Recreational Cannabis and Opioid Distribution*

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abstract — Twenty-one U.S. states have passed recreational cannabis laws as of November 2022. Cannabis may be a substitute for prescription opioids in the treatment of chronic pain. Previous studies have assessed recreational cannabis laws' effects on opioid prescriptions financed by specific private or public payers or dispensed to a unique endpoint. Our study adds to the literature in three important ways: by 1) examining these laws' impacts on prescription opioid dispensing across all payers and endpoints, 2) adjusting for important opioid-related policies such as opioid prescribing limits, and 3) modeling opioids separately by type. We implement two-way fixed-effects regressions and leverage variation from eleven U.S. states that adopted a recreational cannabis law (RCL) between 2010 and 2019. We find that RCLs lead to a reduction in codeine dispensed at retail pharmacies. Among prescription opioids, codeine is particularly likely to be used non-medically. Thus, the finding that RCLs appear to reduce codeine dispensing is potentially promising from a public health perspective.

Keywords: cannabis | opioids | difference-in-differences | substance use | codeine

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1 Introduction

One in three U.S. residents now live in a state that has legalized adult-use recreational cannabis (ProCon, 2022b). Recreational cannabis legalization (RCL) increases adult cannabis use. Estimates of these increases range from 13% to 38% (Abouk et al., 2021; Cerdá et al., 2020; Maclean et al., 2021; Hollingsworth et al., 2020; National Academies of Sciences, 2017). At the same time, misuse of prescription opioids in the U.S. — which has increased rapidly beginning in 1990s — remains high and contributed to nearly 13,500 overdose deaths in 2021 (Ahmad et al., 2022). Both cannabis and prescription opioids can be used to treat chronic pain (Hill, 2015; National Academies of Sciences, 2017). It remains unclear whether RCLs affect opioid-to-cannabis substitution.

Medical cannabis laws (MCLs) appear to induce opioid-to-cannabis substitution. Thirty-nine states have legalized cannabis for medical use in the U.S. as of November 2022 (ProCon, 2022a). These laws provide legal access to cannabis for medical purposes to patients with qualifying health conditions. Surveyed medical cannabis patients with chronic pain frequently indicate that they use medical cannabis instead of prescription opioids (Corroon et al., 2017; Lucas and Walsh, 2017; Whiting et al., 2015). Consistent with this survey evidence, quasi-experimental studies have found that MCLs reduce opioid prescribing (Bradford et al., 2018; Bradford and Bradford, 2016, 2017; Ozluk, 2017; Powell et al., 2018).

Recreational cannabis laws (RCLs), passed by 21 states as of November 2022, expand cannabis access for medical and recreational use to nearly all adults aged 21 and above (ProCon 2022b). These laws stand in stark contrast to many restrictive MCLs, which limit cannabis access to persons with diagnoses for severe health conditions (Smart, 2015). For example, 14 states with MCLs do not include chronic pain as a qualifying health condition (Boehnke et al., 2019). Whereas roughly 2% of residents of MCL states are enrolled in the medical cannabis program (Abouk et al., 2021), RCLs make licit cannabis available to a much larger portion of the population.

An emerging literature suggests RCLs also may reduce demand for prescription opioids. Post-RCL adoption, opioid prescriptions decline among Medicaid enrollees (Raman and Bradford, 2022; Wen and Hockenberry, 2018), Medicare beneficiaries (Abouk et al., 2021), and those with employer-sponsored insurance (Wen et al., 2021). Using a database of public and private payers, McMichael et al. (2020) and Abouk et al. (2021) and find that opioid prescriptions filled in retail pharmacies decline post-RCL. While we investigate changes to opioid distribution, evaluations using survey data are unable to estimate sufficient evidence of reductions in opioid misuse (Ali et al., 2021). These studies generally find more substantial effects than MCL studies, likely due to the

larger scope of RCLs.

We add to this literature by examining the impact of RCL adoption on opioid shipments to all dispensing endpoints for the pharmaceutical market. As such, out study is not limited to specific populations (e.g., Medicaid enrollees), and we consider all possible legal distribution endpoints, including hospitals. Assessing market-level impacts is arguably more useful to policymakers than analyses which focus on a subset of opioid consumers. We also extend existing analyses by adjusting for opioid prescribing limits, which limit opioid prescribing by quantity and duration and may therefore impact the impact of RCLs on opioid prescriptions. While previous studies adjusted for other policies that could affect demand for and supply of prescription opioids, including prescription drug monitoring programs, naloxone access laws, and good Samaritan laws, they have not previously controlled for opioid prescribing limits.

We estimate causal effects of RCL adoption on all prescription opioid shipments to retail pharmacies, hospitals — a common source of prescription opioids — and all other legal endpoints in the U.S. from 2010 to 2019. Our primary finding is that RCLs lead to a 26% reduction in retail pharmacy-based codeine distribution. This finding is suggestive that RCLs may help achieve reductions in opioid misuse, as codeine is a lower-potency opioid with high potential for misuse (Kinnaird et al., 2019). We do not find statistically significant reductions in the distribution of any other opioids, nor do we find statistically significant reductions in hospital-based codeine distribution. Collectively, our findings are consistent with the hypothesis that reductions in opioid demand affected by RCLs, unlike MCLs, may be evidence of decreased opioid misuse more than decreased use of prescription opioids to manage chronic pain. While both MCLs and RCLs reduce demand for prescription opioids, the mechanisms through which they do so appear to be different.

2 Methods

2.1 Data

Our primary data source is the Drug Enforcement Administration's (DEA) Automation of Reports and Consolidation Orders System (ARCOS). The DEA is the federal law enforcement agency in the U.S. tasked with combating drug trafficking and distribution. The ARCOS tracks flows of Scheduled II to IV controlled sub-

stances,[1] including opioids, up to the point that they are distributed to patients by retail pharmacies, hospitals, specialists, and other outlets. These data track shipments of active ingredients, rather than prescriptions of specific medications. We are the first study, to our knowledge, to leverage ARCOS data which details distribution by endpoint — pharmacies, hospitals, specialists, and narcotic treatment programs — to study the effects of RCLs.

We augment the ARCOS data with five secondary data state-year level data sources. Four of these data sources identify the implementation dates of state policies that could affect the supply of and demand for opioids. The RAND-University of Southern California's Schaeffer Opioid Policy Tools and Information Center (OPTIC) database identifies implementation dates for RCLs, MCLs, good samaritan laws, and naloxone access laws. Horwitz et al. (2021) provide prescription drug monitoring program implementation dates, Carey et al. (2020) list Medicaid expansion dates, and dates for implementation of opioid prescribing limits follow Sacks et al. (2021). Lastly, we include data on the number of practicing physicians and racial demographic composition variables from the Area Health Resource File.

2.2 Sample

Our sample consists of 510 state-year observations in all states from 2010 to 2019. During this time period, eleven states adopted an RCL: Alaska, California, Colorado, DC, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, and Washington. Notably, all states that have adopted an RCL previously had adopted an MCL. One can thus interpret our findings as capturing the incremental effect of an RCL. Neither Vermont nor DC permitted recreational cannabis dispensaries during our study window. Figure 1 shows the temporal variation in our RCL variable; Appendix Figure A1 illustrates the geographic distribution of treatment states. We treat a state as implementing an RCL in a given year if it had implemented the RCL by April 1st (i.e., the law was in place for at least three-quarters of the year). We measure all state-year policy variables in the same fashion.

We display opioid distribution in the U.S. by opioid and endpoint from 2010 to 2019 in Figure 2. While opioid prescribing has been declining since 2012 in the U.S., it remains exceptionally high (see Appendix Figure A4). The primary endpoints we study are those with measurable levels of distribution across our study sample:

[1] The DEA recognizes scheduling of drugs based on both their potential for abuse and their capacity for medical use. Schedule I drugs are those that have been deemed by the U.S. Congress to have a high potential for abuse and no medical use. For example, heroin is categorized as a Schedule I drug. As ARCOS tracks only those drugs expected to have some medical use, Schedule I drugs are not included in the database. Cannabis is a Schedule I drug and is therefore not tracked in ARCOS and we cannot study related shipments.

pharmacies and hospitals. We do not present regression results (see below) for distribution to other distribution endpoints, which make up less than 1% of average annual distribution.[2] Buprenorphine and methadone are primarily used for treatment of opioid use disorder (Shulman et al., 2019) and are thusly omitted from our analysis. While we observe distribution of fentanyl, ARCOS data does not capture the dosage of distributed substances. Fentanyl is accessible in low-potency lozenges and high-potency "patches" often used in hospital settings for pain management; as such, interpretation of changes to fentanyl distribution should be made cautiously.

2.3 Empirical Strategy

We fit a series of two-way fixed-effects (TWFE) regressions to estimate the effects of RCL adoption on opioid distribution. A critical assumption required for TWFE regressions to recover estimates of causal effects is that the data satisfy 'parallel trends.' That is, had the states with an RCL not adopted the policy, we assume they would have followed the same trends in opioid distribution as those states that did not adopt RCLs. This assumption is untestable; however, we offer suggestive evidence on this assumption by conducting a pre-trends test with an event study. Our main specification takes the following form:

$$E[y_{st}] = exp\left(\sum_{j=-4, j\neq -1}^{4} \beta_t RCL_{st}(t = k + j) + \gamma X_{st} + \mu_s + \tau_t\right)$$

Our outcome (y_{st}) is the rate of prescription opioid distribution in grams per 100,000 adults over the age of 21 in state s in year t. We estimate Poisson regressions and weight our observations by state population over the age of 21.[3] Our estimates can therefore be interpreted as an approximation of a percentage change in the rate relative to non-RCL states. The summation term $-\sum_{j=-4, j\neq -1}^{4} \beta_t RCL_{st}(t = k + j) - j$ indexes the year relative to adoption for RCL states — expansion occurs at $j = 0$ — and k represents the RCL adoption year. We are interested in the coefficient estimates for β_t which represent the difference in our outcome between RCL and non-RCL states in time t. We include a vector of covariates, X_{st}, indexed at the state-year level and described in Section 2.1. See Appendix Table A1 for further details. We include state (μ_s) and year (τ_t) fixed

[2] When evaluated using our primary specification, we do not estimate statistically significant effects for these other endpoints. See Appendix Table A2 for details on opioid distribution to these endpoints and Appendix Table A3 for estimates.

[3] A Poisson distribution is well adapted to continuous outcomes and can be estimated when the outcome variable is a rate if the rate denominator is used as observations' weights. Estimation in this setting with robust standard errors is shown to be much less sensitive to misspecification for continuous dependent variables when compared to OLS models (Wooldridge, 2010). Our results are descriptively similar in an OLS setting.

effects.

The staggered adoption of RCLs illustrated in Figure 1 has the potential to bias our β_t coefficient estimates due 'forbidden' comparisons (Goodman-Bacon, 2021). Specifically, TWFE regressions compare later treated units to earlier treated units, which can lead to negative weighting and sign reversals.[4] To assess the importance of this potential source of bias, we apply a Goodman-Bacon decomposition (Goodman-Bacon, 2021) to examine the comparisons which compose our overall TWFE coefficient estimate.

3 Results

3.1 Baseline Results

We report baseline findings graphically in Figure 3 for the four prescription opioids which make up over 90% of average annual distribution: oxycodone, hydrocodone, morphine, and codeine. We estimate separate regressions for all prescription opioids and by specific opioids as described in Section 2.2. We estimate these regressions for all endpoints and by two specific endpoints: pharmacies and hospitals. A full set of coefficient estimates for all endpoints and opioids are presented in Appendix Table A3.

Our primary finding is that RCLs affected a 25.7% (95% confidence interval = -46.2 to -5.2) reduction in pharmacy-based distribution of codeine. As shown in Figure 4, this effect increases in magnitude over time, increasing from -17.5% (95% CI = -34.4 to -0.5) one year after RCL implementation to -37.3% (95% CI = -57.5 to -17.0) four years after implementation. We do not find any evidence of a relationship between RCLs and hospital-based codeine distribution; the decrease in pharmacy-based distribution drives an overall decrease in codeine distribution beginning in the third year after RCL implementation. We do not find other evidence of RCLs affecting changes in other types of opioid distribution. That our findings suggest RCLs affect a reduction specifically in codeine distribution is of particular interest because, among legally distributed opioids, codeine is particularly likely to be misused and diverted.

[4] We have a large comparison group and RCLs are recently adopted, which is a setting where these issues are less likely to lead to substantial bias.

3.2 Robustness Checks

We conduct three robustness checks. First, we evaluate our event study estimates for pre-trends as described in Section 2.3. We do not find significant pre-trends for most of the opioids we examine, including net opioid distribution and codeine (see Figure 4 for net distribution and codeine, and Appendix Table A3 for all estimates). Second, we explore the extent to which staggered policy adoption may bias our TWFE regression coefficient estimates. Goodman-Bacon (2021) decompositions (Appendix Figure A2) show that the large majority (91.2%) of the two-by-two difference-in-differences comparisons that compose our overall TWFE coefficient estimate are derived from 'clean' comparisons of treated units to untreated units. Our results are consistent when estimated with a 'stacked' difference-in-difference design that is robust to bias from staggered implementation (Cengiz et al., 2019). Third, to assess if our findings are driven by a single state's RCL implementation, we iteratively exclude each state that implemented an RCL and re-estimate our primary specification. Our results are stable. See Appendix Figure A3 for additional details.

4 Discussion

In this study, we evaluate the impact of recreational cannabis laws on the distribution of opioids in the U.S. Our study builds on existing literature and provides novel estimates of heterogeneous policy effects across distribution endpoints. Our primary finding is that RCLs affect a roughly 26% reduction in the pharmacy-based distribution of codeine, a lower-potency opioid with especially high rates of misuse. That our results increase in magnitude over time — up to a 37% reduction in codeine dispensing four years after an RCL is implemented — is consistent with the increased availability of recreational cannabis dispensaries in states adopting RCLs. We do not find other significant reductions in opioid distribution, overall, in pharmacies, or in hospitals. That reductions in codeine dispensing only occur in a setting where misuse is possible (i.e., pharmacies rather than hospitals), and that we do not find other reductions, suggests that RCLs decrease opioid dispensing by affecting a reduction in prescription opioid misuse. We cannot rule out that these reductions are due to a reduction in use of codeine as prescribed; however, the lack of other reductions in opioid dispensing suggests that this is not the case. Our findings stand in contrast to the literature on MCLs, which finds that MCLs affect reductions in the dispensing of a variety of opioids that do not have misuse rates as high as codeine.

We note four additional limitations. First, we only observe distribution by drug name rather than more granular

national drug codes. Thus, for some drugs like fentanyl (which has tablet, lollipop, and patch formulations with widely varying dosage strengths) we cannot provide an accurate estimate of changes in morphine milligram equivalent values. Second, we are only able to estimate changes to distribution by endpoint at the state-level, as the DEA does not make more granular data (county or 3-digit ZIP code level) publicly available by specific drug type and business activity. Thus, we are unable to adjust for local cannabis access. Finally, our data end in 2019. As data become available, subsequent studies could investigate the longer-run impact of recreational cannabis policies.

Our results are broadly consistent with prior economic studies finding reductions in opioid prescribing following MCL and RCL adoption (Abouk et al., 2021; McMichael et al., 2020; Ozluk, 2017; Raman and Bradford, 2022; Shi et al., 2019; Wen and Hockenberry, 2018; Wen et al., 2021). We contribute to this literature by identifying that reductions in opioid dispensing due to RCLs are driven by reductions in codeine dispensing at retail pharmacies. Future studies should further explore whether these reductions, and perhaps those in illicit markets, are reflective of decreases in opioid misuse or decreases in prescribed opioid use for pain management.

5 Main Text Exhibits

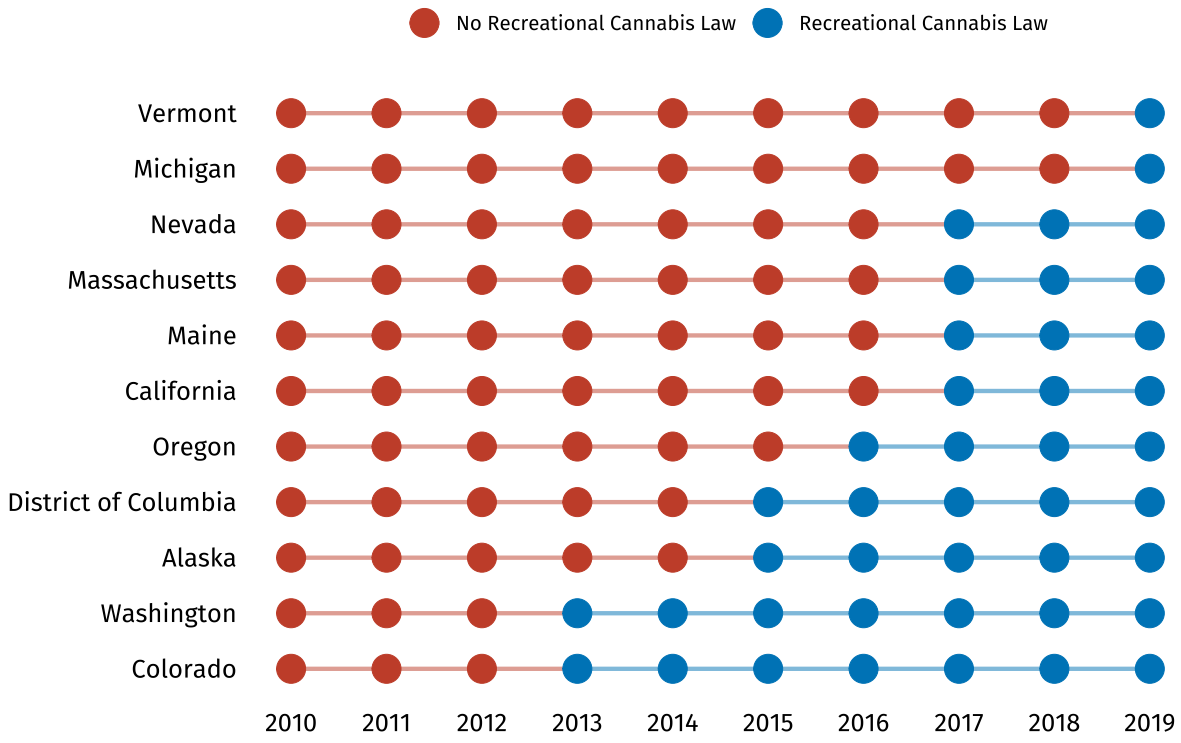

Figure 1: Treatment Timing for Recreational Cannabis Legalizations in Sample

Note: This figure illustrates the variation in recreational cannabis law (RCL) adoption timing among sample states. RCL adoption date data retrieved from the OPTIC database. Displayed are the eleven RCL adopters in our sample and their implementation time across our study window. Our sample includes 510 state-quarter observations across ten years of ARCOS distribution data.

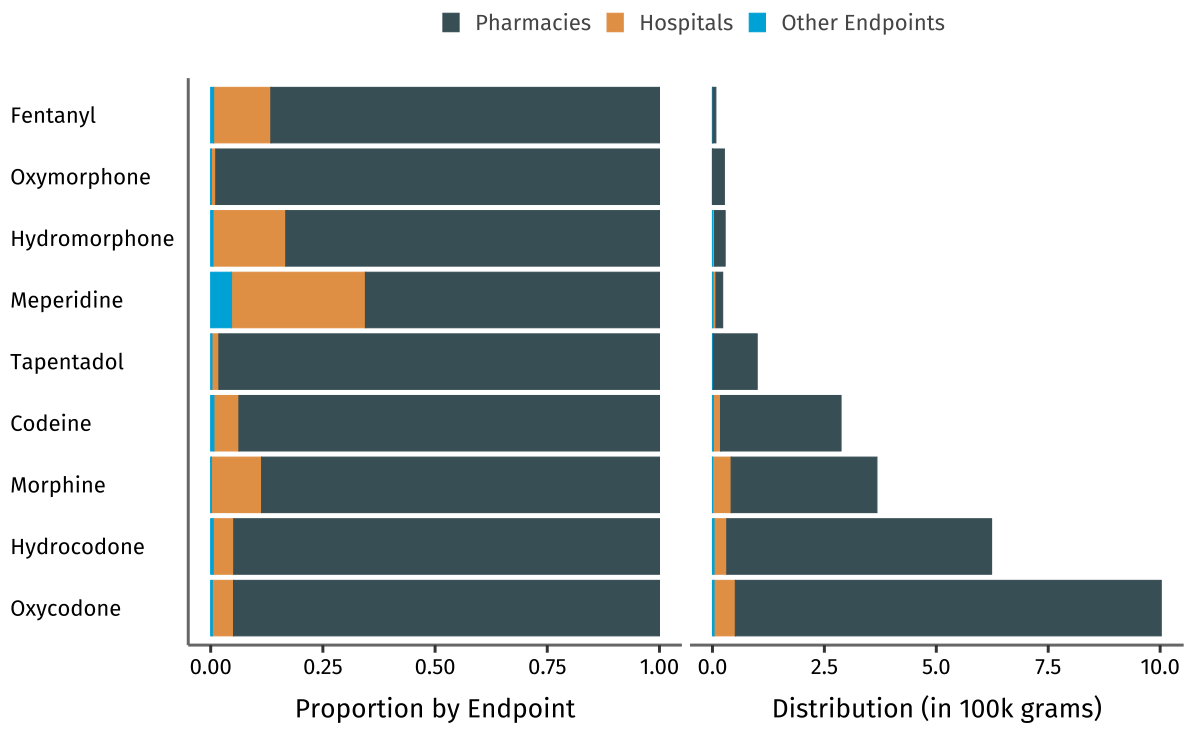

Figure 2: Average Annual Distribution of Opioids by Endpoint in ARCOS Reports (2010-2019)

Note: Data drawn from DEA ARCOS Reports on opioid distribution during our study window: 2010 to 2019. The left hand panel plots the proportion of total distribution by endpoint for each opioid. The right hand panel plots the total distribution in hundreds of thousands of grams by endpoint for each opioid.

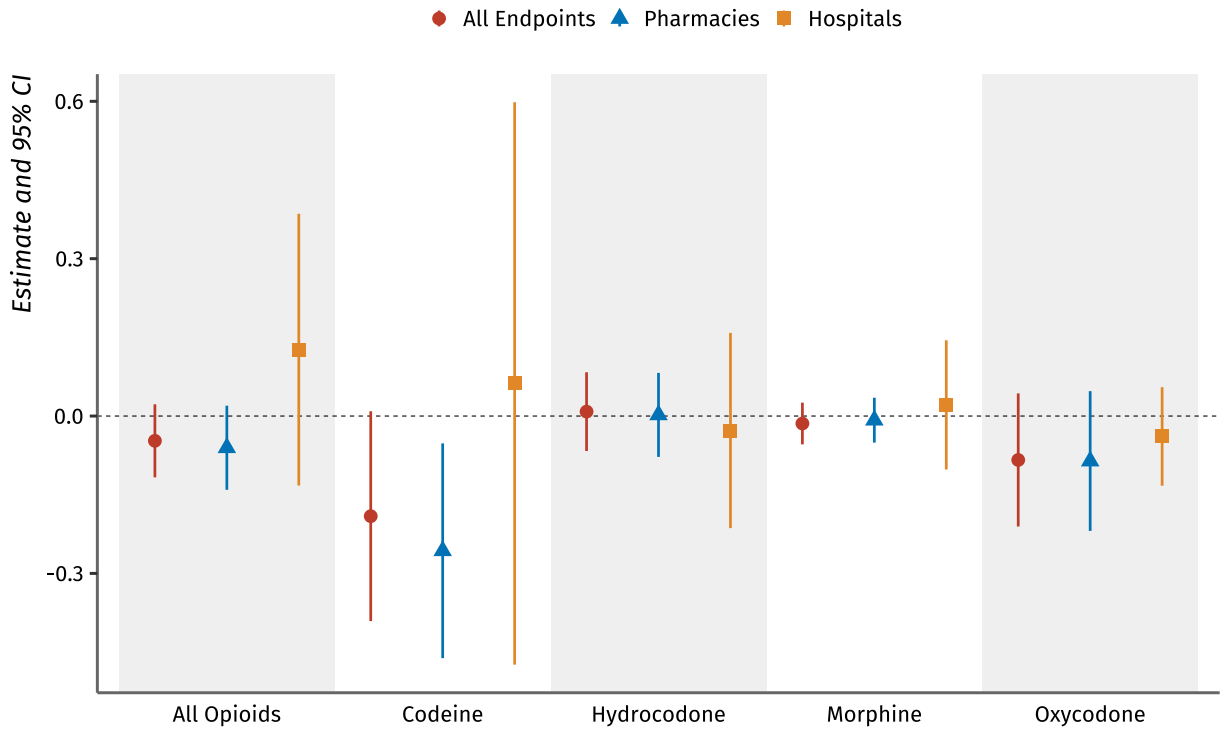

Figure 3: Estimates for Change in Opioid Distribution Following RCL Adoption

Note: This figure displays the average of lagged event study coefficients for recreational cannabis laws' impact on distribution rate of all opioids and oxycodone to pharmacies, hospitals, and all endpoints as captured in ARCOS data. Each coefficient is displayed with 95% confidence intervals. Estimates correspond to the baseline model described in Section 2.3. Coefficient estimates and standard errors can be found in Appendix Table A3. Coefficients are transformed to represent percentage changes in rates and standard errors are expanded using the delta method and account for within-state clustering.

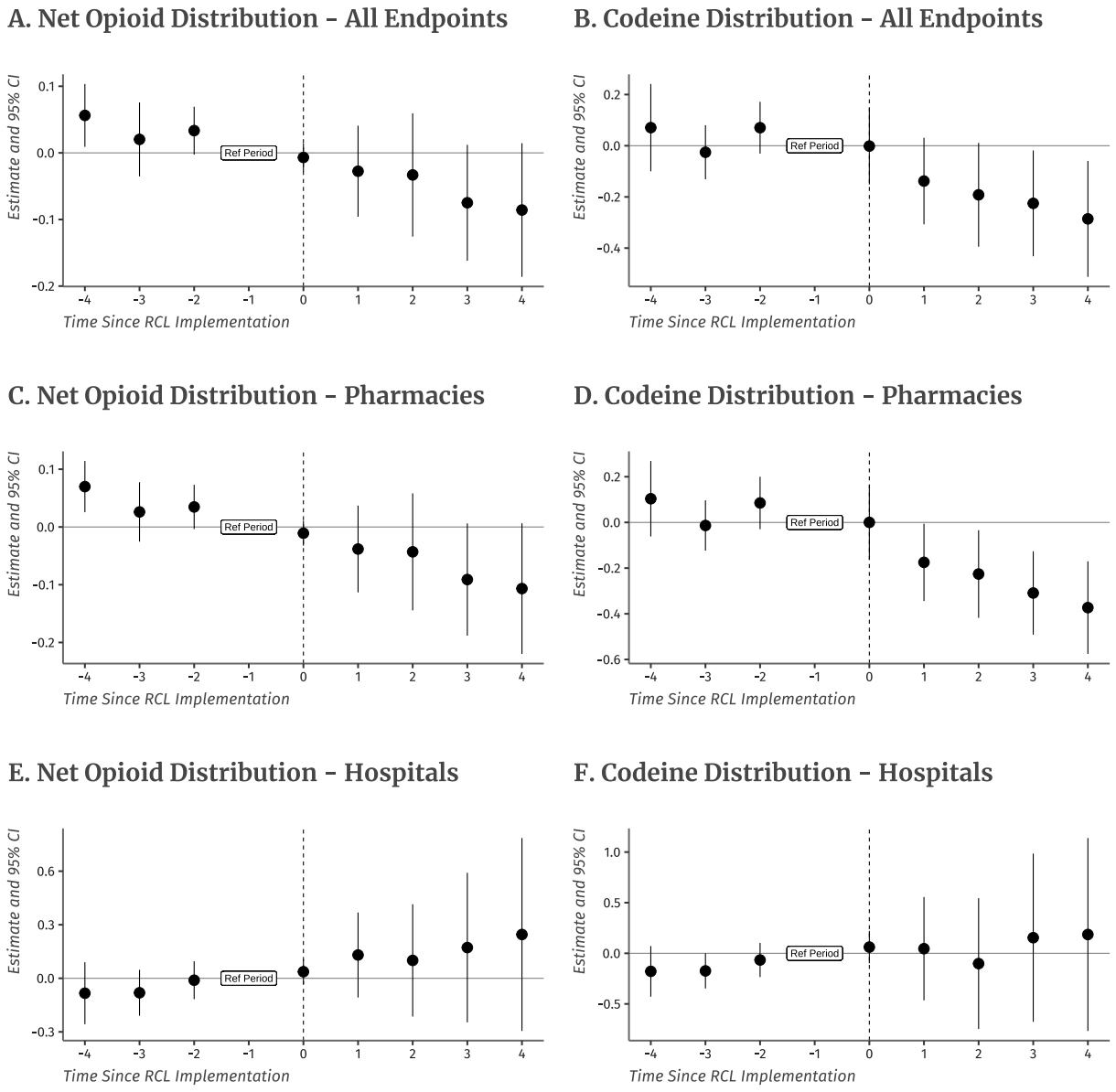

Figure 4: Event Study Estimates for Change in Rate of Opioid Distribution

Note: This figure presents event study estimates of recreational cannabis laws' impact on distribution rate of all opioids and oxycodone to all endpoints, pharmacies, and hospitals as captured in ARCOS data. Estimates correspond to the baseline model described in Section 2.3. Coefficient estimates and standard errors can be found in Appendix Table A3. Estimates are transformed to represent percentage changes in rates and cluster robust standard errors are expanded using the delta method. Opioid names are displayed as the title for each subplot. Future adopters (states which adopted an RCL after 2019) are included in this specification, though we control for existing cannabis policies as well as all covariates discussed in Section 2.1.

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