Using Penalized Synthetic Controls on Truncated data: A Case Study on Effect of Marijuana Legalization on Direct Payments to Physicians by Opioid Manufacturers

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Abstract

Amid increasing awareness regarding opioid addiction, medical marijuana has emerged as an alternative for pain management. Concurrently, opioid manufacturers are putting significant research into making opioids safer yet effective. Interactions between these manufacturers and physicians are critical to advance existing pain management protocols. Direct payments from opioid manufacturers to physicians are established conduits to facilitate such interactions. We study the effects of passage of a medical marijuana law (MML) on these direct payments to physicians. To draw causal conclusions, we develop a novel penalized synthetic control (SC) method that accommodates the zero-payment related latent structures inherent in these payments. Under a truncated flexible additive mixture model, we show that the SC method has uncontrolled maximal risk without the penalty; by contrast, the proposed penalized method provides efficient estimates. Our analysis finds a significant decrease in direct payments from opioid manufacturers to pain medicine physicians as an effect of MML passage. We provide evidence that this decrease is due to the availability of medical marijuana as a substitute. Additionally, physicians in states with an MML are prescribing fewer opioids. Finally, the substitution effect is comparatively higher for female physicians and in localities with higher white, less affluent, and more working-age populations.

Keywords: Access to medication; average treatment effect; latent structure; pain management; penalized estimation;

1 Introduction

Opioids are a class of drugs used to reduce pain. Opioids can be prescribed by physicians to treat moderate to severe pain but may also involve serious risks and side effects (DHAS, 2022). Misuse and overuse of opioids have led to significant increase in opioid addictions and deaths. Opioid overdose-related deaths in the US rose from $21,088$ in 2010 to $68,630$ in 2020 (NIDA, 2022). As such, opioid consumption and

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its effects are highly debated objects in the current public discourse as well as a topic of vibrant academic research (Blanco et al., 2007, Cohn and Zubizarreta, 2022, Jacobs et al., 2022, Nam et al., 2020, Neuman et al., 2020, Prochaska et al., 2021, Zhang et al., 2020).

We consider two notable consequences in light of the opioid epidemic. First, advocacy of marijuana as a substitute for opioids gained traction (Boehnke et al., 2019, Cooper et al., 2018, Hollenbeck and Uetake, 2021), arguing for its effectiveness as a painkiller while lower the chances of addiction and overdose death than opioids (NIDA, 2021). Many states have legalized medical consumption of marijuana, which in part is aimed at reducing opioid-induced harm (Bachhuber et al., 2014, Powell et al., 2018, Shi, 2017). However, there is no consensus on whether marijuana use is altogether effective or harmless. Second, opioid manufacturers are continually putting significant effort into research and development to make opioids safer, e.g., by including an abuse-deterrent formulation (Evans et al., 2019, FDA, 2015).

In the wake of this evolving pain management paradigm, physicians must remain updated on drugs for appropriate patient care. Without the latest information regarding the drugs, physicians may be unable to prescribe opioids appropriately for pain management (Guo et al., 2021). There is significant concern that a subsequent decrease in opioid prescription could lead to opioid being a niche product or, in the extreme, could potentially lead to severely diminished usage of opioids (Feinberg, 2019, Szalavitz, 2023). Further, as a cascading effect, it can negatively affect research and development on opioids as well as decrease in the number of opioid manufacturers. Therefore, opioid manufacturers use different forms of interactions to engage with physicians on a regular basis. One of the most common conduits to facilitate such interactions is through direct payments to physicians from opioid manufacturers (Jones and Ornstein, 2016, Schwartz and Woloshin, 2019). These direct payments may be in the form of consulting and speaker fees, conference travel reimbursements, or meal vouchers.

In this paper, we study the effects of legalization of medical marijuana on these direct payments made by opioid manufacturers to opioid-prescribing physicians. In 2021, the direct payments to physicians made by US pharmaceutical companies amounted to $10.88 billion.[2] While some have criticized such payments on ethical grounds, these payments serve as a medium of interaction between physicians and pharmaceutical companies through which physicians get introduced to new drugs, get updated about

[2]Based on OpenPayment data from CMS: https://openpaymentsdata.cms.gov/summary

existing drugs, augment funding of residency and other programs, and gain significant insights through discussions with fellow physicians in sponsored conferences (Korenstein et al., 2010, Rosenbaum, 2015).

Here, we study the impact that passage of marijuana legalization laws (MML) in different US states had on the opioid ecosystem by analyzing the changes in these direct payments to opioid prescribers over time. To derive causal conclusions, we follow the popular synthetic control (SC) method (Abadie et al., 2010, Abadie and Gardeazabal, 2003). The widely used SC criterion of Abadie et al. (2010) cannot be directly applied in our context due to an idiosyncratic nature of the physicians' payment data, which we describe in details later. To provide consistent inference we develop a novel penalized SC method akin to Abadie et al. (2015) and Ben-Michael et al. (2021b). In addition to the overall effect of MML passage on direct payments to opioid prescribing physicians, we also explore the disparities in the said effect across physicians' speciality, tenure, and gender as well as the communities these physicians are serving.

1.1 Causal Study of Marijuana Legalization Effects on Direct Payments to Physicians by Opioid Manufacturers

Our exposure of interest is the passage of a law legalizing medical marijuana consumption (MML). We study its impact on the direct payments made to physicians by opioid manufacturers. Since pharmaceutical companies care about their returns-on-investment, these direct payments by the manufacturers are strategic, and usually targeted to physicians based on their patient type, practice area, and type of drugs they tend to prescribe (Angell, 2018, Schwartz and Woloshin, 2019). Therefore, availability of opioid substitutes in the market can affect these payments. In states that have passed MML, a physician may recommend medical marijuana for pain (Black, 2022). In such cases, marijuana becomes a substitute for opioids and consequently, opioid manufacturers may reduce payments to physicians whose patients are likely to use marijuana for pain management.

Our research looks at how the direct payments from opioid manufacturers to physicians change in the states where a law legalizing medical marijuana was passed. We use a synthetic control method to match a physician from a state with MML to physicians in states that have not passed MML. However, some care in the use of SC methods is warranted. These payments received by a physician are typically discontinuous; there are often significant periods of time when no payments are made to the physician.

Nonetheless, controlling for these no-payment periods in our estimation is critical. For example, maybe a physician receives payment periodically, every six months, while another physician receives payments every five months. Direct use of a SC method while comparing these two physicians ignores these distinct latent patterns and thus will result in interpolation bias in the estimated effect (Abadie et al., 2015). We customize the synthetic control method (Abadie et al., 2010, Abadie and Gardeazabal, 2003) to pay attention to these varied patterns in physician payments when matching.

As we work with fine-grained datasets containing information at physician-level granularity, we are able to investigate the heterogeneity in the effect based on physicians' specialties and their genders. We also study the heterogeneity in the effect on physician payments based on income, age, and racial composition of their respective patient communities by merging demographic and socioeconomic information of the zip codes that each physician serves. We describe the main contributions of our work below.

1. We develop a novel penalized synthetic control method to accommodate the zero-payment related idiosyncrasies of our physician payments data set. Most physicians' payment histories contain instances of no payments, which do not allow direct application of the widely used synthetic control (SC) method of Abadie et al. (2010). Motivated by penalized SC (PSC) approaches suggested in Abadie et al. (2015), Ben-Michael et al. (2021a), we develop a novel penalty that can prevent interpolation biases and can capture the varied patterns of non-payments in the pre-treatment period.

2. We explain the role of the penalty and the working principle behind the developed PSC method in a truncated flexible additive mixture model that consists of a latent factor model and a mixture process. The model is more complex than the models for which operating characteristics of SC methods have been studied in the existing literature (Abadie et al., 2010, Ben-Michael et al., 2021a,b). The truncation is for non-negative payments and the mixture accommodates varying patterns of zero-payments among the physicians. In Section 3.3, we rigorously explain how the proposed penalty produces efficient SC estimates by accurately learning the factor model coefficients as well as mixture group memberships (see Theorem 1). Further, we illustrate the necessity of the penalty by showing that unpenalized SC method will have uncontrolled maximal risk in the concerned additive mixture models (see Lemma 3). These results may be of independent interest in understanding the role of SC methods in mixture models.

3. We present a primary analysis of the effect on direct payments to pain-medicine physicians using the proposed PSC method. In each quarter 5%–15% of the physicians had no payments. Physicians in the MML states ('treated' states) and the non-MML ('control' states) had no payments on an average of 0.99 and 1.04 quarters respectively during the pre-treatment period (see Section 2). We show that the penalized SC method provides a good match for each physician and their synthetic counterpart during this pre-treatment period. Assuming the validity of the synthetic control method, we find a statistically significant decrease in payments because of the MML passage.

4. We stress-test our estimated effect of MML passage by testing a possible substitution mechanism that could explain the inference from the PSC method. First, we find a consistent effect in Florida, although it passed the MML in 2016 Q4, two quarters after the other treated states in our primary analysis. Second, for Anesthesiologists, who are less likely to switch to marijuana from opioids, we observe an immediate negative effect after MML passage, but it later bounces back to a non-significant effect. Third, we find a negative correlation between increase in marijuana patient registration and opioid-prescribing physician payments.

5. Finally, we investigate the variability in the MML effect on payments across different subgroups. This heterogeneity analysis uses the estimated individualized treatment effect of the pain-medicine physicians. The effect varies between areas with comparatively higher white and black populations and seems more substantial in areas with more lower-income and working-age populations. Additionally, the effects of MML passage are lower in magnitude on female physicians.

1.2 Organization of the paper

Section 2 elaborates on our data sets. We develop our PSC method aimed at varied zero-payment patterns and study its theoretical properties in Section 3. In Section 4, we present simulation experiments comparing the PSC method with the existing methods. Section 5.1 presents the primary analysis result for pain-medicine physicians. Section 5.2 provides the mechanism analysis. Section 6 probes the heterogeneity of the effect across physicians' gender, experience, and their serving communities' age, income, and racial composition. Finally, Section 7 has additional discussion. The supplement contains all the proofs and computer code to reproduce the numerical results.

2 Data Description

To operationalize our research objectives, we needed access to the details on direct payments by opioid manufacturers to opioid prescribing physicians. While these payments are endogenous decisions made by each manufacturer, due to the "Sunshine Act," pharmaceutical manufacturers are now mandated by law to report such payments (Richardson et al., 2014). The act was a federal response to concerns of potential conflict of interest in physicians accepting these payments, the subsequent possibility of bias in treatment, and rising health-care costs (Carey et al., 2021, DeJong et al., 2016, Engelberg et al., 2014, Jones and Ornstein, 2016). In September 2014, the first batch of data was made public. This dataset contains the dollar value of the gift/payment that transpired between a named physician and a named pharmaceutical manufacturer, associated products for their interaction, and payment date.

We aggregated the payment information for each physician in our treated and control states for each of the 16 quarters from 2014 to 2017. In 2016, six states passed a medical marijuana law: Pennsylvania (PA), Ohio (OH), North Dakota (ND), Louisiana (LA), Florida (FL) and Arkansas (AR). We excluded the two small states, ND and AR, which had less than three eligible physicians for our primary analysis. Three out of these four states, PA, OH, and LA passed an MML in the second quarter of 2016, while FL passed the law in the last quarter of 2016. Since the passage of MML in PA, OH, and LA can confound the estimated effect of MML on direct payments to Florida physicians, we analyze the treatments effects on physicians in the former three states separately from physicians in Florida. We use 10 control states which did not did not pass an MML till 2017.

Against any payment made to a physician, the data lists the drug category or therapeutic area of each drug promoted during that interaction. Notably, a single payment entry could enlist up to five drugs. For identifying the payments related to opioids, any payment that mentioned "pain" was marked and subsequently, those payments were retained which mentioned opioid as one of the drugs. Further, we only chose those opioid manufacturer–drug combinations against which direct payments were made to physicians in our pre-MML (pre-treatment) period, i.e., between 2014 and 2016. After this data pre-processing, we had 15 opioid brands promoted by 5 manufacturers.[3] Thus, more precisely, our analysis

[3]Different dosages of the same drug are considered as a single brand of opioid.

looks at the effect of an MML passage on payments to physicians related to these 15 opioid brands.

Since multiple drugs, including a mix of opioids and non-opioids, are often associated with a single payment, there is no logical way to attribute a fraction of the payment to only the opioids. Therefore, to be conservative, we attributed any financial transaction to opioid-related payment if one or more opioids were mentioned in that payment. Figure 1 shows the distribution of the proportion of opioids promoted during each payment and the corresponding average payment amount. The figure shows that the most common payment type in our data is when only one opioid is promoted, followed by the case where two drugs are promoted within which one or both might be opioids. Also, between these two types of payments, higher payments occur when only one opioid is promoted.

Figure 2 describes the payments to physicians in the states we include in our study. Although not identical, the payments do not look very different between our treated and control states in the pre-treatment period. The payments however vary with physician specialities. In 2015, the year prior to our treatment year, 'Anesthesiologists' received the highest proportion of payments in dollar value, about 30%, while 'Pain Medicine' physicians received the second-highest proportion, about 19%. Anesthesiologists and pain medicine physicians likely prescribe opioids for different purposes. Pain medicine physicians primarily deal with chronic pain management. Anesthesiologist, on the other hand, deal with pre- and post-operative acute pain management. Since marijuana drugs are not yet federally approved (FDA, 2020), anesthesiologists are less likely to be able to recommend or prescribe marijuana as an alternative medium for acute pain management. Consequently, if medical marijuana were to work as a substitute for opioid in pain management, we are likely to see a more pronounced effect of MML passage on direct payments to pain medicine physicians than Anesthesiologists. Therefore, we primarily study pain medicine physicians to explore the causal effect of MML passage on direct payments, and subsequently include the effect on Anesthesiologists as part of the mechanism analysis behind the causal effect.

Table 1: Percent of physicians by the number of quarters with zero payments

Number of quarters	0	1	2	3	4	5	6	Total
Control states	50	26	8	7	6	3	0	100
Treated states	53	23	10	9	2	2	2	100

Combining Anesthesiologists or pain medicine physicians, our analysis had 138 and 356 physicians from the four treated and ten control states, respectively, after removing 11 and 28 physicians from the

treatment states and control states for extreme and irregular values. Figure 2 shows that in each quarter, 5%–15% of the physicians had no payments. Physicians in the treated and control states had zero payments on an average of 0.99 and 1.04 quarters, respectively, between 2014 Q1 and 2016 Q2. An incidence of zero payment during a period between an opioid manufacturer and a physician is informative about the latent behaviors of both parties. Clearly, the latent behaviors vary across physicians. Thus, our method, described in the next section, includes an additional penalty to closely match these zero-payment related latent patterns for a physician and its synthetic counterpart.

We supplement the payments data with the corresponding prescription data for each physician from the Medicare Part D Prescriber Public Use File.[4,5] To calculate the number of opioid-related prescriptions, we separated the opioid and non-opioid drugs prescribed by the pain-medicine physicians. Figure 3 shows the yearly average opioids related payments and number of opioids related prescriptions. The figure shows a decrease in payments, while the average number of prescriptions increase marginally, although not significantly, from 2015 to 2017. Later, we look at a difference-in-differences comparison for opioid vs non-opioid prescription patterns for the treated and control states across the years.

We use additional data for further analysis to determine and subsequently elaborate on the heterogeneity in the effect of MML passage. Our supplementary analyses use zip-code level data on demographics and income characteristics from the US census bureau's American Community Survey. Additionally, we use information on physicians' years of experience, gender, and the size of their practice. Finally, we use longitudinal data on the number of medical marijuana patients in Florida after it passed its MML. For parsimony, further details on these datasets used for heterogeneity analysis are provided in Section 6.

3 Methodology

3.1 Set-up and notations

Let b be arbitrary unit that received treatment. The set $\mathcal{C}$ of all control units is indexed by $c = 1, \ldots, C$. We observe payments y_{ct}, $c = 1, \ldots, C$ and $t = 1, \ldots, T$ received by units in $\mathcal{C}$. For simplicity, assume

[4]The Part D Prescriber PUF is from CMS's Chronic Conditions Data Warehouse, which contains Prescription Drug Event records submitted by Medicare Advantage and stand-alone Prescription Drug Plans (https://www.cms.gov/Research-Statistics-Data-andSystems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/ PartD2013.html).

[5]Unlike the detailed payments dataset, the prescription dataset only gives yearly aggregated information per physician.

that the treatment was applied between time $T-1$ and T. We observe payments $y_{bt}, t = 1, \ldots, T-1$ received by unit b in the pre-treatment period and the payment $\breve{y}_{bT}$ received by unit b post-treatment. Noting that unit b would have received y_{bt} if they were not in the treatment set, the treatment effect is given by $\text{TE}_b = \breve{y}_{bT} - y_{bT}$.

Now, if $\mathcal{B}$ be a set of treated units indexed by $b = C+1, \ldots, C+B$, the average treatment effect on the treated (ATT) over the set $\mathcal{B}$ is given by $\text{ATT}_{\mathcal{B}} = B^{-1} \sum_{b=C+1}^{C+B} \text{TE}_b$. Our goal is to estimate $\text{ATT}_{\mathcal{B}}$ as well as the subgroup average treatment effect $\text{ATT}_{\mathcal{A}} = |\mathcal{A}|^{-1} \sum_{b \in \mathcal{A}} \text{TE}_b$ over various interesting subsets of $\mathcal{A} \subseteq \mathcal{B}$, where $|\mathcal{A}|$ denotes the cardinality of $\mathcal{A}$. For that purpose we next develop a synthetic control method to estimate the unknown y_{bT} for each $b \in \mathcal{B}$. The estimates $\hat{y}_{bT}$ are then used to estimate $\text{ATT}_{\mathcal{A}}$ by $\widehat{\text{ATT}}_{\mathcal{A}} = |\mathcal{A}|^{-1} \sum_{b \in \mathcal{A}} (\breve{y}_{bT} - \hat{y}_{bT})$.

3.2 Proposed Penalized Synthetic Control Method

For unit $b \in \mathcal{B}$, we estimate y_{bT} by using the synthetic control (SC) method (Abadie, 2021, Abadie et al., 2010, Abadie and Gardeazabal, 2003) that prescribes estimating y_{bT} by linearly aggregating the payments received by the controls $\hat{y}_{bT} = \sum_{c=1}^{C} w_{bc} y_{cT}$ where the weights $w_{bc} \geq 0$ and $\sum_{c=1}^{C} w_{bc} = 1$ for all $b \in \mathcal{B}$. Let $\boldsymbol{w}_b$ be the C dimensional vector $(w_{b1}, \ldots, w_{bC})$ and W denote the $B \times C$ matrix whose row b is $\boldsymbol{w}_b'$. Define

$$f(W; \lambda, \nu) = \frac{1}{B} \sum_{b \in \mathcal{B}} \left[\sum_{t=1}^{T-1} \left(y_{bt} - \sum_{c=1}^{C} w_{bc}\, y_{ct} \right)^2 + \sum_{c=1}^{C} w_{bc} \exp\left\{ \lambda \left(\sum_{t=1}^{T-1} \left(y_{bt} + y_{ct} \right) I\{\, y_{bt} \cdot y_{ct} = 0 \} \right) \right\} \right] + \nu \sum_{t=1}^{T-1} \left\{ \frac{1}{B} \sum_{b \in \mathcal{B}} y_{bt} - \sum_{c=1}^{C} \left(\frac{1}{B} \sum_{b \in \mathcal{B}} w_{bc} \right) y_{ct} \right\}^2, \quad (1)$$

where $I\{\}$ denotes the indicator function. For any fixed $\lambda, \nu \geq 0$ consider the following minimization:

$$\arg\min_{W} f(W; \lambda, \nu) \text{ such that } \boldsymbol{w}_b \geq 0 \text{ and } ||\boldsymbol{w}_b||_1 = 1 \text{ for all } 1 \leq b \leq B. \quad (2)$$

The objective criterion produces a penalized synthetic control (PSC) estimator. Penalized synthetic controls are increasingly being used (Abadie, 2021, Abadie et al., 2015, Ben-Michael et al., 2021a) to incorporate relevant structural constraints particularly while dealing with disaggregate level data. See Section

1 of Ben-Michael et al. (2021a) for a comprehensive review on usages of penalized synthetic controls. Here, we have two penalty parameters λ and ν which imparts two different types of regularization on the estimators. We next elaborate on the motivation behind (1) and the role of the penalization parameters.

We are interested in not only estimating the average treatment effect on the treated $\text{ATT}_{\mathcal{B}}$ over different concerned subsets of physicians $\mathcal{B}$ but also in studying the heterogeneity among the individual treatment effects TE_b. For the first goal, it is best to use pooled SC based criterion that minimizes the average pre-treatment imbalance across members in $\mathcal{B}$. However, for the second goal it is optimal to use separate SC criterion which estimates weights by separately minimizing the pre-treatment imbalance for each treated unit $b \in \mathcal{B}$. The estimators from the pooled SC and the separate SC based criteria often significantly disagree and subsequently producing highly sub-optimal inference in either one of the two goals. Partially pooled SC (Ben-Michael et al., 2021b) provides a framework for construction of SC estimator whose risk can be simultaneously well-controlled in both the aforementioned inferential goals. We consider a partially pooled SC framework. The ν hyper-parameter in (1) balances the sum of squared imbalances (Im) from the individual SC and the pooled SC criteria. As such, note that the objective criterion minimized here is the sum of three components. Denote the three terms in (1) respectively by

(a) $\text{Im}_{\texttt{sep}}$, which is the sum of squared pre-treatment imbalances for each separate treated units,

(b) $\text{Pen}_{\texttt{sep}}(\lambda)$, which is an additive penalty that is separable across treated units, and

(c) $\text{Im}_{\texttt{pool}}$, which is the sum of squared pre-treatment imbalances for the average payment in $\mathcal{B}$.

Thus, we have: $f(W;\lambda,\nu) = \text{Im}_{\texttt{sep}} + \text{Pen}_{\texttt{sep}}(\lambda) + \nu\,\text{Im}_{\texttt{pool}}$. When $\nu = 0$, $f(W;\lambda,\nu)$ decouples into B separate unit-level minimization problems. Also, as $y_{it} \geq 0$ for all i and t in our data application, $\text{Pen}_{\texttt{sep}}(\lambda)$ is an increasing function of λ. At $\lambda = 0$, $\text{Pen}_{\texttt{sep}}(0) = 1$. When both $\lambda = 0$ and $\nu = 0$, $f(W;\lambda,\nu)$ is the canonical SC criterion prescribed in Abadie et al. (2010). When $\lambda = 0$ and $\nu > 0$, it is the partially pooled SC criterion where ν balances the separate unit level and pooled sum of squared imbalances between the treated unit and their synthetic controls in the pre-treatment period.

We develop and use the penalty $\text{Pen}_{\texttt{sep}}(\lambda)$ in (1) to prevent interpolation biases particularly when the control set is large and have highly heterogeneous members. Such uses of penalties in SC methods were suggested in Abadie et al. (2015) and later further developed in Ben-Michael et al. (2021b). However, $\text{Pen}_{\texttt{sep}}(\lambda)$ differs in fundamental aspects from penalties that have been prescribed in the existing literature

on PSC. This is because we have developed $\text{Pen}_{\text{sep}}(\lambda)$ so that the resulting estimators are adaptive to the following important structural characteristics of the physicians' payment data set that we analyze here. This adaption in the proposed PSC method is crucial (explained later in Section 3.3) in controlling the error rates of the synthetic control based estimators of TE in this application.

While the observed payment y_{it} is non-negative, we witness (see Table 1 and Figure 2) non-significant proportion of zero-payments, i.e., $y_{it} = 0$. As the event of a zero-payment is intrinsically much different from the event of a positive payment, considering a uniform metric such as L_2 distance used in Im_{sep} across all time points can lead to erroneous estimation. To mitigate the severe interpolation bias that can happen due to using sum of squared differences between treated and its estimates, we append the penalty $\text{Pen}_{\text{sep}}(\lambda)$ to the minimization criterion. A natural choice of penalty is the weighted L_1 distance between the treat unit b and each of the control units: $\text{Pen}^{(\ell_1)}_{\text{sep}}(\lambda) = \lambda\{\sum_{c=1}^{C} w_{bc} \left(\sum_{t=1}^{T-1} |y_{bt} - y_{ct}|\right)\}$. The proposed penalty $\text{Pen}_{\text{sep}}(\lambda)$ differs from it by emphasizing the difference between the treated and control units in the occurrence of zero-payments. Unlike this L_1 penalty, the proposed penalty is not linear but exponential and it only considers the gaps between the treated and control units when one of them is zero and the other positive: $\text{Pen}_{\text{sep}}(\lambda) = \sum_{b=1}^{B}\sum_{c=1}^{C} w_{bc} \exp\left(\sum_{t=1}^{T-1}\{\lambda\, y_{ct} I(y_{bt} = 0) + \lambda\, y_{bt} I(y_{ct} = 0)\}\right)$.

Heuristically, the penalty helps in the construction of SC estimates by restricting estimates for treated unit b to only corresponding control units that have similar patterns of zero-payments; subsequently, the ν-weighted sum of separate and pooled imbalances are minimized producing SC estimates for any treated unit $b \in \mathcal{B}$ that (a) have controlled imbalances for positive y_{bt} in $t = 1, \ldots, T-1$, and (b) are based on control units $\mathcal{C}_b \subset \mathcal{C}$ such that $\sup_{c\in\mathcal{C}} y_{ct} \approx 0$ whenever $y_{bt} = 0$ for any $t = 1, \ldots, T$. We show below in Section 3.3 that not only the former but the second condition is also needed in our application to produce good estimates of y_{bT} for $b \in \mathcal{B}$. Thus, the role of the penalty is very important in (1). Next, we formally explain the role of the penalty function and then provide the implementation details for constructing the proposed PSC estimates in Section 3.4.

3.3 Risk properties and the role of the penalties

An additive mixture model. To study the risk properties of the proposed PSC estimators we consider a flexible additive mixture model. Readers interested in the implementation of the PSC method and our

empirical study may skip ahead to Section 3.4.

Without loss of generality, consider y_{it} as truncated observations from unobserved pay-offs z_{it} that varies over $\mathbb{R}$, i.e., $y_{it} = \max(z_{it}, 0)$. Consider an additive model for the pay-offs:

$$z_{it} = f_{it} + \delta_{it} + \epsilon_{it}, \text{ for } i = 1, \ldots, C, C+1, \ldots, B+C \text{ and } t = 1, \ldots, T, \tag{3}$$

where, f_{it} is a low-dimensional factor model and ϵ_{it} are independent noise with $E(\epsilon_{it}) = 0$, $E(\epsilon_{it}^2) = \sigma^2$ and $E(\epsilon_{i_1 t_1} \cdot \epsilon_{i_2 t_2}) = 0$ whenever $i_1 \neq i_2$ or $t_1 \neq t_2$. Let f_{it} be a K dimensional latent factor model as in Abadie et al. (2010), i.e., $f_{it} = \sum_{k=1}^{K} \phi_{ki}\, \mu_{kt}$. The coefficient $\boldsymbol{\phi}_i = (\phi_{ik} : 1 \leq k \leq K)$ varies across units but is invariant across time whereas the factor $\boldsymbol{\mu}_t = (\mu_{kt} : 1 \leq k \leq K)$ is invariant across units but varies across time.

For each i, let $\Delta_i = (\delta_{i1}, \ldots, \delta_{iT})$ be a dampening sequence, i.e, $\Delta_i \leq \mathbf{0}$. If $\Delta_i = \mathbf{0}$ for all i in (3), and $T - 1 \gg K$, then for any treated unit $b \in \mathcal{B}$ the parameters $\boldsymbol{\phi}_b$ and $\{\mu_t : 1 \leq t \leq T\}$ can be well approximated leading to good SC based estimates of y_{bT} (see appendix B of Abadie et al., 2010 and the proof of Thm. 1 in Ben-Michael et al., 2021a).

When δ_{it} is highly negative for some t, it would dominate the other terms in (3) producing negative pay-off z_{it} and so, the observation y_{it} would be a zero-payment. Represent the support of the negative spikes of this dampening process by the vector $\boldsymbol{q}_i = I\{\Delta_i < \mathbf{0}\}$. There can be 2^T different types of $\boldsymbol{q}_i$s. However, for our application the $\boldsymbol{q}_i$s are not random sequences but are based on specific temporal patterns. As such, we can impose further constraints on the model and assume that there are only L different types of dampening sequences where L is an unknown but fixed number. The presence of such regularity structures among the zero-payment patterns is important for consistent estimation. Under this constraint, Δ_i is generated from a mixture model, i.e., $\Delta_i = \bar{\Delta}_{h(i)}$ where $h : \{1, \ldots, B+C\} \to \{1, \ldots, L\}$ is an unknown function that maps the units to groups containing on similar dampening sequences.

We observe $y_{it} = \max(z_{it}, 0)$ for $i \in \mathcal{B} \cup \mathcal{C}$ and $t = 1, \ldots, T-1$ and $y_{iT} = \max(z_{it}, 0)$ for $i \in \mathcal{C}$ and the goal is to estimate $y_{iT} = \max(z_{bT}, 0)$ for $b \in \mathcal{B}$. The factors $\boldsymbol{\mu}_t$ in the factor model are global (invariant across units) whereas $\bar{\Delta}_h = (\bar{\delta}_{h(c),t} : 1 \leq t \leq T)$ varies between groups with different dampening patterns. Compared to the latent factor model analyzed in Abadie et al. (2010), it is more

challenging to construct efficient SC estimates in the presence of these complex, additive structures in Δs. See supplement for an illustrative example. Equipping (1) with the penalty $\text{Pen}_{\text{sep}}(\lambda)$ helps us in correctly learning the coefficients $\boldsymbol{\phi}_b$ for any treated unit b. Next, we explain the risk properties of the proposed PSC method in an asymptotic regime where $T \to \infty$ and λ is large. In practice, the tuning parameter λ is chosen by cross validation and the penalized criterion is seen to produce good estimates across varied non-asymptotic regimes which are presented later in Section 4.

Risk analysis of the proposed estimator. To facilitate a formal but intuitive understanding on the role of the aforementioned penalty for producing consistent SC based estimates, henceforth in this subsection, we assume that the noise component ϵ_{it} in (3) are generated from Gaussian distribution. All the results in this subsection can be easily extended to additive mixture models with sub-gaussian noise. To provide rigorous mathematical proofs of the risk properties, we consider $T \to \infty$ and impose the following assumptions on (3):

A1. The factor model has significant signal strength. Let $\gamma = (2\log C + 4\log T)^{1/2}\sigma$. Assume $f_* := \inf\{f_{it} : 1 \le i \le B + C,\ 1 \le t \le T\} \ge \gamma$.

A2. For any two dampening sequences $\bar{\Delta}_g, \bar{\Delta}_h$, if $\bar{\boldsymbol{q}}_g = I\{\bar{\Delta}_g < \mathbf{0}\}$ and $\bar{\boldsymbol{q}}_h = I\{\bar{\Delta}_h < \mathbf{0}\}$ are such that $\sum_{t=1}^{T-1} |\bar{q}_{g,t} - \bar{q}_{h,t}| = 0$ then $q_{q,T} = q_{h,T}$. This is a benign assumption that ensures that two distinct dampening sequences must differ at least once in the pre-treatment era. It is essential for identifiable estimate of y_{bT} in (3) based on observing y_{it} for $t = 1, \ldots, T-1$ and $i = 1, \ldots, B+C$.

A3. There is at least one instance where the dampening sequence has large enough negative signal to dominate the factor model. For any h, assume $\inf_t \bar{\delta}_{h,t} \le -f^* - \gamma$ where $f^* := \sup\{f_{it} : 1 \le i \le B + C,\ 1 \le t \le T\}$.

A4. Two distinct dampening sequences must differ significantly in at least one time point in the pre-treatment era, i.e., $\sup_{1 \le t < T} |\bar{\Delta}_{g,t} - \bar{\Delta}_{h,t}|\, I\{\bar{\Delta}_{g,t}\bar{\Delta}_{h,t} = 0\} \ge f^* + \gamma$. Note that, by assumption A3, if two distinct dampening sequences have disjoint supports, i.e., $\sum_{i=1}^{T-1} \bar{q}_{g,t}\, \bar{q}_{h,t} = 0$, then this condition is trivially satisfied.

A5. Each dampening sequence has a non-trivial fraction of zeros: $\inf_h \underline{\lim}_{T\to\infty} T^{-1} \sum_{t=1}^{T} (1 - \bar{q}_{h,t}) > 0$. This implies each treated unit can have a non-trivial proportion of non-zero payments in (3). This

is a benign assumption mainly set to prevent degeneracy in the proof. Estimates of any treated unit not satisfying the condition can be just set to 0. We further assume that for any treated unit b, the sum of squared imbalances based on controls with same dampening sequences is well-controlled:

$$\min_{\boldsymbol{w}\geq 0,\,||\boldsymbol{w}||_1=1} \sum_{t=1}^{T} \big(y_{bt} - \sum_{c\in\mathcal{C}_b} w_c\, y_{ct}\big)^2 I\{\delta_{bt}=0\} \leq O(T\log T) \text{ as } T\to\infty, \tag{4}$$

where, $\mathcal{C}_b = \{1 \leq c \leq C : \Delta_c = \Delta_b\}$. This again is a very flexible assumption as the asymptotic behavior of the square error of imbalances from any reasonable model in the pre-treatment period is typically linear in T and we allow a poly-log margin over it. It holds as long as we have a sensible control set such that no group in (3) that has too few or no control units.

A6. Our final assumption is not on the model but on criterion (6). We restrict the weight corresponding to each control unit to be either 0 or at least $1/(CT)$. Let $\mathcal{W}$ be the set of all such weight vectors which satisfy $\sum_{c=1}^{C} w_c = 1$ and $w_c = \{0\} \cup [(CT)^{-1}, 1]$ for all c. We assume (4) also holds for the reduced weight space $\mathcal{W}$.

Under these assumptions, we concentrate on estimating Y_{bT} where Y_{bT} is generated from (3) and $b \notin \mathcal{C}$. We consider estimators of the form $\hat{y}_{bT}(\boldsymbol{w}) = \max(\hat{z}_{bT}(\boldsymbol{w}), 0)$ where $\hat{z}_{bT}(\boldsymbol{w}) = \sum_{c=1}^{C} w_c\, y_{cT}$ where the weights $w_c \geq 0$ for all c and $\sum_c w_c = 1$. We concentrate on criterion (1) with $\nu = 0$. The effect of the pooling penalty parameter has been extensively studied in Ben-Michael et al. (2021a) and similar impact will be seen here. With $\nu = 0$, the optimization of (1) decouples in optimization for each treated unit separately. For constructing $\hat{Y}_{bT}$, consider only controls in the following subset of the control set $\mathcal{C}$:

$$\hat{\mathcal{C}}_b = \{c \in \mathcal{C} : y_{ct} \leq \kappa^{-1} \text{ if } y_{bt} = 0 \text{ and } y_{ct} > 0 \text{ if } y_{bt} \geq \kappa^{-1} \text{ for all } t = 1, \ldots, T-1\}, \tag{5}$$

for some $\kappa > 0$. Note that, unlike $\mathcal{C}_b$ which depends on the model parameters, $\hat{\mathcal{C}}_b$ depends only on the observations. Next, consider the sequence of penalty parameter $\{\lambda_T : T \geq 1\}$ with $\lambda_T^2 = 2\kappa(\log(CT) + \log\log T)$. We have an additional off-shoot term in the penalty akin to hard thresholding penalty in Donoho and Johnstone (1994). Our first results show that with very high probability for any treated unit b the PSC estimate based on λ_T is solely based on control units in $\hat{\mathcal{C}}_b$. As such, the probability is at least $1 - T^{-2}$ as $T \to \infty$.

Lemma 1. *Under assumptions A1–A6, for any treated unit b, the optimal weight vector $\hat{\boldsymbol{w}}^{(b)}$ for the minimization (2) with $\lambda \geq \lambda_T$ satisfies*

$$\lim_{T\to\infty} T^2\, P\big(\hat{w}_c^{(b)} \neq 0 \textit{ for some } c \in \mathcal{C} \setminus \hat{\mathcal{C}}_b\big) = 0.$$

The proofs of all the results stated in this section and additional discussion are given in the supplement.

Next, we use the naive upper bound on the estimation error of the target y_{bT} by PSC estimates: $|y_{bT} - \hat{y}_{bT}| \leq |z_{bT} - \hat{z}_{bT}|$, and concentrate on the estimation error for the non-truncated pay-offs from (3). The residual of PSC estimates $\hat{z}_{bT}$ decomposes into three constituents corresponding to the factor model, the dampening sequence and the noise respectively. For any PSC estimate based on weights $\boldsymbol{w}$,

$$\begin{aligned} &z_{bT} - \hat{z}_{bT}(\boldsymbol{w}) = R_f(\boldsymbol{w}) + R_\delta(\boldsymbol{w}) + R_\epsilon(\boldsymbol{w}), \text{ where, } R_f(\boldsymbol{w}) = \sum_{k=1}^{K} \mu_{kT}\big(\phi_{kb} - \sum_c w_c \phi_{kc}\big), \\ &R_\delta(\boldsymbol{w}) = \sum_c w_c(\bar{\delta}_{h(b),T} - \bar{\delta}_{h(c),T}), \text{ and } R_\epsilon(\boldsymbol{w}) = \epsilon_{bT} - \sum_c w_c \epsilon_{cT}. \end{aligned} \tag{6}$$

Any weight vector $\boldsymbol{w}$ that is trained on the pretreatment period as in (1) is independent of $\{\epsilon_{cT} : c = 1, \ldots, C\}$ and so, $R_\epsilon(\boldsymbol{w})$ is stochastically dominated by $N(0, v)$ where, $v = \sigma^2(1 + ||\boldsymbol{w}||^2) \leq 2\sigma^2$ as $||\boldsymbol{w}_b||_1 = 1$. Thus, we concentrate on controlling the two other terms.

Controlling R_δ is critical since if there exists d with positive weight w_{bd} and $\bar{\Delta}_{h(c)} \neq \bar{\Delta}_{h(b)}$ then $R_\delta(b, T)$ can be very large as the dampening sequence can have very large spikes. We next show that if we restrict ourselves to controls in $\hat{\mathcal{C}}_b$, then $R_\delta = 0$ with probability at least $1 - T^{-1}$ as $T \to \infty$.

Lemma 2. *Under assumptions A1–A6, for any $b \in \mathcal{B}$ and $\alpha < 1/2$*

$$\lim_{T\to\infty} T(\log T)^\alpha\, \boldsymbol{P}\left(\sup_{c\in\mathcal{C}} \sum_{t=1}^{T} |\delta_{ct} - \delta_{bt}| \cdot I\{c \in \hat{\mathcal{C}}_b\} > 0 \right) = 0. \tag{7}$$

Next, consider the term R_f in (6), which can be well-controlled if the PSC method learns the factor model coefficients $\{\phi_{kb} : 1 \leq k \leq K\}$ pertaining to treatment b well, i.e., $\sum_c \hat{w}_{bc}\phi_{kc} \approx \phi_{kb}$. For any weight vector $\boldsymbol{w}$ define $\Phi(b; \boldsymbol{w}) = (\phi_{kb} - \sum_c w_c \phi_{kc} : 1 \leq k \leq K)$. Then, $|R_f(\boldsymbol{w})| \leq ||\boldsymbol{\mu}_T||_2 ||\Phi(b; \boldsymbol{w})||_2$.

In the latent factor model where $\delta_{it} = 0$ for all i, t in (3), it follow directly from Appendix B of Abadie

et al. (2010), that $||\Phi(b;\boldsymbol{w})||_2$ is upper bounded by a multiple of the imbalance between the treated unit and the PSC estimates in the pre-treatment period. The multiplier is proportional to the lowest eigenvalue of H where $H = \sum_{t=1}^{T-1} \boldsymbol{\mu}_t \boldsymbol{\mu}_t'$. Using lemma 2 and applying similar derivations for SC estimates restricted to the class $\hat{\mathcal{C}}_b$ of controls, we obtain an analogous upper bound for $|R_f(\boldsymbol{w})|$. Combining these bounds on the three terms on the right side of (6) we arrive at our main result which states a probabilistic upper bound on the estimation error of the proposed PSC estimates. For PSC estimate $\hat{y}_{bT}(\boldsymbol{w})$ of the bth treated unit based on weight $\boldsymbol{w}$, the upper bound depends on the sum of squared imbalances from positive time points $\text{Imp}(\boldsymbol{w}, b) = \sum_{t=1}^{T-1}(y_{bt} - \sum_{c=1}^{C} w_c y_{ct})^2$ as well as on the parameters of the factor model in (3).

Theorem 1. *Under assumptions A1–A6, for any treated unit $b \in \mathcal{B}$ and for any weight $\boldsymbol{w} \in \mathcal{W}_b := \{\boldsymbol{w} \in \mathcal{W} : w_i = 0$ for $i \notin \hat{\mathcal{C}}_b\}$*

$$|y_{bT} - \hat{y}_{bT}(\boldsymbol{w})| \leq m_b^{-1/2} ||\boldsymbol{\mu}_T||_2 \left(\kappa_b \, \{s_b^{-1} \textit{Imp}(\boldsymbol{w}, b)\}^{1/2} + 8\sigma \sqrt{s_b^{-1} \log T} \right) + 2\sigma \sqrt{\log T}, \tag{8}$$

with probability at least $1 - 1/T$ where m_b and κ_b are respectively the smallest eigenvalue and condition number of $s_b^{-1} \sum_{t=1}^{T-1} \boldsymbol{\mu}_t \boldsymbol{\mu}_t' I\{y_{bt} > 0\}$ and $s_b = \sum_{t=1}^{T-1} I\{y_{bt} > 0\}$.

Note that in Theorem 1 $\mathcal{W}_b$ is the weight space with support concentrated on the control subset $\hat{\mathcal{C}}_b$. For moderately large T, the non-coverage probability of (8) is very small. Also, with K fixed as $T \to \infty$ when the factor loadings are well-regulated, we have $m_b = O(1), \kappa_b = O(1)$. Thus, in this case (8) gives

$$|y_{bT} - \hat{y}_{bT}(\boldsymbol{w})| \leq K ||\boldsymbol{\mu}_T||_\infty \{s_b^{-1} \text{Imp}(\boldsymbol{w}, b)\}^{1/2} + 2\sigma \sqrt{\log T}. \tag{9}$$

By assumptions A5 and A6, the right side above for the optimal weighted PSC estimate is $O(\sqrt{\log T})$.

Now, to illustrate the importance of the penalty $\text{Pen}_{\text{sep}}(\lambda)$ we show that the SC estimator based on minimizing criterion (1) with $\lambda = 0$ have extremely high maximal risk as compared to the proposed PSC estimator. Consider the set Θ_T of all parameters $\boldsymbol{\theta} = (\boldsymbol{\mu}_k, \, \phi_{ik}, \, \bar{\Delta}_l : k = 1, \ldots, K; i = 1, \ldots, B + C; l = 1, \ldots, L)$ of (3) which along with assumptions A1–A4 also satisfy $\sup_k |\boldsymbol{\mu}_k| \leq \psi$ for some prefixed $\psi > 0$ and $\inf\{|\boldsymbol{\phi}_b - \boldsymbol{\phi}_c|_\infty : c \in \mathcal{C}$ and $\Delta_c = \Delta_b\} \leq \log T$. The following asymptotic result shows that with probability $1 - 1/T$, the worst case risk over Θ_T of the PSC estimate is $O(\sqrt{\log T})$ whereas the worse case risk of the SC estimate is higher than T.

Lemma 3. *Consider the PSC estimator $\hat{y}_{bT}(\hat{\boldsymbol{w}}_{psc})$ and the SC estimator $\hat{y}_{bT}(\hat{\boldsymbol{w}}_{sc})$ where the two weight vectors are selected by the minimization problem (2) with $\lambda \geq \lambda_T$ and with $\lambda = 0$ respectively. For any $a > 1/2$, there exists $C > 0$ such that,*

$$\lim_{T\to\infty} \min_{\boldsymbol{\theta}\in\Theta_T} T\left[1 - P_{\boldsymbol{\theta}}\left((\log T)^{-a}\left|y_{bT} - \hat{y}_{bT}(\hat{\boldsymbol{w}}_{psc})\right| < C\right)\right] = 0.$$
$$\lim_{T\to\infty} \max_{\boldsymbol{\theta}\in\Theta_T} T\left[1 - P_{\boldsymbol{\theta}}\left(T^{-1}\left|y_{bT} - \hat{y}_{bT}(\hat{\boldsymbol{w}}_{sc})\right| > C\right)\right] = 0.$$

3.4 Implementation of the method for analysis of physician payments data

We discuss implementation details of the method, specifically regarding the calculations of ν, λ and confidence interval. First, we follow Ben-Michael et al. (2021b)'s guide for the calculation of ν. We calculate W separately by minimizing $\text{Im}_{\texttt{sep}}$ and $\text{Im}_{\texttt{pool}}$. Then ν is set as $\sqrt{\text{Im}_{\texttt{sep}}}/(\sqrt{\text{Im}_{\texttt{pool}}} - \sqrt{\text{Im}_{\texttt{sep}}})$. Next, we use a cross-validation method to calculate λ. The cross-validation method leaves one of the pre-treatment time periods out at a time and fits the penalized synthetic control for a given λ. The λ is chosen as the one that minimizes the penalized partial sum of squared imbalance of the left out time period to the synthetic control fit.

In our payments data analysis, we analyze the average treatment effect on the treated (ATT) and the overall average treatment effect (ATE). The ATE calculation finds a synthetic control physician for each of the physicians from the states passing an MML as well as a synthetic counterpart physician from the pool of treated physicians for each of the physicians from the control states. We fit two W matrices for this purpose by solving two minimization problems, one finding a vector of weights of length equal to the number of control physicians for each treated state physician and the second finding a vector of weights of length equal to the number of treated physicians for each control state physician.

Finally, the confidence interval calculations use a leave-one-out calculation where one at a time each physician is left out; the penalized synthetic controls/counterparts are calculated by solving the minimization problem using the remaining physicians and ATE/ATT calculation is done. The 2.5% and 97.5% quantiles of these leave-one-out effect estimates give a 95% confidence interval to the corresponding estimand.

4 Simulation

This section evaluates the relative performance of the proposed penalized synthetic control method to the existing methods. Our simulation model generates 30 units observed for $T = 55$ periods. Three of these 30 units are exposed to a treatment at time 45 and the rest 37 units remain unexposed. The original synthetic control method of Abadie and Gardeazabal (2003) and Abadie et al. (2010) is developed for a single exposed unit. This method is adapted when there are multiple exposed units by separately calculating the synthetic controls for each of the exposed units from the pool of all control units. Ben-Michael et al. (2021b) show that this method of separate calculations of the synthetic controls can be inefficient and propose a new method for simultaneous calculation of synthetic controls. We compare our method to these two state-of-the-art methods for synthetic control analysis.

In the notation introduced in the previous section, we generate data for unit i at time t as

$$y_{it} = \max(z_{it} + \tau_i W_{it}, 0); \text{ where } z_{it} = a_i + (t-1)/4 + \lfloor (t-1)/4 \rfloor + \delta_{it} + \epsilon_{it},$$

where a_i are iid uniform on $[10, 60]$, W_{it} are the treatment indicator which is 1 only when $t > 45$ and unit i is exposed, and τ_i is the treatment effect. The noise ϵ_{it} are independently drawn for each i, t from a normal distribution with mean 0 and standard deviation 5. We consider three clusters of the units and each cluster is specified by its units' common dampening sequence δ_{it}. How similar or different these dampening sequences are determine how similar or different these clusters are. One unit from each cluster is selected to be treated where the probability of treatment for unit i is proportional to $\sum_{t=20}^{45} y_{it}$.

We specified three models for the δ_{it}s in the three clusters in our simulations, varying the similarity of the clusters. Specifically, we set $\delta_{it} = -80 \times q_{it}$ where q_{it} is 0 or 1, indicating the time when the process is dampened. The first two models are probabilistic and use exponential waiting time processes. Consider one of the three clusters, c. Starting at time $t = 0$, it waits for an exponential time with the rate θ_c when a dampening starts. After that, the process is dampened for an exponential time length with the rate η_c. Following this, the first process starts again to find the next starting time for dampening. This model can be thought of as physicians and drug manufacturers following a similar exponential waiting process to decide when they would interact.

Our first dampening model sets $\theta_c = 1/10$ for all $c = 1, 2, 3$ and $\eta_1 = \eta_2 = \eta_3 = 1/3$; the second model sets $\theta_1 = 1/10$, $\theta_2 = 1/15$, $\theta_3 = 1/7$ and $\eta_1 = \eta_2 = \eta_3 = 1/3$. The last model sets deterministic $q_i = 1$ for $i = 20, \ldots, 24, 40, \ldots, 44$ in cluster 1, $q_i = 1$ for $i = 30, \ldots, 34, 45, \ldots, 49$ in cluster 2, and $q_i = 1$ for $i = 40, \ldots, 44, 50, \ldots, 54$ in cluster 3. Figure 4 provides plots of data generated from these models.

Table 2: Simulation comparison for different synthetic control methods when $\tau_i = 0$ for all: best performance in each row is in bold. Results are based on averaging over 500 simulations; standard errors are in the parentheses

	Synthetic control	Pooled SC	Proposed Penalized SC
clusters are probabilistically similar			
l_2 Imbalance	19.14 (0.26)	5.50 (0.08)	**4.04 (0.03)**
RMSE for ITT	20.69 (0.36)	5.87 (0.09)	**5.35 (0.11)**
RMSE for ATT	13.16 (0.39)	3.61 (0.11)	**2.36 (0.11)**
clusters are probabilistically different			
l_2 Imbalance	19.40 (0.27)	5.58 (0.10)	**4.07 (0.03)**
RMSE for ITT	21.33 (0.37)	5.81 (0.10)	**5.81 (0.18)**
RMSE for ATT	14.03 (0.37)	3.63 (0.13)	**2.89 (0.16)**
clusters are deterministic and different			
l_2 Imbalance	16.65 (0.17)	6.61 (0.08)	**4.50 (0.02)**
RMSE for IIT	26.30 (0.31)	6.56 (0.08)	**5.38 (0.04)**
RMSE for ATT	13.89 (0.22)	4.01 (0.10)	**2.54 (0.05)**

Table 3: Simulation comparison for different synthetic control methods when $\tau_i = 15, 25$ and -10 in the three exposed units respectively: best performance in each row is in bold. Results are based on averaging over 500 simulations; standard errors are in the parentheses

	Synthetic control	Pooled SC	Proposed Penalized SC
clusters are probabilistically similar			
l_2 Imbalance	19.50 (0.26)	5.50 (0.08)	**4.07 (0.03)**
RMSE for ITT	21.18 (0.36)	5.80 (0.09)	**5.33 (0.11)**
RMSE for ATT	13.74 (0.39)	3.52 (0.11)	**2.42 (0.11)**
clusters are probabilistically different			
l_2 Imbalance	19.54 (0.27)	5.64 (0.10)	**4.07 (0.03)**
RMSE for ITT	21.24 (0.37)	5.96 (0.10)	**5.81 (0.18)**
RMSE for ATT	13.41 (0.37)	3.81 (0.13)	**2.81 (0.16)**
clusters are deterministic and different			
l_2 Imbalance	16.33 (0.17)	6.79 (0.08)	**4.53 (0.02)**
RMSE for IIT	25.88 (0.31)	6.67 (0.08)	**5.38 (0.04)**
RMSE for ATT	13.70 (0.22)	4.15 (0.10)	**2.55 (0.05)**

The simulation results are summarized in Tables 2 and 3 which report three performance measures.

The 'l_2 imbalance' is the average of the three euclidean distances of the pre-treatment outcomes of the three treated units and their synthetic controls. The 'RMSE for ITT' is the average of simulation-based root mean squared errors for estimating the individual treatment effect τ_i for each of the three treated units. Finally, the 'RMSE for ATT' is the simulation-based root mean squared error for estimating the average treatment effect $\sum_i W_{iT}\tau_i/3$ of the three treated units.

These simulation results show that the original synthetic control method adapted to this situation performs very poorly in all measures. Comparatively, the pooled SC method performs better than the original method. Still, the proposed method has the best performance among all the methods in better fit and estimation. Further, the performance of pooled SC becomes progressively worse with three structures of the clusters that create increasing distinctions between the latent structures in the clusters. By contrast, the proposed method provides consistently good performance across different cluster structures.

5 Results

5.1 Synthetic control analysis of the MML passage on physician payments

Our primary analysis considers all pain medicine physicians from 13 states, of which three (PA, OH, LA) were 'treated' states that passed an MML in the second quarter of 2016. The method, described in Section 3.4, produces synthetic controls for each physician in the treated states using physicians in the control states, and likewise produces synthetic counterparts for each physician in the control states using physicians in the treated states.

The accompanying Figure 5 in its left panel shows the average of the differences in the payments of 190 pain-medicine physicians against their synthetic counterparts. The difference in payments is nearly 0, with a confidence interval between $-\$27.0$ and $\$0.3$, in the pre-treatment periods. Thus, the match provides a good fit, which is an important requirement to draw causal conclusions from the calculated differences during the post-treatment period (Abadie, 2021, Abadie et al., 2010).

Assuming there is no endogeneity that could have affected the analysis, Figure 5 shows an estimate of the average treatment effect (ATE) of the passage of an MML on payments to physicians. In the left panel of this figure, we observe a negative and significant ATE for pain medicine physicians, indicating that the

payments to these physicians go down post-passage of MML. The negative effect on payments to these physicians continues to increase over time, except for a small kink from the first to the second quarter of 2017. This shows a changing dynamic in the interaction between pain medicine physicians and opioid manufacturers. The estimated decrease in payments is also substantial and estimated to be $\$1217.41$ in the third quarter of 2017.

Unlike the treated states in the above analysis, Florida passed an MML in the last quarter of 2016. We explore whether the payment activities in Florida were affected by the laws passed in other states (PA, OH and LA) in the quarter before Florida passed its own law. A potential spillover effect, stemming from MML passed in other states in the second quarter of 2016, can bias the treatment effect on Florida's pain medicine physicians estimated by the synthetic control method (Schuler et al., 2021).

We performed two analyses on physician payments in Florida. In our first analysis, for each physician in Florida, we create synthetic control from a pool of physicians residing in the 10 control states using their payment history till the second quarter of 2016. In our second analysis, we create synthetic controls using physicians' payment history till the fourth quarter of 2016. Figure 6 shows the difference in payments to Florida physicians and their synthetic controls from these two analyses. The estimates from the first analysis have a similar pattern to the estimates from the earlier analysis shown in the left panel of Figure 5. The first analysis on payments to Florida physicians post-passage of MML shows a negative effect even during the third and fourth quarters of 2016. This effect is likely attributable to a spillover effect from the passage of MMLs in the other states. However, the spillover effect only amplifies the negative effect of MML. Thus even after controlling for concurrent passage of MML in other states, estimated in our second analysis on Florida physicians, we still find a significant negative effect of the law on physician payments in Florida. This effect could be because opioid manufacturers could have anticipated the passage of MML in Florida, leading to a decrease in their interactions with physicians.

5.2 Mechanism

We now elaborate on the possible mechanism behind the declining payments to pain medicine physicians due to MML passage. We attribute that this decline in direct payments from opioid manufacturers to the evolution of marijuana as a superior substitute in states that have legalized medical marijuana consump-

tion. As noted earlier, medical marijuana, although not federally regulated for treating pain, is perceived, both by physicians and patients, to be a viable substitute to manage chronic pain (Powell et al., 2018). Further, marijuana is arguably less addictive compared to opioids (Okusanya et al., 2020). Therefore, under circumstances where marijuana is perceived equally effective as opioids, the former becomes a superior alternative to the latter. This would lead to a decline in opioid prescriptions when marijuana is a potential substitute and the state decriminalizes medical marijuana consumption. Consequently, opioid manufacturers, being profit maximizing enterprises, would decrease direct payments to physicians when faced with a potential irreversibly-declining opioid market in those states (Ingraham, 2017).

However, the declining opioid payments in the treated states can potentially happen due to factors other than MML passage. For example, some states might have stricter laws to curb opioid usage, such as through stricter PDMPs or Pill Mill laws (Moyo et al., 2017). In those states, the pressure on physicians to move away from opioids can lead to opioid manufacturers strategically decreasing their presence and thus investing less on financial inducements to physicians. And if those states pass MML, it might be difficult to identify the substitution effect that can be attributed to MML passage separately from the effect induced by opioid-restricting policies of those states. However, such identification issue will arise only if the MML and opioid-curbing policies were implemented simultaneously. The opioid-restricting policies in our treatment states were passed before 2016 (i.e., not simultaneously with the passage of MML), e.g., Ohio passed the MML in April 2016 while the pill mill law was passed in 2011. Thus, our analysis would be able to adjust for these systematic differences between the states in the pre-treatment period. Therefore, we can cleanly attribute the decrease in payment to opioid physicians to substitution effect arising due to MML passage.

Among the potentially other factors that could explain the estimated decline, it could also be that the treated states were able to pass the MML because of potentially weak lobbying power of the opioids manufacturers in those states (Frances, 2021). This could have led to the opioid manufacturers selectively reducing their activities in the treated states and hence a spurious negative effect in our analysis is manifested. If this conjecture is valid, we would see a negative effect on payments to physicians agnostic of their specializations. To test such a theory, we also analyzed direct payments to Anesthesiologists, who

received the second highest payments after pain medicine physicians.[6]

Both specializations, pain medicine and anesthesiology, regularly prescribe opioid. However, pain medicine physicians mostly use opioid for chronic pain management where marijuana is a good substitute (Powell et al., 2018). Anesthesiologists, on the other hand, primarily use opioid to manage acute pain in hospital settings. As mentioned in Section 1, marijuana, for the most part, is not FDA approved, rendering it inapplicable in acute pain management. Hence, if the marijuana substitution theory is valid, the payments to anesthesiologists should not show a consistent decline post MML passage. In contrast, if the opioid manufacturers reduced payments only because they lost ground in blocking MML passage, the decline of payments seen for pain medicine physicians will be mirrored in the payments to anesthesiologists. Similar to the analysis conducted for the pain medicine physicians (the left panel of Figure 5), we analyzed the payments to anesthesiologists between MML and non-MML states using our proposed synthetic control method. The corresponding plot for ATE on payments to anesthesiologists is provided in the right panel of Figure 5. We find that although payments to Anaesthesiologists declined initially immediately after MML passage, the decline in payments bounced back within a quarter's time to pre-treatment patterns.

The support for the substitution effect of marijuana in explaining the change in direct payments to pain medicine physicians is still incomplete, as this decrease in payments may not have been driven by the perceived invasion of medical marijuana. Instead, the decline in payments from opioid manufacturers to physicians may have led to reduced opioid prescriptions and thus made room for increased medical marijuana use. We attempt to differentiate between these two mechanisms using data on medical marijuana patient registration.

Florida provides bi-weekly updates regarding medical marijuana activities in the state. From their updates, we collected information on the locations of active dispensaries over time and the number of registered medical marijuana patients in those time periods in the state.[7] Figure 7 displays a rolling average of payments to physicians grouped by an active dispensary in their area. Joining the marijuana patient registration data with the payments data we conducted two regressions: we first regressed the

[6] All the other specializations, e.g., internal medicine and family medicine, had less than 10% of opioids related payments.

[7] Data related to bi-weekly updates on locations of active dispensaries and the number of registered medical marijuana patients are available at https://knowthefactsmmj.com/2018/07/28/2017-ommu-updates-archive/

Table 4: Regression analysis results in cities where physicians practice across Florida

Dependent Var.:	Log of Payment Rec.	Log of Payment Rec.	Log of Payment Rec.	Percent Change Mari. Patient
Lag of % Change in Mari. Patients	−0.3626. (0.1886)		−0.3701** (0.188)	
Whether City has Marijuana Dispensary		−0.1435*** (0.0243)	−0.1439*** (0.0243)	
Log of Payment Rec.				0.0011 (0.0010)
Fixed-Effects: Physician Specialty	Yes	Yes	Yes	Yes
S.E. type	Heteroskeda.-rob.	Heteroskedast.-rob.	Heteroskedast.-rob.	Heteroskedast.-rob.
Observations	8,467	8,467	8,467	9,235
R2	0.05255	0.05569	0.05613	0.004
Within R2	0.00044	0.00375	0.00421	0.0004

log of payment on the lagged bi-weekly change in marijuana patients, and whether the city in which a physician was practicing had a marijuana dispensary, and subsequently we regressed the bi-weekly change in marijuana patients to lagged payment activity. The results reported in Table 4 show a significant negative correlation between an increase in marijuana patients in preceding period as well as presence of a marijuana dispensary with opioid-prescribing physician payment; however, there is no significant association between physician payment and change in marijuana patients in the following period. These results provide us with further support that the substitution effect of marijuana is indeed the dominating factor in reducing payments to pain medicine physicians post-passage of MML.

6 Heterogeneity

In the previous section, we have seen evidence that the passage of MML led to a reduction of direct payments to pain medicine physicians from opioid manufacturers. We argued that this reduction is possibly stemming from opioid manufacturers realizing that increasing substitution from opioids to marijuana, particularly for chronic pain management. However, the above analysis does not tease out whether the substitution is initiated by choice(s) made by physicians or patients or if it is happening because of a societal shift. Therefore, it is interesting to explore if some distinct patterns in the data can motivate future studies to extend the understanding of this mechanism. Our proposed synthetic control method allows us

to estimate the individual treatment effects (ITEs), i.e., the treatment effect of MML on payments made to each physician. We use these ITEs to perform a secondary analysis wherein we investigate how the treatment effect varies as a function of physician characteristics and the demographics of where the respective physicians were practicing. In Figures 8–10, the vertical axes plot the estimated ITEs of physicians from 13 states averaged over the four quarters following MML passages in PA, OH, and LA in 2016 Q2.

We first look at the two physician characteristics, namely gender and year of graduation, in Figure 8. While the ITEs for the year of graduation do not show any defined pattern, we find that the decreases in payments to male physicians are less pronounced than female physicians. Historically, empirical research involving physician care has under-studied female physicians (Kimball and Crouse, 2007). However, significant differences exist in practice patterns between male and female physicians. Research shows that female physicians are more patient-centric, more open to patient concerns, have longer visits, and ask more questions (Hall et al., 1994, Roter et al., 2002). Our current finding emphasizes that in the context of pain relief, there is significant heterogeneity in how the introduction of medical marijuana affects physicians based on gender and, consequently, the population they serve.

Analyzing the ITEs based on the demographics of where the physicians practice, in Figure 9, we find that the payments show a greater decrease in low-income areas. Low income areas would have a higher proportion of people who engage in blue-collar jobs and, therefore, have more requirements for chronic pain management (Jacobsen et al., 2013). Also, poorer regions have shown higher instances of opioid misuse (Ghertner and Groves, 2018). Arguably, substituting into marijuana will help these communities (Compton et al., 2017). The recent governmental intervention to reduce opioid misuse has focused on these vulnerable communities (The White House, 2016, USDA, 2019). The larger substitution effect that we witness in lower income communities could be a manifestation of a combination of governmental efforts and societal awareness regarding the potential harmfulness of opioids.

In Figure 9, ITE patterns with respect to the median age of the population reveal that the substitution to medical marijuana is possibly the largest in the regions with a median age between 30-40 years. Populations younger than this bracket will have lesser requirements for chronic pain management; therefore, lesser substitution is probably not surprising. However, regions with an older population, who are more prone to chronic pain, also show lesser substitution to medical marijuana. We are limited in this study to

discern if the slower adoption of medical marijuana among older people is driven by their inertia against alternative pain management methods or if physicians are generally risk-averse in recommending medical marijuana for these older patients.

Next, analyzing the ITEs with respect to racial demographics of a physician's practice, in Figure 10, we find no discernible patterns as the proportion of Asian or Hispanic increases. However, ITEs show a sharp decline for physicians practicing in populations with a higher percentage of blacks. Recent studies have shown considerable differences in opioid prescribing patterns between black/African-American and white patients (SAMHSA, 2020). For example, Blacks/African-Americans are significantly less likely to be prescribed opioids for pain by medical providers than white patients. We find notable differences in the substitution effects between a higher proportion of white population and higher proportion of black/African American population. In Figure 10, a population with a higher than the national average of white population shows a relatively higher effect of MML passage compared to a population with a higher than the national average of black/African American population.[8]

In the above findings, we show that physicians' characteristics and demographics of where they practice are differently affected by payment reduction by the opioid manufacturers, possibly due to inherent differences in the physicians' and patients' substitution patterns. Motivated by our results, hypothesis-driven studies would be helpful to establish the modifiers of the substitution effect on treating pain.

7 Discussion

In the wake of opioid epidemic in the US (Feinberg, 2019), several measures were instituted at the federal and state levels to regulate the proper management of opioid consumption. Some states also passed laws legalizing medical marijuana consumption partly in response to the opioid epidemic. However, the FDA notes that, to date, "[it] has not determined that cannabis is safe and effective for any particular disease or condition;"[9] while, opioid still remains a potent treatment for chronic pain. Physicians are the primary gatekeepers for deciding medication for patients needing pain management. This paper connects these

[8]By April, 2020 estimates, the demography of the United States has about 59.3% non-Hispanic white and 13.6% black/African American population. https://www.census.gov/quickfacts/fact/table/US/PST040221

[9]https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd

three pieces: medical marijuana laws, opioid manufacturers and their interaction with opioid-prescribing physicians.

Our study finds a significant decrease in financial interactions between opioid manufacturers and physicians as an effect of MML passage. The finding that the opioid manufacturers in states that passed MML are stepping away from this particular form of interaction is concerning, for such activity can significantly affect the opioids ecosystem. It calls for detailed studies on the opioid-related healthcare industry in these states. If physicians are not actively engaged with opioid manufacturers in getting updates and driving research, eventually, patients are deprived of optimal care. As we currently do not have a comprehensive understanding of the effects of medical marijuana on individuals and society at large, intensive research on opioids and their safe consumption are needed for optimal pain management in the immediate future.

While our study focuses on opioid manufacturers and physicians, it is worth considering for a moment MML's effect on patient pain management. To set the context, physicians typically prescribe medication of a certain amount in 30 days' fills but also specify medication for the number of days of use. Additionally, it is expected that pain medicine physicians would tend to prescribe more opioid than non-opioid medication. Analyzing the annual prescription data (mentioned in Section 2), we found that, in 2015, they prescribed 49% more opioids than non-opioids in 30 days' fill and a similar 49% more days of prescription for opioid vs non-opioid. From 2015 to 2017, in the states not passing an MML, 30 days' fill of opioid vs non-opioid remained flat at a 1.38:1 ratio. However, in the states passing an MML, from 2015 to 2017, 30 days' fill of opioid vs non-opioid decreased from a 1.57:1 ratio to a 1.52:1 ratio. The ratios for the number of days of prescription in the MML states also decreased from a 1.57:1 ratio in 2015 to a 1.52:1 ratio in 2017. In particular, the pattern of opioid vs non-opioid prescriptions did not change in the control states, while there was a relative decrease in opioid prescriptions in the MML states from 2015 to 2017. We leave further analysis of the possible effect of MML passage on patient care for future research.

As a methodological contribution, we develop a novel penalized synthetic control method. This method estimates an average treatment effect from a longitudinal dataset on multiple treated and control individuals. We create a synthetic counterpart of each treated and control unit by closely matching on the target unit's and their groups' average pre-treatment outcome history using the pooled synthetic

control strategy. Further, we use a novel penalty so that the resulting estimators are adaptive to the latent groups in the data whose members have similar quarterly non-payment patterns. The penalty reduces interpolation bias by closely matching individuals and their synthetic counterparts on their non-payment patterns. Finally, we study the proposed method under an additive mixture model appropriate for our study. We show that an unpenalized synthetic control method will have uncontrolled maximal risk in the additive mixture models while the proposed method produces efficient SC estimates. In future, it will be useful to develop penalized synthetic control methods that can operate in the presence of more complex latent structures in the data.

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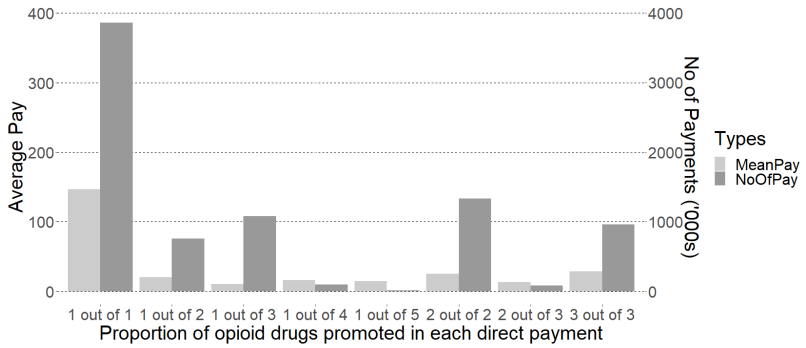

Figure 1: Distribution of average payment (in US dollars) and the number of payments related to opioid, categorized by the ratio of opioid to non-opioid drugs promoted during each payment.

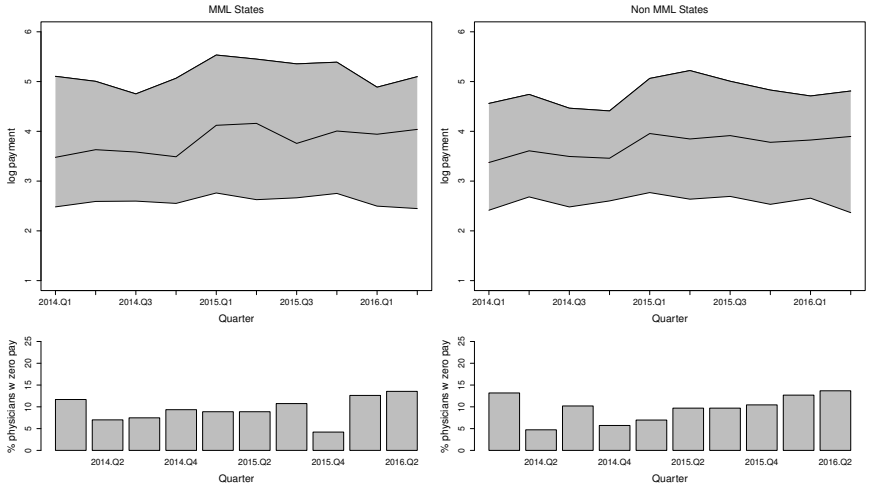

Figure 2: Summary of the payments to physicians in different quarters of pre-treatment period by the states that did and did not pass medical marijuana laws. The MML states are 'FL', 'LA', 'OH' and 'PA'; the non MML states are 'AL', 'GA', 'IN', 'NC', 'NE', 'SC', 'TX', 'UT', 'VA' and 'WI'. The plots on the top two panels show the 85th, 50th and 15th percentiles of log payments.

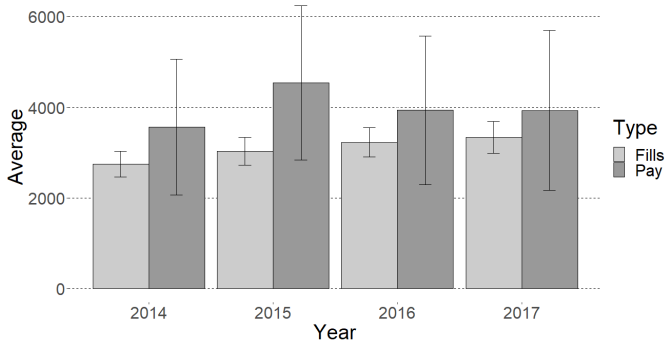

Figure 3: Distribution of average annual payments (in US dollars) to pain-medicine physicians and the corresponding average number of prescriptions (in '000s) written by those physicians across our analysis window (i.e., 2014-2017).

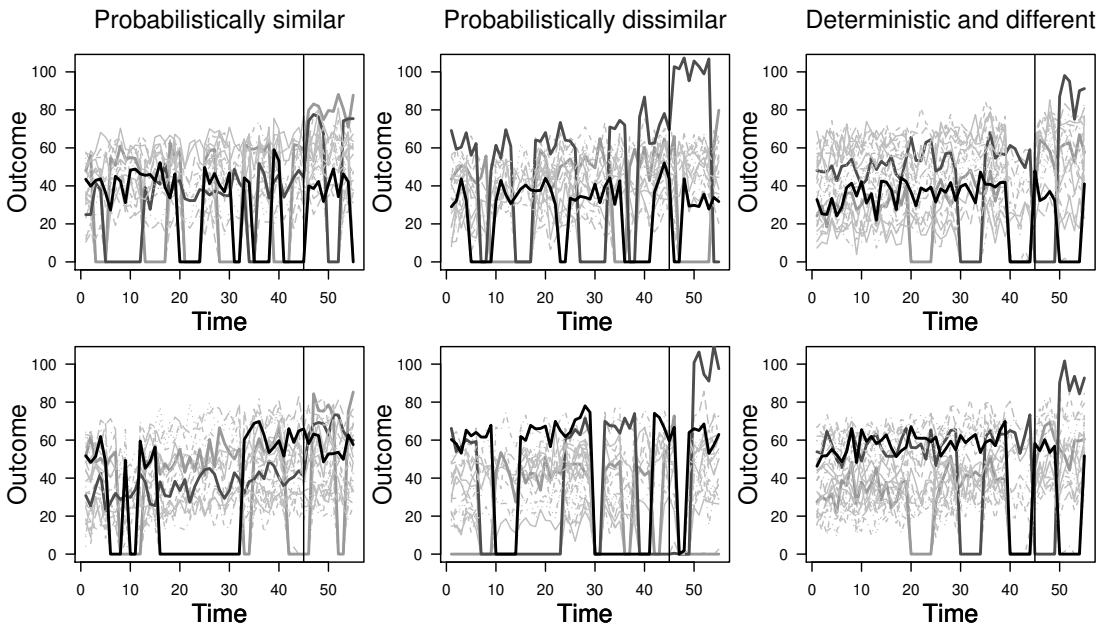

Figure 4: Two sets of simulated data in each the tree columns from the three simulation models. The three treated units from the three clusters are in colors 'black', 'dark gray' and 'gray' respectively; the vertical line shows the treatment adoption time.

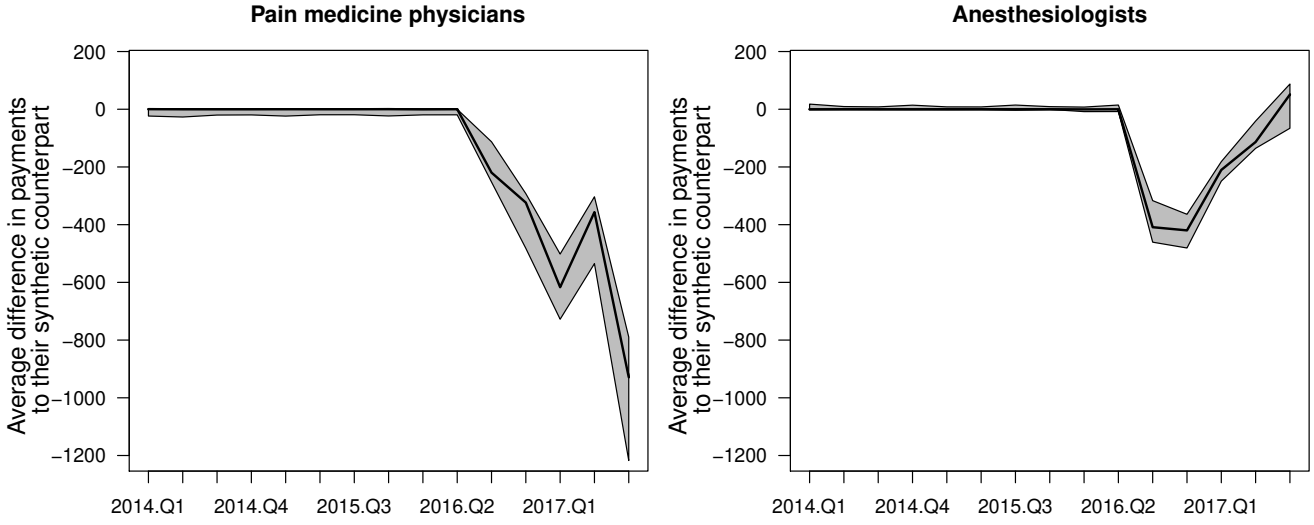

Figure 5: Synthetic counterpart analysis for MML passage on payments to physicians from 13 states in the US.

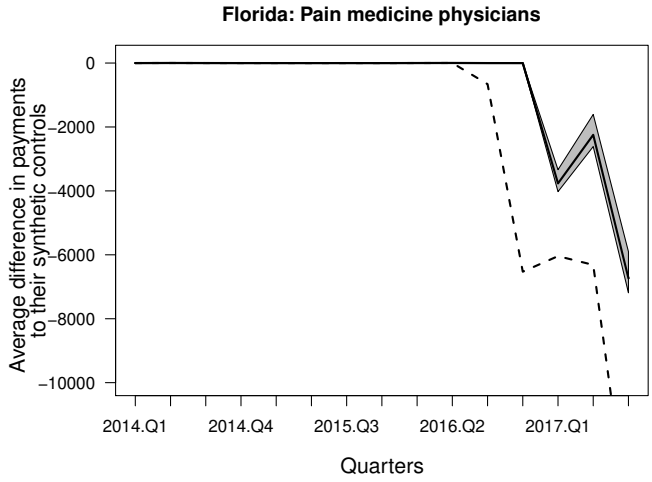

Figure 6: Synthetic control analysis for MML passage on payments to pain medicine physicians in Florida. The dashed line pretends MML passage in FL happened in the second quarter of 2016.

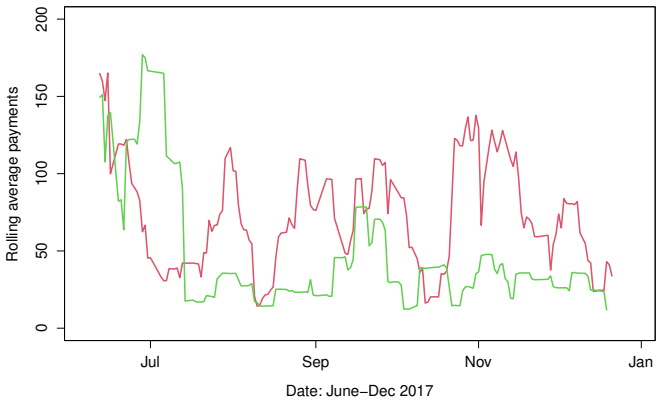

Figure 7: Payments to physicians in Florida between June and Dec 2017 in the cities without any marijuana dispensary at that time in red and with a marijuana dispensary at that time in green.

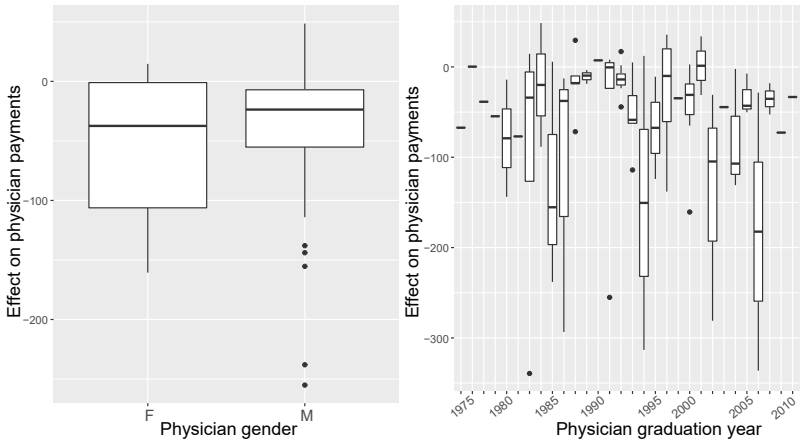

Figure 8: Effect heterogeneity by physician gender and year of graduation.

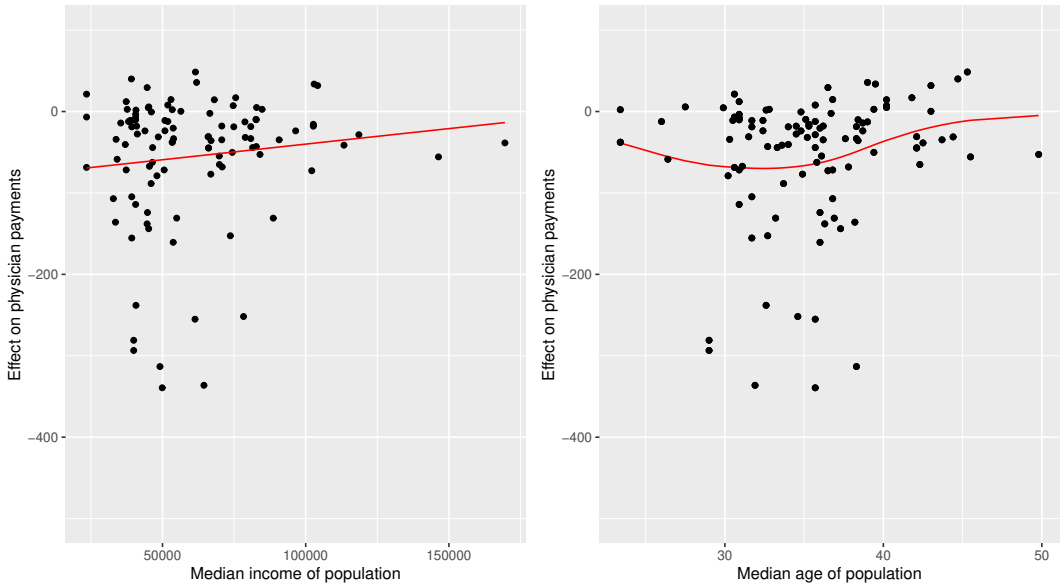

Figure 9: Effect heterogeneity by median income and the age of the zip code.

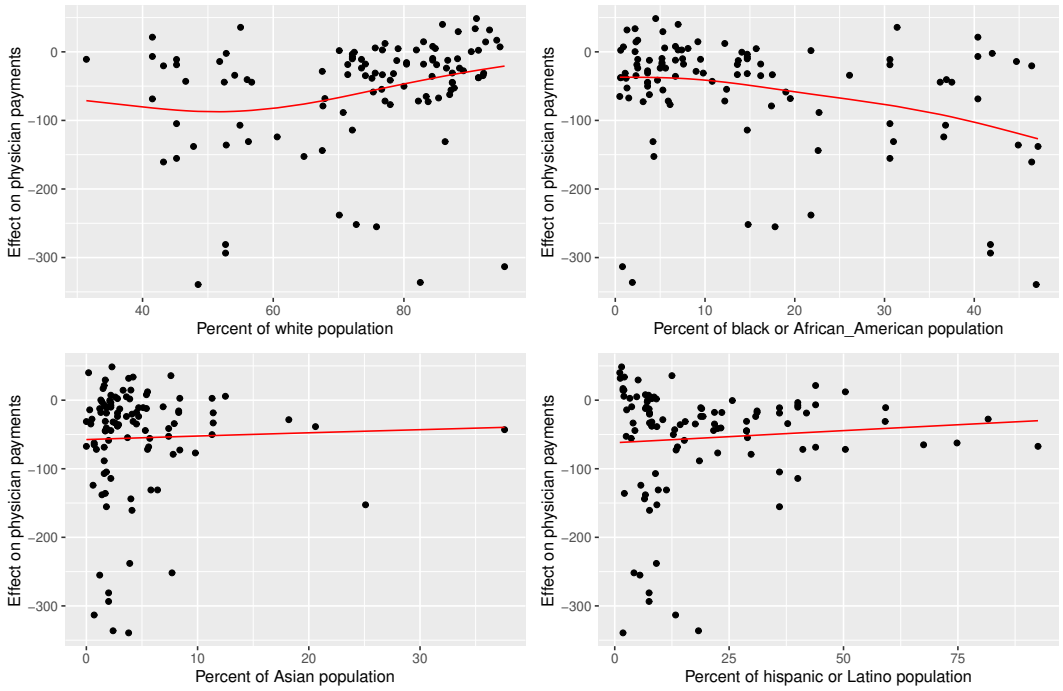

Figure 10: Effect heterogeneity by racial composition of the zip code.