Haultfoeuille, 2020; Goodman-Bacon, 2021). We follow the approach by Callaway and Sant'Anna (2020) and separate the analysis in two steps. First, we rely on nonparametric identification of group-time average treatment effects, which we aggregate in the second step to form summary measures of the causal effects. For the first step, we apply the doubly-robust difference-in-differences estimator developed by Sant'Anna and Zhao (2020) and extended to the multiple-period case by Callaway and Sant'Anna (2020). This approach yields a disaggregated causal parameter that is called the group-time average treatment effect, i.e., the average treatment effect for group g at time t, where a group is defined by the time period when states introduce their PDMP. In the second step, we aggregate the group-time estimates into an overall average treatment effect on the treated, which we can compare to our main estimates.

Appendix Table A.10 shows the disaggregated effects, replicating the structure of Table 1. States are divided in three groups as follows: early PDMP adopters, intermediate PDMP adopters, and late PDMP adopters. In general, we observe that effects are significant primarily for early and intermediate adopters. In terms of magnitude, the largest effects are found among early adopters. Appendix Table A.11 presents the overall estimate of the group-time effects. We find that the aggregated effects are consistent with both the exponential model (Table 1) and the linear model (Appendix Table B.1). The new estimates are actually slightly larger than our main estimates. In sum, we do not find large differences in the results when using an alternative difference-in-differences estimator. However, for the interpretation of the results, it is important to underscore that primarily early PDMP adopters are driving the effects for prescriptions. As shown in Table A.13, the estimates are also not driven by other state policies.

[14] Since methadone for medication treatment is only dispensed through licensed, SAMHSA-certified opioid treatment programs, the prescriptions for methadone we observe in our data are exclusively for non-OUD treatments and most likely issued for chronic pain.

Table 2: The Effect of Prescription Drug Monitoring Programs on Drug Shipments (Oxycodone/Hydrocodone)

	MANUFACTURER DRUG ORDERS BY ENTITY				
	(1) Total shipments	(2) Shipments to pharmacies	(3) Shipments to retail pharmacies	(4) Shipments to chain pharmacies	(5) Shipments to practitioners
PDMP	–0.063	–0.057	–0.107	–0.030	–0.804
	(0.026)	(0.023)	(0.045)	(0.015)	(0.263)
	[0.000]	[0.000]	[0.000]	[0.000]	[0.000]
Covariates	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51
Observations	459	459	459	459	459

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Shipments are based on the DEA's Automation of Reports and Consolidates Orders System data, accessed using the Washington Post's ARCOS API (`https://github.com/wpinvestigative/arcos-api`).

5.1.2 Scheduled Drug Orders and Manufacturer Shipments to Pharmacies

The results for prescriptions are confirmed when we look at the effect of PDMPs on shipments of scheduled drugs (Table 2). All shipments of scheduled drugs face mandatory registration with the DEA, allowing us to track shipments from manufacturers to pharmacies and practitioners. We find that total shipments of oxycodone and hydrocodone are reduced by 6.3%. Similarly, shipments to pharmacies are reduced by 5.7%. Distinguishing between retail and chain pharmacies, we find that smaller retail pharmacies are more affected by the policy change and reduce their orders to a larger degree. Chain pharmacies, which account for more than 60% of shipments, are less affected and only reduce their order volume by about 3%. Notably, direct dispensing by practitioners is most affected as shipments to practitioners fall by 80% following the introduction of a PDMP. However, direct shipments to practitioners only account for about 1% of all shipments.

The effect size of the reduction in shipments is smaller than that of prescriptions for three reasons. First, the units of measurement are different: while the BCBS data is based on prescriptions, ARCOS measures number of pills. Second, the BCBS claims data covers the full spectrum of opioid medication, while ARCOS considers only two major types of opioid medication (oxycodone and hydrocodone). Third, ARCOS covers the full population, whereas BCBS covers a sub-population of commercially-insured individuals. This point is most relevant in light of the generally smaller estimates in the literature for non-commercially insured populations.

5.1.3 Prescriptions to Chronic Opioid Users and Opioid-Naive Patients

Two groups of users are of particular concern from a policy perspective: opioid-naive patients who receive first-time prescriptions, and chronic users who have received high doses of opioids for a longer period. On the one hand, it is important to limit opioid-naive patients' exposure due to the large potential for misuse and harmful side effects of opioids, and prescribe opioids only in cases where their use is clearly indicated and no alternative treatment is available.[15] On the other hand, chronic users, who may already be suffering from side-effects of long-term opioid use like physical and psychological dependence, risk getting cut off from their supply of medication. The concern is that abrupt discontinuation or reduction in opioid treatment precipitates withdrawal, which is extremely distressing to patients. Indeed, in select populations the risk of overdose or suicide is increased following discontinuation of chronic opioid therapy (Oliva et al., 2020). Rather than ceasing prescribing completely, physicians could start users on opioid dependence treatment or help them taper off.

In Table 3, we study how physicians adjust their prescribing to these two patient groups. In panel A, we estimate the effect of PDMPs on initial use. We assess first-time prescriptions (columns 1-2) and dosage (column 3). Since initial prescriptions are unique, reductions in prescriptions correspond to reductions in users. We find large effects: prescriptions to opioid-naive patients are reduced by about 22.5%. High-dosage prescriptions are reduced even more, by about 25%. We find a similarly large reduction of about 25% for the dosage amount. This finding mirrors the conclusion of a recent paper by Sacks et al. (2021), who find that must-access PDMPs limit exposure to opioids for new users.

Next, we look at chronic opioid users (panel B). Prescriptions to these patients make up the bulk of all opioids dispensed. Our results indicate that the number of chronic users exceeding 90 days' supply or more is reduced by 12.4%, a magnitude comparable to our main estimate. We then extend the conventional 90-day chronic use definition to specifically estimate effects on long-term users with prescriptions exceeding 180 and 360 days' supply in total. These patients are more likely to have developed opioid dependence. Our results suggest that the reduction in the number of chronic users is stable at about 12%-13%. The results for prescriptions (not reported) indicate a similar reduction. When considering dosage (panel C), we again find a similar reduction. The total MME amount dispensed to chronic users falls by about 10%, and up to 13% when we consider chronic users who have previously received more than a full year's supply of opioids.

To investigate prescribing behavior, we again consider effects on the individual dosage amount. As

[15] For this reason, opioids were mostly used in inpatient settings and take-home prescriptions of opioids were limited until the early 1990s. Although opioids are not first-line treatment for chronic pain, chronic opioid treatment can be appropriate in select cases where alternative pain therapies do not achieve an acceptable level of functioning or quality of life.

Table 3: The Effect of Prescription Drug Monitoring Programs on Initial and Long-Duration Opioid Prescriptions

(A) Initial Opioid Users and Dosage

	(1) Total enrollees/ prescriptions	(2) Enrollees with MME $\geq$ 50 mg prescriptions	(3) MME amount
PDMP	–0.225	–0.246	–0.255
	(0.065)	(0.080)	(0.087)
	[0.001]	[0.002]	[0.003]

(B) Chronic Opioid Users

	Enrollees with prescriptions for more than 90 days	Enrollees with prescriptions for more than 180 days	Enrollees with prescriptions for more than 360 days
PDMP	–0.124	–0.118	–0.132
	(0.032)	(0.031)	(0.033)
	[0.000]	[0.000]	[0.000]

(C) Chronic Opioid Users: Total Dosage

	MME for enrollees with prior duration $\geq$ 90 days	MME for enrollees with prior duration $\geq$ 180 days	MME for enrollees with prior duration $\geq$ 360 days
PDMP	–0.097	–0.090	–0.136
	(0.060)	(0.062)	(0.040)
	[0.105]	[0.146]	[0.001]

(D) Chronic Opioid Users: Individual Dosage

	Per-claim MME, prior duration $\geq$ 90 days	Per-claim MME, prior duration $\geq$ 180 days	Per-claim MME, prior duration $\geq$ 360 days
PDMP	–0.025	–0.017	0.037
	(0.076)	(0.083)	(0.031)
	[0.736]	[0.840]	[0.216]
Covariates	Yes	Yes	Yes
State FE	Yes	Yes	Yes
Time FE	Yes	Yes	Yes
States	51	51	51
Observations	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Data are from the Blue Cross Blue Shield Axis® database.

before, we do not find any significant reductions in the dosage amount per claim, indicating that physicians do not taper off chronic users by gradually reducing prescription amounts, but instead cut off some patients altogether. This abrupt discontinuation of chronic opioid therapy is concerning given its potentially harmful effects on patients, as well as the possibility that it could induce substitution to illicit drugs.

5.2 Patient Responses

5.2.1 Evasion and Doctor Shopping

One potential patient response to the supply restriction is to seek prescriptions from multiple doctors, or "doctor shopping." Doctor shopping may also partially explain the results in the previous section: with a PDMP, physicians discover that their patients are already receiving opioid prescriptions from other providers and then refuse to prescribe further. In light of this, obtaining further prescriptions from other in-state physicians may be futile when a PDMP is in place. For this reason, we explicitly investigate whether enrollees engage in doctor shopping behavior with out-of-state physicians. We measure doctor shopping using the number of patients who receive prescriptions from at least three different providers, differentiating between prescriptions from in-state and out-of-state providers.

Since the net value of visiting out-of-state providers is diminished when neighboring states also have PDMPs, we adjust our main specification to interact the PDMP indicator with the percent of neighboring states lacking a PDMP in a given year. Table 4 shows that PDMP introduction reduces the number of patients with three or more *in-state* prescribers within a three-month window by 16.5% (column 2), and this effect is not counteracted by neighboring states without PDMPs. The number of patients who receive at least 2 or at least 3 prescriptions from out-of-state prescribers also falls after a PDMP is introduced, however this effect is partially offset in proportion to the percent of neighboring states without PDMPs (columns 4-5). These estimates point to a substantial amount of evasion that depends on the monitoring environment in neighboring states. If we extend the time frame and consider prescriptions from multiple providers within the last six months, we find the same pattern of increases in out-of-state doctor shopping. Patients whose prescriptions are abruptly discontinued try to obtain prescriptions by visiting multiple other health care providers out-of-state.

5.2.2 Consumption and Drug Substitution

If individuals who have developed opioid dependence or who misuse opioids are unable to obtain sufficient amounts of opioids via legal prescriptions, an option is to buy diverted prescription drugs or other

Table 4: The Effect of Prescription Drug Monitoring Programs on Doctor Shopping

	USERS WITH MULTIPLE PRESCRIBERS WITHIN 3 MONTHS				
	(1)	(2)	(3)	(4)	(5)
	3+ providers	3+ providers all in-state	3+ providers 1+ out-of-state	3+ providers 2+ out-of-state	3+ providers 3+ out-of-state
PDMP	–0.196	–0.165	–0.281	–0.236	–0.187
	(0.049)	(0.050)	(0.055)	(0.048)	(0.033)
	[0.000]	[0.001]	[0.000]	[0.000]	[0.000]
% of neighbor states w/o PDMP	–0.009	–0.009	–0.013	–0.010	–0.010
	(0.010)	(0.010)	(0.008)	(0.005)	(0.004)
	[0.364]	[0.368]	[0.127]	[0.030]	[0.010]
(PDMP)*(% of neighbor states w/o PDMP)	0.010	0.010	0.012	0.009	0.009
	(0.010)	(0.010)	(0.008)	(0.004)	(0.004)
	[0.304]	[0.319]	[0.133]	[0.042]	[0.014]
Covariates	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51
Observations	306	306	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Data are from the Blue Cross Blue Shield Axis® database.

illicit opioids on secondary markets. We use the NSDUH to investigate consumer behavior in response to the supply side restriction. The NSDUH elicits information on whether respondents have used pain relievers without a prescription from a doctor, and whether they use heroin or other types of drugs. Since the market for diverted pain medication dries up quickly as more states introduce PDMPs and curb loose prescribing practices, heroin constitutes a cheaper alternative. We find that the number of people who use pain killers without having a prescription increases by 3% (Table 5, column 1).

Drug substitution occurs frequently: the number of people who report using heroin increases by 8.5% (column 2). Drug users also appear to use other substances that are not direct substitutes for opioids. Non-medical use of sedatives or tranquilizers rises by 5.2%. This is largely driven by an increase in use of benzodiazepines, another highly addictive class of medication (columns 3-4). Even though illicit drug use increases for a wide range of substances, there is no increase in the number of people who seek or receive treatment for drug use (column 5).

While these effects are substantial, the relative increases are smaller than the relative reductions in prescriptions. One caveat is that some patients who were previously receiving legitimate opioid prescriptions may have already been using illicit drugs – the NSDUH asks respondents whether they "ever used" a specific drug, effectively measuring incidence instead of prevalence. In light of this, the smaller estimate for prescription drug misuse compared to heroin suggests that pre-PDMP drug misuse was mostly limited to prescription opioids and not heroin, and that PDMPs increase the likelihood of switching to

Table 5: The Effect of Prescription Drug Monitoring Programs on Opioid Consumption

	Respondents drug use by substance				
	(1)	(2)	(3)	(4)	(5)
	Ever used pain relievers w/o prescription	Ever used heroin	Ever used sedatives or tranquilizers w/o prescription	Ever used benzodiazepines	Received treatment for illicit drug use
PDMP	0.029	0.085	0.052	0.053	–0.046
	(0.013)	(0.051)	(0.021)	(0.023)	(0.052)
	[0.030]	[0.094]	[0.016]	[0.019]	[0.378]
Covariates	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51
Observations	306	357	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Survey on Drug Use and Health (NSDUH). The sample size differs for heroin compared to the other outcomes due to data availability for one additional survey year.

Heroin. As previously, these results are invariant to controlling for other time-varying state policies (see Appendix Table A.14).

The results for drug consumption also permit inference on the rate of substitution between heroin and prescription drugs, $\Delta_{H,P} = \mathrm{d}q_H/\mathrm{d}q_P$. Based on our relative effects, we first compute the elasticity of substitution between heroin and prescription drugs, $\varepsilon_{H,P}$. Due to the differences in the population base, the magnitude of the elasticity itself is difficult to interpret. We adjust the elasticity by base population to compute the absolute rate of substitution, $\Delta_{H,P} = \varepsilon_{H,P}\, q_H/q_P$. Since we observe changes in consumption of prescription drugs for the privately insured only, but adoption of heroin for the general population, we can only bound the elasticity (and the rate of substitution in turn). We apply the law of total expectation to the elasticity, decomposing the effect on prescription drug consumption. This yields

$$\Delta_{H,P} = \frac{\frac{\partial q_{\mathrm{H}}}{q_{\mathrm{H}}}}{\frac{\partial q_{\mathrm{P}}}{q_{\mathrm{P}}}} \frac{q_{\mathrm{H}}}{q_{\mathrm{P}}} = \frac{\frac{\partial q_{\mathrm{H}}}{q_{\mathrm{H}}}}{\mathbb{P}(\text{Private}) \frac{\partial q_{\mathrm{P}}^{\text{Private}}}{q_{\mathrm{P}}^{\text{Private}}} + [1 - \mathbb{P}(\text{Private})] \frac{\partial q_{\mathrm{P}}^{\text{Public}}}{q_{\mathrm{P}}^{\text{Public}}}} \frac{q_{\mathrm{H}}}{q_{\mathrm{P}}}. \tag{2}$$

We insert the known population shares for the privately insured and non-privately insured population based on Census data. We then calculate the bounds based on different assumptions about the effect of PDMP operation on the consumption of prescription drugs. As a lower bound, we assume that all non-privately insured stop taking any prescription opioids. As an upper bound, we assume that the non-privately insured do not change drug consumption at all. As a middle ground, we assume homogeneous effects: the relative reduction in prescription drug use is the same for the privately and non-privately

Table 6: Elasticity of Substitution Between Heroin and Prescription Drugs

	$\Delta_{H,P}$
Lower bound	-0.06
Upper bound	-0.26
Homogeneous effects	-0.18
Estimate based on Buchmueller and Carey (2018)	-0.24

Note: Based on estimation results from BCBS Axis®, NSDUH and Census data.

insured.[16]

Results in the literature tend to suggest smaller effects for the publicly insured population, somewhere between the zero effect assumption for the upper bound and the homogeneous effect. Meara et al. (2016) find no effect of PDMPs using Medicare data. Buchmueller and Carey (2018) find an overall reduction of 2.4% in the share of Medicare Part D enrollees taking opioids in response to must-access PDMPs, and larger declines for misuse outcomes (5% reduction in the share of opioid takers with overlapping claims, 6% for those with more than seven months' supply). We also use their main estimate to compute the rate of substitution. The results are shown in Table 6.

We find a lower bound for the rate of substitution of about 0.06, assuming consumption by the publicly insured ceases completely as a response to the PDMP. Conversely, in the opposite extreme case, assuming the change is driven by the privately insured population alone, the estimate is 0.26. Using the Buchmueller and Carey (2018) estimate for the non-commercially insured population, the effect is still substantial at 0.24. If we assume homogeneous effects, we estimate a middle-ground of about 0.18. This implies that for every prescription recipient not receiving opioids due to the PDMP, about 0.18 initiate heroin use (or conversely, approximately one out of six prescription users initiates heroin consumption).

Although our substitution estimates for consumption are sizeable, they are smaller than existing substitution estimates for mortality in other settings. Specifically, the conversion rate from prescription opioid consumption to heroin consumption we estimate is lower than the conversion rate other studies have found for prescription opioid mortality to heroin mortality. For example, analyzing the reformulation of OxyContin, Evans, Lieber, and Power (2019) find a one-to-one replacement of prescription opioid deaths with heroin deaths. Alpert, Powell, and Pacula (2018) find that per 1 percentage point reduction in OxyContin misuse, heroin mortality increases by 3.1 deaths per 100,000. Given a baseline of about one death per 100,000, this suggests a three-fold increase. The most likely explanation for the difference between consumption and mortality substitution is the high fatality risk associated with heroin specifi-

[16] We assume our estimate for the privately insured also covers the population receiving public benefits through private entities. Alternative assumptions change the bounds estimates slightly.

cally compared to prescription opioids. The large overdose risk compensates for the smaller user base, resulting in a higher substitution estimate for mortality.

Two important notes regarding the interpretation of elasticity estimates are needed. First, the estimates also incorporate effects operating through diversion of opioids to secondary markets. Our estimate covers the response in relation to those observed as receiving opioids through a legal prescription. The rate of substitution estimate includes individuals who were relying on diverted prescription opioids for consumption and therefore do not appear in the prescription data, but who nevertheless initiate heroin use in response to PDMP supply restrictions. This population is likely to be non-negligible in size; survey evidence from the NSDUH suggests that 50% of people who misused prescription opioids in the last year obtained some of them from friends or relatives. This implies that our estimates in general are a conservative upper bound for the total rate of substitution, as we underestimate the population in the denominator.

Second, with our data it is not possible to verify empirically that those individuals whose lose access to prescription opioids on account of the PDMP are necessarily the same individuals who increase uptake of heroin. This is, however, the most plausible behavior according to the literature. Of those individuals who began abusing opioids in the 2000s, 75% reported that their first opioid was a prescription drug (Cicero et al., 2014). An estimate for heroin is reported by Jones (2013), who examines national-level general population heroin data and shows that nearly 80 percent of current heroin users used prescription opioids prior to heroin. More generally, the incidence of heroin initiation is approximately 19 times higher among those who reported prior pain reliever use than among those who did not (Muhuri, Gfroerer, and Davies, 2013).

5.2.3 Street Prices and Purchases

Lower prescription rates reduce the supply of diverted opioids on the street. At the same time, the reductions should also increase the demand from chronic users addicted to opioids. Both of these factors are likely to drive up prices. At the same time, the substitution towards heroin will lower demand and prices for diverted prescription drugs. Which of these effects prevail is an empirical question. We study this effect using publicly posted price data on street purchases of prescription drugs from streetrx.com. Table 7 shows how street prices measured in $/mg for different opioid and non-opioid drugs react to PDMP introduction.

Table 7: The Effect of Prescription Drug Monitoring Programs on Drug Prices

	(1) Oxycodone	(2) Hydrocodone	(3) Morphine	(4) Codeine	(5) Methadone	(6) Benzodiazepines	(7) PDE5 inhibitors	(8) Methylphenidate
PDMP	0.145	−0.010	0.183	0.225	0.109	0.249	0.001	0.001
	(0.075)	(0.056)	(0.089)	(0.272)	(0.239)	(0.092)	(0.257)	(0.162)
	[0.054]	[0.860]	[0.039]	[0.409]	[0.647]	[0.007]	[0.995]	[0.994]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51	51	51
Observations	255	255	250	227	235	255	207	254

Note: Results from Poisson regression. Prices are standardized and measured in $/mg. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP. Data are from the StreetRx database.

We find that the street price of oxycodone increases by about 15% following tighter prescription drug regulation. For morphine, we find a similar effect of about 18%. Effects for Codeine and Methadone are in a similar range but noisy and insignificant. We do not find any effect on hydrocodone. Mirroring the results from the consumption data, we also find increases in the prices of benzodiazepines. We also conduct a series of placebo checks using prescription drugs that should be unaffected by PDMPs: PDE5 inhibitors (e.g., Sildenafil/Viagra, Tadalafil/Cialis) and Methylphenidate (Ritalin). Reassuringly, we do not find any effect on the street prices of these substances. Both estimates are indistinguishable from zero.

5.3 Health Consequences of Drug Substitution

5.3.1 Mortality

We now focus on the analysis of opioid-related mortality. The mortality results are shown in Table 8, divided into two sets. The first set (columns 1 and 2) considers the entire time period, mixing both ICD-9 and ICD-10 classifications. In this first set we distinguish between all fatal opioid poisonings (overdoses) and drug-related deaths due to opioid dependence. The second set of results (columns 3 to 9) focuses on the ICD-10 period, i.e., 1999-2017. The advantage of the second set of results is that we can disentangle the opioid category into its subgroups and thus examine how mortality due to each specific opioid derivate is affected by a PDMP introduction. We also focus on the sum between heroin and synthetic opioid deaths because fentanyl or heroin/fentanyl mixtures are often illicitly sold as heroin. Finally, we analyze composition changes directly by using the ratio of heroin deaths over total opioid deaths as the dependent variable (column 8).

PDMP introduction has no effect on aggregate opioid mortality for the period 1993-2017 (column 1). Regarding mortality due to long-term use of opioids (column 2), we also cannot reject the null hypothesis that PDMP exposure has no effect on this type of opioid mortality. Note that there might be two countervailing effects induced by the PDMP introduction: PDMPs may reduce direct mortality from prescription drugs, while increasing mortality from illicit substitute drugs at the same time. If both mortality estimates cannot be separated clearly in the data, this would also lead to a noisy estimate centered around zero.

To resolve this issue, we consider the period 1999-2017, where we can isolate each type of opioid in the ICD-10 data (columns 3 through 8). Column 3 replicates column 1 for the restricted time period and we still find an effect indistinguishable from zero. When examining the single classes of opioids, we find that the introduction of a PDMP significantly reduces mortality due to semi-synthetic opioids (column

Table 8: The Effect of Prescription Drug Monitoring Programs on Mortality

	MORTALITY BY CAUSE OF DEATH							
	1993-2017 (ICD-9 and ICD-10)		1999-2017 (ICD-10)					
	(1) All opioids	(2) Opioid dependence	(3) All opioids	(4) Semi-synthetic opioids	(5) Heroin	(6) Heroin or synthetic	(7) Methadone	(8) Share heroin
PDMP	–0.006	–0.036	0.014	–0.073	0.106	0.140	–0.014	0.092
	(0.065)	(0.231)	(0.063)	(0.053)	(0.097)	(0.090)	(0.056)	(0.130)
	[0.837]	[0.643]	[0.598]	[0.009]	[0.003]	[0.000]	[0.489]	[0.014]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51	51	51
Observations	1,275	1,275	969	969	969	969	969	969

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Vital Statistics System (NVSS).

4). This effect has a magnitude of -7.3% and is statistically significant at the 1% level. The category semi-synthetic opioids includes popular prescription medications such as oxycodone (e.g., OxyContin, Percocet), hydrocodone (Vicodin), and hydromorphone (Dilaudid), indicating that PDMPs achieve the goal of reducing mortality due to opioid pain medications. But do PDMPs induce a substitution effect toward illicit opioids? Columns 5 and 6 show the results for heroin mortality and heroin plus fully synthetic opioid mortality. Both coefficients are positive, sizable, and statistically significant at the 1% level. Overall, the results indicate that while PDMPs reduce mortality rates due to opioid medications, they also lead to an increase in mortality due to heroin and synthetic opioids. The increase in heroin and fentanyl mortality fully offsets the decrease in mortality due to prescription opioids. In column 8, we show further evidence of change in the composition of deaths by using heroin's share of all opioid deaths as the dependent variable. The share of deaths due to heroin increases by 9.2% upon PDMP introduction. As we show in Table A.15 in the appendix, these mortality patterns are not driven by other state policies.

Finally, we find no effect on methadone mortality (column 7), which is expected, as methadone is frequently used for medication treatment of OUD and its effects differ from those of heroin or more conventional opioid medications. In special cases, methadone is prescribed for cancer or other chronic pain when side effects of other opioids limit dosage escalation or pain remains poorly controlled. However, while methadone has a similar analgesic effect, it does not cause euphoria compared to morphine, heroin, oxycodone or similar drugs. As such, it does not constitute an attractive alternative for recreational use.

Table 9: The Effect of Prescription Drug Monitoring Programs on Hospitalizations

(A) ALL HOSPITALIZATIONS: POISONINGS

	(1) All opioids	(2) Opioid medication	(3) Heroin	(4) Other/unspecified	(5) Share heroin
PDMP	–0.010	–0.067	0.076	0.047	0.130
	(0.012)	(0.013)	(0.028)	(0.024)	(0.043)
	[0.392]	[0.000]	[0.006]	[0.054]	[0.002]

(B) EMERGENCY HOSPITALIZATIONS: POISONINGS

	(1) All opioids	(2) Opioid medication	(3) Heroin	(4) Other/unspecified	(5) Share heroin
PDMP	–0.006	–0.061	0.108	0.035	0.142
	(0.015)	(0.015)	(0.032)	(0.027)	(0.048)
	[0.702]	[0.000]	[0.001]	[0.208]	[0.003]
Covariates	Yes	Yes	Yes	Yes	Yes
Hospital FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
Hospitals	2,973	2,973	2,973	2,973	2,973
Observations	16,369	16,369	16,369	16,369	16,369

Note: Results from Poisson regression. Standard errors clustered at the hospital level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include hospital size (on a logarithmic scale), state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Inpatient Sample (NIS).

5.3.2 Hospitalizations

Given the mortality results in the previous section, we now turn to the analysis of hospitalizations. Hospitalizations constitute a more frequent outcome and are a reliable measure of public health and related morbidity changes. At the same time, hospitalizations are associated with non-trivial health care spending, providing a broader, relevant measure of population health and costs. In contrast, mortality, while costly, is a low incidence, terminal outcome.

Table 9 presents the results. We first focus on all types of hospitalizations, i.e., inpatient stays, both scheduled (e.g., withdrawal treatment, drug-related illnesses and infections) and those resulting from emergency admission (e.g., overdoses). In a second step, we repeat the analysis focusing on emergency admissions only.

Looking at the number of hospitalizations for all opioids in panel A, column (1), we find no effect of PDMP exposure on hospitalizations. However, once we disaggregate hospitalization into those driven by prescription opioid medications, and those due to heroin, we find a pattern of opposing incidence effects. PDMP introductions reduce hospitalizations due to prescription opioids by 6.7% (column 2). At the same time, hospitalizations due to heroin increase by 7.6% (column 3). This opposing pattern indicates that

some opioid users change their consumption pattern, substituting illicit drugs for prescription medication. A similar picture arises for the share of hospitalizations that are due to heroin (column 5). The share of hospitalizations due to illicit drug consumption increases by 13%. All estimates are highly significant at conventional levels. The composition change slightly affects the residual category of opioids (by 4.7%). This category includes Fentanyl, but potentially also other drugs that are negatively affected by the restrictions, explaining the moderate effect. As previously, these patterns are not driven by other state policies (see Table A.15 in the appendix).

When we restrict our attention to emergency hospitalizations only (panel B), the pattern of results is exacerbated for heroin poisonings. While the PDMP coefficient for all opioid hospitalizations is still statistically indistinguishable from zero and the coefficient for prescription medication is quite similar to that in panel A, the estimates for heroin are substantially larger (column 3). We observe an 11% increase in heroin hospitalizations, corresponding to about a 6% of a standard deviation increase in inpatient-stay hospitalizations per year. Moreover, heroin's share of emergency hospitalizations increases by 14%.

This latter set of estimates underscores the substantial shift of prescription opioid users towards heroin and illicit markets, substituting for prescription use with a more potent substance of the same drug class. Moreover, the results emphasize the dangers of consuming street drugs, whose potency and active ingredients are often unknown and vary drastically. In contrast to this, the consumption of prescription drugs, manufactured by pharmaceutical companies in sterile environments, with strict quality control and standardization of dose and potency, is associated with fewer health risks, as users can easily ascertain the drug amounts they consume. In addition, heroin is often consumed through routes that carry additional risks (i.e., injection, smoking), which further exacerbate the health risks inherent to illicit drugs. Since our results are based on measures of drug poisonings, we are likely to underestimate the real health care costs as we do not capture other complications linked to drug use (e.g., infections).

One important advantage of using the NIS data is that it is possible to examine each hospitalization in detail. This additional analysis allows us to understand the underlying mechanisms by focusing on two dimensions. The first dimension is hospital costs. The composition change in hospitalizations potentially influences both hospital charges and length of stay. The second dimension is patient characteristics, where we investigate which type of patient (gender, ethnicity) is driving the results presented previously. Overall, the additional analyses are key information for policy, in order to better target prevention and treatment campaigns when supply restrictions are imposed.

Table 10 shows the results for hospital costs, divided into hospital charges in inflation-adjusted 2017-dollars (panel A) and length of stay (panel B). In terms of total charges, we find that charges associated

with heroin poisonings increase by 21.8% after PDMP introduction. This large and significant increase is likely driven by the additional hospitalizations due to heroin poisonings and not by an increase in treatment costs, because the share of charges due to heroin (column 5) is very similar to the effect of PDMPs on the share of heroin poisonings over total opioid cases (Table 9, column 5). We observe no statistically significant change in hospital charges for opioid medication or other/unspecified opioids. The net effect of PDMPs on hospital charges is positive: the total costs associated with all opioid poisonings increase by 3% upon PDMP introduction. This net effect amounts to approximately $7,000 per hospital-year and is – as the results in Table 9 imply – primarily driven by an increase in the number of heroin poisonings.

In terms of the total number of hospital days (Table 10, panel B), we find a strong increase for poisonings due to both heroin (25.5%) and other/unspecified opioids (10.9%). These increases are completely offset by a decrease in the total number of hospital days due to opioid medication poisonings (12.0%), resulting in a zero net effect for all opioids poisonings (column 1). Similar to charges, the heroin share for total hospital days (column 5) is comparable to the heroin share for hospitalizations presented in Table 9. Note that these are effects on total hospital days, not per-case length of stay. For per-case length of stay, we find a smaller intensive margin increase of 0.11 for heroin hospitalizations (not reported). This pattern of findings suggests a change in the marginal consumer of heroin or in consumption habits. Novel users are inexperienced in the consumption of heroin and more likely to overdose severely, leading to longer hospitalization spells.

When looking at patient characteristics (Appendix Table A.12), we find that both the reduction in opioid hospitalizations and the increase in heroin hospitalizations are slightly larger for men than for women. Regarding race – classified as white or non-white patients – we find significant effects of PDMPs on heroin and opioid medication poisonings exclusively for white patients. The effects for non-white patients are much smaller in relative terms and not statistically significant.[17]

5.3.3 Pill Mills in Florida

Pill mills are facilities resembling specialty pain care clinics that prescribe and/or dispense excessive quantities of opioids, beyond that which would be considered medically appropriate. At these facilities, physicians typically prescribe controlled substances without proper examination, diagnosis, documentation, or background checks of patients' medical history. Most pill mills imitate pain clinics and specialize in prescribing opioids and benzodiazepines. Clients usually pay cash to obtain prescriptions. Since pre-

[17] A more disaggregated analysis of racial categories does not reveal any other significant results.

Table 10: The Effect of Prescription Drug Monitoring Programs on Hospital Costs

(A) HOSPITALIZATIONS: CHARGES

	(1) All opioids	(2) Opioid medication	(3) Heroin	(4) Other/unspecified	(5) Share heroin
PDMP	0.030	–0.031	0.218	0.038	0.143
	(0.017)	(0.020)	(0.044)	(0.037)	(0.055)
	[0.088]	[0.117]	[0.000]	[0.295]	[0.009]

(B) HOSPITALIZATIONS: TOTAL HOSPITAL DAYS

	(1) All opioids	(2) Opioid medication	(3) Heroin	(4) Other/unspecified	(5) Share heroin
PDMP	–0.018	–0.120	0.255	0.109	0.159
	(0.016)	(0.018)	(0.043)	(0.042)	(0.059)
	[0.260]	[0.000]	[0.000]	[0.010]	[0.007]
Covariates	Yes	Yes	Yes	Yes	Yes
Hospital FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
Hospitals	2,973	2,973	2,973	2,973	2,973
Observations	16,369	16,369	16,369	16,369	16,369

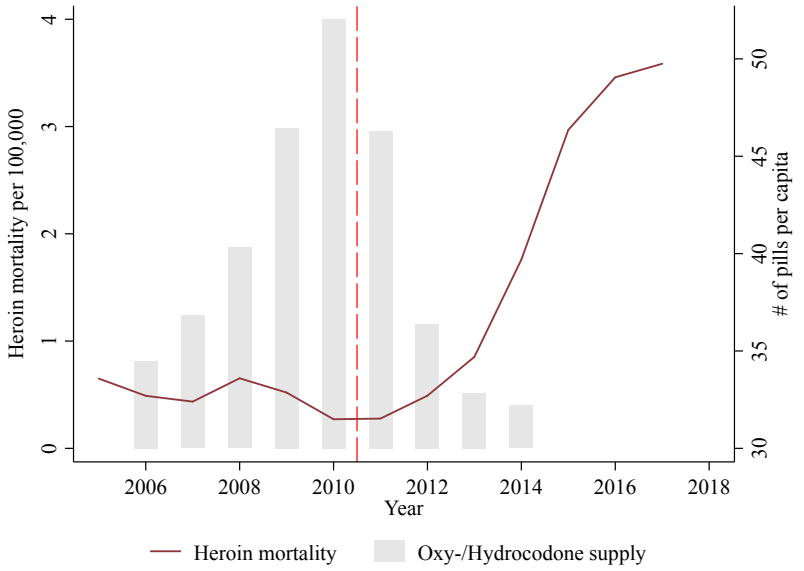
Note: Results from Poisson regression. Standard errors clustered at the hospital level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include hospital size (on a logarithmic scale), state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Inpatient Sample (NIS).

scriptions are easy to obtain, and can be obtained from multiple such facilities, pill mills are likely to have facilitated the proliferation of opioids and addiction. Anecdotal evidence suggests that pill mill prescriptions have been used by both consumers and drug dealers as a source of drug supply.

PDMPs challenge the operation of pill mills: excessive prescribing that promotes drug addiction rather than curing or relieving pain is a violation of medical ethics. Physicians may face professional consequences and prosecution if found out, and facilities will be shut down. When physicians have to register opioid prescriptions in a PDMP that can also be accessed by law enforcement, providers with excessive opioid prescribing can be identified easily, threatening pill mills' business model and continued operation.

One U.S. state that has been notorious for widespread operation of pill mills and easy access to prescription drugs is Florida (e.g., Higham, Horwitz, and Rich, 2019). Other Southern states introduced PDMPs (or other legislation to limit pill mill operation) years before Florida did so in 2011. Florida became known as the "pill mill capital" of the U.S. According to the DEA, Florida had over 900 unregulated pain management clinics in 2010, employing 90 of the top 100 oxycodone-dispensing physicians in the United States. Of the top 50 oxycodone-dispensing clinics across the country, 49 were located in

Figure 3: The Impact of PDMPs and the Closure of Florida Pill Mills on Prescription Drug Consumption and Heroin Mortality



Note: Oxy-/Hydrocodone pills dispensed per capita and heroin mortality per 100,000 of population over time. Sources: DEA ARCOS, National Vital Statistics System.

Florida, selling in excess of a million oxycodone pills a month (Florida Board of Medicine, 2014). For this reason, we conduct a case study of how pill mills in Florida have sustained drug use and addiction, as it clearly highlights the impact of an electronic PDMP on prescribing behavior and its unintended consequences when opioids are widely prescribed.

We track the dispensation of oxy-/hydrocodone and heroin mortality (based on the ARCOS and NVSS data) before and after the state of Florida begins operation of the mandatory E-FORCSE PDMP reporting system. The results are shown in Figure 3. We find that immediately following the introduction of the PDMP, dispensation of oxy- and hydrocodone begins to decrease, falling by about 30% over four years. We also observe a steep increase in heroin mortality. From a relatively low base, heroin mortality increases five-fold between 2010 and 2015. The comparatively large increase suggests the marginal consumer switching to heroin is unfamiliar with its consumption. The high fatality rate is likely to be explained by users being accustomed to unadulterated prescription drugs with consistent dosage amounts and unfamiliar with the higher potency of heroin and its consumption risks.

5.3.4 Trends and Dynamics

In this final section, we take a dynamic perspective on the issue of drug substitution. In terms of preventing addiction, restricting easy access to prescription opioids is arguably a beneficial policy in the long-run – if considered in isolation. However, as our results indicate, drug users switching to heroin

can be associated with significant public health costs in the short-run. Moreover, there is the possibility that increases in both demand and supply of heroin following PDMP introduction sufficiently increase exposure to illicit drugs in at-risk subpopulations such that there is a net increase in drug consumers, potentially mitigating or even reversing the effects of the access restriction. To investigate this issue, we conduct event study estimations for the major health outcomes. Results are shown in Appendix Figures A.2 and A.3. Note that these analyses also implicitly test for significant pre-trends, and we find no systematic pre-trend effect that might violate the key identification strategy discussed in the empirical strategy section.

Regarding mortality, we find that mortality due to semi-synthetic prescription opioids is permanently lowered (Appendix Figure A.2, panel B). This suggests that PDMPs are effective in reducing mortality due to prescription medications. However, as our previous analysis indicates, we also observe a concurrent increase in mortality due to heroin and fentanyl (Appendix Figure A.2, panel C). The event-study suggests that this effect occurs immediately and remains stable over time. Overall, opioid mortality does not seem to be strongly affected in the medium- to longer-term (Appendix Figure A.2, panel A). If anything, the results suggest a minor net decline over time.

For hospitalizations, the patterns for hospitalizations due to all opioid poisonings and poisonings due to prescription opioids are very similar to those for mortality. While hospitalizations due to all opioid poisonings are largely stable, those due to prescription opioids exhibit a steady decline over time after a PDMP is introduced. For heroin poisonings, we observe a steady increase in the number of hospitalizations over time.

Considering the pattern of results for heroin mortality and hospitalizations together in context, our interpretation is that as drug users unfamiliar with street drugs and consumption by injection switch to heroin, fatal overdoses that bypass hospitalization spike initially. As users become acquainted with heroin, dosage concentrations and the associated consumption risks, mortality stabilizes while hospitalizations increase. At the same time, paramedics and first responders become more accustomed to treating overdose cases, further increasing the likelihood that an overdose is non-fatal and results in hospitalization. Similarly, the proliferation of naloxone to treat overdose cases increases with the prevalence of heroin consumption, further increasing the likelihood of hospitalizations compared to fatalities.

6 Conclusion

Public health officials have called the current opioid epidemic the worst drug crisis in American history (Dowell, Haegerich, and Chou, 2016). In 2021, drug overdose deaths during the latest 12-month period exceeded 100,000 for the first time in history, corresponding to a mortality rate of more than 30 per 100,000. Our data show that one fifth of all initial opioid prescription claims with the largest commercial insurance association in the U.S. exceed the CDC's prescribing limit guidelines. Unintentional poisoning is now the fatal injury with the most years of potential life lost before age 65, surpassing one million years of potential life lost.[18] It is thus crucial to study the mechanisms behind the opioid epidemic and understand which policies are effective against it.

In this paper, we focus on PDMPs as an important supply-side policy to prevent prescription opioid misuse and addiction. We find that PDMPs are effective in permanently reducing both the number of overall and high-dose/long-duration scripts by about 13%, and successfully limit exposure of opioid-naive patients. However, prescribers respond almost exclusively on the extensive margin, reducing the number of prescriptions, but not the strength or duration of a prescription. This result matches the findings by Zhu et al. (2019) and Buchmueller, Carey, and Meille (2020), who note that prescribers respond to the opioid crisis by ceasing to start some patients on opioids altogether, rather than prescribing opioids at safer doses and durations. In light of the fact that many prescriptions are considered unnecessarily strong, this result calls for further research on physician's prescribing behavior. Moreover, we find that prescribers frequently cease prescribing further opioids to chronic users. Abrupt discontinuation causes distress and has been linked to an array of negative outcomes, including overdose, suicide, and potential drug substitution. Indeed, we find that users react by engaging in doctor shopping to evade the restrictions. They also seek other alternatives: we document a substantial increase in the number of first-time heroin users, as well as users of other illicit drugs.

We establish that PDMPs achieve their intended goal: fewer people initiate opioid treatment, and opioid-naive people are shielded from exposure. Nonetheless, our study reveals that PDMPs also have important unintended consequences. As access to prescription medication is being restricted, some drug users turn to heroin and illicit drugs. The resulting increases in mortality and hospitalizations due to heroin fully reverse the reductions due to prescription opioids. Opioid hospitalizations are associated with more expensive hospital stays, leading to a net increase in hospitalization costs. In addition, our analysis reveals that a large part of the policy incidence falls on commercial enrollees, suggesting that analyses relying on Medicaid or Medicare claims data alone are missing an important part of the picture.

[18] Calculations provided by the CDC, available at the following link: `http://webappa.cdc.gov`.

Moreover, our event study analysis reveals that mortality effects are concentrated in the first few years after PDMP introduction. As heroin use becomes more established, the number of lethal cases stabilizes and hospitalizations increase further.

Given the magnitude of the estimates, our findings have important policy implications. Restricting access to prescription opioids when they are not medically necessary, and/or when they are not being prescribed safely, is a sensible policy. Nevertheless, restricting access to comparatively less risky drugs for a large population of users has important negative unintended consequences which should not be ignored by policy makers. Expecting potentially addicted long-term users to simply stop consuming drugs because access is restricted is unrealistic, especially if substitute drugs are cheaply available on secondary markets. Problems are amplified since illicit substitute drugs are associated with substantially increased health risks. Our main results indicate that drug substitution partially reverses the intended effects of PDMPs and is associated with significant public health and monetary costs. Future research is needed to assess how much of this effect is temporary. This requires a better understanding of whether the current heroin market is limited to those cohorts of consumers which were exposed to the change in access laws, or whether the increased availability of heroin induces new consumers without any history of prescription opioid use to adopt heroin.

To conclude, our study suggests that restricting access to drugs does not eliminate their use completely, but displaces some users to consume other available alternatives. Given this, PDMPs or similarly targeted supply-side restriction policies should be accompanied by policies that improve access to evidence-based OUD treatment. Medications to treat OUD are a far safer substitute than illicit opioids, but treatment capacity has historically been far from adequate in the U.S. (e.g., Volkow, 2018; Volkow et al., 2014; Volkow and McLellan, 2016).[19] Our findings indicate that improving access to preferable substitutes such as OUD treatment may mitigate the negative unintended consequences of supply-side restrictions on prescription opioids.

[19] In additional analyses, we split our estimation sample by the number of Buprenorphine-waivered providers in each state as a measure of OUD treatment capacity. Although the analysis is underpowered, the results suggest that effects for both heroin consumption and heroin mortality are comparatively smaller in states with larger treatment capacity.

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A Appendix: Supplementary Material

Table A.1: Descriptive statistics

	Mean	SD	Min	Max	N
PDMP AND STATE CHARACTERISTICS					
PDMP	0.34	0.48	0.00	1.00	1,326
Unemployment rate	5.47	1.86	2.30	13.70	1,326
Population	5,798,960	6,497,685	473,228	39,250,017	1,326
Income per capita	35,963	11,259	15,667	82,111	1,326
GDP per capita	49,135	18,550	29,599	183,971	1,326
BCBS CLAIMS DATA: USERS AND PRESCRIPTIONS					
Enrollees with opioid prescriptions	127,320	135,124	1,047	652,596	357
Enrollees with opioid prescriptions ex. 50 MME/day	65,438	70,453	534	325,001	357
Enrollees with opioid prescriptions ex. 90 MME/day	51,988	58,289	425	266,577	357
Opioid prescriptions	382,976	409,158	3,078	1,889,955	357
Opioid prescriptions ex. 50 MME/day	260,949	282,421	2,117	1,349,301	357
Opioid prescriptions ex. 90 MME/day	234,474	258,370	1,859	1,231,747	357
Dosage: Dosage prescribed in MME	307,472,169	348,057,139	3,371,442	1,738,444,647	357
Dosage: Days supply prescribed	6,199,656	6,864,123	46,783	31,921,827	357
Dosage: Prescriptions strength (MME/day)	18,982,779	22,334,110	182,547	198,875,074	357
Dosage: Per-claim dosage in MME prescribed	850	961	180	14,339	357
Dosage: Per-claim days supply prescribed	16	2	12	21	357
Dosage: Per-claim prescriptions strength	51	35	13	550	357
Prescriptions: Oxycodone	87,500	100,042	768	594,673	357
Prescriptions: Hydrocodone	176,684	205,253	1,457	1,163,905	357
Prescriptions: Oxymorphone	1,877	2,814	0	15,096	357
Prescriptions: Hydromorphone	4,906	5,317	18	28,852	357
Prescriptions: Morphine	9,641	10,858	99	59,514	357
Prescriptions: Fentanyl	6,752	8,203	48	55,663	357
Prescriptions: Codeine	23,068	39,205	175	369,885	357
Prescriptions: Tramadol	68,587	79,456	442	492,062	357
Prescriptions: Buprenorphine	14,992	17,980	82	97,733	357
Prescriptions: Methadone	3,091	3,519	38	18,093	357
Opioid-naive patients: Enrollees w/ prescr.	37,803	42,674	212	267,346	357
Opioid-naive patients: Enrollees w/ prescr. ex. 50 MME/day	11,605	13,370	72	90,386	357
Opioid-naive patients: Dosage prescribed	7,664,671	9,377,116	43,171	83,495,436	357
Chronic users (ex. 90 days)	17,909	20,143	123	95,057	357
Chronic users (ex. 180 days)	11,633	12,971	82	60,150	357
Chronic users (ex. 360 days)	4,724	5,270	35	25,389	357
Chronic users: Dosage prescribed (ex. 90 days)	261,412,512	300,925,750	2,688,651	1,528,051,519	357
Chronic users: Dosage prescribed (ex. 180 days)	235,845,301	272,811,527	2,414,638	1,401,715,714	357
Chronic users: Dosage prescribed (ex. 360 days)	157,101,653	181,152,770	1,899,730	1,051,908,751	357
Chronic users: Per-claim dosage (ex. 90 days)	1,435	1,920	318	28,637	357
Chronic users: Per-claim dosage (ex. 180 days)	1,652	2,514	369	37,413	357
Chronic users: Per-claim dosage (ex. 360 days)	1,833	326	458	3,210	357
ARCOS MANUFACTURER DRUG SHIPMENTS					
Oxycodone/Hydrocodone manufacturer shipments	213,779,589	215,618,449	6,577,630	1,224,616,448	459
Oxycodone/Hydrocodone shipments to pharmacies	212,303,456	212,421,278	6,508,310	1,195,350,528	459
Oxycodone/Hydrocodone shipments to retail pharmacies	79,214,489	79,812,150	3,081,390	416,663,616	459
Oxycodone/Hydrocodone shipments to chain pharmacies	133,088,967	138,080,883	971,300	780,278,784	459
Oxycodone/Hydrocodone shipments to practitioners	1,476,132	4,819,428	13,080	41,312,796	459
NSDUH DRUG USE SURVEY					
Ever used pain relievers not prescribed by a doctor	542,205	655,162	24,000	5,062,000	459
Ever used heroin	85,802	105,608	2,000	741,000	510
Ever used sedatives or tranquilizers	491,525	604,663	11,000	4,104,000	408
Ever used benzodiazepines	393,503	425,150	11,000	2,657,000	306
Ever received treatment for drug use	28,155	29,574	1,000	195,000	459
NVSS MORTALITY DATA					
Mortality, all opioids	512	667	1	5,769	969
Mortality, semi-synthetic opioids	176	215	0	1,279	969
Mortality, heroin	107	192	0	1,491	969
Mortality, heroin and synthetic opioids	206	425	0	4,636	969
Mortality, methadone	72	83	0	608	969

Sources: Blue Cross Blue Shield Axis® database, DEA ARCOS data provided by the Washington Post, National Survey on Drug Use and Health, National Vital Statistics System.

Table A.2: PDMP Enactment and Operational Dates by State

State	(1) Legislative enactment	(2) Operational (user access)
Alabama	August 2004	April 2006
Alaska	September 2008	January 2012
Arizona	September 2007	December 2008
Arkansas	July 2011	May 2013
California	January 2005	September 2009
Colorado	June 2005	February 2008
Connecticut	October 2006	July 2008
Delaware	July 2010	August 2012
District of Columbia	February 2014	October 2016
Florida	December 2010	October 2011
Georgia	July 2011	May 2013
Hawaii	December 1996	February 2012
Idaho	April 2000	April 2008
Illinois	April 2000	December 2009
Indiana	July 2007	July 2007
Iowa	May 2006	March 2009
Kansas	July 2008	April 2011
Kentucky	July 1998	July 1999
Louisiana	July 2006	January 2009
Maine	January 2004	January 2005
Maryland	October 2011	December 2013
Massachusetts	December 1992	January 2011
Michigan	January 2002	January 2003
Minnesota	July 2007	April 2010
Mississippi	June 2006	July 2008
Missouri	July 2017	n/a
Montana	July 2011	October 2012
Nebraska	August 2011	January 2017
Nevada	January 1996	February 2011
New Hampshire	June 2012	October 2014
New Jersey	August 2009	January 2012
New Mexico	July 2004	August 2005
New York	October 2006	June 2013
North Carolina	January 2006	July 2007
North Dakota	April 2005	October 2008
Ohio	May 2005	October 2006
Oklahoma	January 1991	July 2006
Oregon	July 2009	September 2011
Pennsylvania	June 2015	August 2016
Rhode Island	August 1995	September 2012
South Carolina	June 2006	February 2008
South Dakota	March 2010	March 2012
Tennessee	January 2003	January 2010
Texas	September 1999	August 2012
Utah	July 1995	January 2006
Vermont	May 2006	January 2009
Virginia	September 2003	June 2006
Washington	July 2007	January 2012
West Virginia	June 1995	May 2013
Wisconsin	June 2010	June 2013
Wyoming	July 2003	July 2013

Note: The data are collected by the authors using the following sources: Prescription Drug Abuse Policy System, National Alliance for Model State Drug Laws, Prescription Drug Monitoring Program Training and Technical Assistance Center, states' statutes, and Horwitz et al. (2018).

Table A.3: Test for Endogenous PDMP Adoption: Prescriptions

	All opioid Enrollees			All opioid prescriptions		
Y_{t-1}	−0.035	−0.026	−0.016	−0.034	−0.023	−0.019
	(0.023)	(0.027)	(0.026)	(0.023)	(0.024)	(0.024)
Y_{t-2}		−0.010	−0.028		−0.013	−0.025
		(0.018)	(0.029)		(0.017)	(0.024)
Y_{t-3}			0.001			−0.001
			(0.034)			(0.027)
F-test (p-value)	0.144	0.410	0.564	0.147	0.420	0.573
	MME $\geq$ 50 Enrollees			MME $\geq$ 50 prescriptions		
Y_{t-1}	−0.036	−0.025	−0.015	−0.035	−0.022	−0.019
	(0.024)	(0.028)	(0.027)	(0.023)	(0.023)	(0.024)
Y_{t-2}		−0.012	−0.027		−0.014	−0.024
		(0.018)	(0.028)		(0.016)	(0.022)
Y_{t-3}			−0.002			−0.004
			(0.031)			(0.024)
F-test (p-value)	0.139	0.398	0.566	0.143	0.410	0.577
	MME $\geq$ 90 Enrollees			MME $\geq$ 90 prescriptions		
Y_{t-1}	−0.034	−0.021	−0.010	−0.034	−0.020	−0.017
	(0.023)	(0.028)	(0.029)	(0.023)	(0.023)	(0.025)
Y_{t-2}		−0.012	−0.028		−0.015	−0.024
		(0.017)	(0.028)		(0.016)	(0.022)
Y_{t-3}			−0.001			−0.003
			(0.030)			(0.022)
F-test (p-value)	0.154	0.420	0.571	0.151	0.419	0.584
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.4: Test for Endogenous PDMP Adoption: Dosage

	Total amount of MME			Total amount of days supply		
Y_{t-1}	–0.027	–0.012	–0.003	–0.037	–0.021	–0.019
	(0.020)	(0.020)	(0.032)	(0.025)	(0.023)	(0.026)
Y_{t-2}		–0.018	–0.025		–0.017	–0.025
		(0.016)	(0.023)		(0.016)	(0.023)
Y_{t-3}			–0.007			–0.005
			(0.023)			(0.022)
F-test (p-value)	0.177	0.442	0.604	0.151	0.415	0.591
	Total amount of MME/day			Per-claim average MME		
Y_{t-1}	–0.027	–0.019	–0.014	0.013	0.017	0.009
	(0.019)	(0.023)	(0.031)	(0.014)	(0.014)	(0.023)
Y_{t-2}		–0.012	–0.025		–0.007	–0.001
		(0.017)	(0.024)		(0.008)	(0.006)
Y_{t-3}			–0.002			–0.007
			(0.026)			(0.026)
F-test (p-value)	0.171	0.456	0.582	0.360	0.354	0.594
	Per-claim average days supply			Per-claim average MME/day		
Y_{t-1}	0.073	0.556	0.172	0.016	0.013	0.015
	(0.573)	(0.418)	(0.353)	(0.019)	(0.018)	(0.029)
Y_{t-2}		–0.573	0.480		0.001	–0.003
		(0.991)	(0.581)		(0.015)	(0.011)
Y_{t-3}			–0.740			0.009
			(1.298)			(0.035)
F-test (p-value)	0.899	0.325	0.552	0.401	0.760	0.950
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.5: Test for Endogenous PDMP Adoption: Shipments

	Total Shipments			Shipments to pharmacies			Shipments to practitioners		
Y_{t-1}	–0.821	–0.626	–0.983	–0.834	–0.604	–0.963	0.025	–0.002	0.035
	(0.383)	(0.461)	(0.538)	(0.391)	(0.476)	(0.561)	(0.062)	(0.071)	(0.083)
Y_{t-2}		–0.457	0.096		–0.524	0.008		0.025	0.054
		(0.576)	(0.533)		(0.572)	(0.510)		(0.067)	(0.057)
Y_{t-3}			–0.079			–0.081			–0.020
			(0.711)			(0.713)			(0.073)
F-test (p-value)	0.037	0.109	0.263	0.038	0.109	0.276	0.685	0.927	0.694
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.6: Test for Endogenous PDMP Adoption: Abuse

	Ever used pain relievers non-medically		Ever used heroin		Ever used sedatives or tranquilizers non-medically	
Y_{t-1}	–0.137	–0.166	–0.066	–0.135	–0.134	–0.190
	(0.270)	(0.301)	(0.077)	(0.094)	(0.215)	(0.260)
Y_{t-2}		0.251		–0.063		0.046
		(0.328)		(0.083)		(0.255)
F-test (p-value)	0.614	0.462	0.400	0.329	0.534	0.701
	Ever used benzodiazepines		Received treatment for illicit drug use			
Y_{t-1}	–0.060	–0.004	–0.013	–0.017		
	(0.219)	(0.260)	(0.049)	(0.071)		
Y_{t-2}		0.098		0.054		
		(0.213)		(0.084)		
F-test (p-value)	0.784	0.860	0.798	0.685		
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.7: Test for Endogenous PDMP Adoption: Mortality

	All opioids (ICD-9/10)			Opioid dependence (ICD-9/10)		
Y_{t-1}	0.006	−0.003	−0.008	−0.002	−0.005	−0.008
	(0.024)	(0.019)	(0.024)	(0.017)	(0.013)	(0.013)
Y_{t-2}		0.013	0.016		0.005	0.003
		(0.018)	(0.017)		(0.013)	(0.011)
Y_{t-3}			−0.001			0.006
			(0.025)			(0.013)
F-test (p-value)	0.788	0.742	0.676	0.925	0.733	0.841
	All opioids (ICD-10)			Semi-synthetic opioids (ICD-10)		
Y_{t-1}	−0.008	−0.021	−0.019	−0.029	−0.022	−0.023
	(0.046)	(0.038)	(0.043)	(0.030)	(0.028)	(0.031)
Y_{t-2}		0.020	0.023		0.004	0.028
		(0.032)	(0.032)		(0.021)	(0.026)
Y_{t-3}			−0.003			−0.018
			(0.047)			(0.032)
F-test (p-value)	0.860	0.540	0.655	0.335	0.544	0.066
	Heroin (ICD-10)			Heroin plus synthetic (ICD-10)		
Y_{t-1}	−0.020	−0.011	−0.008	−0.025	−0.029	−0.020
	(0.026)	(0.019)	(0.022)	(0.026)	(0.023)	(0.025)
Y_{t-2}		−0.017	−0.011		0.001	−0.012
		(0.017)	(0.015)		(0.019)	(0.022)
Y_{t-3}			−0.016			0.004
			(0.021)			(0.028)
F-test (p-value)	0.437	0.617	0.730	0.336	0.419	0.855
	Methadone (ICD-10)					
Y_{t-1}	−0.051	−0.039	−0.037			
	(0.032)	(0.027)	(0.030)			
Y_{t-2}		−0.019	−0.003			
		(0.024)	(0.022)			
Y_{t-3}			−0.025			
			(0.027)			
F-test (p-value)	0.117	0.378	0.275			
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.8: Test for Endogenous PDMP Adoption: Hospitalizations (Drug Poisonings)

	All opioids			Opioid medication		
Y_{t-1}	−0.001	0.003	0.003	−0.001	0.005	0.004
	(0.002)	(0.003)	(0.002)	(0.003)	(0.004)	(0.003)
Y_{t-2}		−0.001	−0.001		−0.001	−0.001
		(0.003)	(0.003)		(0.004)	(0.004)
Y_{t-3}			−0.002			0.001
			(0.003)			(0.004)
F-test (p-value)	0.954	0.536	0.337	0.895	0.497	0.429
	Heroin			Other/unspecified		
Y_{t-1}	0.001	0.002	0.001	0.002	0.006	0.001
	(0.002)	(0.002)	(0.003)	(0.009)	(0.016)	(0.014)
Y_{t-2}		0.003	0.002		0.006	0.002
		(0.003)	(0.004)		(0.012)	(0.017)
Y_{t-3}			−0.001			−0.006
			(0.003)			(0.012)
F-test (p-value)	0.936	0.332	0.888	0.845	0.830	0.916
	Share heroin					
Y_{t-1}	0.001	0.001	−0.001			
	(0.001)	(0.001)	(0.001)			
Y_{t-2}		0.001	−0.001			
		(0.001)	(0.001)			
Y_{t-3}			−0.001			
			(0.001)			
F-test (p-value)	0.465	0.815	0.677			
Hospital FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes

Note: Results from linear regression (OLS). Standard errors clustered at the hospital level are shown in parentheses below the coefficients. The dependent variable is $PDMP_{it}$ in all regressions.

Table A.9: The Effect of Prescription Drug Monitoring Programs on Prescriptions by Opioid Medication

	(1) Oxycodone	(2) Hydrocodone	(3) Oxymorphone	(4) Hydromorphone	(5) Morphine	(6) Fentanyl	(7) Codeine	(8) Tramadol	(9) Buprenorphine	(10) Methadone
PDMP	−0.155	−0.217	0.006	−0.138	−0.101	−0.123	−0.116	−0.081	−0.117	−0.077
	(0.034)	(0.056)	(0.047)	(0.041)	(0.037)	(0.033)	(0.076)	(0.036)	(0.030)	(0.034)
	[0.000]	[0.000]	[0.891]	[0.001]	[0.006]	[0.000]	[0.129]	[0.023]	[0.000]	[0.023]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51	51	51	51	51
Observations	306	306	306	306	306	306	306	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Data are from the Blue Cross Blue Shield Axis® database.

Table A.10: The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions, Callaway/Sant'Anna ATT-Estimator

	(1)	(2)	(3)	(4)	(5)	(6)
	(A) PRESCRIPTIONS					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
	Enrollees	Prescriptions	Enrollees	Prescriptions	Enrollees	Prescriptions
Early PDMP adopters	–0.364	–0.351	–0.357	–0.329	–0.350	–0.321
	(0.096)	(0.102)	(0.088)	(0.099)	(0.085)	(0.100)
	[0.000]	[0.001]	[0.000]	[0.001]	[0.000]	[0.001]
Intermediate PDMP adopters	–0.142	–0.136	–0.142	–0.134	–0.123	–0.127
	(0.064)	(0.062)	(0.060)	(0.057)	(0.060)	(0.057)
	[0.029]	[0.028]	[0.019]	[0.020]	[0.043]	[0.026]
Late PDMP adopters	–0.020	–0.029	0.007	–0.028	0.048	–0.009
	(0.010)	(0.012)	(0.019)	(0.017)	(0.018)	(0.016)
	[0.043]	[0.012]	[0.688]	[0.096]	[0.009]	[0.546]
	(B) DOSAGE					
	Total amount			Per-claim average		
	Dosage in MME	Duration in days	Strength in MME/day	Dosage in MME	Duration in days	Strength in MME/day
Early PDMP adopters	–0.289	–0.323	–0.289	0.062	0.028	0.062
	(0.097)	(0.096)	(0.098)	(0.047)	(0.006)	(0.033)
	[0.003]	[0.001]	[0.004]	[0.182]	[0.000]	[0.064]
Intermediate PDMP adopters	–0.036	–0.121	–0.080	0.101	0.016	0.056
	(0.063)	(0.059)	(0.057)	(0.088)	(0.011)	(0.069)
	[0.573]	[0.042]	[0.162]	[0.255]	[0.152]	[0.417]
Late PDMP adopters	–0.017	–0.007	–0.020	0.012	0.022	0.010
	(0.016)	(0.014)	(0.016)	(0.007)	(0.004)	(0.018)
	[0.275]	[0.599]	[0.231]	[0.067]	[0.000]	[0.580]
States	51	51	51	51	51	51
Observations	306	306	306	306	306	306

Note: Results are obtained using the estimator by Callaway and Sant'Anna (2020). All regressions include state fixed effects and time fixed effects. Standard errors clustered at the state level are shown in parentheses below the coefficients, whereas p-values are shown in square parentheses below the coefficients. Data are from the Blue Cross Blue Shield Axis® database.

Table A.11: The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions, Callaway/Sant'Anna ATT-Estimator

	(1)	(2)	(3)	(4)	(5)	(6)
	(A) PRESCRIPTIONS					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
	Enrollees	Prescriptions	Enrollees	Prescriptions	Enrollees	Prescriptions
PDMP	–0.167	–0.163	–0.158	–0.157	–0.137	–0.146
	(0.045)	(0.049)	(0.042)	(0.043)	(0.047)	(0.044)
	[0.000]	[0.001]	[0.000]	[0.000]	[0.004]	[0.001]
	(B) DOSAGE					
	Total amount			Per-claim average		
	Dosage in MME	Duration in days	Strength in MME/day	Dosage in MME	Duration in days	Strength in MME/day
PDMP	–0.094	–0.143	–0.117	0.069	0.020	0.046
	(0.049)	(0.043)	(0.042)	(0.057)	(0.007)	(0.044)
	[0.058]	[0.001]	[0.005]	[0.225]	[0.003]	[0.302]
Covariates	No	No	No	No	No	No
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51
Observations	306	306	306	306	306	306

Note: Results are obtained using the estimator by Callaway and Sant'Anna (2020). Standard errors clustered at the state level are shown in parentheses below the coefficients, whereas p-values are shown in square parentheses below the coefficients. Data are from the Blue Cross Blue Shield Axis® database.

Table A.12: Heterogeneity Analysis for Hospital Admissions

	(1) Opioid medication	(2) Heroin
PDMP effect for men	–0.097	0.080
	(0.016)	(0.029)
	[0.000]	[0.006]
PDMP effect for women	–0.041	0.066
	(0.016)	(0.043)
	[0.009]	[0.126]
PDMP effect for white	–0.070	0.370
	(0.021)	(0.041)
	[0.001]	[0.000]
PDMP effect for non-white	–0.011	0.091
	(0.031)	(0.062)
	[0.729]	[0.138]
Covariates	Yes	Yes
Hospital FE	Yes	Yes
Time FE	Yes	Yes
Hospitals	2,973	2,973
Observations	16,369	16,369

Note: Results from Poisson regression. Standard errors clustered at the hospital level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include hospital size (on a logarithmic scale), state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Inpatient Sample (NIS).

Table A.13: Controlling for state-level policies: The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions

	(A) Users					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
PDMP	–0.126	–0.135	–0.122	–0.127	–0.108	–0.106
	(0.037)	(0.044)	(0.038)	(0.046)	(0.042)	(0.049)
	[0.001]	[0.002]	[0.001]	[0.005]	[0.010]	[0.031]
	(B) Rx					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
PDMP	–0.126	–0.131	–0.112	–0.115	–0.109	–0.107
	(0.034)	(0.040)	(0.033)	(0.039)	(0.035)	(0.040)
	[0.000]	[0.001]	[0.001]	[0.001]	[0.003]	[0.008]
State prescription drug policies	Yes	Yes	Yes	Yes	Yes	Yes
State marijuana disp. policies		Yes		Yes		Yes
Covariates	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51
Observations	306	306	306	306	306	306

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Other state prescription drug policies policies included are prescription duration limits, pill mill regulation, naloxone access and good samaritan laws. Marijuana policies measure access to medical and recreational marijuana through dispensaries. Prescription data are from the Blue Cross Blue Shield Axis® database.

Table A.14: Controlling for state-level policies: The Effect of Prescription Drug Monitoring Programs on Opioid Consumption

	Respondents drug use by substance									
	Ever used pain relievers w/o prescription		Ever used heroin		Ever used sedatives or tranquilizers w/o prescription		Ever used benzodiazepines		Received trea for illicit dru	
PDMP	0.029	0.030	0.086	0.086	0.046	0.048	0.053	0.054	–0.059	–0
	(0.014)	(0.013)	(0.052)	(0.052)	(0.022)	(0.021)	(0.023)	(0.022)	(0.048)	(0
	[0.034]	[0.020]	[0.098]	[0.097]	[0.033]	[0.020]	[0.019]	[0.015]	[0.221]	[0
State prescription drug policies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
State marijuana disp. policies		Yes		Yes		Yes		Yes		
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
States	51	51	51	51	51	51	51	51	51	
Observations	306	306	357	357	306	306	306	306	306	

Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square
ses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state
GDP. Other state prescription drug policies policies included are prescription duration limits, pill mill regulation, naloxone access and good samaritan laws. Marijuan
measure access to medical and recreational marijuana through dispensaries. Drug use data are from the National Survey on Drug Use and Health (NSDUH). The sa
differs for heroin compared to the other outcomes due to data availability for one additional survey year.

Table A.15: Controlling for state-level policies: The effect of Prescription Drug Monitoring Programs on Mortality

	MORTALITY BY CAUSE OF DEATH 1999-2017 (ICD-10)											
	All opioids		Semi-synthetic opioids		Heroin		Heroin or synthetic		Methadone		Share heroin	
PDMP	-0.006	0.007	-0.084	-0.068	0.076	0.085	0.103	0.110	-0.012	-0.011	0.071	0.076
	(0.056)	(0.056)	(0.047)	(0.047)	(0.094)	(0.090)	(0.074)	(0.072)	(0.052)	(0.052)	(0.131)	(0.129)
	[0.820]	[0.772]	[0.000]	[0.003]	[0.074]	[0.049]	[0.008]	[0.002]	[0.541]	[0.559]	[0.069]	[0.052]
State prescription drug policies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State marijuana disp. policies		Yes		Yes		Yes		Yes		Yes		Yes
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51	51	51	51	51	51	51
Observations	969	969	969	969	969	969	969	969	969	969	969	969

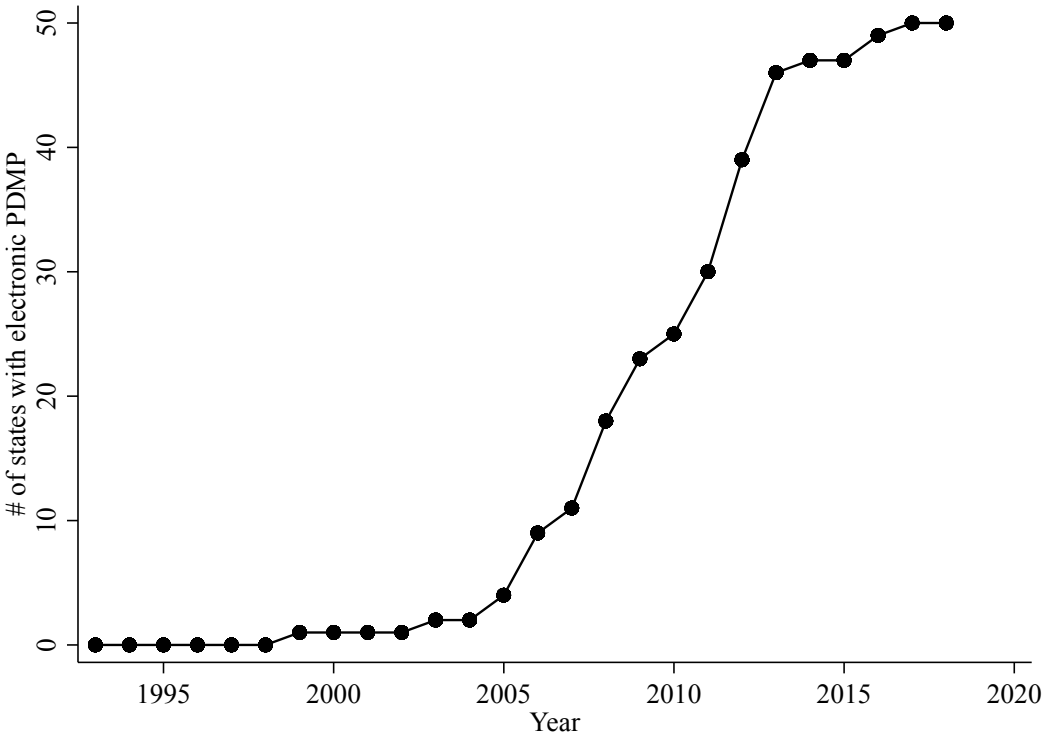
Note: Results from Poisson regression. Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Other state prescription drug policies policies included are prescription duration limits, pill mill regulation, naloxone access and good samaritan laws. Marijuana policies measure access to medical and recreational marijuana through dispensaries. Mortality data are from the National Vital Statistics System (NVSS).

Table A.16: Controlling for state-level policies: The effect of Prescription Drug Monitoring Programs on Hospitalizations

	All opioids		Opioid medication		Heroin		Other/unspecified		Share hero	
PDMP	−0.002	−0.002	−0.062	−0.056	0.131	0.146	0.038	0.030	0.183	0
	(0.012)	(0.012)	(0.013)	(0.013)	(0.028)	(0.028)	(0.025)	(0.025)	(0.043)	(0
	[0.889]	[0.866]	[0.000]	[0.000]	[0.000]	[0.000]	[0.133]	[0.239]	[0.000]	[0
State prescription drug policies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
State marijuana disp. policies		Yes		Yes		Yes		Yes		
Covariates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Hospital FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Hospitals	2,973	2,973	2,973	2,973	2,973	2,973	2,973	2,973	2,973	
Observations	16,369	16,369	16,369	16,369	16,369	16,369	16,369	16,369	16,369	

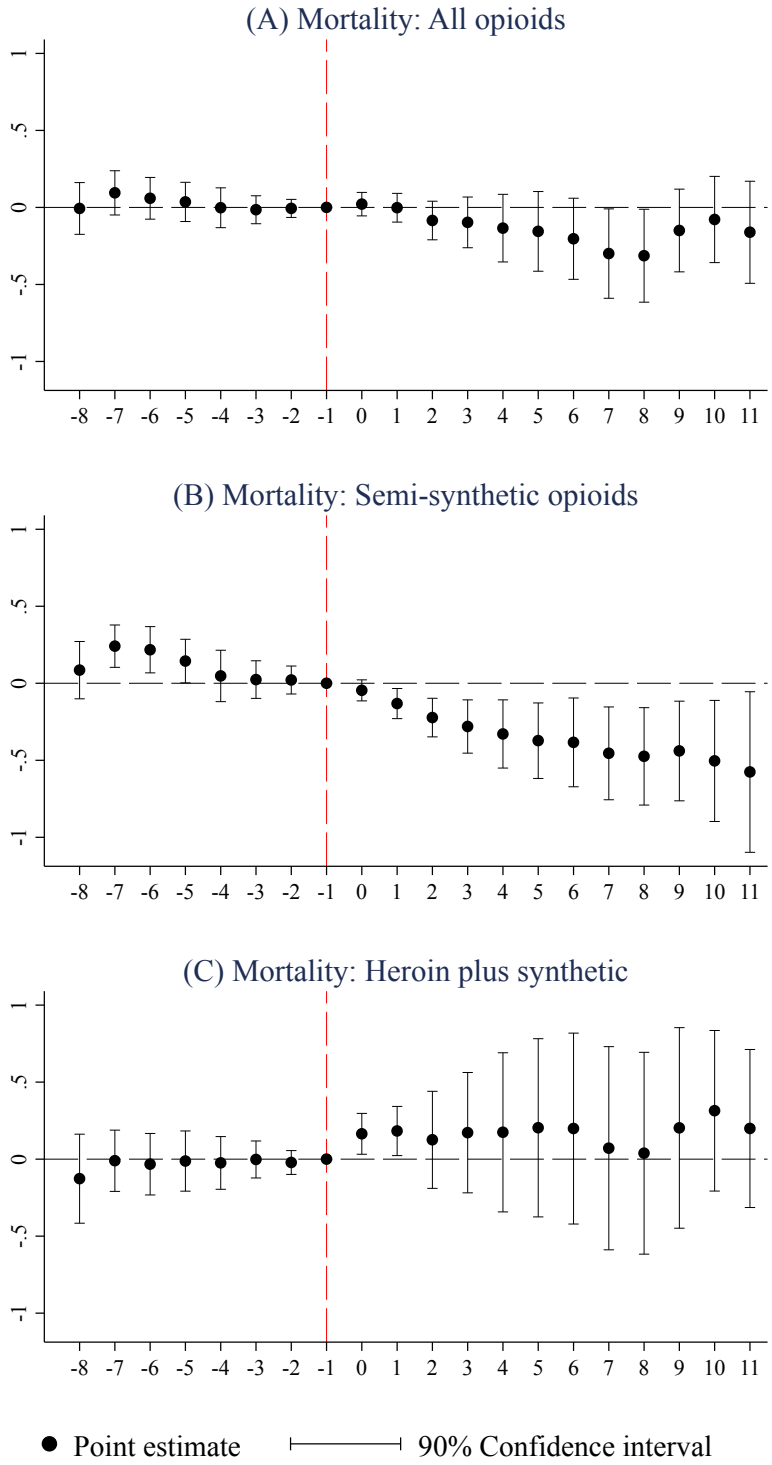
Note: Results from Poisson regression. Standard errors clustered at the hospital level are shown in parentheses below the coefficients. P-values are shown in square pa below the coefficients. Covariates include hospital size (on a logarithmic scale), state census population (on a logarithmic scale), state unemployment rate, state per-c sonal income, and state per-capita GDP. Other state prescription drug policies policies included are prescription duration limits, pill mill regulation, naloxone access samaritan laws. Marijuana policies measure access to medical and recreational marijuana through dispensaries. Hospitalization data are from the National Inpatie (NIS).

Figure A.1: Staggered Implementation of PDMPs Over Time



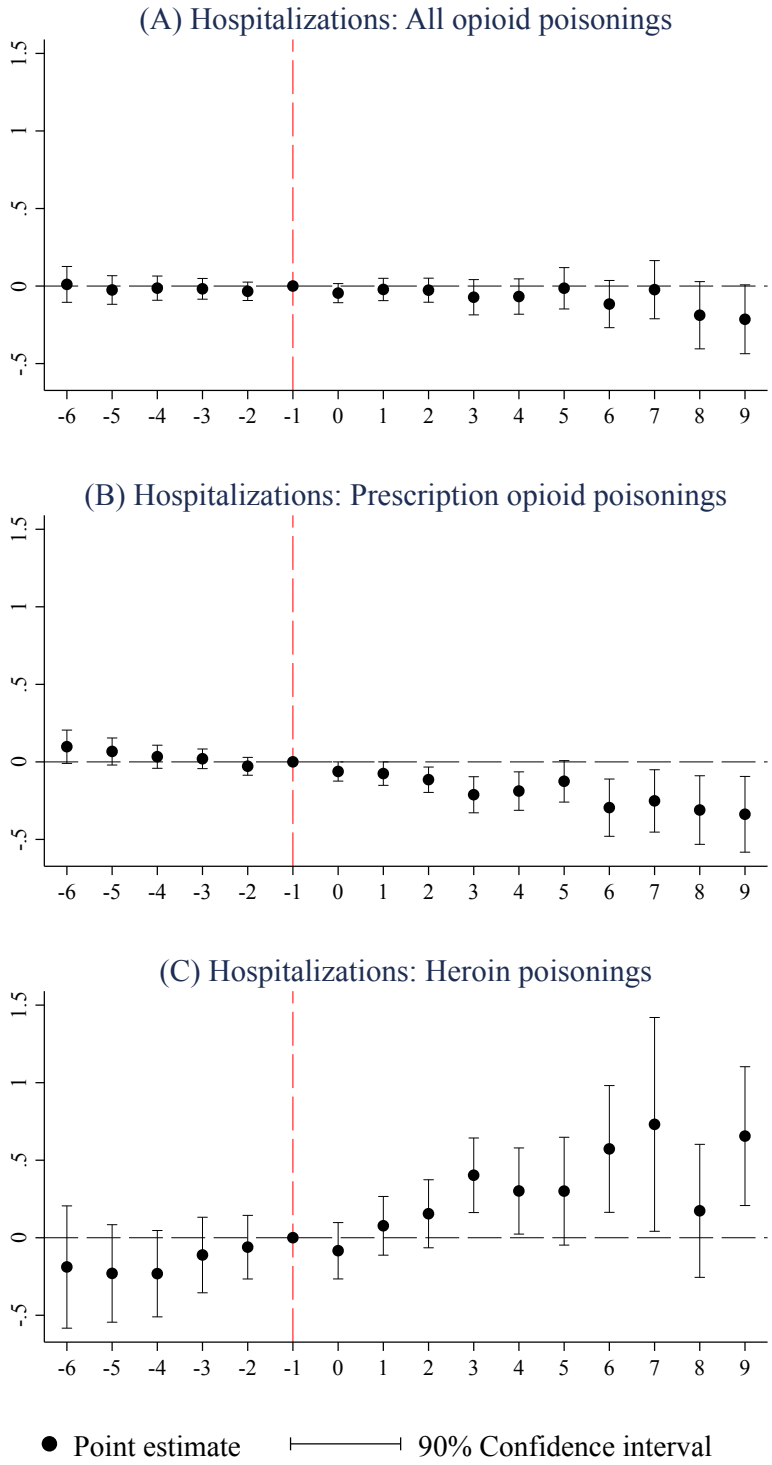
Note: The data are collected by the authors using the following sources: Prescription Drug Abuse Policy System, National Alliance for Model State Drug Laws, Prescription Drug Monitoring Program Training and Technical Assistance Center, states' statutes, and Horowitz et al. (2018).

Figure A.2: Event study analysis: Mortality



Note: Results from Poisson regression, with standard errors clustered at the state level. Data are from the National Vital Statistics System (NVSS).

Figure A.3: Event study analysis: Hospitalizations



Note: Results from Poisson regression, with standard errors clustered at the hospital level. Data are from the National Inpatient Sample (NIS).

B Appendix: Linear Model Results

Table B.1: The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions, Linear Models

	(1)	(2)	(3)	(4)	(5)	(6)
	(A) PRESCRIPTIONS					
	All opioid prescriptions		High dosage (MME/day $\geq$ 50)		Very high dosage (MME/day $\geq$ 90)	
	Enrollees	Prescriptions	Enrollees	Prescriptions	Enrollees	Prescriptions
PDMP	–0.098	–0.105	–0.105	–0.106	–0.075	–0.095
	(0.071)	(0.070)	(0.078)	(0.071)	(0.087)	(0.076)
	[0.032]	[0.029]	[0.023]	[0.035]	[0.093]	[0.051]
	(B) DOSAGE					
	Total amount			Per-claim average		
	Dosage in MME	Duration in days	Strength in MME/day	Dosage in MME	Duration in days	Strength in MME/day
PDMP	–0.140	–0.097	–0.139	–0.035	0.008	–0.033
	(0.090)	(0.074)	(0.083)	(0.053)	(0.010)	(0.049)
	[0.037]	[0.041]	[0.024]	[0.474]	[0.139]	[0.444]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51
Observations	306	306	306	306	306	306

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, state per-capita GDP, and lagged number of BCBS enrollees in the state (on a logarithmic scale). Data are from the Blue Cross Blue Shield Axis® database.

Table B.2: The Effect of Prescription Drug Monitoring Programs on Drug Shipments (Oxycodone/Hydrocodone), Linear Models

	(1) Total shipments	(2) Shipments to pharmacies	(3) Shipments to retail pharmacies	(4) Shipments to chain pharmacies	(5) Shipments to practitioners
PDMP	−0.030	−0.029	−0.044	−0.023	−0.091
	(0.018)	(0.018)	(0.028)	(0.019)	(0.127)
	[0.000]	[0.000]	[0.000]	[0.002]	[0.033]
Covariates	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51
Observations	459	459	459	459	459

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Shipments are based on the DEA's Automation of Reports and Consolidates Orders System data, accessed using the Washington Post's ARCOS API (`https://github.com/wpinvestigative/arcos-api`).

Table B.3: The Effect of Prescription Drug Monitoring Programs on Opioid Consumption, Linear Models

	(1)	(2)	(3)	(4)	(5)
	Ever used pain relievers non-medically	Ever used heroin	Ever used sedatives or tranquilizers non-medically	Ever used benzodiazepines	Received treatment for illicit drug use
PDMP	0.021	0.092	0.034	0.042	−0.031
	(0.023)	(0.051)	(0.033)	(0.035)	(0.091)
	[0.359]	[0.080]	[0.298]	[0.235]	[0.733]
Covariates	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51
Observations	306	357	306	306	306

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Survey on Drug Use and Health (NSDUH).

Table B.4: The effect of Prescription Drug Monitoring Programs on Mortality, Linear Models

	1993-2017 (ICD-9 and ICD-10)		1999-2017 (ICD-10)			
	(1) All opioids	(2) Opioid dependence	(3) All opioids	(4) Semi-synthetic opioids	(5) Heroin	(6) Methadone
PDMP	0.008	−0.034	−0.021	−0.090	0.131	−0.162
	(0.086)	(0.165)	(0.069)	(0.062)	(0.207)	(0.092)
	[0.797]	[0.467]	[0.410]	[0.002]	[0.010]	[0.000]
Covariates	Yes	Yes	Yes	Yes	Yes	Yes
State FE	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes	Yes
States	51	51	51	51	51	51
Observations	1,275	1,275	969	969	969	969

Note: Results from linear regression (OLS). Standard errors clustered at the state level are shown in parentheses below the coefficients. Randomization inference p-values are shown in square parentheses below the coefficients (1,000 resampling replications). Covariates include state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Vital Statistics System (NVSS).

Table B.5: The effect of Prescription Drug Monitoring Programs on Hospitalizations, Linear Models

	(1) All opioids	(2) Opioid medication	(3) Heroin	(4) Other/unspecified	(5) Share heroin
PDMP	−0.005	−0.061	0.110	0.041	1.305
	(0.033)	(0.036)	(0.048)	(0.054)	(0.457)
	[0.877]	[0.085]	[0.021]	[0.443]	[0.004]
Covariates	Yes	Yes	Yes	Yes	Yes
Hospital FE	Yes	Yes	Yes	Yes	Yes
Time FE	Yes	Yes	Yes	Yes	Yes
Hospitals	2,973	2,973	2,973	2,973	2,973
Observations	16,369	16,369	16,369	16,369	16,369

Note: Results from linear regression (OLS). Standard errors clustered at the hospital level are shown in parentheses below the coefficients. P-values are shown in square parentheses below the coefficients. Covariates include hospital size (on a logarithmic scale), state census population (on a logarithmic scale), state unemployment rate, state per-capita personal income, and state per-capita GDP. Data are from the National Inpatient Sample (NIS).