Research Article

Recreational Cannabis Laws and Fills of Pain Prescriptions in the Privately Insured

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ABSTRACT

Objective: Almost half of U.S. states have passed recreational cannabis laws as of May 2024. While considerable evidence to date indicates cannabis may be a substitute for prescription opioids in the treatment of pain, it remains unclear if patients are treating pain with cannabis alone or concomitantly with other medications. **Method:** Using data from a national sample of commercially insured adults, we examine the effect of recreational cannabis legalization (through two sequential policies) on prescribing of opioids, NSAIDS, and other pain medications by implementing synthetic control estimations and constructing case-study level counterfactuals for the years 2007-2020. **Results:** Overall, we find recreational cannabis legalization is associated with a decrease in opioid fills among commercially insured adults in the U.S., and we find evidence of a compositional change in prescriptions of pain medications more broadly. Specifically, we find marginally significant increases in prescribing of non-opioid pain medications after recreational cannabis becomes legal in some states. Once recreational cannabis dispensaries open, we find statistically significant decreases in the rate of opioid prescriptions (13% reduction from baseline, $p < .05$) and marginally significant decreases in the average daily supply of opioids (6.3% decrease, $p < .10$) and number of opioid prescriptions per patient (3.5% decrease, $p < .10$). **Conclusions:** These results suggest that substitution of cannabis for traditional pain medications increases as the availability of recreational cannabis increases. There appears to be a small shift once recreational cannabis becomes legal, but we see stronger results once users can purchase cannabis at recreational dispensaries. The decrease in opioids and marginal increase in non-opioid pain medication may reflect patients substituting opioids with cannabis and non-opioid pain medications, either separately or concomitantly. Reductions in opioid prescription fills stemming from recreational cannabis legalization may prevent exposure to opioids in patients with pain and lead to decreases in the number of new opioid users, rates of opioid use disorder, and related harms.

Key words: = cannabis; cannabis legalization; opioids, pain medication; private insurance

As of May 2024, more than one in three U.S. residents lived in a state that has passed a recreational cannabis law, and the majority of states have passed medical cannabis laws (ProCon.org, 2024; Steuart, 2023). Prior research suggests that legal access to recreational cannabis increases adult use of cannabis by 13 to 38% (Abouk, 2021; Cerdá et al., 2020; Hollingsworth et al., 2020; Maclean et al., 2021). Additionally, 61.9 million people, or about 22% of Americans aged 12 and older, reported using cannabis at least once in 2022 (Substance Abuse and Mental Health

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Services Administration, 2023). New research also shows that, in 2022, for the first time in the history of the US, there were more daily or near daily users of cannabis than alcohol (Caulkins, 2024).

In the years following 2017 when the National Academies of Sciences, Engineering, and Medicine reported "conclusive evidence" supporting the treatment of chronic pain with cannabis, evidence indicating substitution of pain medications for cannabis has grown (National Academies of Sciences, Engineering, and Medicine, 2017). In addition to clinical research, studies using insurance claims data have consistently found that prescribing of opioids decreased following legalization of cannabis, suggesting that patients substitute cannabis for some traditional pain medications (Bradford et al., 2018; Bradford & Bradford, 2016, 2017; McMichael et al., 2020; Raman et al., 2023). While much of the work in this area has focused on medical cannabis legalization, there is reason to believe that recreational cannabis legalization (RCL) will continue this trend because adults over age 21 have easier access to cannabis following RCL implementation (Lucas & Walsh, 2017). In contrast to recreational cannabis users, medical cannabis users must maintain an active state license to purchase, possess, and consume cannabis (Steuart, 2023). This requires medical cannabis users to have medical evaluations, pay fees, and update paperwork on an annual basis (Steuart, 2023), which may prove to be too heavy an administrative burden for some adults with pain conditions. Therefore, in addition to opening the door to adult consumption of cannabis, RCLs may increase access among individuals intending to use cannabis for medical purposes.

While evidence of the substitutability of cannabis for opioids has grown, little is known about the relative substitutability by opioid formulation or strength. Clinical literature indicates cannabis can be an effective treatment for chronic pain, which can alternatively be treated with relatively high doses of extended release opioid formulations (Hill et al., 2017; Kraft et al., 2008; Russo, 2019; Wallace et al., 2007). There is also recent evidence that patients use cannabis concomitantly with lower strength opioids to lower their daily opioid consumption (Steuart & Bradford, 2024). Further, cannabis has been shown to improve the efficacy of opioids and reduce the opioid dose in the treatment of chronic, non-cancer pain (Lynch & Clark, 2003).

Many studies analyzing the effect of cannabis legalization on prescriptions (or fills) of pain medications are limited to opioid utilization and focus primarily on the effects of medical cannabis legalization (Bradford et al., 2018; Bradford & Bradford, 2016, 2017; Lozano-Rojas et al., 2022; McMichael et al., 2020; Raman et al., 2023; Shi et al., 2019; Wen & Hockenberry, 2018; Wen et al., 2021). Using data from a national sample of commercially insured adults from 2007-2020, we examine the effect of recreational cannabis legalization and dispensary openings on prescribing of opioids, NSAIDS, and other pain medications by implementing synthetic control estimations and constructing case-study level counterfactuals. Our study builds upon the existing literature in several ways. First, to the best of our knowledge, we are the first include non-opioid pain medications, such as NSAIDS. Including non-opioid pain medications allows us to gather more evidence on how patients use other pain medications once recreational cannabis is legalized. Second, whereas most work in this area has focused on the publicly insured, our study is focused on Americans who are privately insured. Most Americans are privately insured, therefore our findings are highly generalizable and can inform policymakers regarding the impacts of RCLs on opioid and non-opioid pain medication utilization. Finally, we build on the quasi-experimental work in this area (McMichael et al., 2020; Wen et al., 2021) and contribute new innovations in the econometric literature by addressing the issue of heterogeneous policy adoption timing using a modified synthetic control methodology (SCM) that flexibly accommodates each state's RCL policy adoption timing.

METHODS

Data on all patients who fill prescriptions for opioids, NSAIDs, and other non-opioid pain medications between January 1, 2007 and December 31, 2020 were extracted from Optum's de-identified Clinformatics® Data Mart Database (Clinformatics®). Clinformatics® is derived from a database of administrative health claims for members of large commercial and Medicare Advantage health plans. These administrative claims are submitted for payment by providers

and pharmacies and are verified, adjudicated, adjusted, and de-identified. The database is ICD-10 compliant. Only covered lives with both medical and prescription drug coverage are included. The database includes approximately 15 to 20 million annual covered lives, with over 62 million unique covered lives over a 12-year period.

We limited our analyses to individuals aged 18-64 and excluded claims for Medicare Advantage patients to avoid introducing selection bias, since most Medicare Advantage beneficiaries are aged 65 and older and because Medicare Advantage is not equally representative across the states in this dataset. We also excluded patients who did not have at least six months of continuous enrollment during the study period and patients with a cancer diagnosis at any point during the study period.

Prescription opioid fills were identified using the National Drug Code (NDC) and the NDC-active ingredient crosswalk of all prescription opioids from the Centers for Disease Control and Prevention's National Center for Injury Prevention and Control (CDC, 2021). All opioid pill strengths were converted to Morphine Milligram Equivalent doses (MMEs) to compare at standardized strengths.[1] Length of a prescription was measured in the number of days supplied. Non-pain formulations of opioids, such as buprenorphine formulated for the treatment of opioid use disorder, were omitted from our analysis.[2] Additionally, we omitted all methadone formulations as our data do not allow us to distinguish between formulations for pain versus opioid use disorder.

Prescription fills of NSAIDs and other non-opioid pain medications were identified using American Hospital Formulary Service Pharmacologic-Therapeutic Classification System (AHFS) codes.[3] In addition to opioids, NSAIDs and other non-opioid pain medications, we extracted prescription claims for five additional drug classes as part of a series of placebo tests. The medications included in the placebo tests are primarily prescribed for mental health and sleep disorders (antidepressants, anticonvulsants, barbiturates, benzodiazepines, and z-drugs) and are analyzed only in states without RCLs (See more detailed description below).

We constructed three measures of prescription fills for each class of medications. First, to measure the extensive margin, we calculated the rate of patients with prescriptions filled per 10,000 enrollees in each state-quarter. Second, to measure the intensive margin, we calculated the average number of days supplied per prescription. Third, also to measure the intensive margin, we calculated the average number of prescriptions per patient in each state-quarter.

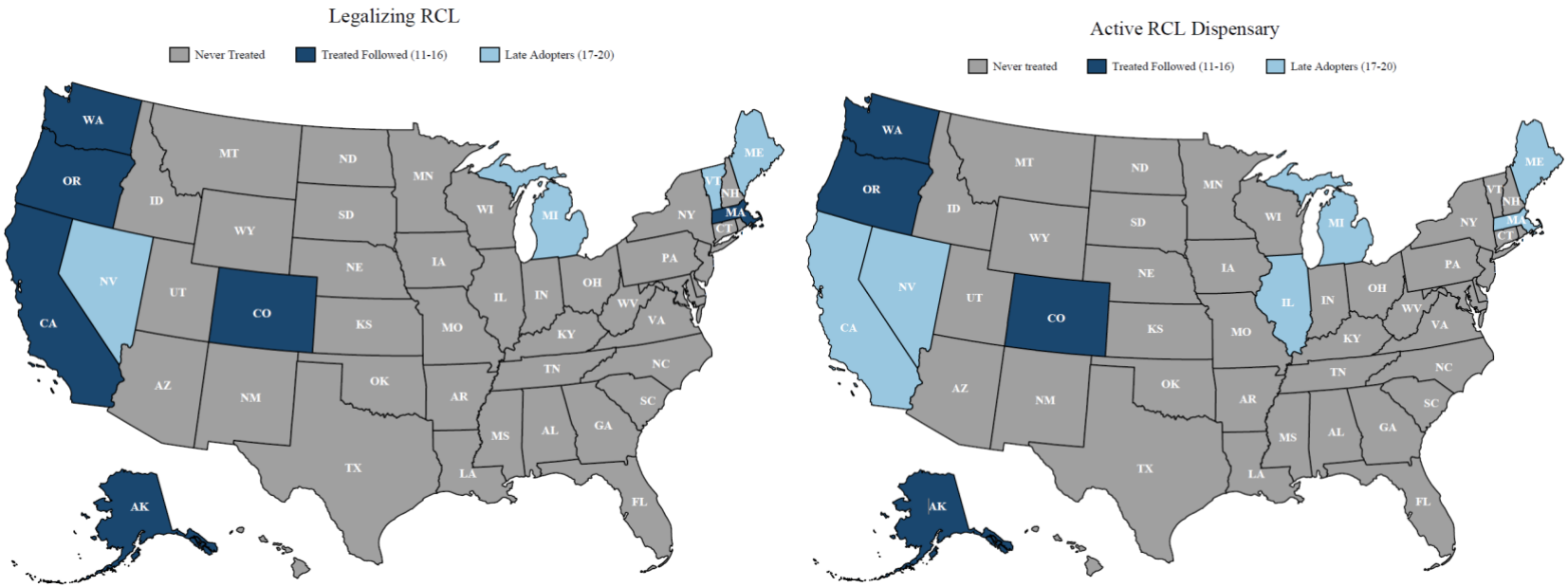
Our independent variables measured whether a state had legal protection to use recreational cannabis (RCL Legal) or had recreational dispensaries open (RCL Dispensary) in each year of the study period. RCL Legal indicates the date when recreational adult-use cannabis was legal to possess in a state. RCL Dispensary indicates the date the first recreational cannabis dispensary opened in a state. We considered legalization as a two-step process: statutory legalization of cannabis followed by a legal mechanism for users to purchase recreational cannabis through dispensaries. While statutory legalization may be enough legal permission for some individuals to become cannabis users, especially given that RCLs are typically passed after several years of medical cannabis legalization, legalization without a recreational dispensary still requires individuals to acquire cannabis on a black or gray market. Therefore, we expect to see some initial substitution of cannabis for pain medications following legalization with larger effects once recreational dispensaries open.

In order to ensure an appropriate pre- and post-treatment window, our analyses included only states that passed recreational cannabis laws between 2011-2017. Specifically, our analyses included seven state case studies where we evaluate the effect of legalization of recreational cannabis (RCL Legal) and four state case studies where we evaluate the effect of the opening of recreational cannabis dispensaries (RCL Dispensary). Figure 1 presents maps with specific states according to the RCL status as of the end of 2022, and Figure 2 presents the timeline of RCL policies and our study period. States with an adequate post-period for our study are shown in navy blue.

[1]See CDC information regarding conversions by different opioids: www.cdc.gov/drugoverdose/modules

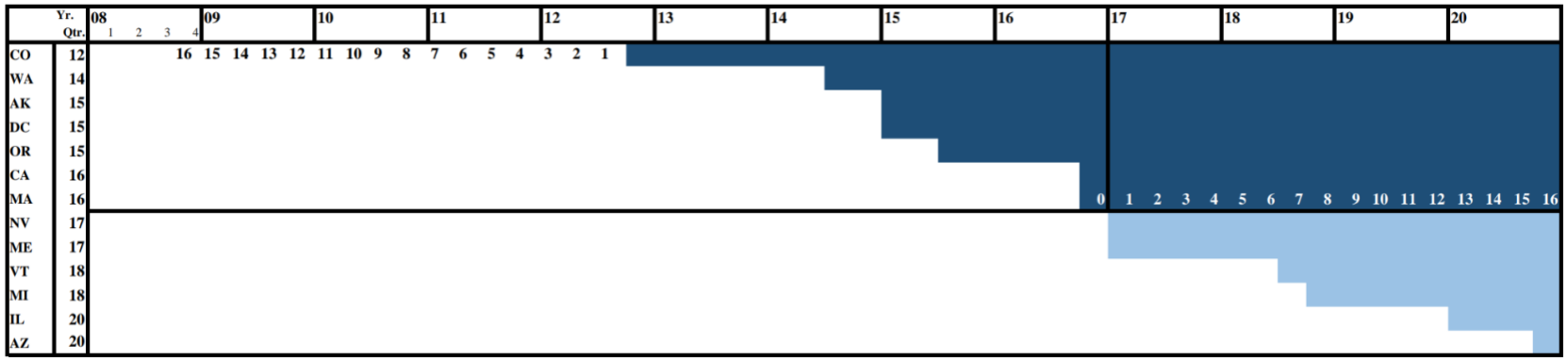
[2]We excluded prescriptions for buprenorphine, except the patch (Butrans), buccal film (Belbuca) and the injection (Buprenex), which are Schedule III buprenorphine formulations for pain. We also exclude Suboxone, which is used for treatment of opioid use disorder (MOUD).

Figure 1. *Geographic Policy Variation*



Note. In this article we follow states whose policy variation started in 2011 or after, and before 2017. This allows us to guarantee that we will always have 16 quarters for the pre- and post-treatment. For RCL Legal, seven states comply with this requirement: AK, CA, CO, DC, MA, OR and WA. For RCL dispensary, four states comply with this requirement: AK, CO, OR and WA.

Figure 2. *RCL Dispensary Timeline*



Analytic Strategy

Our analytic strategy uses a series of synthetic control case-studies at the state-medication level, following Abadie, Diamond, and Hainmueller (2007, 2010; French et al., 2022). A separate synthetic control is constructed for each treated state and policy considered (RCL Legal or RCL Dispensary). We follow seven states for RCL Legal (AK, CA, CO, DC, MA, OR, WA) and four treated states for RCL Dispensary (AK, CO, OR and WA). The synthetic 'state-medication' series is constructed first using all available information from the time-series structure (lags) up to the policy intervention, and second, donors are constructed from the state-medication series of states that by the end of 2020 had not implemented RCLs.

Hollingsworth and Wing (2020) suggest that, in addition to considering the prescriptions of interest, prescription fills of classes of drugs that are unlikely to be impacted by the pseudo version of the policy can contribute to the donor pool (meaning they are used for comparison in untreated states only; Hollingsworth & Wing, 2020). Following this logic, we include prescription fills of additional medications (benzodiazepines, z-drugs, barbiturates, antidepressants, and anticonvulsants) in the donor states to widen the donor unit pool and improve power. Accordingly, in each case study, for the donor states we consider the pain medication series of interest, but we also consider the other medication fill rates as additional placebos. If the RCL policy did not affect pain prescriptions in an untreated state (a state without an RCL policy), it also should not affect the other medication series in an untreated state (Hollingsworth & Wing, 2020). In total, for each untreated state we follow prescription fills for eight therapeutic classes (opioids, NSAIDS, other pain medications, benzodiazepines, z-drugs, barbiturates, antidepressants, and anticonvulsants), aggregated at the state-quarter level. We follow three pain-related therapeutic classes in treated states (opioids, NSAIDS, and other pain medications). Our methodology is further detailed below.

We are interested in analyzing the effect of state recreational cannabis policies (RCL Legal or RCL Dispensary) in treated states, on three measures of pain prescription fills (one extensive, two intensive) of three classes of pain medications (opioids, NSAIDS, and other pain medications). Accordingly, the series of pain medications, Y_{it}, in state i and quarter t, can be defined as follows:

$$Y_{it} = Y_{it}^{N} + \alpha_{it} . D_t ;$$

$$Where\ D_t = \begin{cases} 1\ if\ i = 1\ and\ t \geq 0 \\ 0\ otherwise \end{cases} \quad (1)$$

Where, in the context of potential outcomes notation, Y_{it}^{N} is the value of the prescription fills in the absence of treatment and the treatment effect is α_{it} in state-medication and quarter observations with recreational cannabis policies (when $D_{it} = 1$).

Y_{it}^{N} is always observed for the non-treated states but is observed for treated states only in periods prior to the implementation of recreational cannabis policies. We estimate Y_{it}^{N} for the treated states, in post-treatment observations (separately for legal possession or open dispensaries), by estimating separate state-level case studies.[4] In each case study, the treated state is denoted by $i = 1$, as the remainder of the treated units are not considered jointly, such that in synthetic control estimation there is only a treated state-medication series. The counterfactual outcome of interest is denoted by $\widehat{Y_{it}^{N}}$ and we estimate this term using the ADH synthetic control method with the pool of donor units ($i \geq 2$). The synthetic control estimation procedure generates a set of weights $(w_2^*, \ldots, w_J^*)$, which are used to aggregate the contribution of all donor units to generate the "synthetic" control hat ($\widehat{Y_{it}^{N}}$). This synthetic series ($\widehat{Y_{it}^{N}}$) is constructed such that it approximates, as closely as possible, the treated unit when $Y_{it} = Y_{it}^{N}$, in the pre-policy period ($t < 0$), by minimizing the root mean square

[3]AHFS codes of 280804 capture Nonsteroidal Anti-inflammatory Agents (NSAIDs) including COX-2 inhibitors, Ibuprofen and Naproxen. AHFS codes of 280892 capture other pain medications including miscellaneous analgesics and antipyretics such as formulations of Acetaminophen, salicylamides, Sodium Thiosalicylate and Ziconotide.

[4]I.e., 36 case studies for RCL Legal (3 drug classes x 3 outcomes x 4 states) and 63 case studies for RCL Dispensary openings (3 drug classes x 3 outcomes x 7 states with RCL Dispensary).

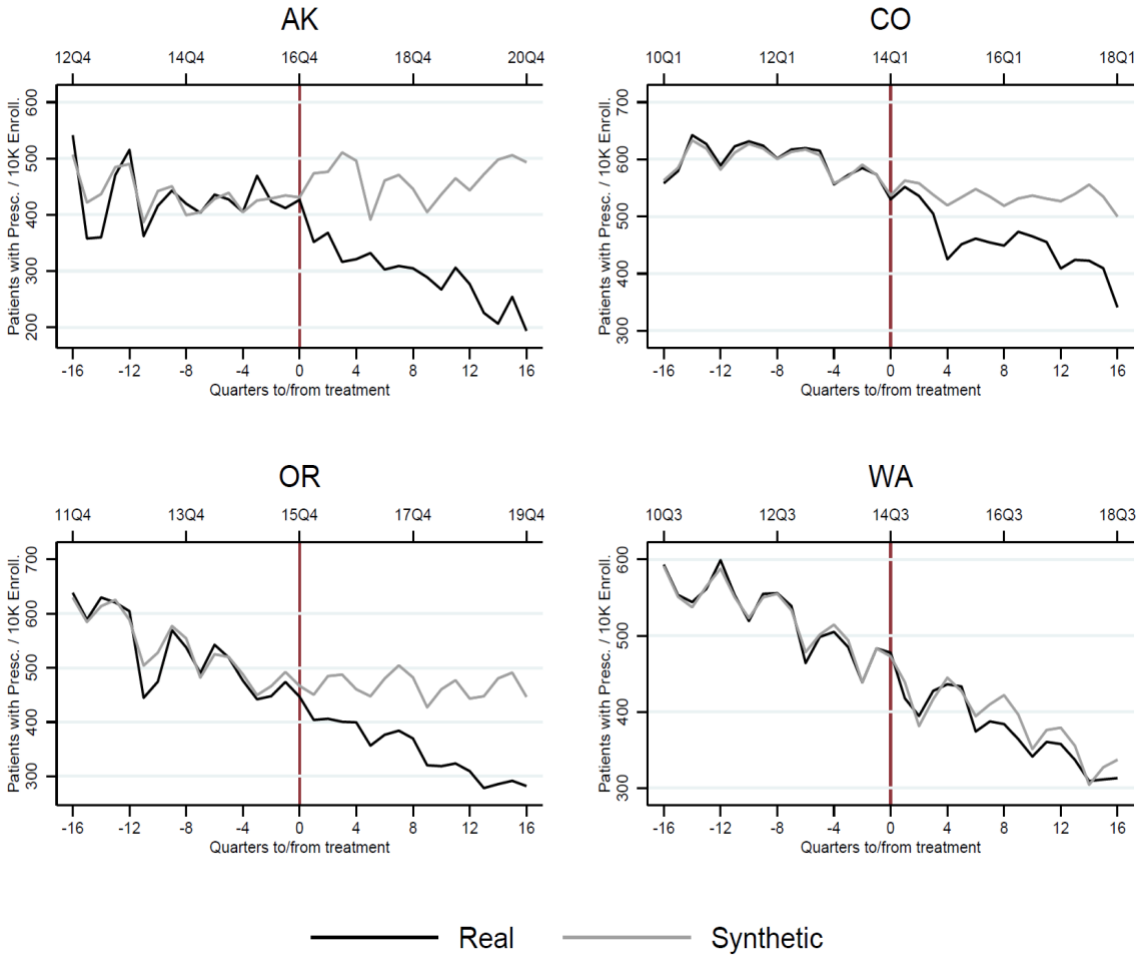
prediction error (RMSPE).[5] We want to consider donor series where the synthetic control can be estimated accurately. Hence, we trim 5% of placebo donor units with the highest RMSPE (Root Mean Square Prediction Error) in the pre-treatment period for each case study, resulting in the set used for analysis: approximately, 326 donor units to examine the effects of RCL Legal and 304 donor units to examine the effect of RCL Dispensary, in each state-level case study.

The estimated synthetic control hat, $(\widehat{Y_{it}^N})$, is then projected into the post-policy period and used as the counterfactual outcome against which the treated state's observed outcome is compared. The difference between the two is interpreted as the treatment effect of the policy in period *t*, represented as:

$$\widehat{\alpha_{1t}} = Y_{1t} - \widehat{Y_{1t}^N} \text{ , where } \widehat{Y_{1t}^N} = \sum_{i=2}^{J} w_i^* \cdot Y_{it} \qquad (2)$$

The synthetic control method often provides very close matches in the pre-policy period to the state it is approximating. The closely overlapping synthetic and actual lines in the graphs in Figure 3 illustrate this, for RCL Dispensary.

Figure 3. *Synthetic Control Time Series of Opioid Prescription Rates by State Time Series of Opioid Prescription Rates by State (Active RCL Dispensary)*



[5]The RMSPE is the average Euclidean distance between the treated series and the synthetic control in pre-policy period and measures how well the synthetic series replicates the treated series prior to the intervention.

In order to recover DD-equivalent point estimates to summarize the treatment effects captured in the post-treatment period, we follow Hollingsworth and Wing (Hollingsworth & Wing, 2020) and average the differences between the actual series and the synthetic series, for each period during the post-treatment time frame, up to four s post-policy. This aggregation can be represented as:

$$\overline{\alpha_1} = \frac{1}{17} \cdot \sum_{t=0}^{T=16} \left(Y_{1t} - \widehat{Y_{1t}^{N}} \right) \quad (3)$$

The baseline synthetic control model does not include a parametric form to conduct statistical inference. Thus, we rely on placebo inference by comparing how large or small the RCL effect on a given treated state is in comparison to the donor series from untreated states (Abadie, 2021; Buchmueller et al., 2011; Hagemann, 2019). Our placebo test estimates the likelihood of attaining similarly large treatment effects if treatment were assigned to non-treated donor units. Specifically, we derive the *p*-value of the synthetic control treatment effects from the percentage of placebo treatment effects as large as the true treatment effects. The key assumption, similar to Difference-in-Difference assumptions, is that the true treatment effect only occurs for the actually treated states, at the timing of the treatment, with otherwise no systematic changes in outcomes in the placebo-treated units at the exact timing of the assigned placebo-treatment. The treatment effect can be considered statistically significant if the treatment effects fall outside the bulk (99%, 95%, or 90%) of the placebo treatment effects.

So far, the methodology we have described allows us to estimate the treatment effect for a particular case-study exercise of a state-medication, but we are measuring the treatment effect across several treated states. To obtain the point estimate of the average treatment effect on the treated (ATT), we average across all treated case studies. For instance, we average across four states when following the effect of RCL dispensaries. We follow the procedure proposed by Cavallo et al. (2013), which draws samples of untreated series to approximate a placebo average treatment effect, one series for each treated unit. We draw 5,000 combinations of the more than 300 donor series on the four treated units (RCL Dispensary) or seven treated units (RCL Legal).

Currently, some concern exists about the plausibility of overfitting following synthetic control estimation. This stems from the inclusion of the time-series structure of each outcome series in the construction of the counterfactual, even if only up to the policy intervention (Abadie, 2021; Chernozhukov et al., 2022). To address this concern, we implement the methodology suggested by Chernozhukov et al. (2020), where a *k*-fold cross-fitting procedure is estimated for each case-study. In their procedure, the pre-period is split into *k* subgroups,[6] and in each cross-fitting attempt, the weights from Equation 2 are estimated without one of the pre-period subgroups. With the weights estimated in a fraction of the pre-period, the *k* subgroup is forecasted along with the post-period treatment effects. The forecast in the *k* subgroup is used to assess the bias. The process is repeated and an average bias from over-fitting is obtained. The result is a treatment effect net of the overfitting bias. Furthermore, their procedure is also based on the demonstration that inference can be conducted by the implementation of a *t*-test on the case-study coefficient. For the results we present we also implement this approximation to inference, but for the general exercise we consider the placebo inference as it does not require assumptions or the imposition of this structure. We present the results of this exercise in the Appendix and discuss how this exercise compares to our main results in the last part of the results section.

RESULTS

Results of synthetic control estimates overall show statistically significant decreases in the rate of opioid prescriptions and marginally significant decreases in the rate of the average daily supply of opioids and number of opioid prescriptions per patient (See Tables 1-4).

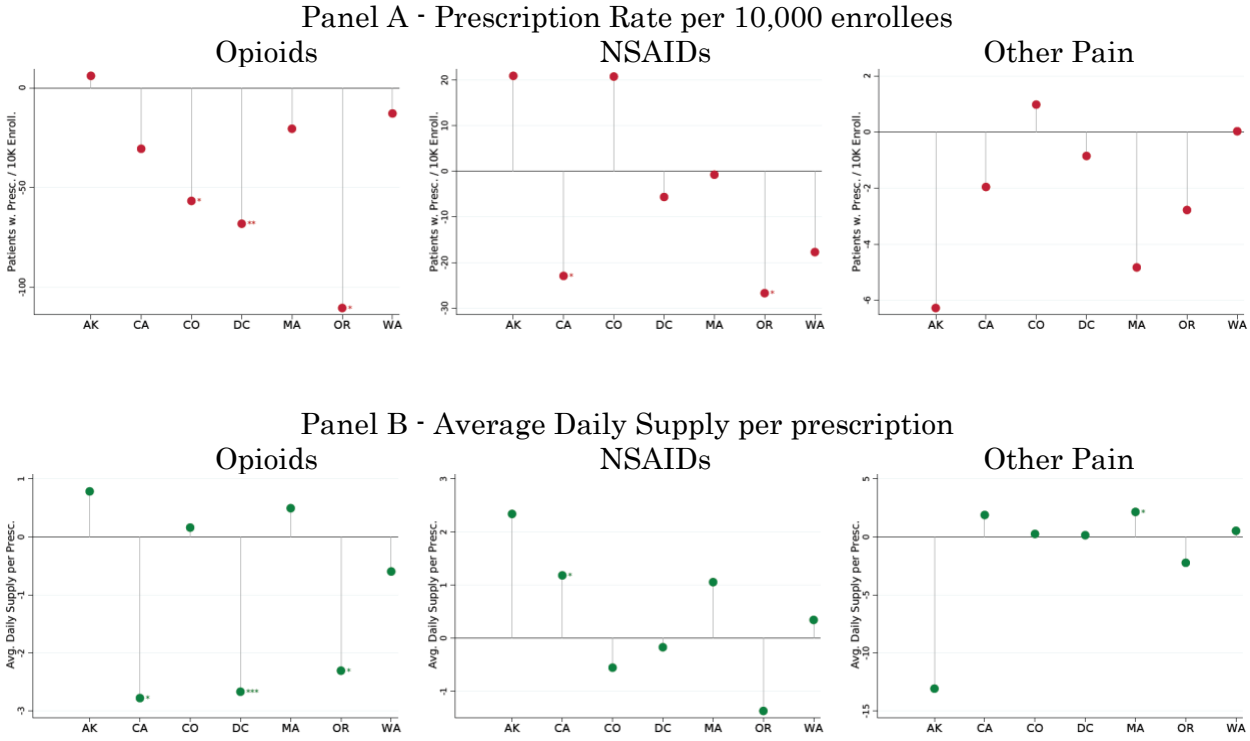
[6]Their recommendation is $k = 3$, and for larger pre-periods they recommend $k = 4$. We report $k = 3$, where the attenuation over the treatment effects is bigger, and the estimated statistical significance renders a more conservative outcome.

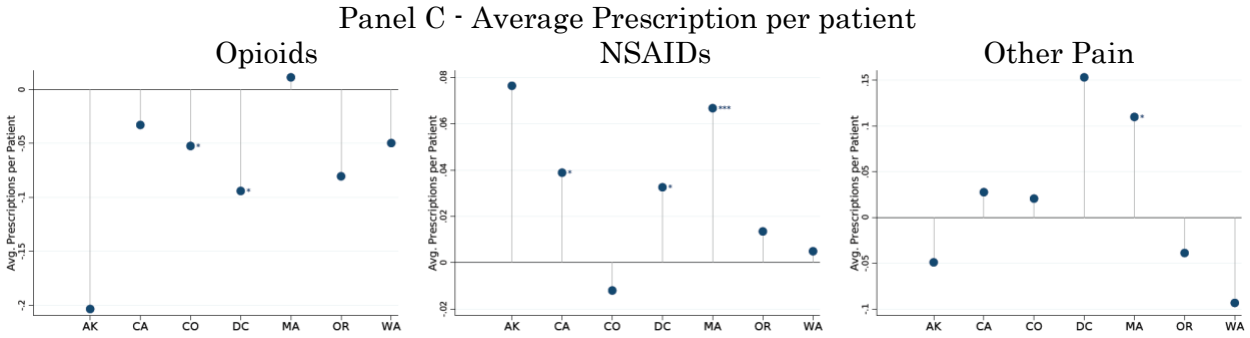
We estimate effects separately by state case studies and provide nationally aggregated estimates.

First, we estimate the effect of recreational cannabis legalization (RCL Legal) to evaluate whether legal protection or legal access to cannabis is the mechanism causing fills of medications to decrease. We calculate the average treatment effects of recreational cannabis legalization by subtracting average outcome values of placebos from average outcome values across the 16-quarter post-treatment period. Figure 3 displays these effects on extensive and intensive opioid prescribing in select states. We find statistically significant decreases in the number of patients per 10,000 enrollees who are filling opioid prescriptions in Colorado (56.68 fewer patients per 10,000; $p < 0.05$), D.C. (68.13 fewer patients per 10,000; $p < 0.01$), and Oregon (110.40 fewer patients per 10,000; $p < 0.10$) following recreational cannabis legalization. We additionally find reductions in the average daily supply of opioids per prescription in some states, with estimated prescribing changes in California (2.78 reduction in the average daily supply of MMEs; $p < 0.10$), D.C. (2.67 reduction in the daily supply of MMEs; $p < 0.01$), and Oregon (2.31 reduction in daily supply of MMEs; $p < 0.10$), demonstrating statistically significant reductions in average daily opioid supply in terms of milligram morphine equivalents. Finally, legalization results in a lower average number of opioid prescriptions per patient in Colorado (0.05 reduction in the number of opioid prescriptions per patient; $p < 0.10$), D.C. (0.12 reduction in the number of opioid prescriptions per patient; $p < 0.05$), Oregon (0.7 reduction in the number of opioid prescriptions per patient; $p < 0.10$), and Washington (0.06 reduction in the number of opioid prescriptions per patient; $p < 0.10$). Interestingly, we find statistically significant decreases in opioid prescribing in D.C. for all measured extensive and intensive outcomes after recreational cannabis legalization.

Aggregate analyses for RCL Legal can be found in Figure 4. In the aggregate analyses, we only find a decrease in the average daily supply of opioids (1.70 decrease in average daily supply, $p < 0.10$). We do not find any national, statistically significant effects on NSAID or other non-opioid pain medication prescribing following legalization of recreational cannabis.

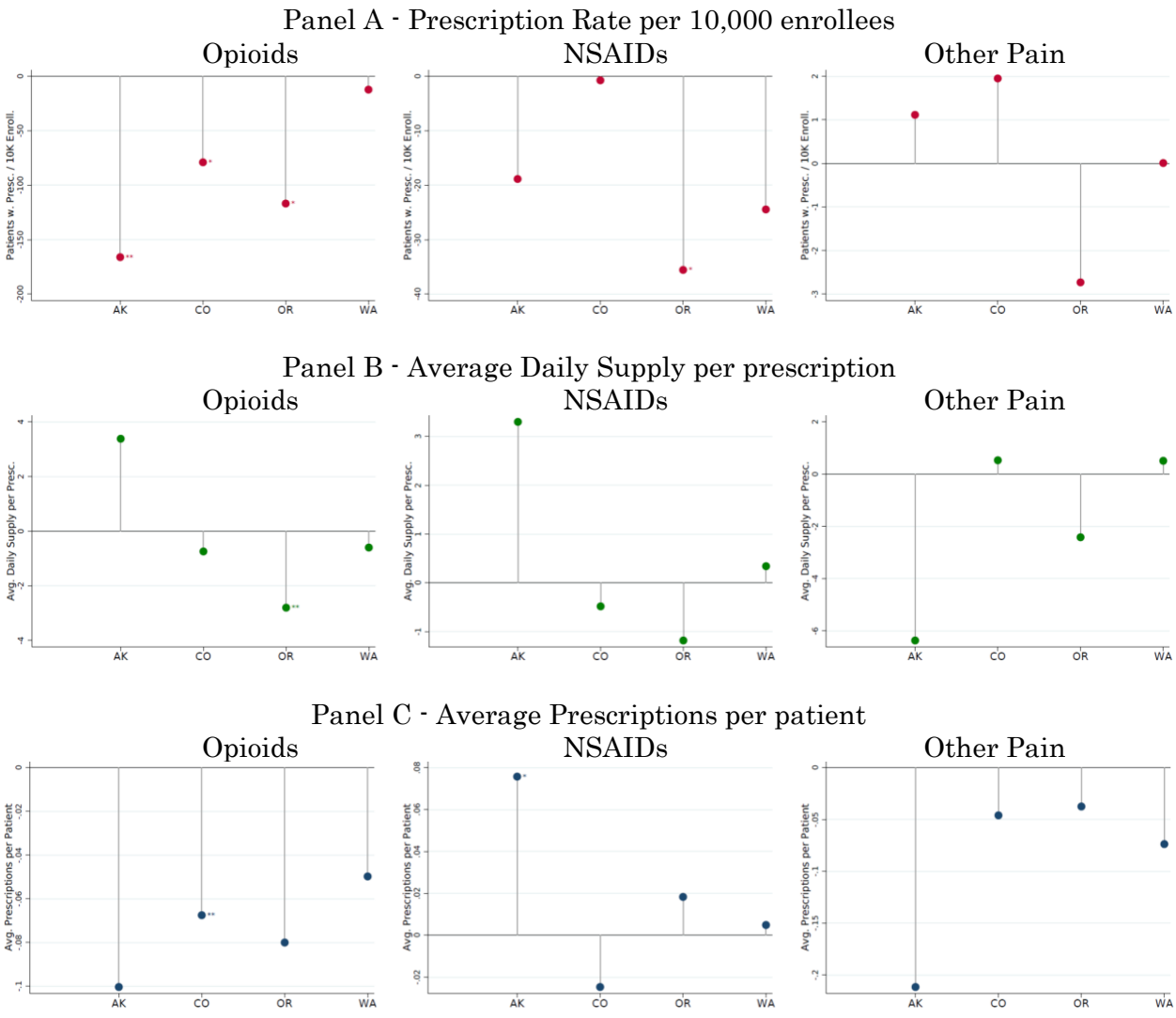
Figure 4. *Synthetic Control Time Series of Opioid Prescription Rates by State Time Series of Opioid Prescription Rates by State (Active RCL Dispensary)*





The lollipop graphs in Figure 5 provide a visual interpretation of the state-level point estimates and indicate decreases in opioid prescribing across most states and outcomes for recreational dispensary openings (RCL Dispensary).

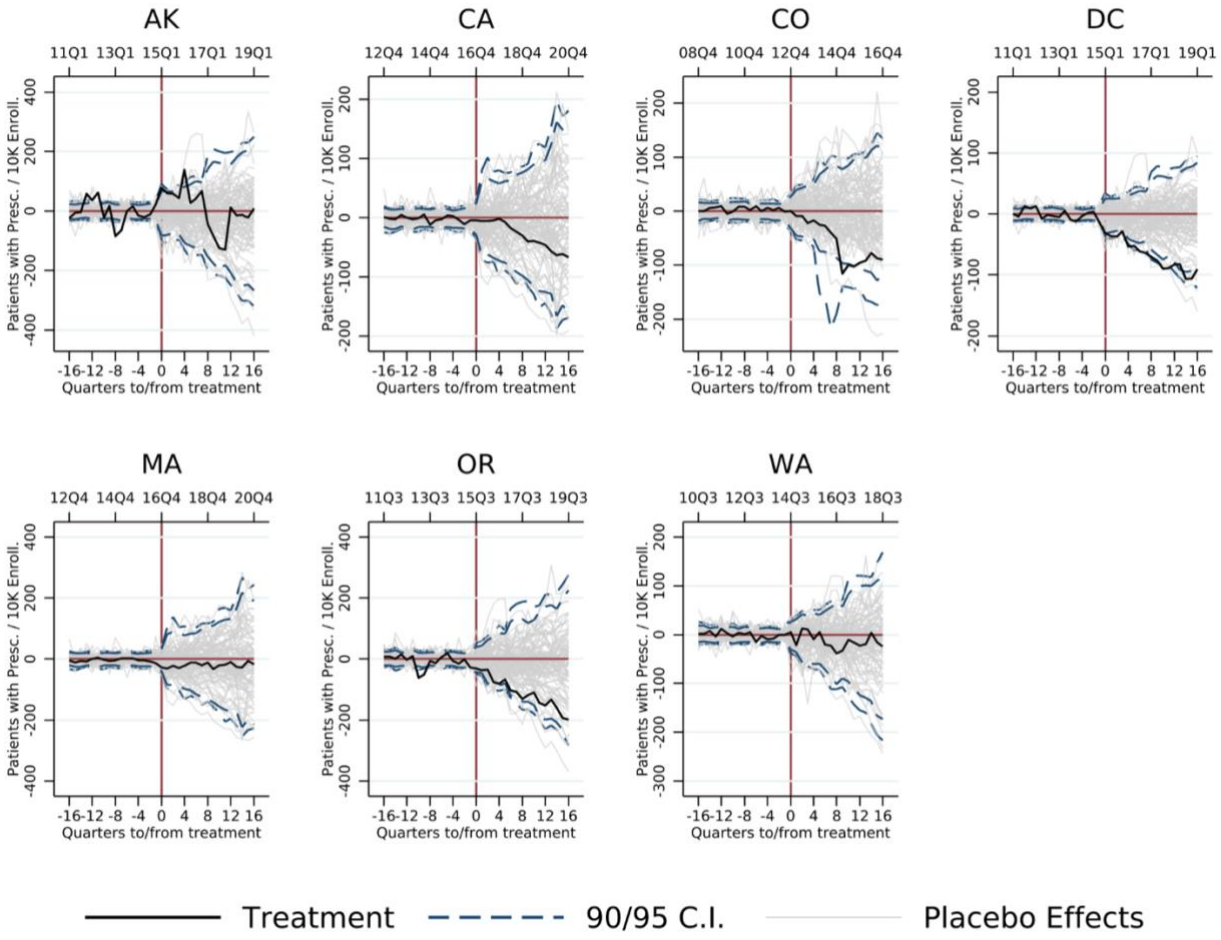
Figure 5. *Causal Synthetic Controls - RCL Legalization Effect on Opioid Outcomes*



The overall trends displayed in the lollipop graphs can be understood in detail using the state-level point estimates in Table 3. Following recreational dispensary openings, all states except for Washington show statistically significant decreases in the rate of patients with prescriptions of opioids. RCL Dispensary models for Alaska show a 166.1 decrease ($p < 0.05$) from a baseline of 427.5. Colorado shows a 78.98 decrease ($p < 0.10$) in the rate of patients per 10,000 enrollees with opioid prescriptions, from a baseline of 571.8. In Colorado, the average opioid fills per patient also decrease by 0.052 ($p < 0.10$) from a baseline of 2.1. Oregon RCL Dispensary models show a 116.88 decrease ($p < 0.10$) from a baseline of 460.06 in the number of opioid prescriptions per 10,000 patients and a 2.8 decrease ($p < 0.05$) in the number of days supplied by the average opioid prescription, from a baseline of 26.8 days. We see no statistically significant effects on opioid prescriptions from recreational cannabis dispensaries opening in Washington state.

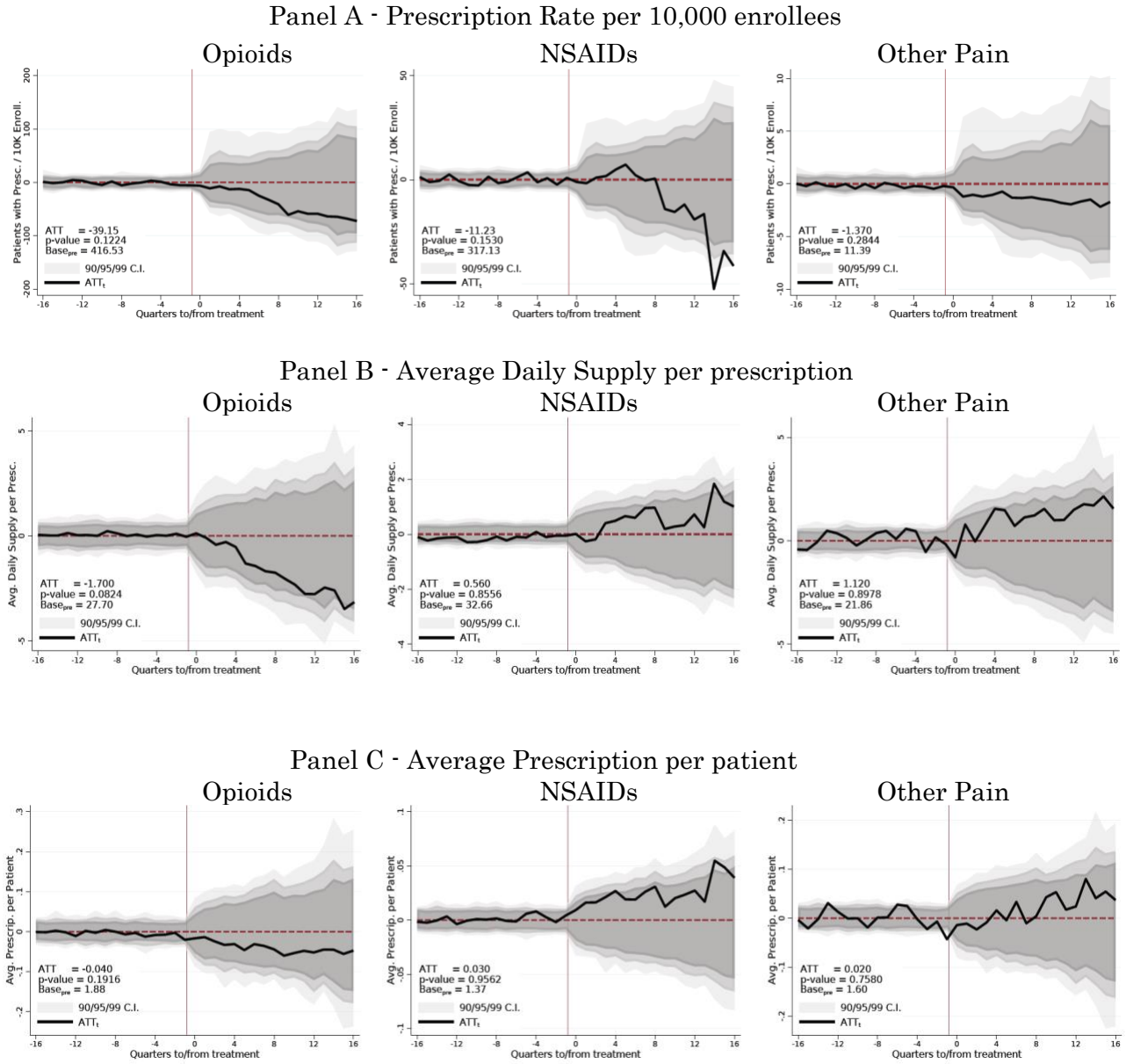
One important evaluation of the fit provided by a synthetic control is the matching of the synthetic and actual state in the pre-policy period. The synthetic control method often provides very close matches in the pre-policy period to the state it is approximating. This is evidenced by the synthetic control case studies in Figure 5. All the case study states match on most quarters in the pre-policy period, with Colorado and Washington matching almost perfectly. These case studies, except for Washington state, also indicate a deviation between the synthetic and actual in the post-policy period, although the placebo tests (Figure 6) should be used to infer and calculate causal effects.

Figure 6. *Causal Synthetic Controls - RCL Legalization Effect on Opioid Outcomes*



We aggregate all states to detect the overall effect of recreational cannabis dispensary openings on fills of opioids and non-opioid prescription pain medications at the national level. We find a statistically significant 70.21 reduction ($p < 0.05$) in the number of patients with opioid prescriptions per 10,000 enrollees, about a 13% change from the baseline (531.85; Table 4). Similarly, we see a decrease of 0.07 ($p < 0.05$) opioid fills per patient following recreational dispensary openings. Changes in the average daily supply of opioids are not statistically significant. We do not see statistically significant effects in the prescriptions of NSAIDs or other non-opioid pain medications, on extensive or intensive margins. However, it is worth noting the baseline average number of prescriptions of NSAIDs is less than half of opioids. Other non-opioid pain medications are rarely prescribed, so it is possible that any change in prescribing as a result of recreational dispensaries is too small to detect. These results can also be seen in the causal synthetic control event study graphs (Figure 7).

Figure 7. *Causal Synthetic Control Event Studies of RCL Dispensary Effects on All Outcomes - RCL Legalization effect on Pain Prescriptions*



DISCUSSION

We analyze the effects of RCL implementation on opioid and non-opioid pain medication prescribing at the aggregate, national-level and at the state-level by leveraging a synthetic control method estimation. Our state-level case studies allow us to investigate the differential effects resulting from heterogeneous RCL implementation. Overall, we find reductions in opioid prescribing and estimate ambiguous relationships between RCL implementation and non-opioid prescription pain medication outcomes among the commercially insured.

We find marginally significant increases in NSAID prescribing in some states, following recreational cannabis legalization (before dispensaries open). This finding is consistent with the idea that some people may use cannabis and non-opioid pain medications concomittantly for pain following recreational legalization (and perhaps decrease opioid usage to a level sub-perceptual for our methodology), but the larger effects of recreational cannabis legalization are likely to occur once there is a mechanism for cannabis users to legally purchase cannabis through dispensaries. Prior work shows that, while some subset of the population uses cannabis when it becomes recreationally legal, many wait until dispensaries open. Still, many more wait until dispensaries have been open for several years (Montgomery et al., 2022).

Results from our state-level case studies indicate that, aside from estimating an increase in the average daily supply of opioids prescribed in Alaska, we find decreases in the rate of patients with opioid prescriptions and average opioid prescription fills per patient in all case study states when using the opening of recreational dispensaries as the treatment. In Colorado, Oregon, and Washington state, we also find decreases in the average daily supply of opioids following recreational dispensary openings. In Alaska, we estimate the largest magnitude decreases in rates of patients with opioid fills and average opioid fills per patient despite finding a statistically significant increase in the daily supply of opioids. This finding may suggest that a smaller number of patients are receiving a higher frequency of daily doses following recreational dispensary openings. These findings may also suggest that Alaska provides a unique case study.

Following recreational dispensary openings, we only observe a statistically significant increase in the number of NSAID prescriptions per patient in Alaska. However, we do not observe a similar relationship between changes in NSAID and other non-opioid pain medication prescribing in other case-study states. In Oregon, we find a statistically significant decrease in the rate of NSAID prescriptions per patient as well as opioid prescribing reductions following recreational dispensary openings, which potentially supports the pain relieving qualities of cannabis. However, these findings are not replicated in other case study states. In Colorado, Oregon, and Washington state, we largely find non-significant increases and decreases in non-opioid prescription outcomes, which indicates an unclear relationship between RCL implementation and non-opioid pain medication prescribing at the state level. Because we do not observe over-the-counter non-opioid prescription consumption, our inconclusive findings must be considered cautiously. We also acknowledge that the market for cannabis and pharmaceuticals can be influenced by unique factors in each state.

Overall, we find recreational cannabis dispensary openings are associated with a significant decrease in opioid fills among commercially insured adults in the US. At the national level, we find decreases in opioid prescribing on both intensive and extensive margins among the commercially insured following recreational dispensary openings. Our estimates for non-opioid pain medication prescribing are not statistically significant when using RCL dispensary openings as our treatment. NSAIDs are largely available over-the-counter and less frequently prescribed than opioids, so our analyses using these medications as outcomes are relatively under-powered. Our findings may therefore support the analgesic properties of cannabis because patients are prescribed fewer opioids without a statistically significant increase in non-opioid pain medication when cannabis is available.

Alternatively, our results could suggest changes in physician prescribing behavior following RCL implementation. Prescription Drug Monitoring Programs (PDMPs) allow prescribers to monitor patients who are prescribed medical cannabis in some states and there is some evidence this impacts their prescribing practices

(Steuart, 2024), but it is possible that providers may not be informed about their patients' recreational cannabis use. With imperfect information between patients and prescribers in the context of recreational cannabis use, we cannot attribute estimated reductions in average fills per patient or rate of patients with opioid fills solely to provider caution. Whether driven by patients or healthcare providers, reductions in opioid fills stemming from RCL implementation may prevent exposure to opioids in patients with pain and lead to decreases in the number of new opioid users, rates of opioid use disorder, and related harms.

To our knowledge, previous studies examining the impacts of cannabis legislation and prescription pain medication utilization among the commercially insured have largely focused on medical cannabis legislation (Lozano-Rojas et al., 2022; McGinty et al., 2023; McMichael et al., 2020; Wen et al., 2021). We expand on this literature by examining recreational cannabis legislation. Furthermore, we include a novel examination of non-opioid pain medications. While previous works include non-opioid prescription pain medications, they do not look specifically at non-opioid pain medication prescribing (Bradford et al., 2018; Bradford & Bradford, 2016, 2017; Raman & Bradford, 2022). Our study separates non-opioid medications from the aggregate of prescription analgesics, and our results indicate that reductions in pain-related prescriptions following cannabis legislation are driven largely by opioid fill reductions.

Limitations

This study has several limitations. First, we do not observe patient use of cannabis or patient referrals for cannabis; therefore, the reductions we observe are not directly measuring substitutions. As the cannabis literature has evolved, the dates researchers use to measure cannabis policy implementation have changed. Instead of making a definitive assessment about the best moment to consider recreational cannabis "in effect," we use two measures of recreational cannabis legalization and follow this up with robustness exercises evaluating the effects of alternative date definitions and specifications. Second, our individual state case studies are underpowered, so we may be classifying effects as not statistically significant, when in fact they are. Thus, our results should be interpreted as a conservative estimate. Our goal is to be transparent about these unstable results by disclosing which results are affected and including both real and synthetic time series. Further, the unstable case studies do not change the overall results.

It is important to consider that during this timeframe, efforts were being made locally and nationally aimed at decreasing excessive opioid prescribing. Therefore, other contextual factors may have also impacted rates of opioid prescribing. The methodology we use compares states with legal recreational cannabis to states without legal recreational cannabis which controls for any trends that are occurring for both the treated and untreated states (such as national efforts or state policies occurring across states in both groups simultaneously). However, it is possible that states legalizing recreational cannabis were using additional or alternative policies to decrease opioid prescribing. Still, we do not observe patient or prescriber behavior directly, and thus we cannot with certainty distinguish mechanisms. We hope future research can address these topics more directly.

Conclusion

Our study adds to the growing evidence of the substitutability of cannabis for opioids and non-opioid pain medications and highlights state variation in two recreational cannabis policy settings. Importantly, this study provides evidence of potential concomitant use of cannabis and non-opioid pain medications as an alternative to opioids when individuals have easier access to legal cannabis through recreational dispensaries. Reductions in opioid prescription fills stemming from recreational cannabis legalization may prevent exposure to opioids in patients with pain and lead to decreases in the number of new opioid users, rates of opioid use disorder, and related harms. We recommend that future studies explore the relative substitutability of cannabis for opioids or use of cannabis concomitantly with non-opioid pain medications. We also recommend future studies explore observing patient or prescriber behavior directly, to more certainly distinguish mechanisms of cannabis substitution.

Table 1. *State-Level Point Estimates, RCL Legal Effect On All Outcomes*

Opioid Outcomes		Alaska	California	Colorado	District of Columbia	Massachusetts	Oregon	Washing-ton
Rate of Patients with Fills (10,000 enrollees)	ATT	6.0614	-30.519	-56.683**	-68.130***	-20.470	-110.40*	-12.812
	p-value	0.5508	0.2640	0.0767	0.0230	0.4125	0.0759	0.3630
	$Base_{pre}$	410.14	345.09	615.61	281.53	267.26	471.31	478.00
Avg. Daily Supply	ATT	0.7834	-2.7783**	0.1594	-2.6687***	0.4932	-2.3061**	-0.5967
	p-value	0.6234	0.0962	0.5296	0.0065	0.6838	0.0660	0.2716
	$Base_{pre}$	33.947	28.818	28.111	16.456	21.973	27.074	26.587
Avg. Fills per Patient	ATT	-0.1471	-0.0234	-0.0524*	-0.1201**	0.0115	-0.1691*	-0.0577*
	p-value	0.1881	0.3702	0.0514	0.0495	0.6055	0.0660	0.0740
	$Base_{pre}$	2.1345	1.7987	2.1090	1.5332	1.7212	2.0184	2.0485

Table 2. *Aggregated Results, RCL Legal Effect On All Outcomes*

		Opioids	NSAIDs	Non-opioid Pain
Rate of Patients with Fills (10,000 enrollees)	ATT	-39.15	-11.23	-1.370
	p-value	0.1224	0.1530	0.2844
	$Base_{pre}$	416.53	317.13	11.39
Avg. Daily Supply	ATT	-1.700*	0.560	1.120
	p-value	0.0824	0.8556	0.8978
	$Base_{pre}$	27.70	32.66	21.86
Avg. Fills per Patient	ATT	-0.040	0.030	0.02
	p-value	0.1916	0.9562	0.7580
	$Base_{pre}$	1.88	1.37	1.60

Table 3. *State-Level Point Estimates, RCL Dispensary Effect On All Outcomes*

Opioid Outcomes		Alaska	Colorado	Oregon	Washing-ton
Rate of Patients with Fills (10,000 enrollees)	ATT	-166.10**	-78.980*	-116.88*	-12.22
	p-value	0.02778	0.07012	0.07927	0.3628
	$Base_{pre}$	427.50	571.77	460.06	478.00
Avg. Daily Supply	ATT	3.3816	-0.7419	-2.7990**	-0.5994
	p-value	0.7792	0.2690	0.0466	0.2827
	$Base_{pre}$	31.530	28.489	26.777	26.587
Avg. Fills per Patient	ATT	-0.2034	-0.0524*	-0.08049	-0.04969
	p-value	0.1075	0.0533	0.2098	0.1650
	$Base_{pre}$	2.1322	2.1090	1.9532	1.996

Table 4. *Aggregated Results, RCL Dispensary Effect On All Outcomes*

Opioid Outcomes		Alaska	Colorado	Oregon	Washington
Rate of Patients with Fills (10,000 enrollees)	ATT	-166.10**	-78.980*	-116.88*	-12.22
	p-value	0.02778	0.07012	0.07927	0.3628
	$Base_{pre}$	427.50	571.77	460.06	478.00
Avg. Daily Supply	ATT	3.3816	-0.7419	-2.7990**	-0.5994
	p-value	0.7792	0.2690	0.0466	0.2827
	$Base_{pre}$	31.530	28.489	26.777	26.587
Avg. Fills per Patient	ATT	-0.2034	-0.0524*	-0.08049	-0.04969
	p-value	0.1075	0.0533	0.2098	0.1650
	$Base_{pre}$	2.1322	2.1090	1.9532	1.996

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