Impact of "Must-access" Prescription Drug Monitoring Program on Prescription Opioid Overdose Deathrate: A Generalized Synthetic Control Approach[☆]

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Abstract

As of 2019, except Missouri, all the U.S. states have enacted voluntary Prescription Drug Monitoring Program (PDMP), while few other states have enacted a so-called "Must-access" PDMP. Unlike voluntary PDMP, the "Must-access" PDMP states abide by the law to collect data on controlled substance prescriptions. The "Must-access" PDMP states allow authorized individuals to view a patient's prescription history to facilitate the detection of suspicious prescription and utilization behaviors. This paper This paper utilizes panel data (1999-2015) and utilizes the Generalized Synthetic Control Method of Xu (2017) and displays the results with a comparison of the prescription opioid over-dosage death rates among "Must-access" PDMP states with voluntary PDMP states. This paper contributes to the causal inference for program evaluation in a regional context.

Keywords:

JEL codes:

☆ While retaining full responsibility for errors and omissions, I thank Jane Ruseski, Daniel Grossman, Elham Erfanian Sultan Altruki and Danny Bonneau and participants of 58th Annual Meeting Southern Regional Science Association (SRSA) for helpful comments in this work.

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1. Introduction

Deaths related to overdoses of opioids drugs[2], including both prescription drugs and illegal opioids such as heroin are rising in the United States. On average, 130 Americans die every day from an opioid overdose (CDC, 2018). Since 1999, rates of overdose death, drug treatment admissions, and prescription-drug sales have quadrupled, with two-fifths of prescription drugs overdose deaths (CDC, 2018). Prescription-drug abuse started to intensify in the late 1990s after the state medical boards began to relax the restriction on prescribing opioids for the treatment of chronic pain. Around the same time, to maintain patients right to pain reduction, the new pain-management standards added pain to the physician's standard checklist along with other vitals like blood pressure…. Aggressive marketing and promotion[3] of opioid pain relievers by pharmaceutical companies also led physicians to induced demand for prescription pain relievers (Manchikanti et al., 2012). As policy responses to the escalating rates of opioid abuse and overdose, the U.S. states policymakers have tried a diverse state-level policies like quantitative prescription limits, patient identification requirements, doctor-shopping restrictions, Prescription Drug Monitoring Program (PDMPs), provisions related to tamper-resistant prescription forms, and pain-clinic regulations (Meara et al., 2016).

The CDC has been promoting the Prescription Drug Monitoring Programs (PDMPs) as the best defense against the current impending crisis (Birk & Waddell, 2017). Currently, except for the state of Missouri, all the U.S. states have adopted voluntary PDMP, while ten states have enacted a so-called "must-access" or mandatory PDMP. Unlike voluntary PDMP, the "must-access" PDMP states abide by the law to collect data on controlled substance prescriptions that doctors have written for patients. The "must-access" PDMP states allow authorized individuals to view a patient's prescription history to facilitate the detection of suspicious prescription and

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[2] Opioid drugs are formulated to replicate properties of opium –mainly to sooth 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 the legal painkiller like morphine, oxycodone, or hydrocodone prescribed by doctors for acute or chronic pain as well as illegal drugs like heroin and illicitly made fentanyl (CNN, 2019).

[3] The root of the cause of the present US opioid endemic dates to 1995 when Purdue Pharma aggressively marketed OxyContin which is an oxycodone opioid that slowly releases the drug over 12 hours. This extended-release reformulation of oxycodone in OxyContin was initially believed to reduce the abuse liability of drug and was used as an aggressive marketing tool to convince the physician to prescribe OxyContin. However, the abuse of OxyContin by the intravenous (IV), intranasal, and oral routes was still possible. Unfortunately, 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).

utilization behaviors. Existing literature finds no effects of PDMPs (Haegerich, Paulozzi, Manns, & Jones, 2014; Meara et al., 2016) while Buchmuller & 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.

This study examines the effect of the PDMPs in the opioid-related overdose deaths in a regional setting. This study contributes to the literature on program evaluation in a regional context. Contrary to generic synthetic control method (Abadie, Diamond, & Hainmueller, 2010; Abadie & Gardeazabal, 2003) for program evaluation which allows to estimate the policy effect on one treatment unit or state, this study contributes to evaluate impact of must-access PDMPs implementing Xu (2017) generalize synthetic control method which allows multiple intervention units. Thus, this study complements Buchmuller & Carey (2018), which only estimates the effect among elderly and disabled participants between 2007 and 2013. Moreover, this paper offers several novel findings and insights.

Most of the study assume that PDMPs policy intervention as an exogenous shock and exploits PDMPs enactment as the natural experiment to examine the effect of PDMPs on some outcome variables like opioid-related overdose death. However, state specific political, socio-economic and demographic features could affect both "must-access" PDMP enactment and opioid-related overdose deaths. Therefore, for inference, a political, socio-economic and demographic characteristic of the state must be adequately controlled. Failure to control relavant confounders leads to omitted variable bias, however, over-controlling leads to loss of efficiency of estimates. By merging state-level data from several sources, this paper develops a high dimensional panel data of potential confounding variables and use the double-selection post-LASSO[4] method by (Belloni, Chernozhukov, & Hansen, 2013) for proper selection on observables confounders.

However, reverse causality can contaminate the estimates of the impact of PDMPs. This paper argues that the states with high opioid-related overdose death might enact "must-access" PDMPs, but once the PDMPs is enacted, the feedback of high opioid-related overdose death to reenact "must-access" PDMPs is not possible. Thus, simultaneity may not occur. Furthermore, unobservable can also induce biases in the estimation. This paper implements implementing Xu

[4] LASSO represents least absolute shrinkage and selection operator and is a feature selection machine learning algorithm.

(2017) generalize the synthetic control method to absorb unobserved time-varying confounding effect along with state and time fixed effects to maintain the "parallel trend" assumption and to estimate the counterfactual. Therefore, feedback from unobservable becomes less plausible.

Section 2 comprises a literature review. Section 3 explains data and concludes the methodology mainly to focus on policy endogeneity and estimation of counterfactuals in a regional setting. Section 4 reports the results. Section 5 has a summary with a discussion of policy prescriptions.

2. Literature Review

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

Simeone & Holland (2006) study the effect of PDMPs on the supply using Automation of Reports and Consolidated Orders System (ARCOS) and abuse of prescription drugs using Treatment Episode Data Set (TEDS) dataset. They find states with PDMP reduces per capita supply of prescription pain relievers and stimulants while the probability of abuse is higher among non PDMPs states compared to PDMPs states. (Reisman, Shenoy, Atherly, & Flowers, 2009) also, find similar results that PDMP decrease the number of oxycodone shipments and the prescription 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, whereas 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 & 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 multivariable logistic and multinomial regressions. They find reductions in the utilization of targeted prescription 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 covert 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 which use simple multivariate analysis, the health economics literature deals rigorously with identification strategy for proper estimation. For example, Kilby (2015) uses an individual level dataset of prescription claims of 59% of the U.S. population from Truven Health Analytics and merges this dataset with ARCOS dataset. She finds about 10% reduction of oxycodone prescription and a 10% decrease in oxycodone shipment. Similarly, Buchmuller & Carey (2018) uses a claims-level subsample of the universe of Medicare claims, and find must-access PDMPs reduce indicators of opioid abuse while voluntary PDMPs have no effects among elderly and disabled participants between 2007 and 2013. Ayres & Jalal (2018) implements standard difference-in-difference with fixed effect methods on the county-level panel data on all opioid prescriptions 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 prescription rates; however, such 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 prescription opioid-related hospitalizations but see an increase in heroin-related admission.

Contrary to the effect of PDMPs on the prescription rates, the results for the impact of must-access PDMPs on outcomes like opioid overdoses and opioid-related overdoses death rate are mixed. (Patrick, Fry, Jones, & Buntin, 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, I explore the impact of PDMPs on the prescription 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 effect. Unlike, many other studies which utilize difference-in-difference with fixed effect methods, I perform dynamic difference-in-difference which is similar to event study and interactive fixed effect models used by (Mallatt, 2017) and also a generalized synthetic control approach with a machine learning method.

3. Data

This study merges several panel data (from 1999 to 2017) from various sources. The primary dependent variable is prescription opioid overdose deaths per 100,000 (age-adjusted)[5] and retrieved from the National Vital Statistics System multiple cause-of-death mortality files published by CDC. This paper also merges several selected variables from the University of Kentucky Center for Poverty Research (UKCPR) data; Annual State-Level Measures of Human Capital Attainment database of Frank (2009); Measures of Income Inequality database of (M. W. 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. The Automation of Reports and Consolidated Orders System (ARCOS) provides the Morphine mg equivalents of prescribed opioids per 100,000 population. 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

[5] 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 X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent). 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 semisynthetic 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 displayed in this table represent age-adjusted rates per 100,000 population. Natural and Semisynthetic Opioids are category of prescription opioids that includes 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 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 drugs, 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.

a controlled substance while seeking help for himself or another person experiencing an overdose. The state with Naloxone Access Law provide naloxone and other opioid overdose prevention services to individuals who use drugs, their families and friends, and service providers; include 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, and 37 states have passed a drug overdose good samaritan law (Ayres & Jalal, 2018). Table 1 in the results section displays the list of variables, their transformation, units, data sources and summary statistics.

4. Identification Strategy

In this study, Delaware, Kentucky, Louisiana, Nevada, New Mexico, New York, Ohio, Oklahoma, Tennessee, and West Virginia enact a "must-access" PDMP and are considered as treated states (see Figure 2). Except for the state of Missouri, remaining states are comparison states.

The primary research question in this paper is if the treatment variable D ("must-access" PDMPs) affects the outcome variable Y (opioid-related overdose death rate) or not. Therefore, the causal direction flow is from D to Y given as $D \rightarrow Y$. I argue that the states with high opioid-related overdose death rates might enact "must-access" PDMPs, but once the state enacts the PDMPs, the feedback from high opioid-related overdose death rates to reenact "must-access" PDMPs is not possible. Thus, simultaneity may not occur. Therefore, $D \leftarrow Y$ don't exist.

I assume state specific political, socio-economic and demographic features could affect both "must-access" PDMP enactment and prescription opioid-related overdose death rates. Therefore, for inference, political, socio-economic and demographic characteristics of state (say X) 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 process that explains the relationship between the PDMPs and prescription opioid-related overdose deaths is unknown to researcher. However, I use general economic intuition to guide the variable selection.

The actual data generating process (DGP) might comprise the various transformation of X, for example, lags, higher order polynomials, and interactions. Moreover, 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. Under the assumption of sparsity, I utilize double-selection post-Lasso method proposed by Belloni et al. (2013) to select the observable confounders properly.

The difference-in-differences (DID) model aims to attain identification by restricting the way in which unobserved confounders affect the outcome of interest over time (Abadie & Cattaneo, 2018). However, DID identification strategy requires the further assumption that the effect of the unobserved confounders on the average of the outcome variable is additive and does not change in time, which implies "parallel trend.". The presence of unobserved time-varying confounders weakens this assumption (Xu, 2017).

After controlling for these observable explanatory variables implementing double-selection post-Lasso method (Belloni et al., 2013), I perform Generalize Synthetic Control Method (GSC) (Xu, 2017). Unlike Synthetic Control Method (SCM) of (Abadie, Diamond, & Hainmueller, 2010; Abadie & Gardeazabal, 2003) which can study one treatment unit at a time and cannot produce confidence interval for counterfactual, Xu (2017) GSC method allows study of multiple treatment units at a time and develops the confidence interval for counterfactual.

The assumption of the "parallel trend" or the average outcomes of the treated and control units follow parallel paths in pretreatment periods is required to maintain for causal inference. Due to the unobserved time-varying confounding effect, the parallel trend assumption is not directly testable[6] , and visual detection of the parallel trend is also likely not to hold (Xu, 2017). GSC method captures the unobserved time-varying confounding effect semi-parametrically based on Bai (2009) linear interactive fixed effects (IFE) models. However, unlike Bai (2009) IFE model

[6] One way to deal with the problem is matching prior to DID estimation as of Abadie (2005), seems intuitive but still fails to guarantee parallel pretreatment trends. Another approach is the synthetic control method proposed by Abadie, Diamond, and Hainmueller (2010, 2015) which compares the treated with the synthetic control where the synthetic control unit is some optimized weights of few selected control units. However, this method applies to only one treated unit. To model unobserved time-varying heterogeneities, a third strategy is to add in unit-specific linear or quadratic time trends to conventional two-way fixed effects models but doing so consumes large degree of freedom and underlying confounders may not be in the forms of specific trend. Fourth approach is model unobserved time-varying confounders semiparametric ally with unit specific intercepts interacted with time-varying coefficients also known as the interactive fixed effects of Bia (2009) where, the time-varying coefficients are also referred to as (latent) factors while the unit-specific intercepts are labeled as factor loadings.

where the number of factors for the IFE is known in prior, Xu (2017) allows cross-validation to discover the correct number of factors with high probability, therefore reduces the risks of overfitting.

5. Empirical Strategy

5.2 Generalized synthetic control

Several states enacted "must-access" PDMPs in a different period. Instead of performing individual synthetic control method to each treatment unit or state with "must-access" PDMPs, I implement Yu (2017) method of a generalized synthetic control which relies on the potential outcome framework for causal inference (Neyman 1923; Rubin 1974; Holland 1986).

The outcome of interest Y_{it} is opioid-related overdose death rates per 100,000 population, in the state i over the period 1999 to 2015 indexed with t. Let τ denote the states with "must-access" PDMPs and c denote the comparison states which excludes the state of Missouri. 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. Let $T_{0,i}$ be 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 $q_i = T - T_{0,i}$ periods. States in the control group remain unexposed to the treatment in the observed period. Now, assume that a linear factor model can approximate the Y_{it} and express the functional form as:

$$Y_{it} = \delta_{it} D_{it} + x_{it}'\beta + \lambda_i' f_t + \varepsilon_{it}$$

where, the treatment indicator is defined as D_{it} equals 1 after state i has been exposed to the treatment and equals 0 otherwise. The δ_{it} is the heterogeneous treatment effect on state i at time t; x_{it} is $k \times 1$ vector of observed confounding variables selected via double post Lasso selection method (see Appendix A4 for methodological details); $\beta = [\beta_1, ..., \beta_k]'$ is $k \times 1$ vector of unknown parameter, $f_t = [f_{1t}, ... f_{rt}]'$ is $r \times 1$ vector of unobserved common factors which is fixed during the observed period and treatment and control group both are affected by this fixed factor, $\lambda_i = [\lambda_{i1}, ..., \lambda_{ir}]'$ is $r \times 1$ vector of unknown factor loadings and ε_{it} represents unobserved idiosyncratic shock for state i at time t which has zero mean.

The above equation can be formalized using the potential outcome framework or Rubin's Causal Model. Let $Y_{it} = \delta_{it} D_{it} + x'_{it}\beta + \lambda'_i f_t + \varepsilon_{it}$ and $Y_{it} = \delta_{it} D_{it} + x'_{it}\beta + \lambda'_i f_t + \varepsilon_{it}$ be the potential outcome for the state i at a time t when $D_{it} = 1$ or $D_{it} = 0$ respectively. Then, the individual treatment effect on states with PDMP is $\delta_{it} = Y_{it}(1) - Y_{it}(0)$ for any state $i \in \tau$, $t > T_0$. Re-expressing:

$$Y_i = D_i \circ \delta_i + X_i\beta + F\lambda_i + \varepsilon_i$$

where, $i \in \{1, 2, ..., N_{co}, N_{co+1}, ..., N\}$; $Y_i = [Y_{i1}, ..., Y_{iT}]'$; $D_i = [D_{i1}, ..., D_{iT}]'$; symbol $\circ$ stands for the point-wise product; $\varepsilon_i = [\varepsilon_{i1}, ..., \varepsilon_{iT}]'$; $X_i = [x_{i1}, ..., x_{iT}]'$ and $F = [f_1, ..., f_T]'$. Stacking all the control units together we can express the equation as:

$$Y_{co} = X_{co}\beta + F\lambda'_{co} + \varepsilon_{co}$$

Now to identify β, F and λ_{co}, the factors are normalized, i.e. $F'F = I_r$ and are orthogonal to each other, i.e. $\lambda'_{co}\lambda_{co} = diagonal$. These constraints are based on (Bai 2003; Bia 2009) papers. Xu (2017) purposes a leave-one-out-cross-validation procedure for the choice of r (number of factors).

Then, 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:

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

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. Under several assumptions[7], Xu (2017) provides GSC estimator. Essentially, Xu (2017) GSC estimator is a three-step process. First, GSC estimates interactive fixed effect model using only the control group. Second, GSC

[7]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.

estimates factor loadings for each treated unit by minimizing the mean squared error of the predicted treated outcome in pretreatment periods. Third, GSC estimates counterfactuals. In practice, researchers may have limited knowledge of the exact number of factors to be included in the model. Therefore, Xu (2017) develop a cross-validation procedure to select models before estimating the causal effect. It relies on the control group information as well as information from the treatment group in pretreatment periods.

The results section follows several variants of the following data generating process. This framework flexibly incorporates the additive fixed effects, known time trends, and exogenous time-invariant covariates:

$$Y_{it} = \delta_{it} D_{it} + x_{it}'\beta + \gamma_i' I_t + z_i \theta_t + \lambda_i' f_t + \alpha_i + \zeta_t + \varepsilon_{it}$$

As explained earlier, Y_{it}, D_{it}, x_{it}, β, λ_i, f_t and, ε_{it} holds the same interpretation. The I_t is a $(q \times 1)$ vector of known time trend that may affect each unit differently; γ_i is a $(q \times 1)$ unit-specific unknown parameters; z_i is a $(m \times 1)$ vector of observed time-invariant covariates; θ_t is a $(m \times 1)$ unknown parameters, and ζ_t are additive individual and time fixed effects respectively.

6. Results

The results section includes a descriptive statistics table, geographical heat maps of the prescription opioid overdose death rate per 100,000 populations (age-adjusted) from 2000 to 2015, and graphical panel view plot on comparison and treatment states along with intervention year indicator. For inference, the prescription opioid overdose death rate per 100,000 populations (age-adjusted) is the primary dependent variable and enactment of "must-access" PDMPs is the treatment variable. The result section presents the impact of the treatment variable on the dependent variable. For each model, the double-selection post-Lasso method selects the covariates or controls. With these selected covariates, the results section exhibits several difference-in-difference models and generalized synthetic controls in tables and graphs. Later in this section, the results section displays estimates with different treatment samples selection to incorporate the policy heterogeneity.

Table 1: Descriptive statistics (pooled across the state from 2000 to 2015)

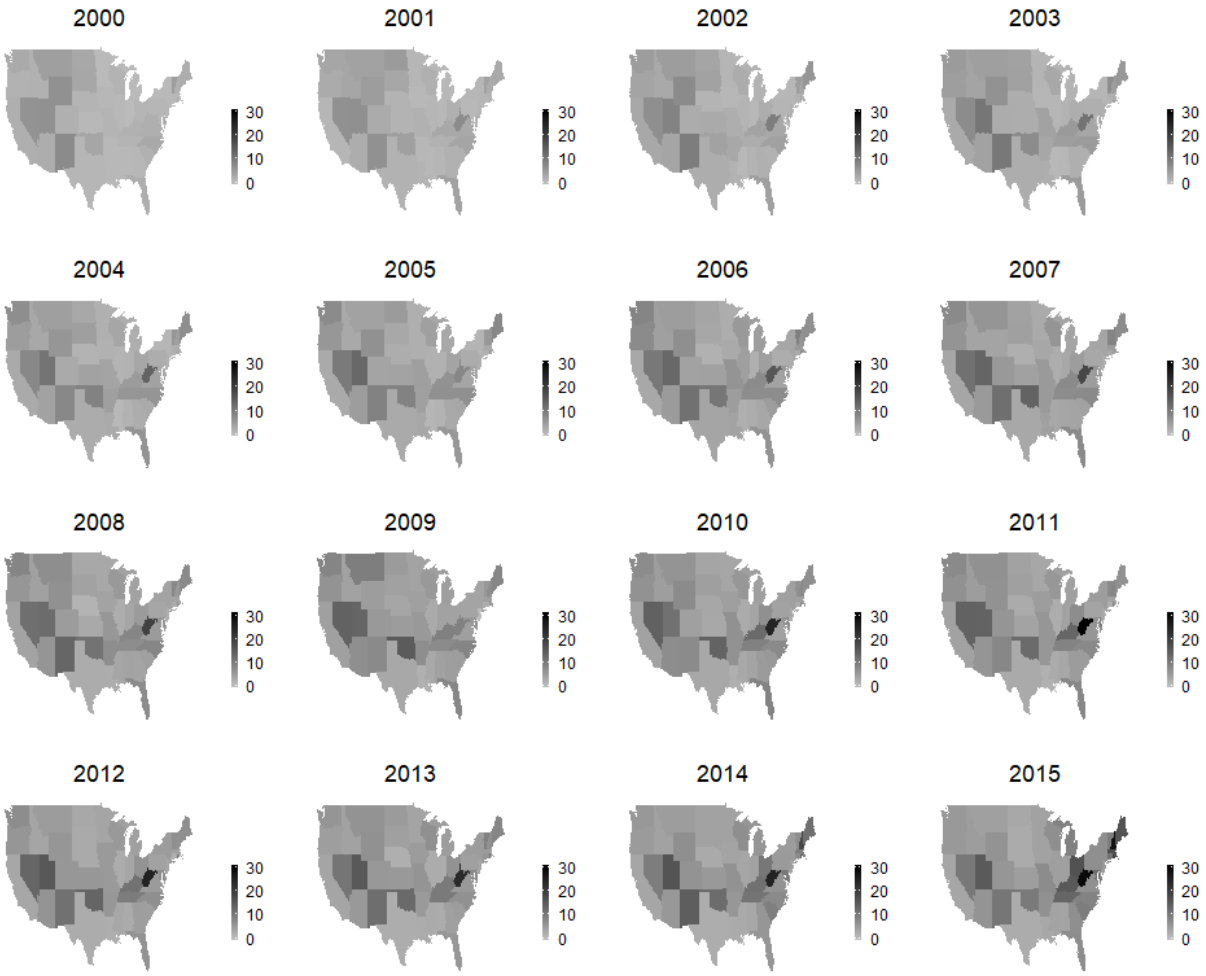
Variables	Min	Max	Mean	Std Dev	Source
Prescription opioid overdose death rate per 100,000 population	0.3	30	5.278	3.786	NVSS
Morphine mg equivalents of prescribed opioids per 100,000 population	0.15	52.29	11.85	9.56	ARCOS
Unemployment rate	2.3	13.7	5.75	2.01	UKCPR
Poverty rate	4.5	23.1	12.56	3.36	UKCPR
The fraction of state house that is the democrat	0	92	49.76	17.52	UKCPR
The fraction of state Senate that is the democrat	0	96	48.77	18.54	UKCPR
2012 PCI state minimum wage (dollars)	0.92	3.98	3.06	0.42	UKCPR
Employment to population (percentage)	38.51	56.12	47.82	3.52	UKCPR
High school completion (percentage)	52.63	74.84	63.86	3.9	Frank (2009)
College level completion (percentage)	10.71	30.56	18.82	4.03	Frank (2009)
Atkinson inequality coefficient	0.22	0.41	0.28	0.04	Frank (2014)
Gini inequality coefficient	0.52	0.71	0.6	0.04	Frank (2014)
Root mean deviation inequality coefficient	0.74	1.02	0.84	0.05	Frank (2014)
Thiel inequality coefficient	0.44	1.5	0.81	0.2	Frank (2014)
Fraction of top 1% income population	0.06	20.07	1.99	3.13	Frank (2014)
Fraction of millionaires' population	0.07	18.27	1.99	3	Frank (2014)
Log of per capita Gross Domestic Product (in thousands, 2014 $)	10.29	11.34	10.76	0.19	UKCPR
Log of per capita income (in thousands, 2014 $)	9.5	10.54	9.95	0.19	UKCPR
Share of private construction industry (percentage)	2.89	11.99	5.59	1.23	Frank (2002)
Share of private manufacturing industry (percentage)	1.61	27.23	12.03	4.85	Frank (2002)
Share of total public industry (percentage)	11.09	31.87	17.2	3.58	Frank (2002)
Share of total private industry (percentage)	68.13	88.91	82.8	3.58	Frank (2002)
Good Samaritan Law	0	1	-	-	PDAPS
Marijuana Law (either Medical and/or recreational)	0	1	-	-	PDAPS
Naloxone Access Law	0	1	-	-	Procon.org
Prescription Drugs Monitoring Programs	0	1	-	-	PDAPS

Note: State minimum wage is deflated using the Consumer Price Index (CPI) for all urban consumers. Gross Domestic Product and Personal Income are deflated using Gross Domestic Product: implicit price deflator. The treatment indicator of "must-access" PDMPs are retrieved from Buchmuller & Carey (2018).

6.1 Descriptive statistics

Table 1 in the results section presents the list of variables, their transformation (log, level, percentage, rate e.t.c.), units, data sources and summary statistics. The summary statistics comprises the minimum, maximum, mean and standard deviation for each variable. Each variable is pooled across time and state. The maximum prescription opioid overdose death is 30 per 100,000 populations. The maximum of Morphine milligram equivalents of prescribed opioids is about 50 per 100,000 population.

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



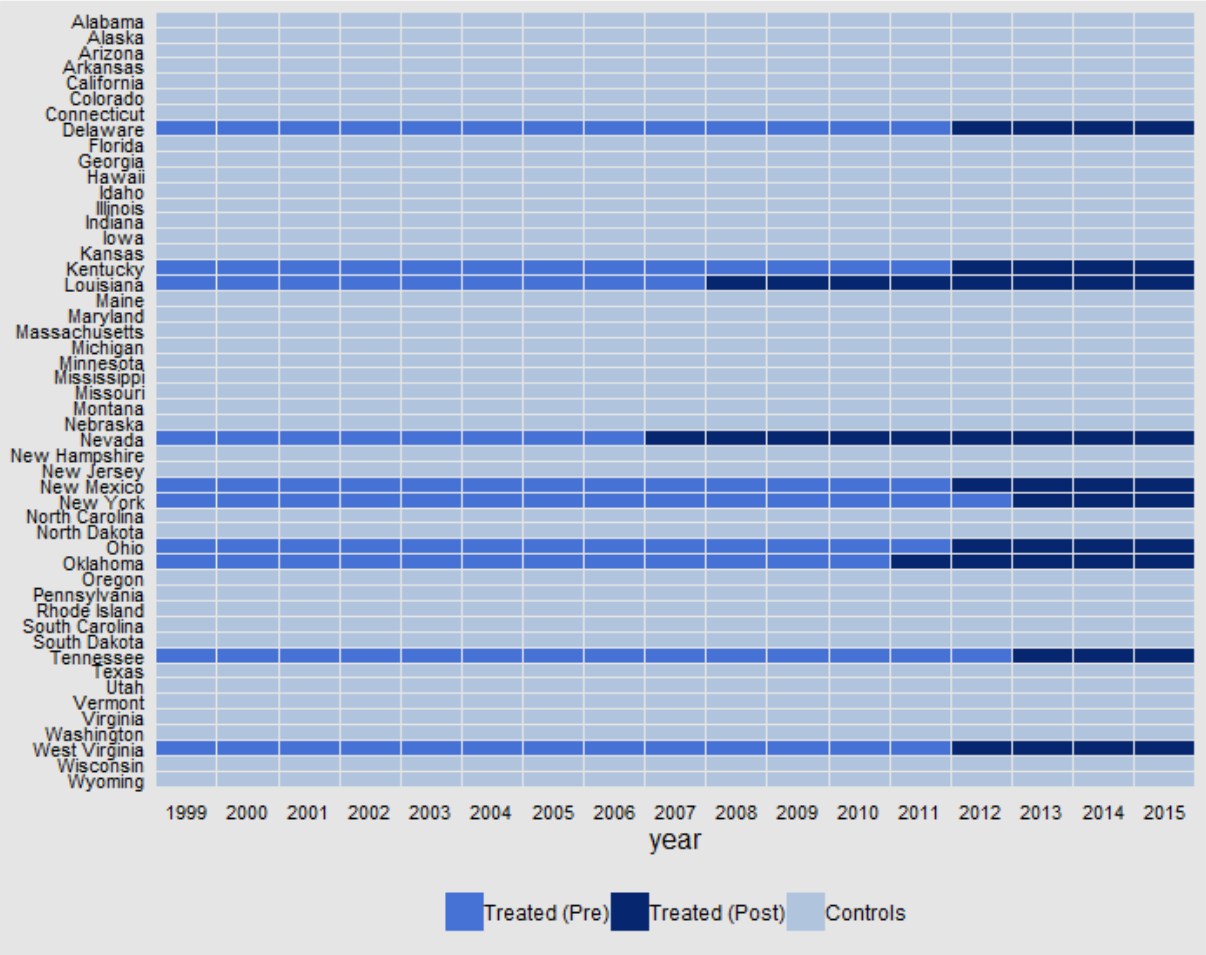
Note: I exclude Alaska. It prohibits proper scaling of geographical plots.

Figure 1 displays geographical heat maps of prescription opioid overdose death rate per 100,000 populations from 2000 to 2015. Darker intensity represents a higher prescription opioid-related overdose death rate. The intensity is fixed between 0 and 30 deaths per 100,000. This allows comparison of each state with others over the period.

Figure 2 is a panel view representation of "must-access" PDMPs enactment states and comparison states. Louisiana and Nevada enacted "must-access" PDMPs in around 2007. Delaware, New Mexico, New York, Ohio, Oklahoma, Tennessee, and West Virginia enacted "must-access" PDMPs after 2010 when opioid abuse widespread. Other than these ten states in the

treatment group, all other states except Missouri are listed in the comparison group. The comparison group states have voluntary PDMPs only.

Figure 2: Comparison and treatment states



The state of Missouri has not enacted any form of PDMPs. Comparison states have enacted only a voluntary PDMPs.

6.2 Main Results

Louisiana and Nevada enacted PDMPs in around 2007-2008, while other states in the treatment group enacted PDMP after 2010 when opioid was becoming an epidemic. The purpose of the enactment of PDMPs in the first wave around 2007 can be different from the objective of enactment of PDMPs in the second wave or post-2010. I present the analysis including Louisiana and Nevada in Appendix A3, while for the main results section, I exclude Louisiana and Nevada.

6.2.1 Difference-in-difference (excluding Louisiana and Nevada)

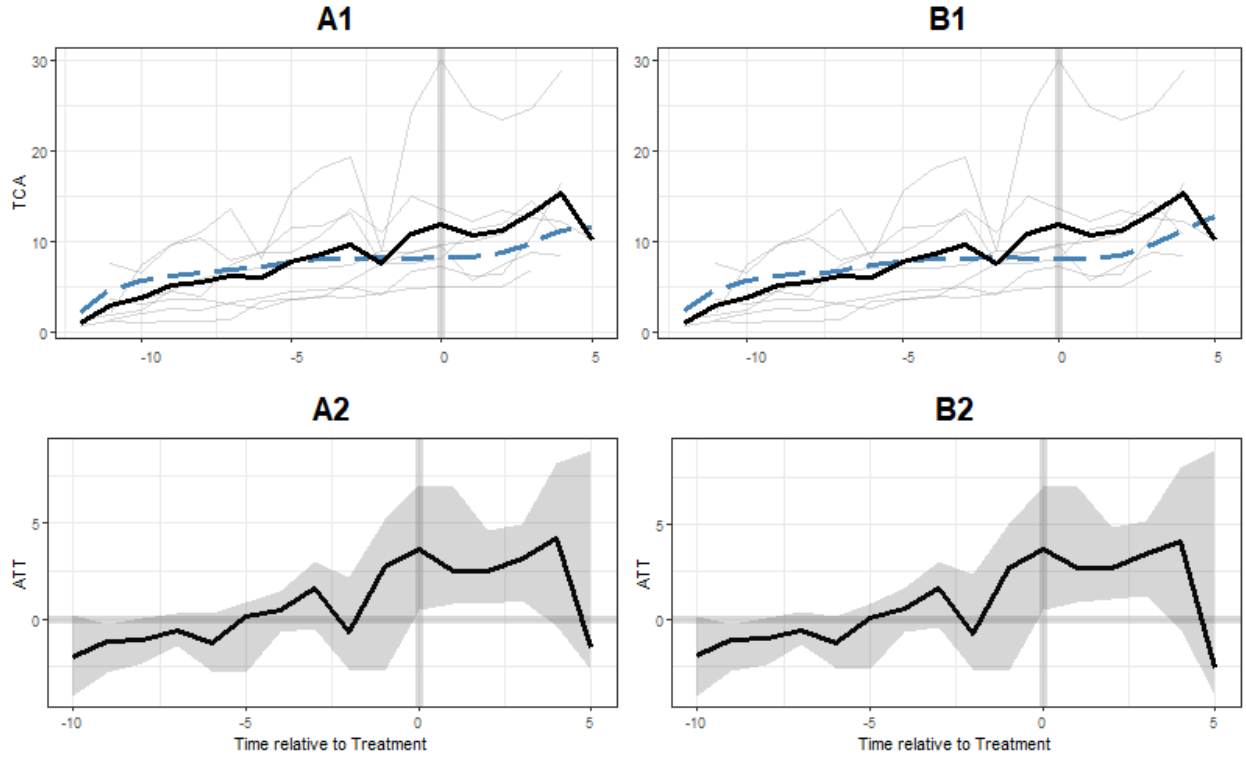
Table 3: Difference-in-difference (excluding Louisiana and Nevada)

Prescription Opioid Overdose Deaths and Death Rate per 100,000 Population (Age-Adjusted)					
Variables	FE				
	DID			Dynamic DID	
	-1	-2	-3	-4	-5
D	2.70***(1.28)	2.61***(1.18)	2.70***(1.13)		
Avg-ATT				2.84***(1.21)	2.94***(1.21)
Employment.to.Population		0.24(0.17)	-1.37(1.82)	0.40***(0.13)	0.03(0.84)
HighSchool		0.22***(0.09)		0.23**(0.1)	
log.Per.capita.PI		3.50(4.92)		-1.31(3.05)	
MillionUS		-0.44(0.44)	-0.33(0.43)	-0.54(0.32)	-0.17(0.28)
Share.Priv.Construction		-0.07(0.15)		-0.09(0.14)	
Share.Priv.Manufacturing		-0.27***(0.1)		-0.22***(0.09)	
SQ_Employment.to.Population			0.02(0.02)		0.00(0.01)
SQ_Share.Priv.Construction			0.00(0.01)		-0.01(0.01)
SQ_Share.Priv.Manufacturing			-0.01***(0.00)		-0.01***(0.00)
State.Minimum.Wage		-0.15(0.14)	-0.20(0.15)	-0.15(0.14)	-0.17(0.14)
total_mme		0.04(0.06)	0.04(0.06)	-0.01(0.04)	0.00(0.04)
_const	5.10***(0.39)	-53.22(49.75)	30.95(41.85)		
State fixed effects	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes
DSPL (List 1)	-	Yes	-	Yes	-
DSPL (List 2)	-	-	Yes		Yes
Factors	-	-	-	0	0
Observation	736	736	736	736	736
Treated states	8	8	8	8	8
Control States	39	39	39	39	39

*Note: 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 *. The estimates are given column (1), (2) and (3) are average treatment effect or ATT. The estimates given in (4), (5), are the average of average treatment effect (A-ATT). DSPL (list 1) is double-selection post-Lasso variable selection using 22 contemporaneous covariates list, and DSPL (list 2) is double-selection post-Lasso variable selection using DSPL (list 1) variables along with second order polynomial, first level all feasible interaction and up to two lags.*

Table 5 shows the DID estimates but excludes Louisiana and Nevada from the treatment group. The DID estimates in column (1), (2) and (3) of Table 5 shows about 2.7 more prescriptions opioid death per 100,000 populations among each treated state compare to comparison states. The dynamic DID estimates in column (4) and (5) of Table 5 shows 2.84, and 2.91 additional prescription opioid deaths per 100,000 populations among each treated state compare to comparison states. Figure 3 exhibits the total counterfactual average and treatment effect for model presented in column (4) and (5) in the panel A1, B1, A2, and B2. These figure exhibits that week violation of the pretreatment trend for proper inference.

Figure 3: Dynamic DID (excluding Louisiana and Nevada)



These estimates may be contaminated by measurement error mainly in the dependent variable. As per 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 semisynthetic 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 may substitute the prescription opioid with cheap illegally produced fentanyl or illegal heroin. CDC (2018) reports such substitution led to another nation-wide crisis known as the third wave of opioid crisis (see Appendix A2). The models presented in Table 3 cannot be distinguished among legally prescribed and illegally produced fentanyl from the prescription opioid overdose deaths rate. One potential solution is to implement this study without incorporating deaths from illegally produced fentanyl using microdata. However, the CDC microdata known as multiple cause of deaths distinguish the overdose death related fentanyl only and cannot attribute such overdose death with legal or illegal fentanyl. Therefore, the estimates in

the Table 3 incorporate the total effect of PDMPs on indented prescription opioid overdose deaths as well as the third wave of opioid crisis (an unintended substitution effect). The positive significant coefficient suggest possibly unintended substitution effect surpasses the intended effect of PDMPs on the prescription opioid overdose deaths rate. Onaway to deal with such a situation is to implement interactive fixed effect model, which helps to control for the latent nationwide time trends in prescription opioid death rate (if such trend exists). The next section explores such possibility.

6.2.2 Generalize synthetic control method (excluding Louisiana and Nevada)

Table 4: Generalize synthetic control method (excluding Louisiana and Nevada)

Prescription Opioid Overdose Deaths and Death Rate per 100,000 Population (Age-Adjusted)			
	G-Synth		
Variables	**(1)**	**(2)**	**(3)**
D	-7.65* (3.08)	-8.20 (3.63)	-8.24 (3.61)
Employment.to.Population		-0.02 (0.10)	0.18 (0.80)
HighSchool		0.05 (0.05)	
log.Per.capita.PI		0.21 (2.24)	
MillionUS		-0.05 (0.31)	-0.04 (0.32)
Share.Priv.Construction		-0.04 (0.10)	
Share.Priv.Manufacturing		-0.05 (0.07)	
SQ_Employment.to.Population			0.00 (0.01)
SQ_Share.Priv.Construction			0 .00 (0.01)
SQ_Share.Priv.Manufacturing			0 .00 (0.00)
State.Minimum.Wage		-0.06 (0.11)	-0.06 (0.11)
total_mme		0.00 (0.03)	0.00 (0.03)
_const			
State fixed effects	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes
DSPL (List 1)	-	Yes	-
DSPL (List 2)	-	-	Yes
Factors	1	1	1
Observation	736	736	736
Treated states	8	8	8
Control States	39	39	39

*Note: All the model comprises of state and year fixed effects. Standard errors are based on parametric 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 *. The estimates are given column (1), (2) and (3) are average of average treatment effect (A-ATT). DSPL (list 1) is double-selection post-Lasso variable selection using 22 contemporaneous covariates list, and DSPL (list 2) is double-selection post-Lasso variable selection using DSPL (list 1) variables along with second order polynomial, first level all possible interaction and up to two lags.*

Table 4 presents estimates of GSE for sample excluding Louisiana and Nevada. The estimates of an average of ATT is about -7.65, -8.20 and -8.24 in GSC model presented in column (1), (2) and (3) respectively. The estimates presented in column (1) is significant in 10% level of

significant while the p-values of estimate (2) and (3) are about 12% and 13% respectively. These estimates suggest a weak statistical significance. These estimates indicate that the states with "must-access" PDMPs on average have 7 to 8 less prescription opioid overdose death rate per 100,000 population compared to states with only voluntary PDMPs.

Figure 4: Generalize synthetic control (second wave of PDMPs)

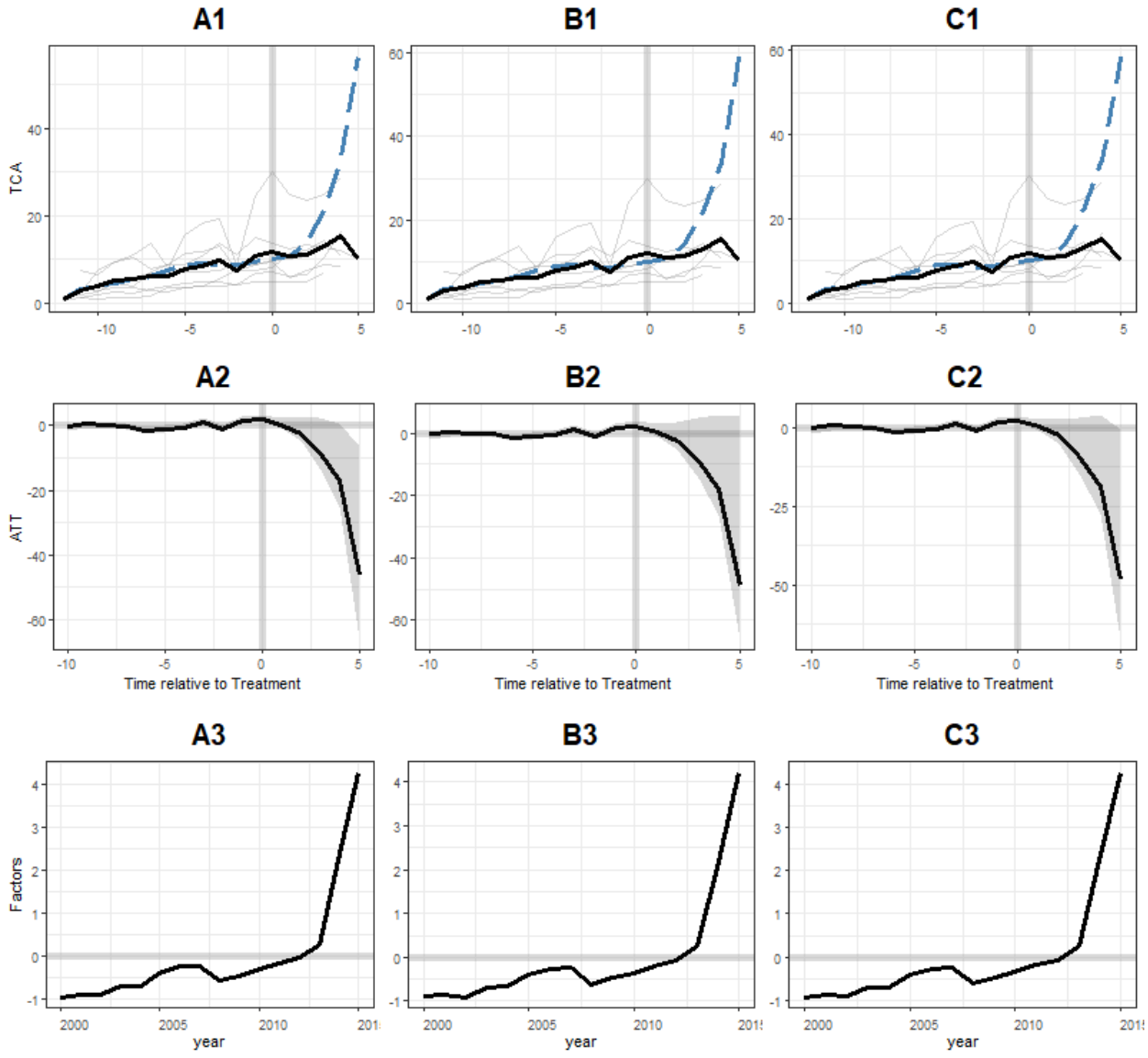


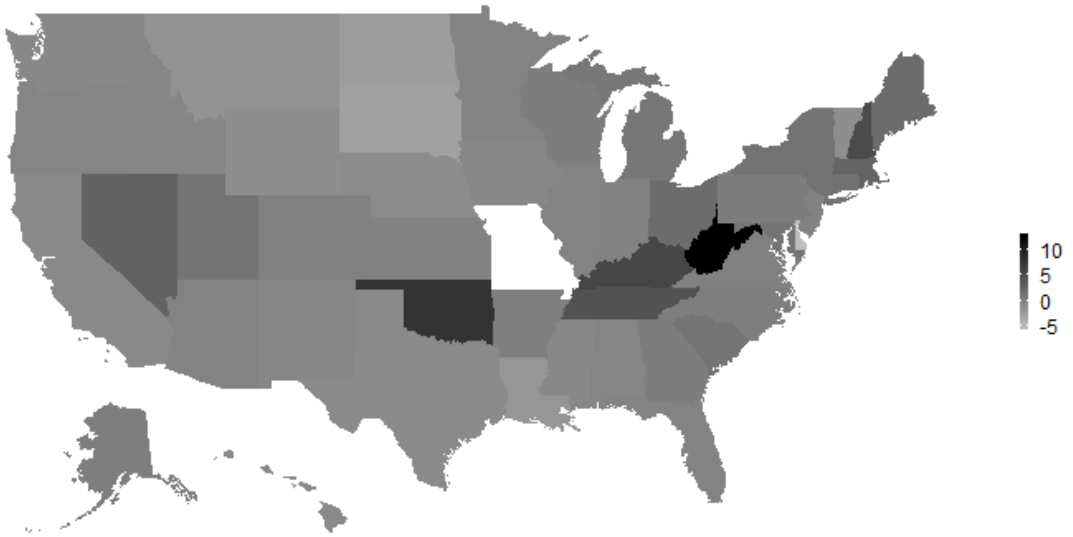
Figure 4, panel A1, B1, and C1 panel shows treatment and counterfactual averages for the GSC model presented in Table 4 column (1), (2) and (3). The cross-validation scheme finds one

unobserved factor to be important (presented in A3, B3 and C3 panel) and after conditioning on both the factors and the additive fixed effects, the estimated ATT based on the GSC method are in panel A2, B2, and C2. It appears that the parallel trend holds in the pretreatment period and PDPMs seems useful to reduce the prescription opioid overdose deaths.

6.2.3 Factors

This section explains the factor presented in Figure 4 in panel A3, B3, and C3. Note these factors appear similar. The x-axis is a year, and the y-axis is the magnitude of factors (rescaled by the square root of their corresponding eigenvalues to demonstrate their relative importance). Bearing in mind the caveat that estimated factors may not be directly interpretable because they are, at best, linear transformations of the true factors, we find that the estimated factors shown in this figure are meaningful.

Figure 5: Factor Loadings

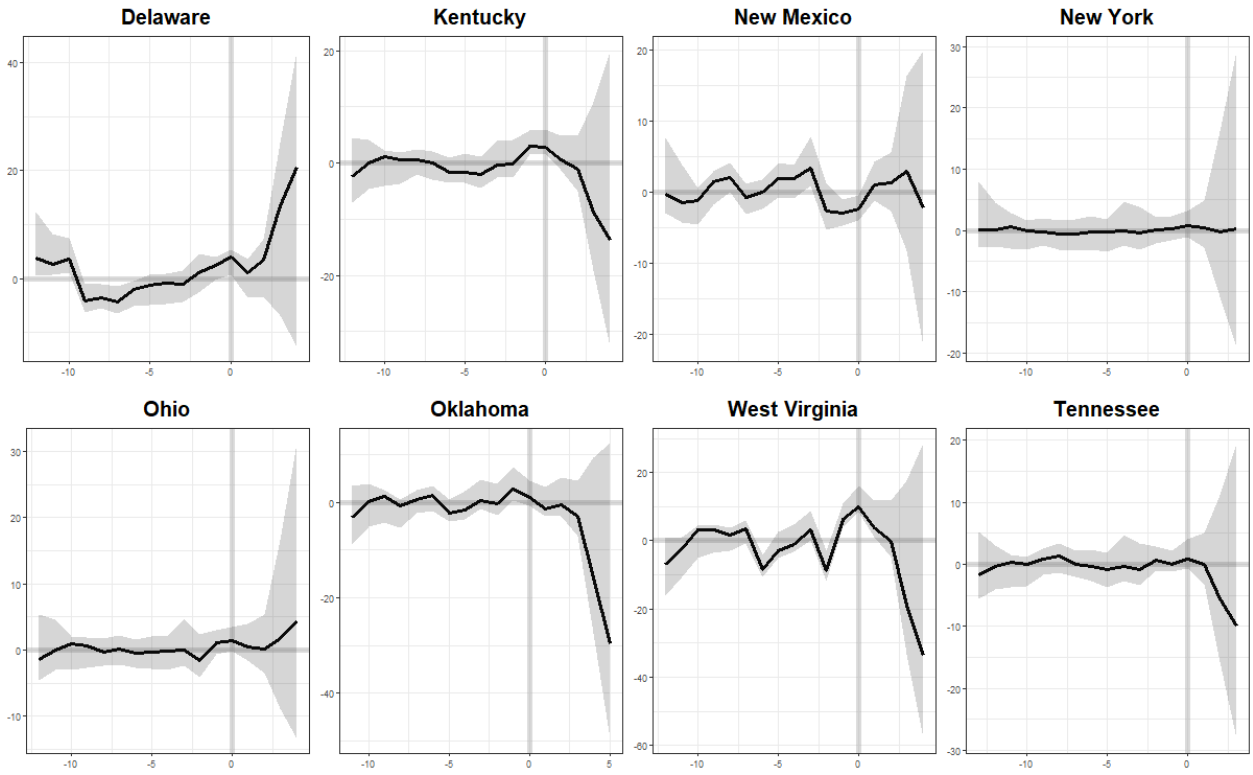


Note: This figure excludes Missouri which hasn't enacted any form of PDMP.

The factor can be thought of as nationwide time trends in prescription opioid which different states are either more or less susceptible, depending on unobservable characteristics of

those states. The basic difference-in-difference model accounts for national non-linear patterns in prescription opioid overdose deaths, and the IFE factor model extends this by accounting for additional non-linear time trends that affect areas to varying degrees. This factor has a gradual increase in prescription opioid overdose deaths from 2004-2012, which then increases exponentially from 2013-2015. States experience the non-linear increase in prescription opioid overdose deaths to differing degrees, which is accounted for in each states' factor loading (See Figure 5). In the case of prescription opioid overdose deaths, a state's factor correlated with the second wave of opioid crisis known as synthetic opioid crisis (See Appendix A1 and A2), implying that prescription opioid overdose deaths-dense states are more sensitive to the third wave of opioid crisis known as increased death rates due to synthetic opioid. This is consistent with the hypothesis that restricting prescription opioids causes opioid abusers toward another illicit opioid, in our case that could be illicit fentanyl. The darkest-color states in Oklahoma, Kentucky, Ohio, West Virginia and New Hampshire experienced the steepest increases in heroin incidents after 2010.

Figure 6: State-level impact of "must-access" PDMPs



6.2.4 State-level impact of "must-access" PDMPs on Opioid-related overdose death rate.

Figure 6 shows the state level impact of "must-access" PDMPs on opioid-related overdose death rate. The "must-access" PDMPs in the state of Kentucky, Oklahoma, Tennessee, and West Virginia effectively reduces the opioid-related overdose deaths. The "must-access" PDMPs in the state of New Mexico, New York, and Ohio has no effect while the program was ineffective in the state of Delaware.

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 (Xu, 2017) unifies the synthetic control method (Abadie, Diamond, & Hainmueller, 2010) with interactive linear fixed effects models (Bia, 2009) under a simple framework, of which DID is a particular case. In short, we conclude that on average the effect of "must-access" PMDPs to reduce prescription opioid-related overdose deaths are successful

In this section, we present some discussions on some of the obvious questions that the reader may have. First is why we choose to discuss the prescription opioid-related overdose deaths and not the prescription rates or other overdose deaths and what are some caveats of our dependent variable. Several papers discuss the impact of PDMPs on the prescription rate. I think that the impact of PDMPs on the prescription rate is obvious that the PDMPs leads to a reduction of prescription rates. However, there may be some heterogeneity (Ayres & Jalal, 2018). I argue that PDMPs are targeted to reduce prescription related opioid overdose deaths. If the prescription rate declines after PDMPs but the trend of prescription opioid overdoses are in rising. This phenomenon could represent either that the Americans are reporting pain (which is not the case), or the opioid user is using more of other opioid drugs (possible heroin/Fentanyl), but the overdose occurred due to prescription opioid. As per 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 semisynthetic 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 suggest that a reduction of prescription opioid would lead to higher demand for substitutes like heroin and fentanyl. In this paper, I show the 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 is enacted, the feedback of high opioid-related overdose death to reenact "must-access" PDMPs is not possible.

Secondly, we discuss why we find evidence the success of PDMP in generalize synthetic control and not in 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 effect. At the same time, GSC allows the interactive fixed effect to potential capture the unobserved heterogeneity. I argue that GSC absorbs the third wave of opioid crisis mainly the switching of prescription opioid to the illicit fentanyl, which is an unintended consequence of PDMPs. DID exhibits the estimates with both intended and unintended consequence of PDMPs while GSC estimates teasel out an intended and unintended consequence of PDMPs.

Third, we 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 unobservable characteristics of those states. The factor correlates with the third wave of opioid (See Appendix A1 and A2) therefore, this factor potentially captures a nationwide trend of prescription opioid switching toward illicit fentanyl as the unintended consequence. Even thou, we don't know the source of switching behavior, but the literature suggests oxytocin reformulation or other supply-side policy that restricts the prescription opioid, or drug lords are moving toward the suburb.

Fourth, the concern can be related to sample size. In Table 4, we find that estimates given in column (1) are appropriate which is just GSC model without covariates since the covariates were insignificant presented in column (2) and (3). Therefore, we implement the estimation with an updated sample from 1999 to 2017, we find similar results. The p-value is about 7% suggesting a weak statistically significant effect. However, I think that this paper presents the story of the economic significance of PDMPs to be able to save people's life. Upon these arguments, we

conclude that “must-access” PDMPs are successful in saving about 7 lives per 100,000 population opioid-related overdoses deaths, however the net effect of PDMPs when including illicit fentanyl (an unintended consequence) we find PDMPs claims around 2.7 lives per 100,000 population.

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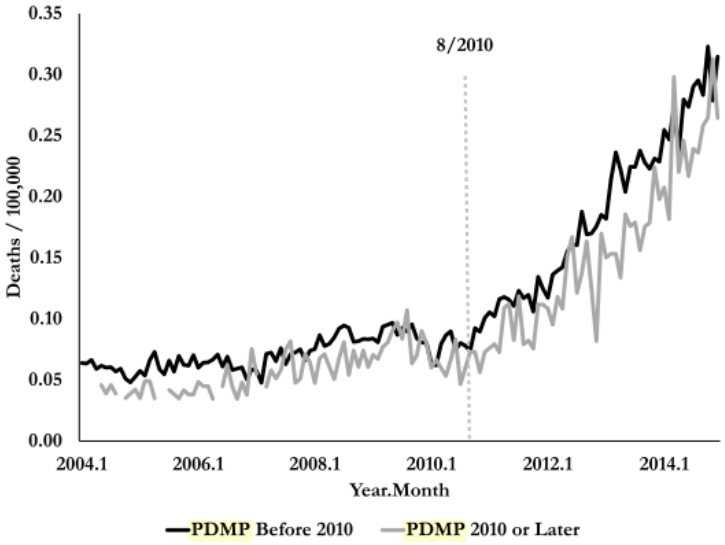
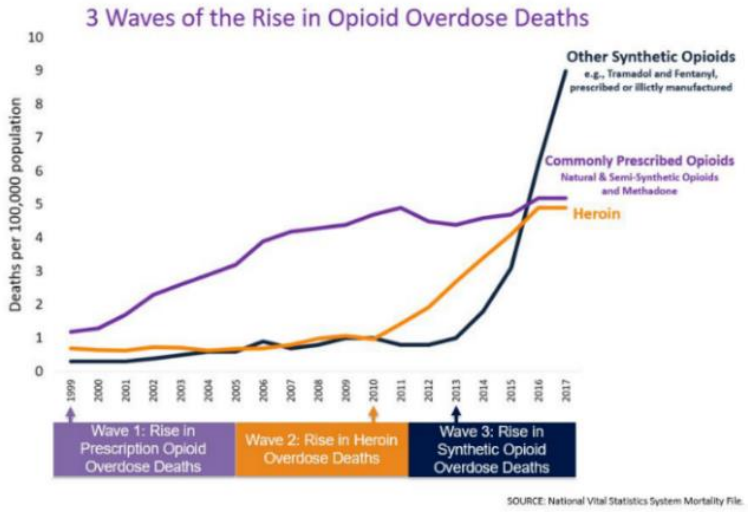
Appendix

A1: Evan et al (2018) plot of deaths by heroin overdose.



A2. Three waves of Opioid Overdose Deaths



Source: www.cdc.gov

A3 Full sample analysis

Table A3.1 displays estimates of several variants of two-way fixed effect models, known as the difference-in-difference (DID) model in the literature. This result comprises 39 comparison states and 10 treatment states but excludes Missouri from the analysis. All the model consists of

state and year fixed effects. 2000 times non-parametric bootstraps (blocked at the state level) produces the standard errors.

The main estimates of interest are the average treatment effect (ATT) and the average of average treatment effect (A-ATT). Table A3.1 columns (1) to (3) shows the average treatment effect (ATT) estimates implementing standard DID under three model specifications. Table A3.1 column (4) and (5) shows A-ATT estimates implementing dynamic DID. Endogeneity can bias these estimates, as parallel trend assumption is not likely to hold (see Figure A3.1).

Table A3.1: Full sample analysis with the difference-in-difference method

Prescription Opioid Overdose Death Rate per 100,000 Population (Age-Adjusted)					
	FE				
	DID			Dynamic DID	
Variables	(1)	(2)	(3)	(4)	(5)
ATT	2.10**(1.03)	2.10**(1.01)	2.28***(0.99)		
Avg-ATT				2.05*(1.09)	2.29**(1.07)
Employment to Population		0.04(0.19)	0.07(0.20)	0.39***(0.14)	0.43***(0.16)
High School		0.19***(0.08)		0.23**(0.10)	
log Per capita PI		1.25(3.71)		-3.10(2.45)	
MillionUS		-0.38(0.42)	-0.33(0.43)	-0.48(0.33)	-0.44(0.34)
Poverty Rate		-0.01(0.07)	0.00(0.06)	0.07(0.06)	0.08(0.06)
Share Priv Manufacturing		-0.22**(0.09)		-0.21***(0.08)	
SQ_log Per capita PI			0.01(0.16)		-0.18(0.11)
SQ_Share Priv Manufacturing			-0.01**(0.00)		-0.01***(0.00)
State Minimum Wage		-0.17(0.14)	-0.20(0.14)	-0.14(0.14)	-0.17(0.14)
Per capita Total_mme		0.06(0.06)	0.07(0.06)	-0.01(0.04)	0.00(0.04)
const	5.15***(0.37)	-18.30(38.09)	2.49(17.22)		
State fixed effects	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes
DSPL (list 1)	-	Yes	-	Yes	-
DSPL (list 2)	-	-	Yes	-	Yes
Factors	-	-	-	-	-
Observation	784	784	784	784	784
Treated states	10	10	10	10	10
Control States	39	39	39	39	39

*Note: 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 *. The estimates are given column (1), (2) and (3) are average treatment effect or ATT. The estimates given in (4), (5), are the average of average treatment effect (A-ATT). DSPL (list 1) is double-selection post-Lasso variable selection using 22 contemporaneous covariates list, and DSPL (list 2) is double-selection post-Lasso variable selection using DSPL (list 1) variables along with second order polynomial, first level all possible interaction and up to two lags.*

In Table 3A.1, column (1) includes the "must-access" PDMP indicator. Column (2), includes additional controls for the "must-access" PDMP indicator. These controls are selected implementing double-selection post-Lasso on a list of 22 contemporaneous variables (list 1). Column (3) comprises additional covariates selected implementing on double-selection post-Lasso on a list of 22 contemporaneous variables, their second-order polynomials, all possible first level

interactions and up to two-year lags (list 1). The average treatment effect of "must-access" PDMPs is 2.21, 2.10 and 2.28 respectively and statistically significant in 1% level of significance. In Table 3A.1, column (4) includes dynamic DID estimates with covariates selected from list 1 and column (5) includes DID estimates with covariates selected from list 2. The average of ATT is 2.05 and 2.29 and statistically significant in 10% and 5% level of significance respectively. All these estimates suggest "must-access" PDMPs are ineffective and treatment states have about 2 additional prescription opioid overdose deaths among per 100,000 populations, compared to comparison states.

Figure 3A.1: Dynamic DID (full sample)

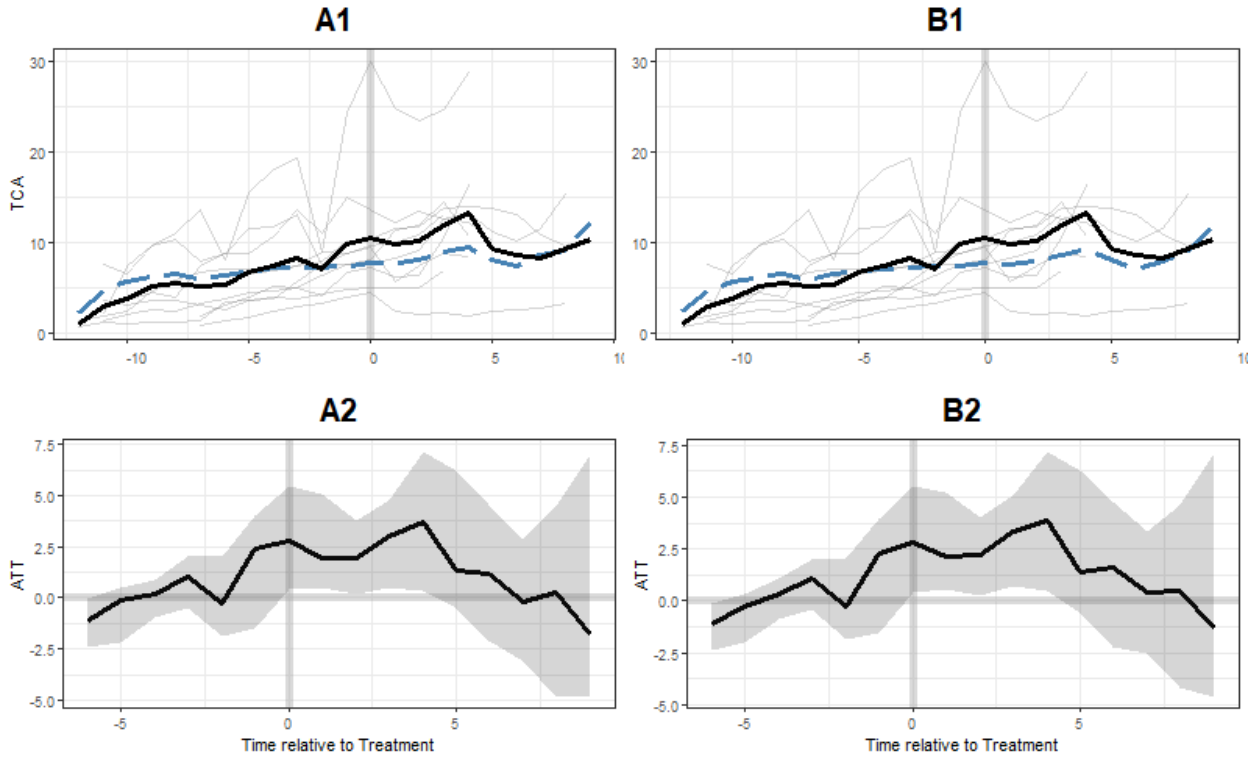


Figure 3A.1 shows that DID models don't hold the preintervention parallel trend. The A1 and B1 panel show the treatment (solid) and counterfactual (dotted) average along with trend (light grey) of prescription-related opioid overdose death rate among treated in relative to the PDMPs enactment period for dynamic DID present in column (4) and (5) respectively. The gap between the actual average and counterfactuals shows the ATT estimates and presented in A2 and B2 panel respectively. The confidence intervals of ATT are based on nonparametric bootstraps (blocked at

the state level) of 2,000 times. It is clear from panel A2 and B2 that the "parallel trends" assumption is not likely to hold since the average predicted prescription related opioid overdose deaths deviates from the average actual prescription related opioid overdose deaths in the pretreatment periods. However, the estimated prescription related opioid overdose deaths are in general downward trended post PDMP suggesting PDMPs states might be reducing the prescription-related opioid overdose deaths.

Table 3B.1: Full sample analysis with the generalize synthetic control method

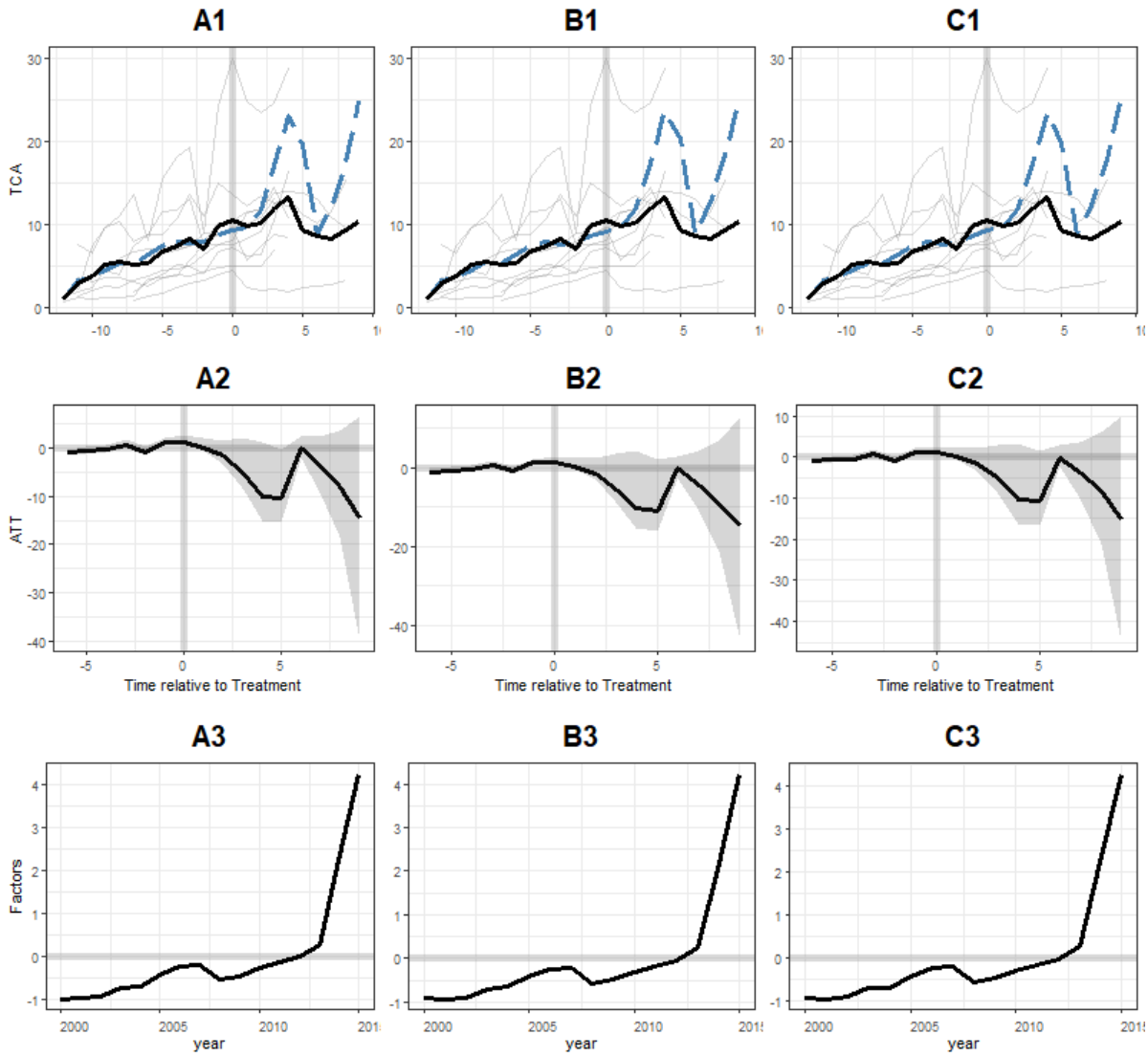
Prescription Opioid Overdose Deaths and Death Rate per 100,000 Population (Age-Adjusted)			
	G-Synth		
Variables	(1)	(2)	(3)
D	-4.56*(1.94)	-4.86(2.22)	-4.71*(2.18)
Avg-ATT			
Employment to Population		-0.08(0.10)	-0.08(0.10)
HighSchool		0.05(0.05)	
log Per capita PI		-0.05(1.92)	
MillionUS		-0.03(0.32)	-0.02(0.31)
Poverty Rate		-0.02(0.04)	-0.02(0.05)
Share Priv Manufacturing		-0.05(0.07)	
SQ_log Per capita PI			-0.01(0.09)
SQ_Share Priv Manufacturing			0.00(0.00)
State Minimum Wage		-0.06(0.11)	-0.07(0.11)
Per capita Total_mme		0.00(0.03)	0.00(0.03)
const			
State fixed effects	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes
DSPL (List 1)	-	Yes	-
DSPL (List 2)	-	-	Yes
Factors	1	1	1
Observation	784	784	784
Treated states	10	10	10
Control States	39	39	39

*Note: All the model comprises of state and year fixed effects. Standard errors are based on parametric 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 *. The estimates are given column (1), (2) and (3) are average of average treatment effect (A-ATT). DSPL (list 1) is double-selection post-Lasso variable selection using 22 contemporaneous covariates list, and DSPL (list 2) is double-selection post-Lasso variable selection using DSPL (list 1) variables along with second order polynomial, first level all possible interaction and up to two lags.*

Table 3B.1 column (1), (2) and (3) presents provides estimates of an average of the average treatment effect of the "must-access" variable implementing generalized synthetic control. Parametric bootstraps (blocked at the state level) of 2,000 times produces the standard error. Column (1) comprises only the "must-access" indicator variable. Column (2) and (3) includes

additional contemporaneous controls selected via double-selection post-Lasso from list 1 and list 2 respectively.

Figure 3B.1: Generalize synthetic control (full sample)



When the unobserved heterogeneity is absorbed using interactive fixed effects in GSE (the models capture 1 factor, discussed later), the estimates of average of ATT is about -4.5 suggesting that the states with "must-access" PDMPs on average have 4.5 less prescription opioid overdose death rate per 100,000 population compared to states with only voluntary PDMPs. However, such a relationship is likely to be significant at 10% level of significance.

Figure 3B.1, the A1, B1, and C1 panel show treatment and counterfactual averages for the GSC model presented in Table 3B.1. The cross-validation scheme finds one unobserved factor to be important (presented in A3, B3 and C3 panel) and after conditioning on both the factors and the additive fixed effects, the estimated ATT based on the GSC method are in panel A2, B2, and C2. It appears that the parallel trend holds in the pretreatment period and PDPMs seems useful.

A4. Double-selection post-Lasso

Consider a basic model set up:

$$y_{it} = \varphi D_{it} + \Theta_{it}'\omega + \nu_{it}$$

Where i indexes states, t indexes times, Θ_{it} are a set of control variables to control for time-varying confounding state-level variables, D_{it} is a binary indicator if the state has "must-access" PDMPs or not and y_{it} is opioid-related overdoses death rate in each state in each time.

This paper depart from the standard literature by allowing a much richer set of control variables Θ_{it} (which comprises a large list of variable based on literature review and economic intutions and their various transformation like higher-order terms, interaction terms, lags e.t.c) to select proper observable confounder x_{it} (few relevant confounders from protential list of Θ_{it}). Such controls allow for the possibility that there may be some feature of a state that affects with both "must-access" PDMPs enactment and prescription opioid-related overdoses death rate. The "must-access" PDMPs enactment and prescription opioid-related overdoses death rate might depend upon the observables socio-economic, political and demographic features of the states.

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 are associated both with "must-access" PDMPs and opioid-related overdoses death rate. Thus, including a large set of variables makes this assumption more plausible. However, naively controlling for redundant variables reduces the ability to distinguish the impact of the interest variable and consequently produces less precise estimates. The double-selection post-Lasso procedure Belloni et al. (2013) is an efficient, data-driven way to search for a small set of essential confounds from among a sensibly chosen broad set of potential confounding variables. The double-post-Lasso procedure comprises the following stpe: First, run Lasso of y on Θ to select a set of predictors for y.

Second, run Lasso of D on Θ to select a set of predictors for D. Third, run OLS regression of y on D, and the union of the sets of regressors selected in the two Lasso runs to estimate φ then correct the inference with usual heteroscedasticity robust OLS standard error. For the theoretical arguments see (Belloni et al., 2013; Belloni, Chernozhukov, & Hansen, 2014; Nowak & Smith, 2017).