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 a substitute to opioids 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 practices that often moderates 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 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 medical marijuana becoming available as a substitute. Finally, our heterogeneity analyses indicate that the decrease in direct payments is comparatively higher for physicians practicing in localities with higher white populations, lower affluence, and a larger proportion of working-age residents.

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. 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 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 (Cooper et al., 2018, Geluardi, 2016, Hollenbeck and Uetake,

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2021), arguing for its effectiveness as a painkiller and in lowering the chances of addiction and overdose death compared to 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 limited medical congruence regarding the efficacy of marijuana in treating acute and chronic pain, and the Food and Drug Administration (FDA) has advocated for more clinical studies before it approves marijuana for pain management (FDA, 2020). Second, opioid manufacturers are increasingly spending more into research and development to make opioids safer, e.g., by including an abuse-deterrent formulation (Evans et al., 2019, FDA, 2015). However, an increased adoption of marijuana could lead to opioid being a niche product or, in the extreme, could lead to severely diminished usage of opioids (Feinberg, 2019, Szalavitz, 2023). Thus, in response to marijuana's entry into pain management, opioid manufacturers are likely to adjust their push-marketing strategies to interact with physicians (Levy et al., 1983, Scherer, 1980). One of the most common practices to facilitate such interactions in pharmaceuticals 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] Some stakeholders in this ecosystem, who have justified these payments, have argued that these payments serve as a conduit to engage with physicians and foster collaboration (Donohue et al., 2007, Korenstein et al., 2010, Rosenbaum, 2015). However, these payment practices have been historically found to have caused biased endorsement of manufacturers' drugs by the payment-receiving physicians (Carey et al., 2021, DeJong et al., 2016, Jones and Ornstein, 2016) and also contributed to higher health care costs (CMS, 2013). Given the potential impact of these payments, it is of societal interest to study how a law affecting a critical domain, such as pain management, impacts these payment-to-physician strategies.

In the context of this research, 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

[2]Based on Open Payments Data from CMS: https://openpaymentsdata.cms.gov/summary

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 detail 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 estimating the overall effect of MML on payments to opioid-prescribing physicians, we also explore how this effect varies across physician specialties, experience levels, gender, and the communities they serve.

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

We study whether the passage of a law legalizing medical marijuana consumption (MML) affects direct payments from opioid manufacturers to physicians. These payments are typical of the push marketing strategies used by pharmaceutical firms (Levy et al., 1983), strategically aimed at physicians based on patient demographics and prescription preferences (Angell, 2018, Schwartz and Woloshin, 2019). In MML states, where physicians can recommend medical marijuana for pain relief (Black, 2022), marijuana emerges as an opioid substitute. This could prompt adjustments in payments by opioid manufacturers, potentially impacting the pain management ecosystem.

Our research explores how 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, on payments they received before MML, to physicians in states without MML. Synthetic control methods are suitable for panel data because they provide causally interpretable estimates of post-treatment effect over time under appropriate assumptions; see details in Abadie et al. (2015) and Ben-Michael et al. (2021b). These methods are further appropriate for us since an MML passage is a staggered treatment; consequently, there are distinguished pre and post-treatment periods. However, as we discuss below, some care in using SC methods is warranted for our study.

Briefly, the synthetic control (SC) method is used with panel data where it (Abadie et al., 2010, Abadie and Gardeazabal, 2003) fits the pre-treatment observations of a target treated unit using a convex combination of the pre-treatment observations of the control units, which is called the synthetic control (SC) unit

for this treated unit. The post-treatment outcome of the SC unit estimates the unobserved counterfactual post-treatment outcome of the target unit. Most applications of the SC method in the literature have used aggregated units, e.g., states and countries, as their study units. Aggregated observations average over latent patterns in the finer units' data and retain the common factors that might have different loadings in different units. Intuitively, in aggregated data, weights in the SC methods attempt to equate the factor loading of the target unit to the weighted average of the loadings of the control units.

Our direct payments data are available at the physician-level and have latent patterns. Specifically, these payments received by a physician are typically discontinuous, with 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, consider a scenario where a physician in the treated group receives payments every other quarter, while many control physicians receive payments quarterly. The standard Synthetic Control (SC) method, assessing the overall fit of payments received by the target physician, may assign positive weights to control physicians receiving quarterly payments. This could result in biased estimates of post-treatment counterfactual outcomes if zero-payment patterns correlate with confounding variables like differing promotional strategies across months and physicians. If these zero-payment patterns persist post-treatment, standard SC methods can yield highly biased estimates of the effect during zero-payment quarters for the target physician. In general, if post-treatment control outcomes vary systematically across various pre-treatment zero-payment patterns, the usual SC method will exhibit finite sample bias. As a possible remedy to this bias, Abadie et al. (2015) recommend "restricting the donor pool to units that are similar to the [target unit]." For our study, we customize the synthetic control method (Abadie et al., 2010, Abadie and Gardeazabal, 2003) to account for varied zero-payments patterns in physician payments while matching as these patterns are latent.

Using detailed physician-level data, we study the heterogeneity in the effect based on physicians' specialties and their genders. Additionally, we explore how income, age, and racial composition of patient communities influence these effects by integrating demographic and socioeconomic zip code data into each physician's area of practice. Our contributions are summarized 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. The proposed penalty involves two parameters λ and ν (defined in Sec. 3.2). While ν is associated with a pooling-penalty akin to Ben-Michael et al. (2021b), λ involves a new penalty that is designed to adjust for different patterns of non-payments.

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 analyze the impact on pain-medicine physicians' direct payments using our PSC method. Quarterly, 5%-15% of physicians had no payments. In the pre-treatment period, physicians in MML states (treated) and non-MML states (control) had no payments on an average of 0.99 and 1.04 quarters respectively (see Section 2). Our penalized SC method effectively matches physicians with synthetic counterparts during this period. Assuming the validity of the proposed synthetic control method, we find a statistically significant payment decrease due to MML passage on pain-medicine physicians.

4. We stress-test the effect of MML passage by examining a potential substitution mechanism. First, we identify a consistent effect in Florida, despite Florida passing MML two quarters after other

treated states in our main analysis. Second, for Anesthesiologists, who are less prone to shifting from opioids to marijuana, we observe an initial negative post-MML effect that subsequently levels to a non-significant impact. Third, we find a negative correlation between increased 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 lower-income and working-age populations.

1.2 Organization of the paper

Section 2 describes our data. We develop our PSC method aimed at varied zero-payment patterns and study its theoretical properties in Section 3. Section 4 presents simulation experiments comparing our PSC method with existing methods. Section 5.1 presents the primary analyses for pain-medicine physicians. Section 5.2 provides the mechanism analysis. Section 6 probes the heterogeneity in effects across physicians' gender, experience, and demographics of their patient communities. We conclude with additional discussion in Section 7. The supplement includes proofs and additional results.

2 Data Description

To meet our research goals, we needed access to the details on the direct payments from opioid manufacturers to prescribing physicians. These payments, although endogenously decided by each opioid manufacturer, are now legally mandated to be reported under the "Sunshine Act" (Richardson et al., 2014). This law was a federal response to address concerns over possible conflicts of interest, potential treatment bias, and healthcare costs (Carey et al., 2021, DeJong et al., 2016, Engelberg et al., 2014, Jones and Ornstein, 2016). Data became publicly available in September 2014, including payment amounts between physicians and manufacturers, drugs promoted through these payments, and payment dates.

We aggregated the payment information for each physician in our treated and control states for each of the 16 quarters from 2014 to 2017. No states passed an MML in 2015, and in 2016, six states passed an MML: 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. This gap of over a quarter in Florida's MML passage could sway attitudes of physicians and patients on marijuana adoption, based on outcomes seen in PA, OH, and LA. FL policymakers and voters might also have been influenced by these states' MML passage, posing potential confounding concerns. Therefore, to prevent this confounding bias, we analyze FL separately from PA, OH, and LA. We use 10 control states that did not pass an MML till 2016 Q2.[3] For each payment made to a physician, the data indicates the drug category promoted during the interaction, with up to five drugs listed per entry. To isolate opioid-related payments, we first flagged payments mentioning "pain," and subsequently retained those payments that mentioned opioids among the promoted drugs. We focused only on opioid manufacturer-drug combinations with payments in our pre-MML (pre-treatment) period (2014–2016). This led to 15 opioid brands from 5 manufacturers.[4] Our analysis precisely examines how MML impacts payments to physicians from these 15 opioid brands.[5]

A single payment can involve both opioids and non-opioids. As there was no logical way to allocate a fraction of the payment solely to opioids, to be conservative, we deemed any transaction as opioid-related if one or more opioids were mentioned. Figure 1 depicts the distribution of opioid proportion promoted in each payment and its corresponding average amount. The graph highlights two prominent payment types: payments promoting a single opioid, and payments involving two drugs, one or both of which could be opioids. Notably, payments featuring a single opioid tend to be associated with higher amounts.

Figure 2 outlines physician payments in the states under our study. While not identical, the payments exhibit similar patterns between treated and control states pre-MML. These payments, however, differ based on physician specialties. In 2015, the year before our treatment, 'Anesthesiologists' received roughly 30% of payments by dollar value, with 'Pain Medicine' physicians following at around 19%.

[3]These are: VA, NC, IN, GA, TX, WI, NE, SC, UT, AL. Twenty states had not passed an MML till 2016 Q2. Our control states were selected from them first, based on their geographical proximity to the treated states. Then, because of the population and economy sizes relative to our treated states, we included TX as a control state and removed smaller states TN and WV. Due to the limitation of having only 20 donor states, synthetic control estimation with state-level aggregated data will lead to poor balance. The quarter-year time scale also minimizes treatment anticipation bias in our analysis.

We run a robustness test where we include all 20 donor states in our estimation. Results from this robustness exercise are consistent with our main findings (For more details, please refer to Supplement S3).

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

[5]We anticipate minimal interference from new opioid brand introductions in our post-MML analysis period, as only one brand from a new manufacturer was introduced in 2017, our post-MML period. (For more details, refer to Supplement S3).

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	47	29	13	6	4	2	0	100
Treated states	47	29	12	8	2	1	1	100

Anesthesiologists and pain medicine physicians likely prescribe opioids for different purposes. Medical pain management involves various specialists for treating chronic pain conditions, including family physicians, internal medicine physicians, and psychiatrists (Chou et al., 2009, INTEGRIS, 2020). Anesthesiologists, on the other hand, specialize not only in treating chronic pain but also in acute pain, and may use advanced intravenous techniques, particularly in peri-operative settings (INTEGRIS, 2020). Despite marijuana's growing use for chronic pain, its effectiveness in acute pain is limited (Corliss, 2022). With FDA yet to endorse marijuana for pain (FDA, 2020), anesthesiologists cannot use marijuana in intravenous acute pain treatment. 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.

Combining anesthesiologists and 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.[6]

We supplement the payments data with the corresponding prescription data for each physician from

[6]We could have avoided this technical challenge by aggregating the payments data at the state level. However, with only 20 control possible control states for 4 treated states and 10 pre-treatment time periods to match for, we found that the synthetic control method does not give good matches.

the Medicare Part D Prescriber Public Use File.[7,8] 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 of the heterogeneity in the effects on direct payments due to an MML passage. Supplementary analyses involve zip-code level data on demographics and income characteristics from the US Census Bureau's American Community Survey. We also use data on physicians' experience, gender, and practice size. Further, we analyze longitudinal data on medical marijuana patients in Florida post-MML. Section 6 gives additional information on these datasets.

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 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 $\check{y}_{bT}$ 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 $\text{TE}_b = \check{y}_{bT} - y_{bT}$.

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 $\widehat{\text{ATT}}_{\mathcal{A}} = |\mathcal{A}|^{-1} \sum_{b \in \mathcal{A}} (\check{y}_{bT} - \hat{y}_{bT})$.

[7] 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).

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

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 unit,

(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 $\text{Pen}_{\texttt{sep}}(\lambda)$ 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 $\text{Im}_{\texttt{sep}}$ 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 $\text{Pen}_{\texttt{sep}}(\lambda)$ 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: $\text{Pen}^{(\ell_1)}_{\texttt{sep}}(\lambda) = \lambda\{\sum_{c=1}^{C} w_{bc}\,(\sum_{t=1}^{T-1} |y_{bt} - y_{ct}|)\}$. The proposed penalty $\text{Pen}_{\texttt{sep}}(\lambda)$ 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: $\text{Pen}_{\text{sep}}(\lambda) = \sum_{b=1}^{B}\sum_{c=1}^{C} w_{bc} \exp\left(\sum_{t=1}^{T-1}\{\lambda\, y_{ct} I(y_{bt}=0) + \lambda\, y_{bt} I(y_{ct}=0)\}\right)$. Table S1 in the supplement compares these two choices of penalties through a simulation study and shows that the proposed penalty is more suitable for our context.

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 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 $f_{it} = \sum_{k=1}^{K} \phi_{ki}\, \mu_{kt}$ be a K dimensional latent factor model as in Abadie et al. (2010), with 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 $\gamma = 2(\log C + \log T)^{1/2}\sigma$. 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 $\inf_{1 \le t < T} \bar{\delta}_{h,t} \le -f^* - \gamma$ where $f^* := \sup\{f_{it} : 1 \le i \le B+C,\, 1 \le t \le T\}$. Additionally, post intervention $\delta_{h,T}$ are either very large or well-controlled: $\delta_{h,T} \in (-\infty, -f^* - \gamma] \cup [-\sigma(\log T)^{1/2}, 0]$ for all h.

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:

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

where, $\mathcal{C}_b = \{1 \le c \le C : \Delta_c = \Delta_b\}$. 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 (1). 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 $\hat{y}_{bT}(\boldsymbol{w}) = \sum_{c=1}^{C} w_c\, y_{cT}$ where weight $\boldsymbol{w} \in \mathcal{W}$. 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 $\mathcal{C}$:

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

for some $\psi > 0$. 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 $\lambda_T^2 = 2\psi(\log(CT) + \log\log T)$. The additional off-shoot term in the penalty akin to hard thresholding penalty in Donoho and Johnstone (1994). Lemma 1 shows 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. We next show that if we restrict ourselves to controls in $\hat{\mathcal{C}}_b$, then with very high probability, we will be considering only controls which has the same dampening sequence as the b^{th} treated unit.

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

$$\lim_{T\to\infty} T(\log T)^{\alpha}\, P\left(\sup_{c\in\mathcal{C}} \sum_{t=1}^{T} |\delta_{ct} - \delta_{bt}| \cdot I\{c \in \hat{\mathcal{C}}_b\} > 0\right) = 0. \tag{6}$$

Equipped with the above results, we next establish a probabilistic upper-bound on the error of the proposed PSC estimator. It involves several steps. The essential part of the analysis is that when $y_{bT} > 0$, then with very high probability, $y_{bT} - \hat{y}_{bT} = z_{bT} - \sum_c w_c z_{cT}$ for the proposed estimator, and we can

concentrate on the estimation error for the non-truncated pay-offs from (3). For any weight $\boldsymbol{w}$, this error decomposes into three constituents corresponding to the factor model, the dampening sequence and the noise respectively:

$$R_f(\boldsymbol{w}) + R_\delta(\boldsymbol{w}) + R_\epsilon(\boldsymbol{w}), \text{ where, } R_f(\boldsymbol{w}) = \sum_{k=1}^{K} \mu_{kT}\big(\phi_{kb} - \sum_c w_c \phi_{kc}\big),$$
$$R_\delta(\boldsymbol{w}) = \sum_c w_c(\bar{\delta}_{h(b),T} - \bar{\delta}_{h(c),T}), \text{ and } R_\epsilon(\boldsymbol{w}) = \epsilon_{bT} - \sum_c w_c \epsilon_{cT}. \tag{7}$$

By lemma 2, R_δ is well-controlled for the proposed PSC estimator. Also, as any weight vector $\boldsymbol{w}$ that is trained on the pretreatment period as in (1) is independent of $\{\epsilon_{cT} : c = 1, \ldots, C\}$, $R_\epsilon(\boldsymbol{w})$ is stochastically dominated by $N(0, v)$ where, $v = \sigma^2(1 + ||\boldsymbol{w}||^2) \leq 2\sigma^2$ as $||\boldsymbol{w}_b||_1 = 1$. R_f in (7) 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 in (7) we arrive at our main result which provides an explicit upper-bound on the loss of the PSC estimator $\hat{y}_{bT}(\boldsymbol{w})$ for the bth treated unit based on weight $\boldsymbol{w}$. The bound depends on the sum of squared imbalances from positive time points $\text{Imp}(\boldsymbol{w}, b) = \sum_{t=1}^{T-1}(y_{bt} - \sum_{c=1}^{C} w_c y_{ct})^2 I\{y_{bt} > 0\}$ as well as on the factor model parameters 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 $i \notin \hat{\mathcal{C}}_b\}$ and $\psi > 0$, we have,*

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

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

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. With K fixed as $T \to \infty$ when the factor loadings are well-regulated, we have $m_b = O(1), \kappa_b = O(1)$; also, by assumption A5, $T/s_b = O(1)$. 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 $\text{Pen}_{\texttt{sep}}(\lambda)$ 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 $\sup_k |\boldsymbol{\mu}_k| \leq \zeta$ for some prefixed $\zeta > 0$ and $\inf\{|\boldsymbol{\phi}_b - \boldsymbol{\phi}_c|_\infty : c \in \mathcal{C} \text{ and } \Delta_c = \Delta_b\} \leq \log T$. 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 worst 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 the implementation details of the method, specifically our 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 timeperiods 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. Our simulation comparisons evaluate the proposed PSC where ν and λ are calculated this way.

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-state-out calculation as in Rubinstein et al. (2021). For each state we create a new data set, leaving out all the physicians in that state, and calculate the ATE for the remaining physicians using our PSC method. We then estimate the standard error of our ATE by taking the squared root of the Jackknife variance formula ((17) of Rubinstein et al.). The calculation of standard errors for the ATT of FL leaves out control state physicians one state at a time. In an alternative approach, Keele et al. (2023) address correlated observations by estimating the correlation from the residuals from an outcome model fit. Our PSC method does not use an outcome model.

4 Simulation

We evaluate 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, with the proposed selection of the ν and λ, 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

$$y_{it} = \max(z_{it} + \tau_i W_{it}, 0); \text{ where } z_{it} = a_i + (t-1)/2 + \lfloor (t-1)/4 \rfloor + \delta_{it} + \epsilon_{it},$$

where a_i are iid uniform on $[10, 60]$, W_{it} is 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 determines 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. We let $\delta_{it} = -80 \times q_{it}$ 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. Specifically, in cluster c, starting at time $t = 0$, after an exponential time with the rate θ_c a dampening starts. After that, the process is dampened for an exponential time length with the rate η_c. Following this, the first process restarts 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 for deciding 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, for $i = 30, \ldots, 34, 45, \ldots, 49$ in cluster 2, and 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)**

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.

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)**

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.

Figure S2in the supplement, which shows that the RMSEs are lowest for the proposed λ over a grid of choices of λs, provides an empirical justification of the cross-validated choice of λ. As in Kern et al. (2016), we further conduct a simulation study "calibrated" to the physician payments data set to judge our method's performance in practice. Results reported in the supplement show that the proposed method performs better in this calibrated simulation study; see Figure S3.

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 $-\$143.0$ and $\$142.0$, 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). Recently, Parast et al. (2020) proposed a new type of measure that is similar to the commonly used standardized differences in matched studies for balance diagnosis of a synthetic control analysis. Using this measure, Figure S4 in the supplement shows that the synthetic counterparts are good matches for the target physicians.

Figure 5 shows the average treatment effect (ATE) of MML on payments to physicians, estimating the effect on physicians from treated as well as control states where an MML might be enacted in the future. In the left panel, a significant and negative ATE is observed for pain medicine physicians, indicating declining payments after MML passage.[9] The negative impact on payments persists, except for a minor shift from Q1 to Q2 of 2017. This reflects evolving dynamics in the interaction between these physicians and opioid manufacturers. The estimated payment decrease is substantial, around $\$753.11$ in Q2 2017.

Unlike the treated states mentioned earlier, Florida enacted an MML in the final quarter of 2016. We explore whether actions in other states (PA, OH, and LA) during the quarter before Florida's MML passage influenced payment activities in Florida. Such potential spillover effects from MML in other states in Q2 2016 could bias the estimated treatment effect for Florida's pain medicine physicians using the synthetic control method (Schuler et al., 2021). We conducted two analyses on Florida physician

[9] We have conducted placebo-in-time tests to address concerns related to anticipation bias (details in Supplement S3). The results do not indicate such a bias.

payments. In the first, we created synthetic controls from physicians in the 10 control states, considering payment history up to Q2 2016. In the second, we used payment history up to Q4 2016. Figure 6 contrasts payments to Florida physicians with their synthetic controls from these two analyses. Estimates from the first analysis are similar to estimates from the earlier analysis shown in left panel of Figure 5. This analysis reveals a negative effect on Florida physicians' payments as early as Q3 and Q4 of 2016, possibly due to spillover from MML passage in other states. However, this spillover only accentuates the negative MML effect. Controlling for concurrent MML passage in other states in our second analysis, the significant negative MML effect on payments to Florida physicians persists. This suggests that opioid manufacturers could have anticipated marijuana legalization, thus reducing direct payments 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. Scherer (1980) theorizes that upon entry of a substitute, existing competitors in the market respond in one of the following ways: by counterattacking (increased marketing spending), retreating (by cutting back on marketing spending), or remaining passive (no reaction) (Hanssens, 1980, Lambin et al., 1975). Gatignon et al. (1989) suggest that existing players may reduce marketing spending as a profit-maximizing move when they are unable to effectively counter new entrant(s) (Oxenfeldt and Moore, 1978). In our context, research shows a shift in consumption from opioids (existing players) to marijuana (the new entrant) (Boehnke et al., 2019, Cooper et al., 2018, Hollenbeck and Uetake, 2021, NIDA, 2021). Thus, opioid manufacturers may curtail marketing spending where the substitution to marijuana is inevitable.

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 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 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 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 this theory, we also analyzed direct payments to anesthesiologists. Along with pain medicine physicians, they were the top two groups receiving the majority of direct payments.[10]

Both specializations, pain medicine and anesthesiology, regularly prescribe opioid. Pain medicine physicians primarily address chronic pain, while anesthesiologists manage both chronic and acute pain, often necessitating intravenous interventions (INTEGRIS, 2020). Despite increasing medical marijuana acceptance, its lack of FDA approval and its limited efficacy in treating acute pain make it unsuitable for anesthesiologists' intravenous procedures (Corliss, 2022, FDA, 2020). Therefore, pain medicine physicians are more likely to switch to marijuana compared to anesthesiologists. Consequently, post-MML, opioid manufacturers may reduce the payments to pain medicine physicians in response to the evitable substitution to marijuana, but may not decrease payments to anesthesiologists. Alternatively, if reduced payments to pain medicine physicians were solely due to opioid manufacturers losing ground in blocking MML passage, then a similar payment decline would be seen for anesthesiologists. We analyzed payments to anesthesiologists in MML and non-MML states, akin to the analysis on pain medicine physician (left panel of Figure 5), using our synthetic control method. The corresponding ATE plot for anesthesiologist payments is shown in the right panel of Figure 5. Results indicate that though anesthesiologist payments initially dropped post-MML passage, they rebounded within a quarter to pre-treatment levels.

Another plausible explanation for the observed effects could be at play. The decline in payments might

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

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** (0.1882)	
Whether City has Marijuana Dispensary		−0.1435*** (0.0243)	−0.1439*** (0.0243)	
Log of Payment Rec.				-0.0001 (0.0001)
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	9,453
R2	0.04408	0.04725	0.04757	0.00280
Within R2	0.00044	0.00375	0.00421	0.00001

not directly result from medical marijuana but could instead be due to reduced payments prompting fewer opioid prescriptions and consequently an increase in medical marijuana recommendations. We seek to differentiate between these mechanisms using medical marijuana patient registration data. Florida's provides bi-weekly updates on medical marijuana activity in the state, detailing active dispensary locations and number of registered patients over time.[11] Figure 7 depicts a rolling average of physician payments linked to active dispensaries in their regions. By merging marijuana patient registration data with payment data, we performed two regressions. First, we regressed log of payment against lagged bi-weekly change in marijuana patients and whether the physician's city had a marijuana dispensary. Second, we regressed bi-weekly change in marijuana patient against lagged payment activity. Table 4 indicates a significant negative correlation between marijuana patient increase in the preceding period, presence of a marijuana dispensary, and opioid-prescribing physician payments. However, there's no significant association between physician payments and subsequent change in marijuana patients. This suggests the primary factor in reducing payments to pain medicine physicians post-MML is the substitution effect of marijuana.

6 Heterogeneity

In Section 5, we found the passage of MML led to reduced direct payments to pain medicine physicians from opioid manufacturers. We argued this might arise from manufacturers recognizing increased opioid-to-marijuana substitution, especially for chronic pain management. Exploring distinct data patterns can

[11] Information is available at https://knowthefactsmmj.com/2018/07/28/2017-ommu-updates-archive/

inspire further studies to extend our understanding of this mechanism. Our synthetic control method offers insight into individual treatment effects (ITEs), i.e., how MML affects each physician's payments. Using ITEs, we conduct a secondary exploratory analysis to study variations in ITEs based on physician characteristics and practice demographics. We report the statistical significance of the observed differences between groups using standard two-sample t-tests (though ITEs are not independent, a significant p-value still guides future research questions). Figures 8–10 display estimated ITEs for physicians in 13 states, averaged over four quarters following MML passages in PA, OH, and LA in 2016 Q2.

We begin by investigating the impact of MML passage on physician characteristics: graduation year and gender. Figure 8 shows no discernible pattern regarding graduation year. Empirical research in physician care has historically understudied female physicians (Kimball and Crouse, 2007). However, numerous studies have highlighted significant differences in practice patterns between male and female physicians, such as patient-centricity and visit duration (Hall et al., 1994, Roter et al., 2002). Figure 8 suggests a less pronounced decrease in payments to male physicians compared to female physicians, although no statistically significant difference between genders was found (p-value = 0.14).

Analyzing ITEs based on demographics of where physicians practice, in Figure 9, we find the payments show a greater decrease in low-income areas (p-value $= 0.049$). Low-income areas would have a higher proportion of people who engage in blue-collar jobs and, thus, 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 observed larger decrease in payments to physicians practicing 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 decrease in payments is the largest in the regions with a median age between 30-40 years compared to other ages (p-value $= 0.045$). Populations younger than this bracket will have lesser requirements for chronic pain management; therefore, opioid manufacturers might feel less threatened by the entry of marijuana and may not decrease payments significantly. However, regions with older populations, who are more prone

to chronic pain, also show lesser decrease in payments to physicians, suggesting lesser threat to substitution to medical marijuana. Focusing on racial dispersion, in Figure 10, ITEs show a sharp decline for physicians practicing in populations with a higher percentage of blacks (p-value $= 0.024$ for comparing populations with higher than 13.6% blacks with the ones that have less than 13.6% blacks; 13.6% is the average of the proportion of black in the US population). Recent studies have shown Blacks/African-Americans are significantly less likely to be prescribed opioids for pain by medical providers than white patients (SAMHSA, 2020). In Figure 10, we also observe that areas above the national average in White population demonstrate a greater MML passage effect than those exceeding the national average in Black/African American population (p-value $= 0.01$).[12]

Motivated by the heterogeneity results, hypothesis-driven studies would be helpful to (a) establish whether decrease in payments to opioid prescribing physicians is causally related to substitution to medical marijuana and (b) subsequently identify the modifiers of the substitution effect on treating pain.

7 Discussion

Amidst the US opioid epidemic (Feinberg, 2019), various federal and state measures were introduced to regulate opioid consumption. Additionally, some states passed laws legalizing medical marijuana use, partly in response to the opioid crisis. While adoption of medical marijuana is on the rise (Geluardi, 2016), the FDA notes that, to date, "[it] has not determined that cannabis is safe and effective for any particular disease or condition;"[13] resulting in opioids remaining potent for pain mitigation. Physicians are key decision-makers in prescribing pain management medication. Our research links these three key factors: medical marijuana laws, opioid manufacturers, and their engagement with prescribing physicians. Specifically, we examine how the emergence of medical marijuana as a transformative competitor affects direct payments to physicians from opioid manufacturers. We find MML leads opioid manufacturers to decrease direct payments to physicians prescribing opioids. Our analyses suggest this shift is due to increased adoption of marijuana for pain management, indicating that opioid manufacturers perceive marijuana as a superior substitute and respond by reducing these payments (Gatignon et al., 1989).

[12] 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

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

While our focus is on opioid manufacturers and physicians, it's crucial to consider how MML affects patient pain management. Pain medicine physicians often prioritize opioid prescriptions, typically providing a 30-day supply along with medication for the number of days of use. The annual prescription data (mentioned in Section 2) shows that, 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 as well as the number of days of prescription of opioid vs non-opioid decreased from a 1.57:1 ratio to a 1.52:1 ratio. 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.

Methodologically, we develop a novel penalized synthetic control method that estimates an average treatment effect from a longitudinal dataset on multiple treated and control individuals. Using the pooled synthetic control strategy, 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. Further, we use a novel penalty to adapt the resulting estimators 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, under an additive mixture model appropriate for our study, we show that an unpenalized synthetic control method will have uncontrolled maximal risk while the proposed method produces efficient SC estimates. In the future, developing penalized synthetic control methods for more complex latent structures in the data will be useful.

Supplementary Materials

An online supplement includes proofs of our technical results, additional empirical evaluation of our proposed method and provides further analysis of our case study.

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Disclosure Statement

The authors report there are no competing interests to declare.

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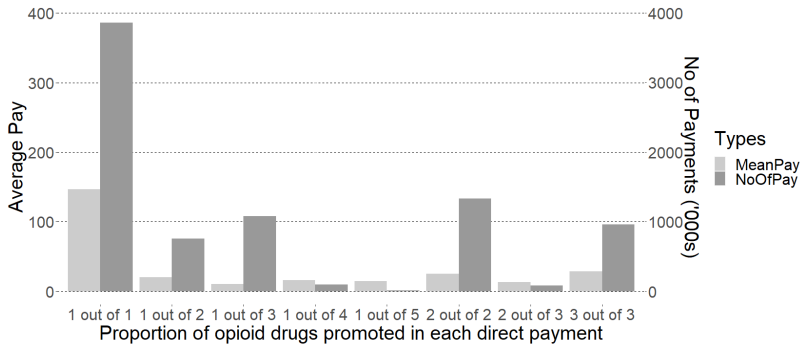

Figure 1: Distribution of average payment (in US dollars) and the number of payments related to opioid, categorized by the ratio of opioid to non-opioid drugs promoted during each payment.

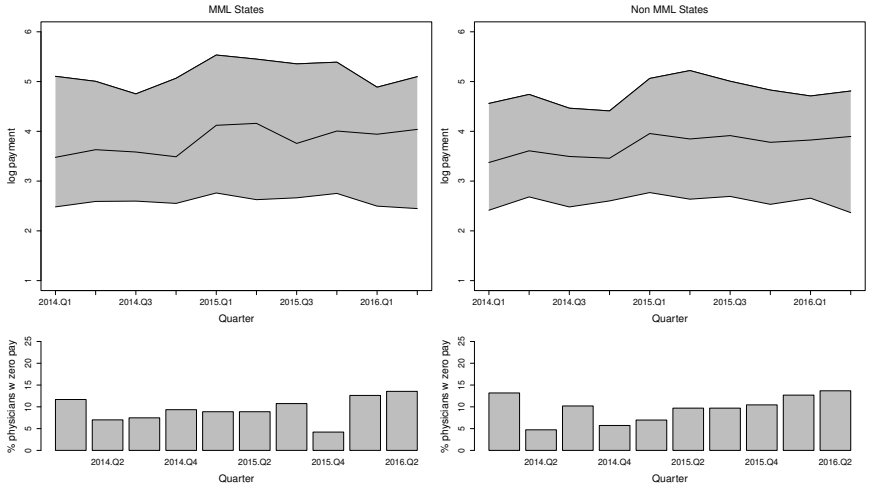

Figure 2: Summary of the payments to physicians in different quarters of pre-treatment period by the states that did and did not pass medical marijuana laws. The MML states are 'FL', 'LA', 'OH' and 'PA'; the non MML states are 'AL', 'GA', 'IN', 'NC', 'NE', 'SC', 'TX', 'UT', 'VA' and 'WI'. The plots on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

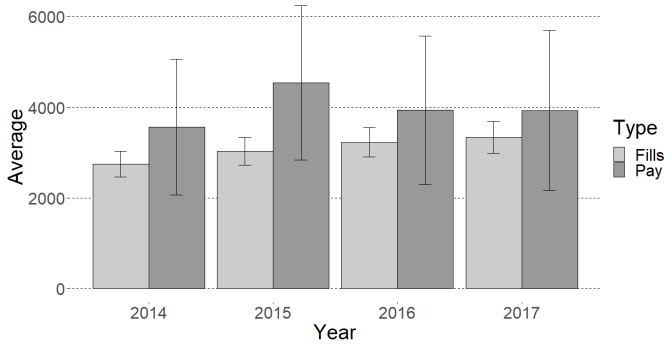

Figure 3: Distribution of average annual payments (in US dollars) to pain-medicine physicians and the corresponding average number of prescriptions (in '000s) written by those physicians across our analysis window (i.e., 2014-2017).

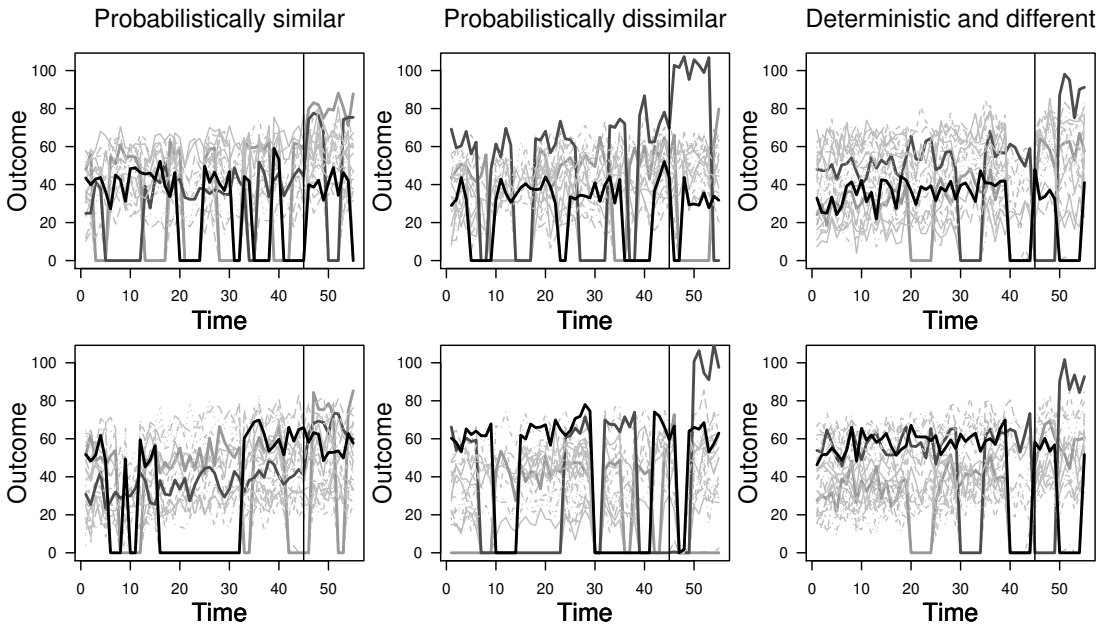

Figure 4: Two sets of simulated data in each the tree columns from the three simulation models. The three treated units from the three clusters are in colors 'black', 'dark gray' and 'gray' respectively; the vertical line shows the treatment adoption time.

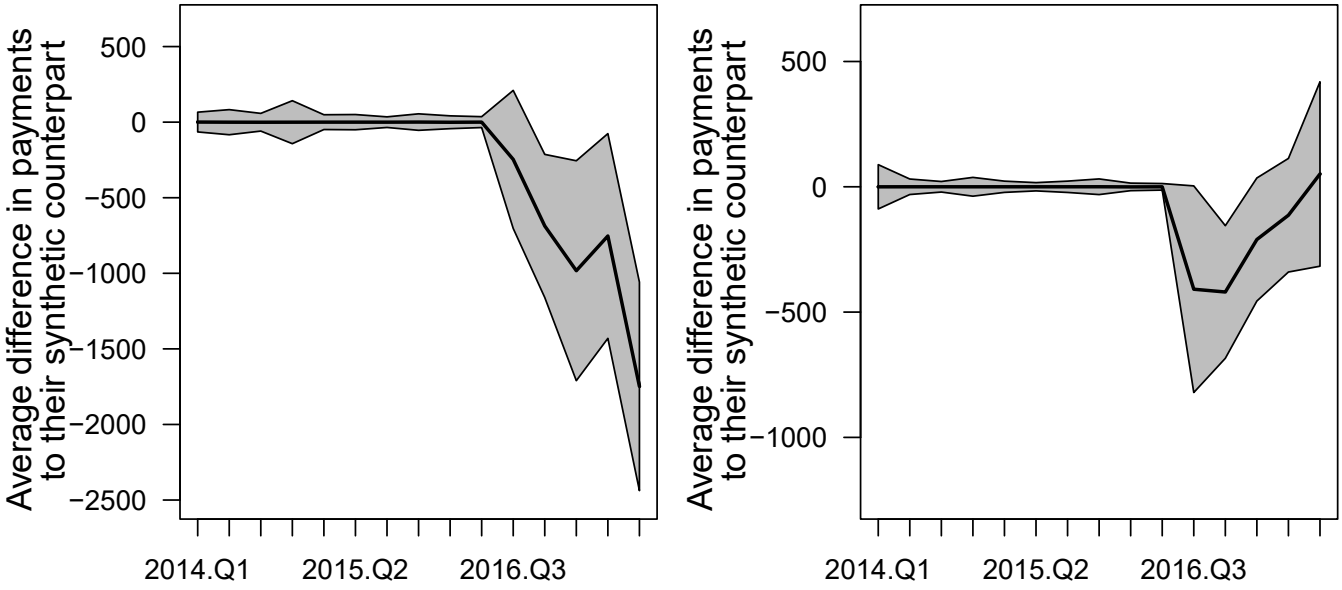

Figure 5: Synthetic counterpart analysis for MML passage on payments to physicians from 13 states in the US.

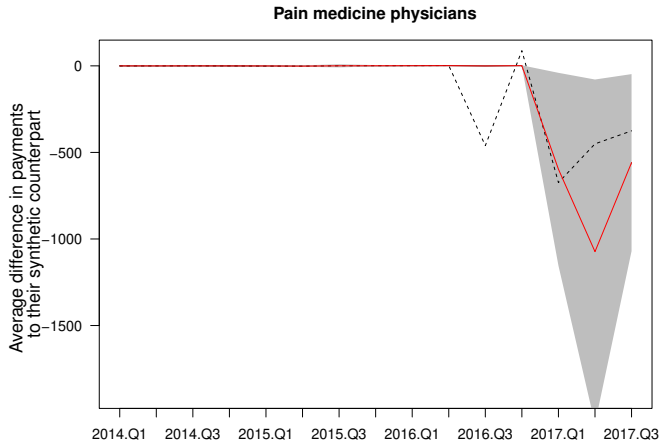

Figure 6: Synthetic control analysis for MML passage on payments to pain medicine physicians in Florida. The dashed line pretends MML passage in FL happened in the second quarter of 2016.

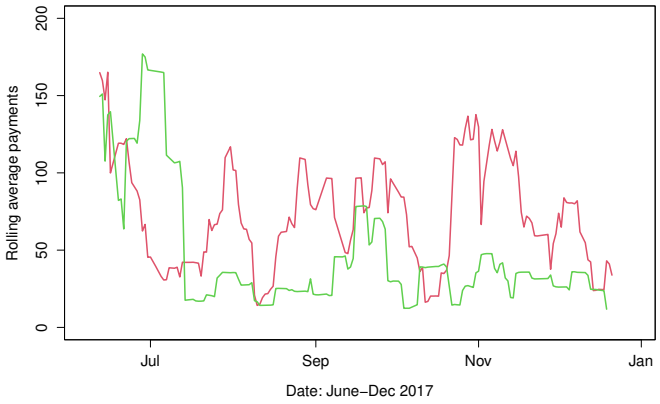

Figure 7: Payments to physicians in Florida between June and Dec 2017 in the cities without any marijuana dispensary at that time in red and with a marijuana dispensary at that time in green.

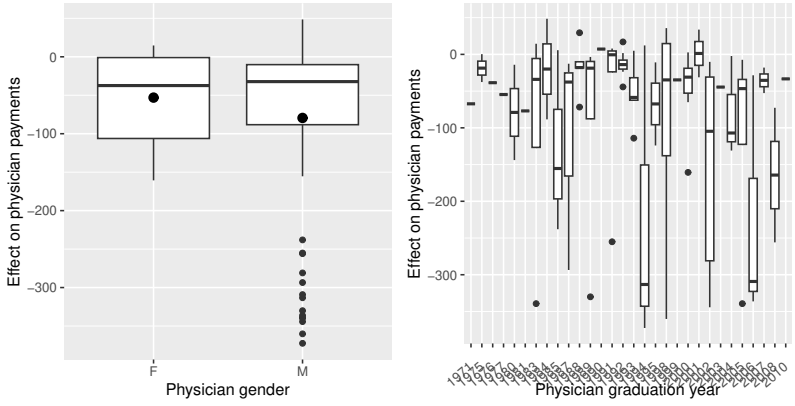

Figure 8: Effect heterogeneity by physician gender and year of graduation.

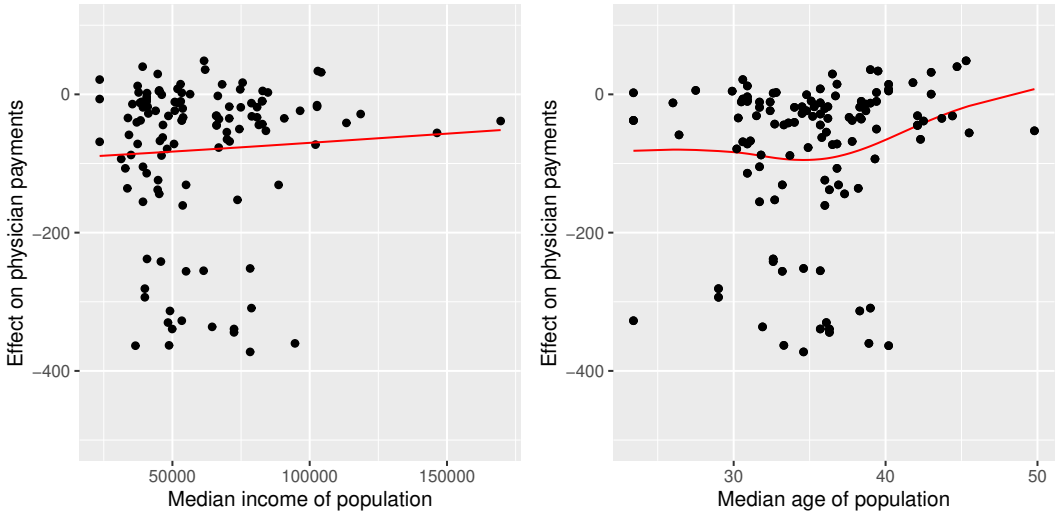

Figure 9: Effect heterogeneity by median income and the age of the zip code.

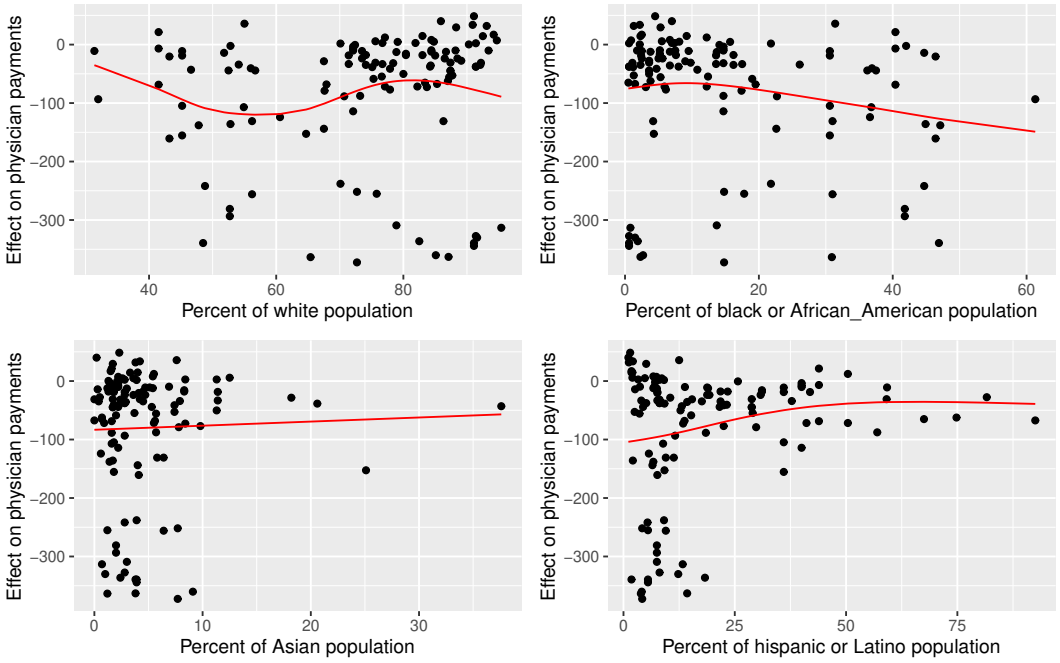

Figure 10: Effect heterogeneity by racial composition of the zip code.