

# Impact of Must-access Prescription Drug Monitoring Program on Prescription Opioid Overdose Death Rates\*

Shishir Shakya<sup>†</sup>

## Abstract

As of 2019, all U.S. states, except Missouri, have enacted voluntary Prescription Drug Monitoring Programs (PDMPs). In response to the relatively low uptake of voluntary access, several states have strengthened their PDMPs by requiring providers to access information regarding prescription drug use under certain circumstances. These “must-access” PDMPs require states to view a patient’s prescription history to facilitate the detection of suspicious prescription and utilization behaviors. This paper develops causal evidence of the effectiveness of “must-access” PDMP laws in reducing prescription opioid overdose death rates relative to voluntary PDMP states. I find that PDMPs are ineffective in reducing prescription opioid overdose deaths overall, but the effects are heterogeneous across states with “must-access” PDMP states. I find that marijuana and naloxone access laws, poverty level, income, and education confound the impact of must-access PDMPs on prescription opioid overdose deaths.

---

\*While retaining full responsibility for errors and omissions, I thank Jane Ruseski, Daniel Grossman, Elham Erfanian, Sultan Altruqi and Daniel Bonneau from West Virginia University; participants of 58th Annual Meeting Southern Regional Science Association (SRSA); and Yiqing Xu University of California, San Diego for helpful comments in this work.

<sup>†</sup>Shishir Shakya, John Chambers College of Business and Economics & Regional Research Institute (RRI), West Virginia University, Morgantown WV 26506 E-mail: ss0088mix.wvu.edu.

# 1 Introduction

The United States (U.S.) is amid an opioid drug epidemic<sup>1</sup>. From 1999 to 2017, over 700,000 people have died from a drug overdose, and nearly 400,000 people have died from an overdose involving prescription (Rx) opioids and illicit opioids like heroin and illicitly manufactured fentanyl (CDC, 2019). In 2017, opioid overdoses claimed about 130 American lives each day<sup>2</sup>. In 2017, the number of overdose deaths involving opioids (including Rx opioids and illegal opioids) was six times higher than 2006 (CDC, 2019). The dramatic increase in opioid-related deaths has reversed the declining midlife mortality trend for middle-aged Whites (Case and Deaton, 2015). Florence et al. (2016) estimate the total economic burden of Rx opioid overdose along with opioid abuse, dependence, loss of productivity, and criminal justice costs to be \$78.5 billion annually.

In 2011, the Centers for Disease Control and Prevention (CDC) classified Rx abuse as an “epidemic”. Among many policy responses, the CDC promotes the Prescription Drug Monitoring Programs (PDMPs) as the best defense against the current Rx opioid crisis (Birk and Waddell, 2017)<sup>3</sup>. The PDMP is a supply-side policy to restrict over-prescription and over-utilization of controlled substances while maintaining compassionate care. PDMPs collect data on prescriptions of controlled substances and allow authorized healthcare providers, law enforcement officials, PDMP administrators, and other authorized stakeholders (Meinhofer, 2018) to identify patients who are possibly abusing Rx drugs, doctor shopping, and are at high risk of an overdose (Grecu et al., 2019)<sup>4</sup>.

Currently, 49 U.S. states, along with the District of Columbia and the U.S. territory of Guam has implemented some form of PDMPs. The only state without a PDMP is Missouri<sup>5</sup>. The stringency of the PDMPs varies by state along several dimensions<sup>6</sup> and also evolve over time<sup>7</sup>. As of 2018, 18 different states have enacted “must-access” or mandatory PDMP, while the remaining states have so-

---

<sup>1</sup>Opioid drugs are formulated to replicate properties of opium, mainly to soothe pain and emotions and to release the dopamine hormone to create a feeling of euphoria, and can lead users to dependence and later to the addiction. These opioid drugs include both legal painkillers like morphine, oxycontin, or hydrocodone prescribed by doctors for acute or chronic pain and illegal drugs like heroin and illicitly made fentanyl (CNN, 2019).

<sup>2</sup>Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2017. Available at <http://wonder.cdc.gov>.

<sup>3</sup>Various state-level policy responses have been pursued to address the escalating rate of opioid abuse and overdose, including quantitative prescription limits, patient identification requirements, doctor-shopping restrictions, Prescription Drug Monitoring Programs (PDMPs), provisions related to tamper-resistant prescription forms, and pain-clinic regulations (Meara et al., 2016).

<sup>4</sup>The data collected generally includes the names and contact information of the patient, prescriber, and dispenser, the name and dosage of the drug, the quantity supplied, the number of authorized refills, and the method of payment (Meinhofer, 2018).

<sup>5</sup>St. Louis County that accounts for more than half of the population of Missouri have implemented their PDMP and appeal to other counties and cities in Missouri to conjoin (PDMPTTAC, 2019).

<sup>6</sup>States can differ in who may access the database (e.g., prescribers, dispensers, law enforcement), in the agency that administers the PDMP (e.g., department of health, pharmacy boards), in the controlled substances (C.S.) that are reported (e.g., some do not monitor CS-V), in the timeliness of data reporting (e.g., daily, weekly), in how to identify and investigate cases of potential doctor shoppers (e.g., reactive, proactive), and on whether prescribers are required to query the database (Meinhofer, 2018).

<sup>7</sup>For instance; initially, several states implemented paper-based PDMPs. Still, eventually, these and others shifted to electronic-based PDMPs (Meinhofer, 2018).

called “voluntary” PDMPs. Authorized individuals in the states that passed must-access PDMP are required by law to check the PDMP before prescribing controlled substances ([Buchmueller and Carey, 2018](#)).

Most of the previous literature finds that PDMPs, in general, have limited, inconsistent, or no effect on mortality and abuse ([Meara et al., 2016](#); [Brady et al., 2014](#); [Reifler et al., 2012](#); [Haegerich et al., 2014](#)). These inconsistencies in results may be caused by not differentiating among voluntary and must-access PDMPs because, when then provider’s access not mandatory, only a small share of providers create PDMP logins and request patient histories ([PDMP Center of Excellence, 2014](#); [Buchmueller and Carey, 2018](#))<sup>8</sup>. Therefore, previous studies that do not differentiate between voluntary and mandatory PDMPs are likely to consider lower provider utilization of PDMPs when estimating the possible impacts.

A few recent studies differentiate between “must-access” and voluntary PDMPs in the research design. [Buchmueller and Carey \(2018\)](#) find must-access PDMPs reduce indicators of opioid abuse while voluntary PDMPs have no effects among elderly and disabled participants between 2007 and 2013. [Ali et al. \(2017\)](#) find limited impact based on self-reported measures of Rx drug abuse. [Grecu et al. \(2019\)](#) find a reduction in opioid abuse among young adults (ages 18 to 24) and substitution toward other illicit drugs and a corresponding decrease in admissions related to cocaine and marijuana abuse.

This paper contributes to this limited literature in several aspects. First, I examine the effect of the must-access PDMPs and develop some of the first evidence of state-level heterogeneous effects of must-access PDMPs. Second, I control for observable confounders using a high dimensional panel data from 1999 to 2017, implementing the double-selection post-LASSO method ([Belloni et al., 2013](#)). Most previous studies exploit variation PDMP policies as an exogenous shock to examine the effect of PDMPs on some outcome variables like opioid abuse, poisoning, and overdose death. However, state-specific political, socioeconomic, and demographic features could affect both PDMP enactment and opioid-related outcome variables. Therefore, for inference, the state’s political, socioeconomic, and demographic characteristics must be adequately controlled. The double-selection post-LASSO method helps with causal inference by utilizing the strengths of machine learning methods to select adequate observables and instruments.

Third, I examine Rx opioid overdose deaths in a state setting and contribute to the literature of program evaluation in a regional context. The synthetic control method of [Abadie and Gardeazabal \(2003\)](#); [Abadie et al. \(2010, 2015\)](#) only allows estimating the policy effect on one treatment unit or state; how-

---

<sup>8</sup>For example, when New York implemented a must-access PDMP in 2013, the number of registrants increased fourteen-fold. The number of daily queries rose from fewer than 400 to more than 40,000 ([PDMP Center of Excellence, 2016](#)). Similarly, in Kentucky, Tennessee, and Ohio, implementing a “must access” provision increased by order of magnitude the number of providers registered and the number of queries received per day ([PDMP Center of Excellence, 2016](#)). In contrast, in the first year after a voluntary PDMP was established in Florida, a state with a well-publicized opioid misuse problem, fewer than one in ten physicians had even created a login for the system ([Electronic-Florida Online Reporting of Controlled Substances Evaluation, 2014](#)).

ever, this study evaluates the impact of “must-access” PDMPs by implementing a generalized synthetic control method which allows multiple intervention units (Xu, 2017). This approach also allows modeling the unobserved time-varying heterogeneity by explicitly implementing the interactive fixed effects (IFE) model of Bai (2009), while the previous studies model the unobserved time-varying heterogeneity using unit-specific linear or quadratic time trends in a conventional two-way fixed effects models Grecu et al. (2019); Mallatt (2018). Fourth, to generalize the results to the national context, I implement weighted regressions, which allows for investigating the impact of “must-access” PDMP provisions across states.<sup>9</sup>

My findings show that “must-access” PDMPs states do not reduce the Rx opioid overdose deaths while these effects are heterogeneous across “must-access” PDMP states. I find evidence that marijuana and naloxone access laws, poverty level, income, education confound the impact of must-access PDMPs on the Rx opioid overdose deaths. I show that the unobserved time-varying heterogeneity possibly relates to the illicit fentanyl-overdose death rate, which cannot be identified from the overall Rx opioid overdose death rate. Furthermore, this paper explains why the existing literature does not reach a consensus regarding the effect of PDMPs. I show evidence that the definition of the Rx opioid death rate provided by the CDC can lead to inconclusive results. Among the deaths with drug overdose as the underlying cause, the CDC reports the Rx opioid deaths following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2); methadone (T40.3); and synthetic opioids, other than methadone (T40.4). Deaths from illegally-made fentanyl cannot be distinguished from pharmaceutical fentanyl in the data. For this reason, deaths from both legally prescribed and illegally produced fentanyl are included in these data.

Section 2 comprises a background of Rx opioids and PDMPs. Section 3 provides a literature review. Section 4 layouts detailed empirical strategies. Section 5 explains the data. Section 6 reports the results with a discussion. Section 7 concludes the study.

## 2 Prescription drug epidemic

In the 1840s, opium and morphine were sold as miracle cures and syrup. Diverse users<sup>10</sup> triggered the first U.S. opium and morphine epidemic that lasted until the 1910s. The 1960’s heroin epidemic, the 1980’s cocaine/crack epidemic, and 2000s methamphetamine epidemic are evidence that the United States has a persistent insatiable demand for intoxicating substances, legal and illegal (Pacula and Powell, 2018),

---

<sup>9</sup>Grecu et al. (2019) suggest utilizing weighted regressions because unweighted regressions impose the constraint of a similar effect for the entire population which may mask heterogeneity and policy effects.

<sup>10</sup>Mothers dosed themselves and their children with opium tinctures and patent medicines. Soldiers used opium and morphine to treat diarrhea and painful injuries. Drinkers alleviated hangovers with opioids. Chinese immigrants smoked opium, a practice that spread to the white underworld. But the primary source of the epidemic was iatrogenic morphine addiction, which coincided with the spread of hypodermic medication during 1870–1895. The model opioid-addicted individual was a native-born white woman with a painful disorder, often of a chronic nature (Kolodny et al., 2015).

and the U.S. is always on the war on drugs.

The root causes of the present U.S. opioid epidemic dates back to the 1980s. [Portenoy and Foley \(1986\)](#)'s conclusion that long-term usages of opioid pain relievers are safe (based on the sample size of 38 chronic pain patients) was widely cited to support the use of opioid pain relievers for chronic non-cancer pain. The practice to prescribe opioid pain relievers for chronic non-cancer pain gradually rose and accelerated rapidly after 1995 when Purdue Pharma introduced "OxyContin" as an extended-release formulation of oxycodone with aggressive marketing and promotion strategies<sup>11</sup>. This extend-release formulation contained a much higher concentration of oxycodone ([Singer, 2018](#)), which slowly releases into the bloodstream and can be taken less frequent intervals (every 12 hours for control of chronic pain) than other immediate-release counterparts products ([Soni, 2018](#)). Bootleggers diverted a considerable amount of OxyContin to the illegal market for non-medical use, and abusers crush OxyContin into a fine powder to snort (intranasal), or dissolve the powder in water to inject into intravenous, or chew ([Singer, 2018](#)).

Around the same time, in 1995, the president of the American Pain Society's campaign, "Pain is the Fifth Vital Sign" encourage healthcare professionals to assess pain ([Kolodny et al., 2015](#)) along with other four vitals: body temperature, blood pressure, heart rate, and respiratory rate. By 2001, the Veteran Affairs health system and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) – which accredits hospitals and other health care organizations, with the introduction of new pain management standards – made a formal recommendation to include pain as the fifth vital sign in the physician checklist ([Pacula and Powell, 2018](#)).

In 2005, Medicare introduced Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS)<sup>12</sup> linked inpatient reimbursement payments with patients' perspectives on hospital care – one of the measures is "pain management." When the Affordable Care Act passed, value-based incentive payments to hospitals were tied to the value of these patient experience performance measures, which included pain management scores as a core component [Pacula and Powell \(2018\)](#).

[Kolodny et al. \(2015\)](#) defines increasing overdose deaths involving prescription opioids (natural and

---

<sup>11</sup>As per [The United States, General Accounting Office \(2003\)](#), between 1996 to 2002, Purdue Pharma funded direct sponsorship or financial grants for more than 20,000 pain-related educational programs to promoted long-term use of OxyContin for chronic non-cancer pain. Purdue Pharma also provided financial support to the American Pain Society, the American Academy of Pain Medicine, the Federation of State Medical Boards, the Joint Commission, pain patient groups, and other organizations [Faubert \(2012\)](#).

<sup>12</sup>The HCAHPS Survey has three intents. The first is to produce comparable data on the patient's perspective on the care that allows objective and meaningful comparisons between hospitals on domains that are important to consumers. Second is to incentives for hospitals to improve their quality of care by linking Medicare reimbursement. The third is to enhance public accountability in health care by increasing the transparency of the quality of hospital care provided in return for the public investment. The HCAHPS survey contains 21 patient perspectives on care and patient rating items that encompass nine key topics: communication with doctors, communication with nurses, the responsiveness of hospital staff, pain management, communication about medicines, discharge information, cleanliness of the hospital environment, the quietness of the hospital environment, and transition of care. The survey includes four screener questions and seven demographic items, which are used to adjust the mix of patients across hospitals and for analytical purposes. The survey is 32 questions in length. See: <https://www.hcahpsonline.org/>

semi-synthetic opioids and methadone) since at least 1999 to 2010 as the "first wave." The "second wave" began in 2010 with rapid increases in overdose deaths involving heroin (CDC, 2019) and is contemporaneous with the 2010 abuse-deterrent formulations (ADF) or reformulation<sup>13</sup> of OxyContin (Evans et al., 2018), pill mill crackdown, prescription drug monitoring programs (PDMPs) (Meinhofer, 2016). The "third wave" began in 2013, with significant increases in overdose deaths involving synthetic opioids - particularly illicitly-manufactured fentanyl (IMF) (CDC, 2019) and its analogs adulterated with counterfeit pills and heroin which are highly potent, less bulky and – that are sourced primarily from China, Mexican drug trafficking organizations and disseminate using crypto-currencies through internet (Beletsky and Davis, 2017).

### 3 Literature Review

Existing studies associate PDMPs with opioid prescription and opioid-related overdose deaths and poisoning. At the same time, another strand of literature exploits PDMPs as an exogenous source of variation to investigate the heroin-related crime.

Simeone and Holland (2006) study the effect of PDMPs on the supply using Automation of Reports and Consolidated Orders System (ARCOS) and abuse of Rx drugs using Treatment Episode Data Set (TEDS) dataset. They find states with PDMP reduces per capita supply of Rx pain relievers and stimulants while the probability of abuse is higher among non-PDMPs states compared to PDMPs states. Reisman et al. (2009) also, find similar results that PDMP decreases the number of oxycodone shipments and the Rx opioid admission rate for states with these programs. Reifler et al. (2012) implement repeated measures negative binomial regression on quarterly RADARS System Poison Center and Opioid Treatment surveillance data (from 2003 to mid-2009) to estimate and compare opioid abuse and misuse trends. They find compared to non-PDMPs, PDMPs states reduce Poison Center intentional exposures by 1.9% per quarter, exposures opioid intentional exposures by 0.2% per quarter. In contrast, opioid treatment admissions increase, on average, 4.9% per quarter in states without a PDMP vs. 2.6% in states with a PDMP. These findings suggest the effectiveness of PDMPs. Simoni-Wastila and Qian (2012) retrieve 2.2 million records from Coordination of Benefits (COB) MarketScan administrative claims data of Medicare-eligible and their dependents to study analgesic utilization by an insured retiree population among the different types of PDMPs and non-PDMPs states with cross-sectional study implementing

---

<sup>13</sup>By the early 2000s, opioid overdoses and deaths, especially related to OxyContin spiked. In 2007, Prude Pharma pleaded guilty to misbranding OxyContin, a felony under the Food, Drug, and Cosmetic Act, and agreed to pay more than \$600 million in fines (Van Zee, 2009). In April 2010, the Food and Drug Administration approved Purdue Pharma's ADF of the original OxyContin formulation. With no public notice, on the 5<sup>th</sup> August 2010, Purdue Pharma stopped manufacturing the unique formulation of OxyContin and only manufactured and sold the reformulated version from 9<sup>th</sup> August 2010 (Butler et al., 2013) without any change in the price (Coplan et al., 2016). The ADF OxyContin is resistant to crushing, forms a gel not quickly injected when dissolved in solutions, and resists extraction with solvents (Singer, 2018).

multivariate logistic and multinomial regressions. They find reductions in the utilization of targeted Rx opioid analgesics and increases in less scrutinized, lower scheduled opioid analgesics. Contrary to these studies, [Brady et al. \(2014\)](#) find no significant impact on per-capita opioids dispensed among PDMP states. They convert quarterly 1999-2008 ARCOS database to morphine milligram equivalents (MMEs) for each state then implement multivariable linear regression modeling with temporal trends and demographic characteristics.

Contrary to previous studies that use simple multivariate analysis, the health economics literature deals rigorously with an identification strategy for proper estimation. For example, [Kilby \(2015\)](#) uses an individual-level dataset of Rx claims of 59% of the U.S. population from Truven Health Analytics and merges this dataset with ARCOS dataset. She finds about a 10% reduction of oxycodone Rx and a 10% decrease in oxycodone shipment. Similarly, [Buchmueller and Carey \(2018\)](#) uses a claims-level subsample of the universe of Medicare claims, and find must-access PDMPs reduce indicators of opioid abuse. In contrast, voluntary PDMPs have no effects among elderly and disabled participants between 2007 and 2013. [Ayres and Jalal \(2018\)](#) implements standard difference-in-difference with fixed effect methods on the county-level panel data on all opioid Rx in the U.S. between 2006 and 2015 along with county-level demographic controls, other state-level opioid interventions such as Naloxone Access and Good Samaritan laws, Medicaid expansion, and the provision of Methadone Assistance Treatment. They find a reduction of Rx rates; however, such a decline is pronounced among urban, predominantly white counties within more affluent regions. Another recent study [Rivera-Aguirre et al. \(2019\)](#) explores the source of heterogeneity of PDMPs (what populations benefit the most from these programs) and opioid overdoses using county-level, spatiotemporal study design. They find lower rates of Rx opioid-related hospitalizations but see an increase in heroin-related admission.

Contrary to the effect of PDMPs on the Rx rates, the results for the impact of must-access PDMPs on outcomes like opioid overdoses and opioid-related overdoses death rates are mixed. [Patrick et al. \(2017\)](#) perform 1999-2013 period state-level analysis with interrupted time-series with fixed effect and a linear time trend method using Wide-Ranging Online Data for Epidemiologic Research (WONDER) database of multiple causes of death maintained by the Centers for Disease Control and Prevention (CDC). They find an average reduction of 1.12 opioid-related overdose deaths per 100,000 population in the year after PDMPs implementation.

My study is similar to [Patrick et al. \(2017\)](#) in which they explore the impact of PDMPs on the Rx opioid overdose. However, they utilize interrupted time-series with fixed effect and a linear time trend. My study has a more rigorous identification strategy and implements non-linear time trends using interactive fixed effects. Unlike many other studies that utilize difference-in-difference with fixed effect methods, I perform difference-in-difference with event study framework and generalized synthetic

control approach, which is similar to event study models of [Grecu et al. \(2019\)](#) and [Mallatt \(2018\)](#) and interactive fixed-effect models used by [Mallatt \(2018\)](#). However, these studies explore the impact of PDMPs on the Rx opioid prescription and abuse. However, this research examines the impact of PDMPs on the Rx opioid overdose death rate similar to [Erfanian et al. \(2019\)](#). However, [Erfanian et al. \(2019\)](#) study impact of Naloxone access laws on opioid overdose deaths utilizing spatial econometric methods. Several studies exhibit the heterogeneous effects of PDMPs mainly on different age groups within the state population like [Grecu et al. \(2019\)](#); [Mallatt \(2018\)](#); [Ayres and Jalal \(2018\)](#); [Buchmueller and Carey \(2018\)](#). However, I show first-hand evidence of state-level heterogeneous effects of Rx opioid overdose. As my knowledge, this paper is first to utilize the strength and innovation of machine learning and causal inference namely the double-selection post-LASSO ([Belloni et al., 2013](#)) which is a robust method for inference on the effect of a treatment variable (must-access PDMP) on the outcome variable (Rx opioid overdose death) by selecting adequate observable confounders from a list of high dimensional controls which I compile based on the literature review and economic intuition.

## 4 Empirical Strategies

I exploit variation in the timing of adoption of must-access PDMPs, within a variety of difference-in-differences (D.D.) frameworks, to estimate the impact on the Rx opioid overdose death rate. I begin the analysis with a two-way fixed-effect model.

$$Y_{it} = c + \delta D_{it} + \alpha_i + \zeta_t + \varepsilon_{it} \quad (1)$$

where,  $Y_{it}$  is Rx opioid overdose death rates per 100,000 population (age-adjusted);  $c$  is the intercept,  $D_{it}$  is the treatment indicator and equals 1 after state  $i$  has been exposed to the treatment (must-access PDMP) and equals 0 otherwise;  $\delta$  is the average treatment effect,  $\alpha_i$  and  $\zeta_t$  are additive individual state and year fixed effects respectively. One should expect a negative and significant value of  $\delta$  which would suggest the must-access PDMP is successful to reduce Rx opioid overdose death rates. However, a positive and significant  $\delta$  shows that state with must-access PDMP have on average higher Rx opioid overdose death rates compare to comparison state that do not have must-access PDMP.

The state-specific political, socioeconomic, and demographic features could affect both must-access PDMP enactment and Rx opioid overdose death rates. Therefore, for inference, political, socioeconomic, and demographic characteristics of state or observable confounders must be adequately controlled. Failure to conditioning these confounders can lead to omitted variable bias. However, over-controlling leads to loss of efficiency of estimates. The actual data generating a process that explains the relationship



between the must-access PDMPs and Rx opioid overdose death rate is unknown to the researcher. However, one can use general economic intuition to guide the variable selection that is standard in the literature. Table 1 in the results section displays the list of variables, their transformation, units, data sources, and summary statistics. However, the actual data generating process (DGP) might comprise the various transformation of these observable confounders, for example, lags, higher-order polynomials, and interactions. Including and controlling for all these transformations may not be feasible because the covariates space can increase exponentially with high dimensional data, and regression is infeasible when the numbers of covariates exceed the number of observations in data.

To properly select the observable confounders, I exploit the strengths and innovations of machine learning method, namely the “LASSO”<sup>14</sup> and causal inference. Under the assumption of sparsity, I utilize the double-selection post-LASSO method Belloni et al. (2013) to select the observable confounders properly. The double-post-LASSO procedure comprises the following steps (Belloni et al., 2014). First, run LASSO of dependent variables on a large list of potential covariates to select a set of predictors for the dependent variable. Second, run LASSO of treatment variable on a large list of potential covariates to select a set of predictors for treatment. If the treatment is truly exogenous, I should expect this second step should not select any variables. Third, run OLS regression of dependent variable on treatment variable, and the union of the sets of regressors selected in the two LASSO runs to estimate the effect of treatment on the dependent variable then correct the inference with usual heteroscedasticity robust OLS standard error. The following D.D. exhibits the estimation after the double-post-LASSO procedure.

$$Y_{it} = c + \delta D_{it} + \beta x_{it} + \alpha_i + \varsigma_t + \varepsilon_{it} \quad (2)$$

where,  $x_{it}$  are a set of time-varying observable confounders selected by the double-selection post-LASSO.

The DD estimates in equation 1 and equation 2 only show the average impact of the must-access PDMPs. To obtain a more precise understanding of the impact of the must-access PDMPs, I employ an event study methodology, which takes into account the possible dynamic response of must-access PDMP on the Rx opioid overdose death rate. The event study D.D. framework with policy lags and leads to provide visual evidence of the policies’ effect. Furthermore, the event study D.D. framework is visually appealing to detect the parallel trend – in the absence of the treatment, the average outcomes of treated

---

<sup>14</sup>The Least Absolute Shrinkage and Selection Operator (LASSO) is an appealing method to estimate the sparse parameter from a high-dimensional linear model is introduced by Frank and Friedman (1993) and Tibshirani (1996). LASSO simultaneously performs model selection and coefficient estimation by minimizing the sum of squared residuals plus a penalty term. The penalty term penalizes the size of the model through the sum of absolute values of coefficients. Consider a following linear model  $\tilde{y}_i = \Theta_i \beta_1 + \varepsilon_i$ , where  $\Theta$  is high-dimensional covariates, the LASSO estimator is defined as the solution to  $\min_{\beta_1 \in \mathbb{R}^p} E_n \left[ (\tilde{y}_i - \Theta_i \beta_1)^2 \right] + \frac{\lambda}{n} \|\beta_1\|_1$ , the penalty level  $\lambda$  is a tuning parameter to regularize/controls the degree of penalization and to guard against overfitting. The cross-validation technique chooses the best  $\lambda$  in prediction models and  $\|\beta\|_1 = \sum_{j=1}^p |\beta_j|$ . The kinked nature of penalty function induces  $\hat{\beta}$  to have many zeros; thus, LASSO solution feasible for model selection.

and comparison states would have followed parallel paths – which is the key identifying assumption for D.D.

$$Y_{it} = c + \sum_{p=-12}^6 \delta_p D_{i,t+p} + \beta x_{it} + \alpha_i + \varsigma_t + \varepsilon_{it} \quad (3)$$

where  $D_{i,t+p}$  is an indicator equal to one if the must-access PDMP started in state  $i$  in the time  $t+p$  and equal zero in all other time periods. The coefficient  $\delta_p$  capture the measured effect of the must-access PDMP at  $p$  periods after the enactment. The negative value of  $p$  correspond to “leads, which captures the effect of the policy before it is implemented and should be zero under the “parallel trend” assumption (the average outcomes of the treated and control units follow parallel paths in pretreatment periods is required to maintain for causal inference) of the DD framework. The data starts from 1999 to 2017 which is 19 period. In this data sample, Kentucky, New Mexico and West Virginia are the earliest states that enacted must-access PDMP in 2012. From 2012 until 2016 there are 6 periods and prior 2012 there are 13 periods. Therefore, I index  $p$  from  $-12$  to 6 periods. See Figure 2.

The detection of the average outcomes of the treated and comparison states follow parallel paths in pretreatment periods is not sufficient but provides more confidence in the validity of the parallel posttreatment period. But, in many cases, if data do not support the parallel pretreatment trends, it’s likely to fail in the posttreatment period. The “parallel trend” assumption is not directly testable; however, literature provides two broad directions. First is the synthetic control (S.C.) method proposed by Abadie, Diamond, and Hainmueller (2010, 2015). It matches both pretreatment covariates and outcomes between a treated unit and a set of control units and uses pretreatment periods as criteria for suitable matches. Specifically, it constructs a “synthetic control unit” as the counterfactual for the treated unit by reweighting the control units. It provides explicit weights for the control units, making a comparison between the treated and synthetic control units transparent. However, it only applies to the case of one treated unit, and the uncertainty estimates it offers are not easily interpretable. The synthetic control method is not appropriate in this study because must-access PDMPs were enacted in several states at different periods.

The second approach is to model the unobserved time-varying heterogeneities explicitly. A widely used strategy is to add in unit-specific linear or quadratic time trends to conventional two-way fixed effects models. For example, [Grecu et al. \(2019\)](#) imposes a quadratic time trend to their two-way fixed effect model to examine the impact of opioid abuse among young adults; and [Mallatt \(2018\)](#) implements linear, quadratic and cubic time trends to estimate the effect of PDMP on heroin incidents.

An alternative way is to model unobserved time-varying confounders semiparametrically. For example, [Bai \(2009\)](#) proposes an interactive fixed effects (IFE) model, which incorporates the unit-specific

intercepts interacted with time-varying coefficients. The time-varying coefficients are also referred to as (latent) factors, while the unit-specific intercepts are labeled as factor loadings. Unlike explicitly imposing a linear or a quadratic time trend to a model, the IFE allows for additional non-linear time trends that affect areas to varying degrees. The factor captures nationwide time trends in Rx opioid-related overdose deaths to which different states are either more or less susceptible, depending on the unobservable characteristics of those states. The factor loading exhibits the intensity or severity of such nationwide time trends for each state. For example, [Mallatt \(2018\)](#) implements the D.D. framework with the IFE model to identify the effect of PDMPs on opioid painkiller Rx filled and on rates of heroin crimes.

I implement [Xu \(2017\)](#) generalized synthetic control (GSC) method that unifies the synthetic control method with linear fixed-effects models. This method provides several advantages over the S.C. method and IFE. First, it generalizes the synthetic control method to cases of multiple treated units and/or variable treatment periods and can estimate confidence intervals for counterfactual. Therefore, this method is suited for the causal inference for program evaluation in a regional context. Second, it embeds a cross-validation scheme to select the number of factors of the IFE model. The use of cross-validation is crucial because, in practice, researchers may have limited knowledge of the exact number of factors to be included in the model. The GSC estimate is presented as:

$$Y_{it} = \delta_{it}D_{it} + x'_{it}\beta + z_i\theta_t + \lambda'_i f_t + \alpha_i + \zeta_t + \varepsilon_{it} \quad (4)$$

where,  $f_t$  comprise of  $r$  different factor and  $\lambda_i$  are factor loadings. The main quantity of interest is the average treatment effect on the treated (ATT) at the time  $t$  when  $t > T_0$  and given as:

$$ATT_{t,t>T_0} = N_{tr}^{-1} \sum_{i \in \tau} [Y_{it}(1) - Y_{it}(0)] = N_{tr}^{-1} \sum_{i \in \tau} \delta_{it}$$

where,  $Y_{it}(1)$  is the observed for treated units in the posttreatment period, and  $Y_{it}(0)$  is the counterfactual for the treated unit in the posttreatment period. The total number of states is  $N = N_{tr} + N_{co}$ , where  $N_{tr}$  and  $N_{co}$  are the numbers of treated and control states. The  $T_{0,i}$  is the number of pretreatment period for state  $i$  and state are first exposed to the treatment at the time  $(T_{0,i} + 1)$  and observed for  $T - T_{0,i}$  periods. States in the control group remain unexposed to the treatment in the observed period. Under several assumptions<sup>15</sup>, [Xu \(2017\)](#) GSC estimator is a three-step process. First, the GSC method estimates the interactive fixed-effect model using only the control group. Second, GSC estimates factor loadings for each treated unit by minimizing the mean squared error of the predicted treated outcome in

---

<sup>15</sup>Under the assumption of strict exogeneity (unconfoundedness), decomposable time-varying confounders, weak serial dependence of the error term, some regularity conditions and cross-sectionally independent and homoscedastic error terms.

pretreatment periods. Third, GSC estimates counterfactuals with a cross-validation procedure to select the number of factors to be included in the model.

All of the regression presented in this section have clustered standard error at the state level to allow for an arbitrary autocorrelation process within states (Bertrand et al., 2004) and are weighted by the population of the relevant state (Angrist and Pischke, 2009).

## 5 Data

This study merges several panel data (from 1999 to 2017) from various sources. The dependent variable is Rx opioid overdose deaths per 100,000 (age-adjusted)<sup>16</sup> and retrieved from the National Vital Statistics System multiple cause-of-death mortality files published by the CDC. Figure 1 displays geographical heat maps of Rx opioid overdose death rate per 100,000 populations from 2002 to 2017.

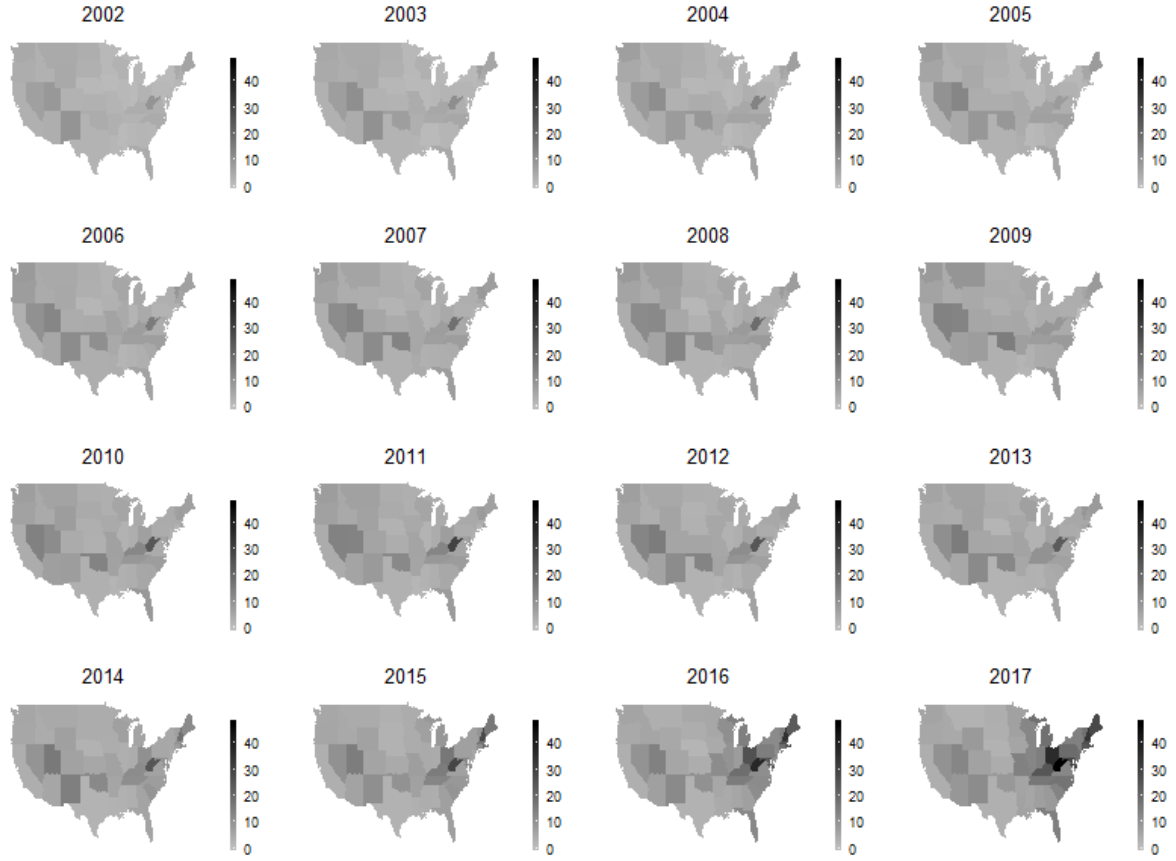
I retrieve the list of states that require prescribers to check the PDMP before prescribing controlled substances or must-access PDMP and the PDMP enactments date from the pdaps.org website. Figure 2 is a visual representation of state and timing of states that enacted must-access PDMP and the state with only voluntary PMDPs.

The supply of opioids along with a health care system – that incentivizes opioid prescription as a quick-fix to complex physical and mental health needs – fuels the U.S. opioid crisis, therefore, I include Morphine mg equivalents of prescribed opioids per 100,000 population in the control variable list. These quantities are available from the Drug Enforcement Administrations Automation of Reports and Consolidated Orders System (ARCOS). ARCOS reports the legal flow of control substances from the manufacturer to retail sales in the zip level and quarterly frequency. Reliance on opioid medication for physical pain, psychological trauma, concentrated disadvantages, isolation, and hopelessness – that are caused by economic and social upheaval – complicates the etiology of the U.S. opioid crisis (Dasgupta et al., 2018). Therefore controlling social and economic confounders (common causes of Rx opioid deaths and PDMPs enactment) is crucial for estimation. I retrieve several socioeconomic variables from

---

<sup>16</sup>As per kff.org, the National Vital Statistics System multiple cause-of-death mortality files were used to identify drug overdose deaths. Drug overdose deaths were classified using the International Classification of Disease, Tenth Revision (ICD-10), based on the ICD-10 underlying cause-of-death codes X4044 (unintentional), X6064 (suicide), X85 (homicide), or Y10Y14 (undetermined intent). Among the deaths with drug overdose as the underlying cause, Rx opioid deaths are indicated by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2); methadone (T40.3); and synthetic opioids, other than methadone (T40.4). Deaths from illegally-made fentanyl cannot be distinguished from pharmaceutical fentanyl in the data source. For this reason, deaths from both legally prescribed and illegally produced fentanyl are included in these data. Rates represent age-adjusted rates per 100,000 population. Natural and Semi-synthetic Opioids are a category of Rx opioids that provides for natural opioid analgesics (e.g., morphine and codeine) and semi-synthetic opioid analgesics (e.g., drugs such as oxycodone, hydrocodone, hydromorphone, and oxymorphone). Synthetic Opioids, other than Methadone, are a category of opioids, including drugs such as tramadol and fentanyl. Synthetic opioids are commonly available by prescription. Fentanyl is legally made as a pharmaceutical drug to treat pain, or illegally made as a non-prescription drug and is increasingly used to intensify the effects (or "high") of other medications, such as heroin. Methadone is a synthetic opioid prescribed to treat moderate to severe pain or to reduce withdrawal symptoms in people addicted to heroin or other narcotic drugs.

Figure 1: Rx opioid-related overdose death per 100,000 population

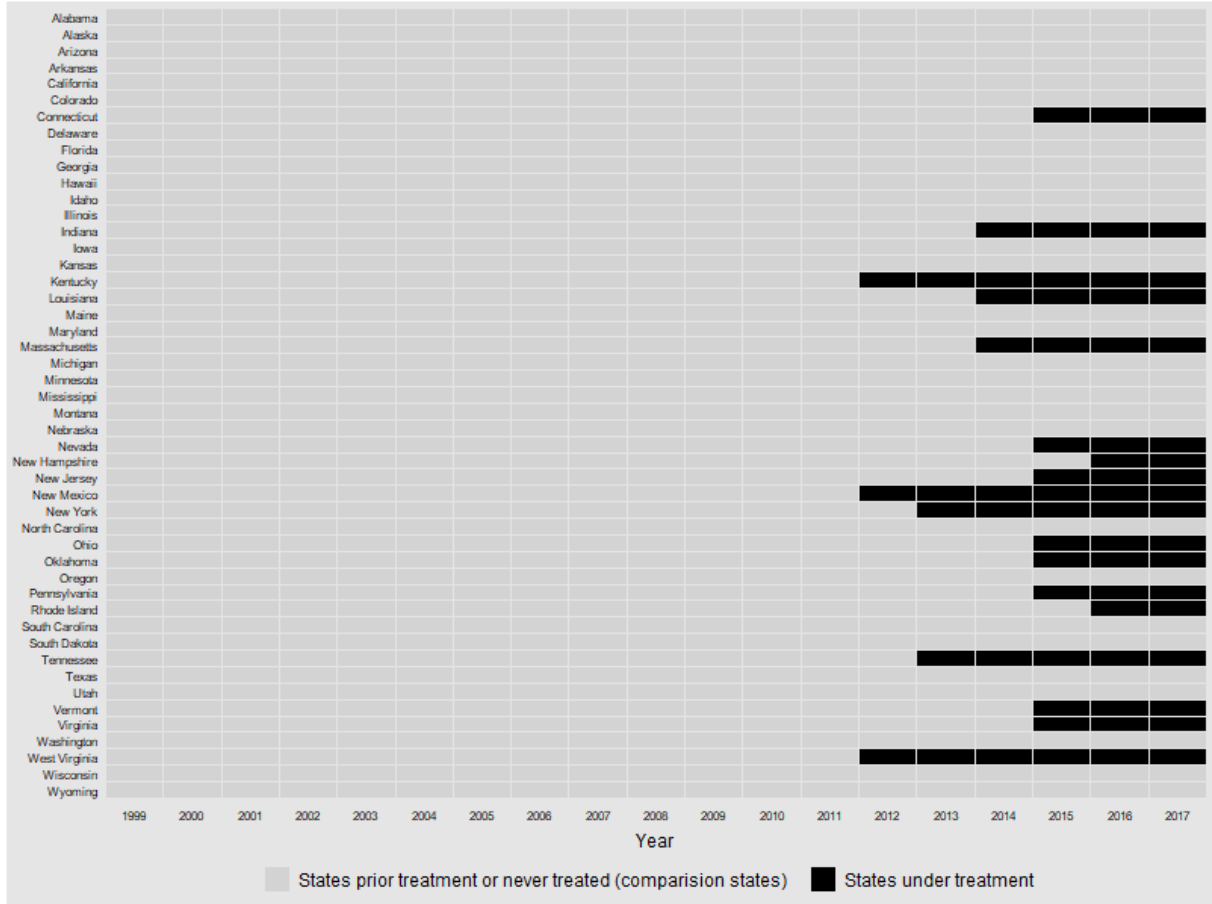


*Notes:* Darker intensity represents a higher Rx opioid-related overdose death rate. The intensity is fixed between 0 and 50 deaths per 100,000. This allows comparison of each state with others over the period. I exclude Alaska for scaling purpose.

the [University of Kentucky Center for Poverty Research \(2019\)](#) database; Annual State-Level Measures of Human Capital Attainment database ([Frank, 2009](#)); Measures of Income Inequality database ([Frank, 2014](#)); Top Income Shares by the State of Frank, State level employment database constructed by Barry and David was created in 2002 and is updated annually. [Monnat \(2016\)](#) briefs opioid crisis also intertwined with political supports, so I also control some political variables like a fraction of statehouse and Senate house that is democrats.

I also use Good Samaritan Laws, Marijuana Law (medical or/and recreational possession of Marijuana), and Naloxone Access Law as indicator variables. States with the Good Samaritan Law provide immunity from prosecution for possessing a controlled substance while seeking help for himself or another person experiencing an overdose. The state with Naloxone Access Law provides naloxone and other opioid overdose prevention services to individuals who use drugs, their families and friends, and service providers, including education about overdose risk factors, signs of overdose, appropriate response, and administration of naloxone. As of 2016, 48 states have authorized some variant of a naloxone access law,

**Figure 2: State requiring prescribers to check the PDMP before prescribing controlled substances.**



*Notes:* I exclude the state of Missouri because it has not enacted any form of PDMPs. Comparison states have enacted only a voluntary PDMPs. I also exclude the state of North Dakota due to the missing data. These data are retrieved from pdaps.org website.

and 37 states have passed a drug overdose good samaritan law ([Ayres and Jalal, 2018](#)).

Table 1 displays the list of variables, their transformation, units, data sources, and summary statistics. The summary statistics comprise the minimum, maximum, mean, and standard deviation for each variable. Each variable is pooled across time and state.

## 6 Results

### 6.1 Main results

Table 2 presents the estimated impact of the PDMP on the age-adjusted Rx opioid overdose death rate per 100,000 population utilizing difference-in-difference (DID), event study and generalized synthetic control with interactive fixed-effect (GSC) methods. When applicable, each of these methods use the double-selection post-LASSO method to select the confounders.

**Table 1:** Descriptive statistics (pooled across the state from 1999 to 2017)

Variables	Min	Max	Mean	Std Dev	Source
Prescription Drugs Monitoring Programs	0.00	1.00	-	-	PDAPS
Prescription opioid overdose death rate per 100,000 population	0.30	47.20	5.96	5.27	NVSS
Unemployment rate	2.30	13.70	5.65	1.97	UKCPR
Poverty rate	4.50	23.10	12.56	3.37	UKCPR
The fraction of state house that is the democrat	0.00	92.00	49.60	17.77	UKCPR
The fraction of state senate that is the democrat	0.00	100.00	48.52	19.02	UKCPR
State minimum wage (in 2014 \$)	2.20	10.62	7.39	1.05	UKCPR
Employment to population (percentage)	38.51	56.12	47.66	3.47	UKCPR
High school completion (percentage)	52.63	74.84	63.95	3.93	Frank (2009)
College level completion (percentage)	10.71	30.56	18.96	4.15	Frank (2009)
Atkinson inequality coefficient	21.60	41.08	28.25	3.62	Frank (2014)
Gini inequality coefficient	52.18	71.14	59.81	3.68	Frank (2014)
Thiel inequality coefficient	0.44	1.50	0.82	0.20	Frank (2014)
Fraction of top 1% income population	0.08	20.07	2.05	3.19	Frank (2014)
Fraction of millionaires population	0.11	18.27	2.05	3.05	Frank (2014)
Log of per capita Gross Domestic Product (in thousands, 2014 \$)	10.34	11.39	10.81	0.19	UKCPR
Log of per capita income (in thousands, 2014 \$)	10.37	11.39	10.82	0.19	UKCPR
Share of private construction industry (percentage)	2.89	11.99	5.59	1.22	unionstats
Share of private manufacturing industry (percentage)	1.61	27.23	11.97	4.87	unionstats
Share of total public industry (percentage)	10.78	31.87	17.08	3.60	unionstats
Morphine mg equivalents of prescribed opioids per 100,000 population	0.15	52.29	11.82	9.62	ARCOS
Marijuana law (either Medical and/or recreational)	0.00	1.00	-	-	PDAPS
Naloxone access law	0.00	1.00	-	-	Procon.org
Good samaritan law	0.00	1.00	-	-	PDAPS

*Notes:* The state of Nebraska don't have state upper and lower house. Missing value imputation were based on the weighted moving average and performed separately for each state.

**Table 2:** The impact of must-access PDMPs on age-adjusted Rx opioid overdose death rate per 100,000 population

Variables	DiD		Event study		GSC	
	(1)	(2)	(3)	(4)	(5)	(5)
ATT	5.45***(1.58)	4.31***(1.42)				
ATT (Average)			6.05***(1.65)	4.95***(1.78)	-0.91(2.39)	-0.82(2.92)
High school		0.29***(0.11)		0.12(0.11)		-0.05(0.05)
Marijuana law		2.01***(0.94)		1.77*(1.14)		-0.27(0.43)
Medicare expansion		1.31(1.09)		-0.94(1.13)		-0.72(0.53)
Fraction of millionaires		-0.18(0.63)		-0.19(0.59)		-0.15(0.36)
Naloxone access law		1.12(1.11)		2.33***(1.07)		-0.57(0.40)
Private manufacturing industry		-0.04(0.18)		-0.23(0.13)		-0.03(0.07)
Morphine		0.07(0.08)		0(0.08)		0.01(0.03)
Intercept	5.5***(0.41)	-13.93(8.19)				
State fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
DSPL	-	22	-	22	-	22
Factor	-	-	-	-	1	1
Observation	950	950	950	950	950	950
Treated states	18	18	18	18	18	18
Control States	30	30	30	30	30	30

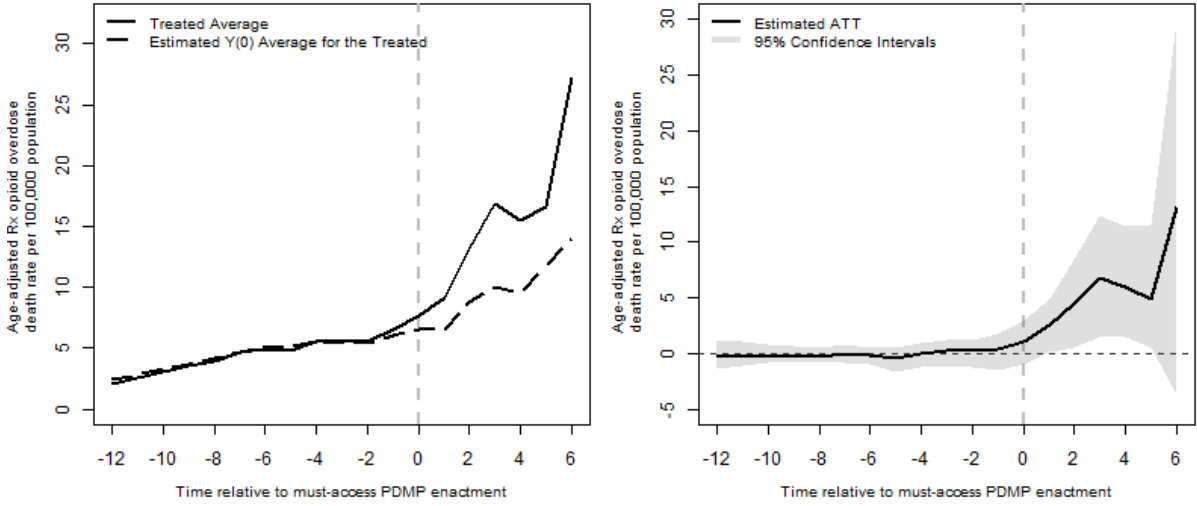
*Notes:* All the model comprises of state and year fixed effects. Standard errors are based on nonparametric bootstraps (blocked at the state level) of 2,000 times. Controls are selected implementing double post-LASSO selection method. Standard errors are enclosed in the parenthesis. The 1%, 5% and 10% level of significance are given as \*\*\*, \*\*, and \* respectively. DSPL shows numbers of variables that are feed to the double-selection post-LASSO method. In this table, the double-selection post-LASSO method was performed using 24 different contemporaneous covariates. Variable Morphine represents Morphine mg equivalents of prescribed opioids per 100,000 population. The event study and generalized synthetic control regressions are weighted based on the relevant state population.

Estimates presented in columns (1) and (2) are the standard two-way fixed effect model, also known as DID in the literature. The estimates in column (1) only include the indicator of must-access PDMP, while column (2) contains additional controls, these controls are selected utilizing the double-selection

post-LASSO method. On average, PMDP enacting states have 5.45 and 4.31 additional age-adjusted Rx opioid overdose death rates per 100,000 population, compared to comparison states with only voluntary PDMP.

The identification strategy of DID is the “parallel trend”, I relax this assumption. In other words, I estimate the effect of must-access PDMP on Rx opioid overdose death in the posttreatment period by subtracting the time intercepts estimated from the control group and the unit intercepts based on the pretreatment data. The predict Rx opioid overdose death for state  $i$  in year  $t$ , therefore, is the summation of unit intercept  $i$  and time intercept  $t$ , plus the impact of the time-varying covariates. The column (3) and (4) exhibits the average of ATT, and Figure 3 provides a visualization. These regressions are weighted based on the population size of relevant states.

**Figure 3:** Estimated Impact of must-access” PDMP on age-adjusted Rx opioid overdose death rate per 100,000 population for Years Before, During, and After Adoption, (based on event study)



The left panel of Figure 3 shows the average actual age-adjusted Rx opioid overdose death rate per 100,000 population (solid line) and average predicted age-adjusted Rx opioid overdose death rate per 100,000 population in the absence of must-access PDMP laws (dashed line); both averages are taken based on the number of terms since (or before) must-access PDMP laws first took effect. The right panel of Figure 3 shows the gap between the two lines or the estimated ATT. The confidence intervals are derived from the standard errors, which are based on nonparametric bootstraps (blocked at the state level) of 2,000 times. It is clear from both figures that the “parallel trends assumption is not likely to hold since the average predicted Rx opioid overdose death deviates from the average actual Rx opioid overdose death in the pretreatment periods.

These estimates presented in column (1) to column (4) may be contaminated by measurement error, mainly in the dependent variable. As per the CDC, among the deaths with drug overdose as the un-



derlying cause, prescription opioid deaths are indicated by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2); methadone (T40.3); and synthetic opioids, other than methadone (T40.4). Deaths from illegally-made fentanyl cannot be distinguished from pharmaceutical fentanyl in the data source. For this reason, deaths from both legally prescribed and illegally produced fentanyl are included in these data.

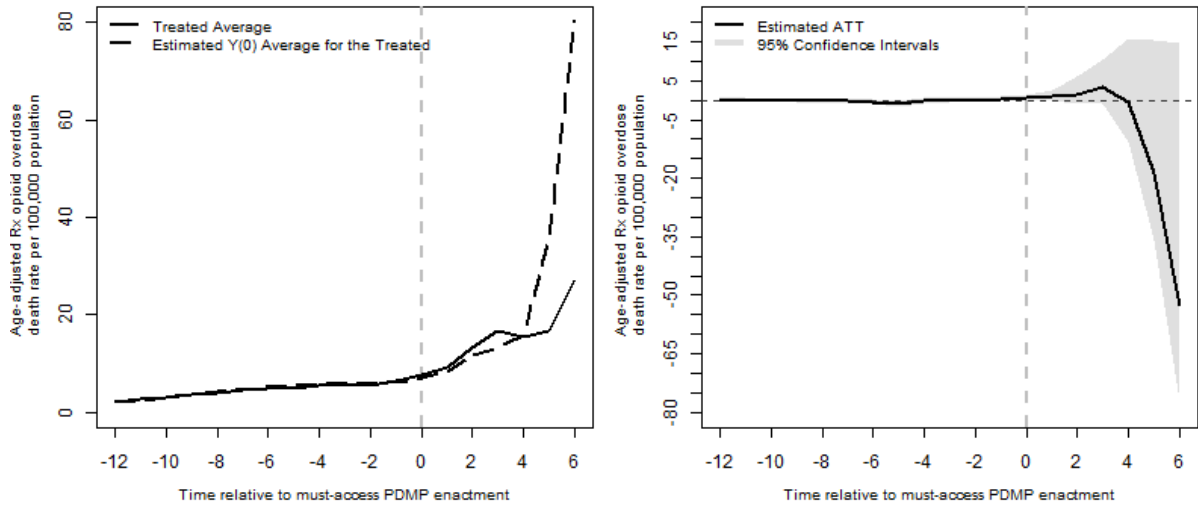
Literature establishes that PDMPs being a supply-side policy, opioid abusers, and dependent users may substitute the Rx opioid with cheap substitutes like illegally manufactured fentanyl or illegal heroin. (CDC, 2019) reports such substitution led to another nationwide crisis known as the third wave of the opioid crisis and illicit manufactured fentanyl are adulterated with counterfeit pills and heroin which are highly potent, less bulky and that are sourced primarily from China, Mexican drug trafficking organizations and disseminate using cryptocurrencies through internet (Beletsky and Davis, 2017).

The estimates presented in Table 2 cannot distinguish deaths from legally prescribed and illegally produced fentanyl. Therefore, the estimates possibly incorporate the total effect of must-access PDMPs on intended Rx opioid overdose deaths as well as the third wave of the opioid crisis (an unintended substitution effect). The positive significant coefficient suggests possibly unintended substitution effect surpasses the intended impact of PDMPs on the Rx opioid overdose death rate. One way to deal with such a situation is to implement an interactive fixed-effect model, which can help to control for the underlying nationwide time trends in Rx opioid death rate (if such pattern exists). The next section explores such a possibility.

Next, I apply the GSC method, which is similar to the synthetic control method but allows multiple treatment units and also allows the possibility of interactive fixed effects. Table 2 columns (5) and (6) reports the estimation from the GSC method. Again, both specifications impose additive state and year fixed effects. In column (5), no covariates are included, while in column (6), controls are selected, implementing the double-selection post-LASSO method. These regressions are weighted based on the population size of relevant states. The cross-validation scheme finds one unobserved factor to be important and after conditioning on both the factors and fixed additive effects. The estimated ATT is -0.91 and -0.82 and insignificant. These estimates suggest that must-access PDMP state laws are not associated with an increase in Rx opioid overdose death. Figure 4 provides a visualization.

The left panel of Figure 4 shows averages taken after the actual and predicted Rx opioid overdose death rates are realigned to the timing of the must-access PDMP enactment. With the GSC method, the average actual Rx opioid overdose death and average predicted Rx opioid overdose death match well in pretreatment periods. It diverged after must-access PDMP laws that took effect. The right panel of Figure 4 shows that the gaps between the two lines are flat in pretreatment periods, and the results shoot downward right after few years of the adoption of ‘must-access’ PDMP. Yet, such a relationship is

**Figure 4:** Estimated Impact of must-access PDMP on age-adjusted Rx opioid overdose death rate per 100,000 population for Years Before, During, and After Adoption, (based on generalized synthetic control study)



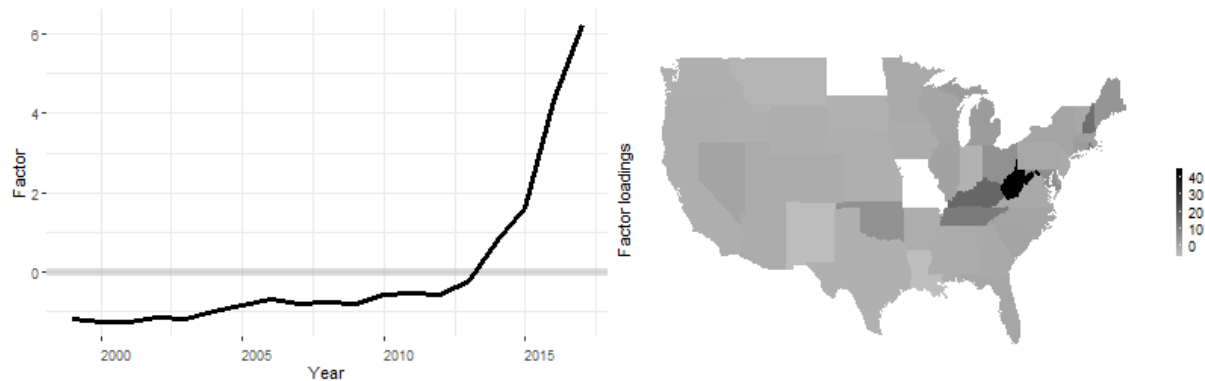
not statistically significant.

## 6.2 A nationwide time trends in Rx opioid

The estimates presented in 2 columns (5) and (6) requires an in-depth interpretation because the GSC includes the factor. Figure 5 shows factor in left panel. The x-axis is a year, and the y-axis is the magnitude of factors (re-scaled by the square root of their corresponding eigenvalues to demonstrate their relative importance). Bearing in mind the caveat that estimated factors might not be directly interpretable because they are, at best, linear transformations of the true factors, I find that the estimated factors shown in this figure are meaningful as this factor correlates with the third wave of the opioid crisis known as the synthetic opioid crisis. In simplest, the factor can be thought of as nationwide time trends in Rx opioid, in which different states are either more or less susceptible, depending on the unobservable characteristics of those states. A widely used strategy is to add in unit-specific linear or quadratic time trends to conventional two-way fixed effects models. For example, [Grecu et al. \(2019\)](#) imposes a quadratic time trend to their two-way fixed effect model to examine the impact of opioid abuse among young adults; and [Mallatt \(2018\)](#) implements linear, quadratic and cubic time trends to estimate the effect of PDMP on heroin incidents. The basic difference-in-difference model accounts for national non-linear patterns in Rx opioid overdose deaths. The GSC factor model extends this by accounting for additional non-linear time trends that affect areas to varying degrees. This factor gradually increases in Rx opioid overdose deaths from 1999-2012, which then increases exponentially from 2013-2015. States experience the non-linear increase in Rx opioid overdose deaths to differing degrees, which is accounted

for in each states' factor loading. In the case of Rx opioid overdose deaths, a states factor correlated with the third wave of the opioid crisis known as synthetic opioid crisis (CDC, 2019), implying that Rx opioid overdose deaths-dense states are more sensitive to the third wave of the opioid crisis that was triggered particularly those involving illicitly-manufactured fentanyl. This is consistent with the hypothesis that restricting Rx opioids causes opioid abusers toward another illicit opioid, in this case, that could be illicit fentanyl.

**Figure 5:** Factor and factor loadings



*Notes:* I exclude the state of Missouri, because it has not enacted any form of PDMPs. Comparison states have enacted only a voluntary PDMPs. I also exclude the state of North Dakota due to the missing data. Factor loading are enclosed in parenthesis with descending order as: West Virginia (43), Kentucky (16.2), New Hampshire (13.9), Tennessee (10.9), Rhode Island (10.1), Maryland (6.1), Oklahoma (5.6), Ohio (5.5), Maine (4.7), Connecticut (3.1), Delaware (3.1), Michigan (3), Massachusetts (1.8), Illinois (1.5), Nevada (1.4), South Carolina (1.2), North Carolina (1.2), New York (1), Wisconsin (0.9), Florida (0.7), Vermont (0.2), Pennsylvania (0.1), Georgia (0), Virginia (-0.1), Minnesota (-0.2), New Jersey (-0.4), Arizona (-0.4), Alaska (-0.5), Utah (-0.5), Alabama (-0.6), Colorado (-0.6), Iowa (-0.7), Mississippi (-0.8), Arkansas (-0.9), Oregon (-1.2), Wyoming (-1.3), California (-1.3), Idaho (-1.3), Nebraska (-1.5), Washington (-1.5), Kansas (-1.5), Hawaii (-1.6), Texas (-1.6), South Dakota (-1.8), Indiana (-2), Montana (-2.6), New Mexico (-4.7), Louisiana (-4.9)

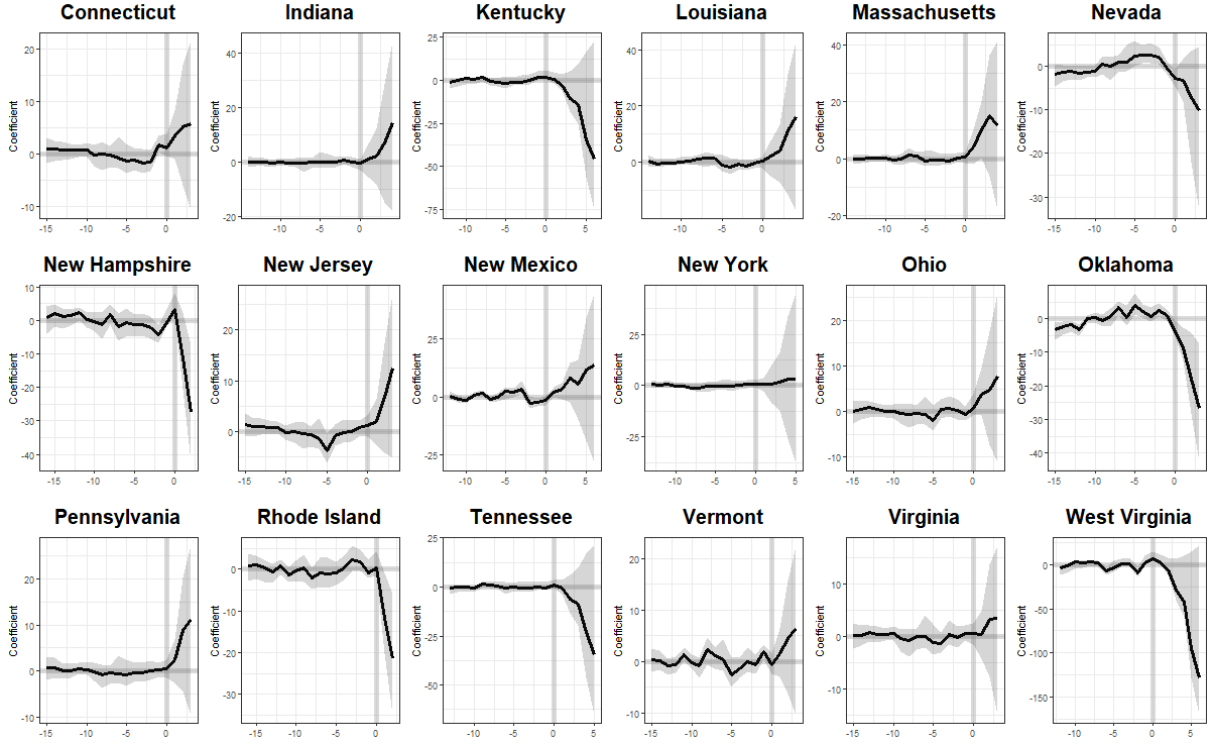
Figure 5 shows factor loadings in right panel. Factor loading exhibits severity of the state's experience of the non-linear increase in Rx opioid deaths (or the factor which correlates with synthetic opioid crisis) to differing degrees, which is accounted for in each state. The states with darker colors are more susceptible to the factor.

### 6.3 State-level impact of must-access PDMPs

Next, Figure 5 shows state-level impact of must-access PDMPs. Note to interpret these plots; we should keep track of the factor loading. The PDMPs seems to reduce the Rx opioid overdose deaths among the state of West Virginia, Kentucky, New Hampshire, Tennessee, Rhode Island, Oklahoma but these states also have higher factor loading – suggesting that possibly these states suffer higher unintended consequences where Rx opioid overdose deaths are substituted by the deaths from the third wave of the opioid crisis. The rest of the states presented in Figure 5 shows that PDMPs are ineffective in reducing Rx opioid deaths, however, the state of Nevada, despite having lower factor loading, seems to reduce the

Rx opioid death successfully.

**Figure 6:** State-level impact of “must-access PDMPs



*Notes:* To interpret these plot, we should keep track of the factor loading for each PDMP law abiding state.

#### 6.4 Validity: consistency using high dimensional covariates

Causal interpretation relies on the belief that there are no higher-order terms of the control variables, no interaction terms, and no additional excluded variables that associate with the PDMPs and Rx opioid overdose deaths. Thus, controlling a large set of variables seems desirable to make this assumption plausible. However, naively controlling redundant variables reduces the ability to distinguish the impact of interest variables and, consequently, produces less precise estimates. Further, literature considers utilizing lagged control rather than contemporaneous control mainly to avoid the potential reverse causality.

In this regard, I have 24 contemporaneous covariates; instead of these contemporaneous covariates, I took the first lag of these variables. Next, I allow second-order polynomial or quadratic of these lagged variables to account for possible non-linear relationships. Further, to allow the possible interaction of controls, I took all the feasible controls. Then to select the adequate controls, I implement the double-selection post-LASSO method using first lag, a second-order polynomial of first lag, all the possible interaction between first lag variables. In total, there are  $24+24+24*23/2=324$  different potential covariates. Table 3 shows the estimates which are very similar to the estimate I presented in the

**Table 3:** The impact of must-access PDMPs on age-adjusted Rx opioid overdose death rate per 100,000 population (variables selection on high dimensional covariates)

Variables	DiD		Event study		GSC	
	(1)	(2)	(3)	(4)	(5)	(6)
ATT	5.35***(1.55)	3.78***(1.27)	-	-	-	-
ATT (Average)	-	-	5.91***(1.63)	4.7(2.64)	-1.23(2.26)	-2.42(3.07)
State fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
DSPL	-	324	-	324	-	324
Factor	-	-	-	-	1	1
Observation	900	900	900	900	900	900
Treated states	18	18	18	18	18	18
Control States	30	30	30	30	30	30

*Notes:* All the model comprises of state and year fixed effects. Standard errors are based on nonparametric bootstraps (blocked at the state level) of 2,000 times. Controls are selected, implementing the double post-LASSO selection method. Standard errors are enclosed in parenthesis. The 1%, 5%, and 10% level of significance are given as \*\*\*, \*\*, and \*, respectively. DSPL shows the number of variables that are feed to the double-selection post-LASSO method. In this table, the double-selection post-LASSO method was performed using the first lag, the second-order polynomial of first lag, all the possible interaction between first lag variables, in total, there are  $24+24+24*23/2=324$  different possible covariates. The regressions (2), (3), (4), and (5) are weighted based on the relevant state population.

main results in Table 2, therefore provides validity of effect as the results have consistency across high dimensional covariates.

## 7 Discussion and conclusion

The results in the previous section are consistent and have relevance in the policy analysis in the regional settings. The GSC approach unifies the synthetic control method with interactive linear fixed-effects models under a simple framework, of which DID is a particular case (Xu, 2017). In short, this paper concludes that, on average, the effect of “must-access PMDPs on reducing Rx opioid overdose deaths is heterogeneous. States, where the “must-access PMDPs seem to reduce Rx opioid overdose deaths (mainly West Virginia, Kentucky, New Hampshire, Tennessee, Rhode Island, Oklahoma) are heavily affected by additional non-linear time trends that correlate with the third wave of the opioid crisis. The rest of the states, except for Nevada, the “must-access PMDPs, seem unsuccessful, and these sates are mildly affected by additional non-linear time trends. In aggregate, the PDMPs do not save lives, mainly due to the third wave of the opioid crisis.

We present some discussions on some of the obvious questions that the reader may have. First is why we choose to discuss the Rx opioid-related overdose deaths and not the Rx rates or other overdose deaths and some caveats of the dependent variable. Several papers discuss the impact of PDMPs on the Rx rate. We think that the effect of PDMPs on the prescription rate is evident that the PDMPs leads to a reduction of prescription rates. However, there may be some heterogeneity (Ayres and Jalal, 2018).

Literature finds the opioid Rx rate declines after PDMPs, but the trend of Rx opioid overdoses is rising. This phenomenon could represent either that the Americans are reporting more pain (which is not

the case), or the opioid user is using more of other opioid drugs (possible heroin/fentanyl). The overdose occurred due to the Rx opioid. As per the CDC, among the deaths with drug overdose as the underlying cause, prescription opioid deaths are indicated by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2); methadone (T40.3); and synthetic opioids, other than methadone (T40.4). Deaths from illegally-made fentanyl cannot be distinguished from pharmaceutical fentanyl in the data source. But simple economic intuition suggests that a reduction of prescription opioids would lead to higher demand for substitutes like heroin and fentanyl.

This paper shows evidence regarding the unintended consequence of the PDMPs using the interactive fixed-effect model. Readers might get concerned about endogeneity as the PDMPs were policy responses to the prescription-related opioid overdose deaths. I argue that the states with high opioid-related overdose death might enact must-access PDMPs, but once the PDMPs are passed, the feedback of high opioid-related overdose death to reenact must-access PDMPs is not possible. However, I also provide an additional analysis with a lagged variable and high dimensional list of covariates to control two sources of endogeneity: reverse causality and omitted variables biases. The results hold validity.

Secondly, I discuss why this paper finds evidence of the ineffectiveness of PDMP in generalize synthetic control and not in a simple Difference-In-Difference framework. The DID framework assumes “parallel trend or the average outcomes of the treated and control units follow parallel paths in pretreatment periods. Due to the unobserved time-varying confounding effect, the parallel trend assumption is not directly testable, and visual detection of the parallel trend is also most likely not to hold. GSC method captures unobserved time-varying confounding effects. At the same time, GSC allows the interactive fixed effect to potentially capture the unobserved heterogeneity. I argue that GSC absorbs the third wave of the opioid crisis, mainly the switching of prescription opioids to the illicit fentanyl, which is an unintended consequence of PDMPs. DID exhibits the estimates with both intended and unintended consequences of PDMPs, while GSC estimates tease out an intentional and unintentional effect of PDMPs.

Third, I discuss the meaning of the unobserved time-varying confounding effect or the factor. The factor captures nationwide time trends in prescription opioid-related overdose deaths to which different states are either more or less susceptible, depending on the unobservable characteristics of those states. The factor correlates with the third wave of the opioid. Therefore, this factor potentially captures a nationwide trend of prescription opioid switching toward illicit fentanyl as the unintended consequence. Even thou, we dont know the source of switching behavior, but the literature suggests Oxycotin re-formulation or other supply-side policy that restricts the prescription opioid, or drug lords are moving toward the suburb. Finally, to conclude, the Rx opioid deaths from illegally-made fentanyl cannot be distinguished from pharmaceutical fentanyl in the data source, therefore to study the impact of PDMPs on Rx opioids is obscure. However, there is clear evidence that abusers possible switch to cheaper opioid

alternatives like fentanyl.

## References

- Abadie, A., Diamond, A., and Hainmueller, J. (2010). Synthetic Control Methods for Comparative Case Studies: Estimating the Effect of California’s Tobacco Control Program. *Journal of the American Statistical Association*, 105(490):493–505.
- Abadie, A., Diamond, A., and Hainmueller, J. (2015). Comparative Politics and the Synthetic Control Method. *American Journal of Political Science*, 59(2):495–510.
- Abadie, A. and Gardeazabal, J. (2003). The economic costs of conflict: A case study of the Basque country. *American Economic Review*.
- Ali, M. M., Dowd, W. N., Classen, T., Mutter, R., and Novak, S. P. (2017). Prescription drug monitoring programs, nonmedical use of prescription drugs, and heroin use: Evidence from the national survey of drug use and health. *Addictive Behaviors*, 69:65 – 77.
- Angrist, J. and Pischke, J.-S. (2009). *Mostly Harmless Econometrics: An Empiricist’s Companion*. Princeton University Press, 1 edition.
- Ayres, I. and Jalal, A. (2018). The impact of prescription drug monitoring programs on U.S. Opioid prescriptions. *Journal of Law, Medicine and Ethics*, 46(2):387–403.
- Bai, J. (2009). Panel Data Models With Interactive Fixed Effects. *Econometrica*, 77(4):1229–1279.
- Beletsky, L. and Davis, C. S. (2017). Today’s fentanyl crisis: Prohibition’s Iron Law, revisited. *International Journal of Drug Policy*, 46(2017):156–159.
- Belloni, A., Chernozhukov, V., and Hansen, C. (2013). Inference on treatment effects after selection among high-dimensional controls. *Review of Economic Studies*, 81(2):608–650.
- Belloni, A., Chernozhukov, V., and Hansen, C. (2014). High-Dimensional Methods and Inference on Structural and Treatment Effects. *Journal of Economic Perspectives*, 28(2):29–50.
- Bertrand, M., Duflo, E., and Mullainathan, S. (2004). How much should we trust differences-in-differences estimates?
- Birk, E. and Waddell, G. R. (2017). The mitigating role of prescription drug monitoring programs in the abuse of prescription drugs.
- Brady, J. E., Wunsch, H., DiMaggio, C., Lang, B. H., Giglio, J., and Li, G. (2014). Prescription drug monitoring and dispensing of prescription opioids. *Public Health Reports*, 129(2):139–147.



- Buchmueller, T. C. and Carey, C. (2018). The effect of prescription drug monitoring programs on opioid utilization in medicare. *American Economic Journal: Economic Policy*, 10(1):77–112.
- Butler, S. F., Cassidy, T. A., Chilcoat, H., Black, R. A., Landau, C., Budman, S. H., and Coplan, P. M. (2013). Abuse rates and routes of administration of reformulated extended-release oxycodone: Initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. *The Journal of Pain*, 14(4):351 – 358.
- Case, A. and Deaton, A. (2015). Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. *Proceedings of the National Academy of Sciences*, 112(49):15078–15083.
- CDC (2019). Understanding the Epidemic — Drug Overdose — CDC Injury Center.
- CNN (2019). Opioid Crisis Fast Facts - CNN.
- Coplan, P., Chilcoat, H., Butler, S., Sellers, E., Kadakia, A., Harikrishnan, V., Haddox, J., and Dart, R. (2016). The effect of an abuse-deterrent opioid formulation (oxycontin) on opioid abuse-related outcomes in the postmarketing setting. *Clinical Pharmacology & Therapeutics*, 100(3):275–286.
- Dasgupta, N., Beletsky, L., and Ciccarone, D. (2018). Opioid Crisis: No Easy Fix to Its Social and Economic Determinants. *American Journal of Public Health*, 108(2):182–186.
- Electronic-Florida Online Reporting of Controlled Substances Evaluation (2014). 20112012 Prescription Drug Monitoring Program Annual report. florida Department of Health. Tallahassee, December.
- Erfanian, E., Grossman, D., and Collins, A. R. (2019). The impact of naloxone access laws on opioid overdose deaths in the us. *Review of Regional Studies*, 49(1):45–72.
- Evans, W. N., Lieber, E., and Power, P. (2018). How the reformulation of oxycontin ignited the heroin epidemic. Working Paper 24475, National Bureau of Economic Research.
- Fauber, J. (2012). Painkiller boom fueled by networking: Doctors, researchers with financial ties to drug makers set stage for surge in prescriptions.
- Florence, C., Luo, F., Xu, L., and Zhou, C. (2016). The Economic Burden of Prescription Opioid Overdose, Abuse and Dependence in the United States, 2013 HHS Public Access. *Med Care*, 54(10):901–906.
- Frank, L. E. and Friedman, J. H. (1993). A statistical view of some chemometrics regression tools. *Technometrics*.
- Frank, M. W. (2009). Inequality and growth in the united states: Evidence from a new state-level panel of income inequality measures. *Economic Inquiry*, 47(1):55–68.

- Frank, M. W. (2014). A New State-Level panel of Annual Inequality Measures Over the Period 1916-2005. *Journal of Business Strategies*, 31(1):241–263.
- Grecu, A. M., Dave, D. M., and Saffer, H. (2019). Mandatory Access Prescription Drug Monitoring Programs and Prescription Drug Abuse. *Journal of Policy Analysis and Management*, 38(1):181–209.
- Haegerich, T. M., Paulozzi, L. J., Manns, B. J., and Jones, C. M. (2014). What we know, and don’t know, about the impact of state policy and systems-level interventions on prescription drug overdose. *Drug and Alcohol Dependence*, 145:34–47.
- Kilby, A. (2015). Opioids for the Masses: Welfare Tradeoffs in the Regulation of Narcotic Pain Medications. *Working Paper*.
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., and Alexander, G. C. (2015). The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction. *The Annual Review of Public Health*, 36:559–74.
- Mallatt, J. (2018). The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions and Heroin Crime Rates. *SSRN*.
- Meara, E., Horwitz, J. R., Powell, W., McClelland, L., Zhou, W., O’Malley, A. J., and Morden, N. E. (2016). State Legal Restrictions and Prescription-Opioid Use among Disabled Adults. *New England Journal of Medicine*, 375(1):44–53.
- Meinhofer, A. (2016). The War on Drugs: Estimating the Effect of Prescription Drug Supply-Side Interventions. *SSRN*.
- Meinhofer, A. (2018). Prescription drug monitoring programs: The role of asymmetric information on drug availability and abuse. *American Journal of Health Economics*, 4(4):504–526.
- Monnat, S. (2016). Deaths of Despair and Support for Trump in the 2016 Presidential Election. *Department of Agricultural Economics, Sociology, and Education Research Brief*, pages 1–9.
- Pacula, R. L. and Powell, D. (2018). A Supply-Side Perspective on the Opioid Crisis. *Journal of Policy Analysis and Management*, 37(2):438–446.
- Patrick, S. W., Fry, C. E., Jones, T. F., and Buntin, M. B. (2017). Implementation Of Prescription Drug Monitoring Programs Associated With Reductions In Opioid-Related Death Rates. *Health Affairs*, 35(7):1324–1332.
- PDMP Center of Excellence (2014). Mandating PDMP participation by medical providers: current status and experience in selected states.

- PDMP Center of Excellence (2016). PDMP prescriber use mandates: characteristics, current status, and outcomes in selected states.
- PDMP TTAC (2019). Prescription Drug Monitoring Frequently Asked Questions (FAQ) — The PDMP Training and Technical Assistance Center.
- Portenoy, R. and Foley, K. (1986). Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain*, 25:171–86.
- Reifler, L. M., Droz, D., Bailey, J. E., Schnoll, S. H., Fant, R., Dart, R. C., and Bartelson, B. B. (2012). State Trends in Opioid Abuse/Misuse? *Pain Medicine*, 13(April):434–442.
- Reisman, R. M., Shenoy, P. J., Atherly, A. J., and Flowers, C. R. (2009). Prescription opioid usage and abuse relationships: An evaluation of state prescription drug monitoring program efficacy. *Substance Abuse: Research and Treatment*, 3(1):41–51.
- Rivera-Aguirre, A., Fink, D. S., Wintemute, G. J., Gruenewald, P. J., Cerdá, M., Castillo-Carniglia, A., Marshall, B. D. L., Ponicki, W. R., Gaidus, A., and Martins, S. S. (2019). Prescription Drug Monitoring Programs and Opioid Overdoses. *Epidemiology*, 30(2):212–220.
- Simeone, R. and Holland, L. (2006). *An evaluation of prescription drug monitoring programs*. US Department of Justice, Office of Justice Programs, Bureau of Justice .
- Simoni-Wastila, L. and Qian, J. (2012). Influence of prescription monitoring programs on analgesic utilization by an insured retiree population. *Pharmacoepidemiology and drug safety*, 21(12):1261–1268.
- Singer, J. A. (2018). Abuse-Deterrent Opioids and the Law of Unintended Consequences. (832).
- Soni, A. (2018). Health Insurance , Price Changes , and the Demand for Pain Relief Drugs : Evidence from Medicare Part D.
- The United States, General Accounting Office (2003). OxyContin Abuse and Diversion and Efforts to Address the Problem: Report to Congressional Requesters. Technical report, United States, General Accounting Office.
- Tibshirani, R. (1996). Regression Selection and Shrinkage via the Lasso.
- University of Kentucky Center for Poverty Research (2019). UKCPR National Welfare Data, 1980-2017.
- Van Zee, A. (2009). The promotion and marketing of oxycontin: Commercial triumph, public health tragedy. *American Journal of Public Health*, 99(2):221–227.

Xu, Y. (2017). Generalized synthetic control method: Causal inference with interactive fixed effects models. *Political Analysis*, 25(1):57–76.