Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers?

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Abstract:

Many medical marijuana patients report using marijuana to alleviate chronic pain from musculoskeletal problems and other sources. If marijuana is used as a substitute for powerful and addictive pain relievers in medical marijuana states, a potential overlooked positive impact of medical marijuana laws may be a reduction in harms associated with opioid pain relievers, a far more addictive and potentially deadly substance. To assess this issue, we study the impact of medical marijuana laws on problematic opioid use. We use two measures of problematic use: treatment admissions for opioid pain reliever addiction from the Treatment Episode Data Set (TEDS) and state-level opioid overdose deaths in the National Vital Statistics System (NVSS). Using both standard differences-in-differences models as well as synthetic control models, we find that states permitting medical marijuana dispensaries experience a relative decrease in both opioid addictions and opioid overdose deaths compared to states that do not. We find no impact of medical marijuana laws more broadly; the mitigating effect of medical marijuana laws is specific to states that permit dispensaries. We evaluate potential mechanisms. Our findings suggest that providing broader access to medical marijuana may have the potential benefit of reducing abuse of highly addictive painkillers.

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I. Introduction

Drug overdoses are the leading cause of deaths from injuries in the United States today, exceeding deaths from suicide, gunshot deaths and motor vehicle accidents (Murphy et al., 2013). In 2010, 16,651 deaths were caused by a prescription opioid overdose, representing nearly 60% of all drug overdose deaths, and exceeding overdose deaths from heroin and cocaine combined (Jones, Mack and Paulozzi, 2013). While a modest decline in opioid overdose deaths has occurred since 2012, more than 16,000 lives are lost to prescription opioids even today (NCHS, 2014).

These numbers are the result of a dramatic rise in problems associated with prescription opioid abuse over the past two decades, both in terms of morbidity and mortality. While the number of fatal poisonings due to prescription pain medications quadrupled between 1999 and 2010, the distribution of opioid pain medications also quadrupled during the same period, demonstrating a parallel rise between the distribution of opioid pain medication and its abuse nationally (CDC, 2011). Treatment admissions grew at an even faster rate, increasing nearly six-fold between 1999 and 2009 (CDC, 2011b). Opioid-related ED visits more than doubled from 21.6 per 100,000 in 2004 to 54.9 per 100,000 in 2011, for a total of 1.24 million emergency department visits involving non-medical use of pharmaceuticals and pain relievers in 2011 (SAMHSA, 2013a). It is these trends that led the Centers for Disease Control to deem the misuse of prescription opioids in the United States an "epidemic."

Agencies at the federal, state and local level have been implementing a variety of strategies to tackle the problem, including adopting mandatory prescription monitoring programs, pharmacy lock-in programs, doctor shopping laws, good Samaritan laws, physician exam requirements, and prescriber education programs (Levi et al, 2013; CDC 2013a). Evidence from the most recent waves of the National Household Survey on Drug Use and Health (NHSDUH) and the Drug Abuse Warning Network (DAWN) suggest that some of these policies may have helped slow the increase. According to the most recent NSDUH survey, self-reported annual prevalence and dependence on pain relievers has leveled off

since 2007 and even declined (temporarily) in a few years (e.g., 2011) (SAMHSA, 2013b). Similarly, the DAWN data show that between 2009 and 2011, opiate-involved ED visits saw no significant increase even though nonmedical use of all pharmaceuticals rose 15 percent (SAMHSA, 2013a).

The effectiveness of policy approaches to reducing opioid problems has been relatively understudied. Prescription drug monitoring programs (PDMPs) have received the most serious attention. The research evaluating this policy, however, is currently inconclusive due in part to different definitions of the type of PDMP that is deemed "effective" (Brady et al., 2014; Riefler et al., 2012; Paulozzi et al., 2011; Paulozzi & Stier, 2010; Reisman et al., 2009; Simeone & Holland, 2006). Even less well understood is the potential mitigating role medical marijuana laws might have on opioid misuse. Many reviews find that marijuana is effective medicine for the treatment of chronic pain (Borgelt et al., 2013; Lynch & Cambell, 2011; Lueng, 2011; Martin-Sanchez et al., 2009). Furthermore, patients often seek medical marijuana recommendations for severe or chronic pain (Bowles 2012; Nunberg et al., 2011).[1] To the best of our knowledge, only one study, Bachhuber et al. (2014), considers how medical marijuana laws affect opiate-related harms. That study focuses only on a rare, albeit important, outcome – overdose deaths. It finds that age-adjusted opiate mortality decreased in states that adopted medical marijuana laws but does not discriminate among the features of medical marijuana laws that contributed to this relationship.

In this paper, we examine whether medical marijuana laws reduced prescription opioid misuse. As of June 2015, twenty-four states and the District of Columbia had enacted laws allowing marijuana to be used for medicinal purposes; over half of which were passed since 2007. Thus, laws liberalizing marijuana use were adopted over the same period that opiate problems first exploded and then leveled off. If marijuana is indeed an effective alternative to prescription opioids, then states that provide legal

[1] Nunberg et al (2011) studied over 1600 patients seeking medical marijuana recommendations in California in 2006 – 10 years after California's law passed – and finds half of the patients report seeking medical marijuana to replace prescription opioid medications.

access to patients with these symptoms may have helped stem the rise of prescription opiate use and, most importantly, misuse. Medical marijuana laws, like prescription drug monitoring programs, vary along numerous dimensions. One feature of these laws – an allowance for retail marijuana sales to qualified patients through dispensaries - is associated with greater access to and use of marijuana (Pacula et al., 2015; Wen et al., 2015; Choi, 2014; Pacula et al., 2010) as well as the availability of more potent marijuana (Sevigny et al., 2014). During our sample period, we observe a huge shift in the legal protection of legal dispensaries, with 18 of the 24 states with medical marijuana now allowing for dispensaries, most of which have passed since 2007. Thus, while we study the effects of all medical marijuana laws in some of our analyses, we focus most of our attention on state medical marijuana laws that legally protect dispensaries.

We examine two measures of prescription opioid problems: treatment admissions for addiction to pain relievers (1992-2012) and state-level overdose deaths for opioid medications (1999-2013). We also examine the extent to which state policies influence the distribution of opioid medication (2000–2011), so as to better understand whether medical use of marijuana impacted the legal distribution of opioid analgesics as a possible mechanism for our findings. We first estimate standard differences-in-differences models, exploiting changes in the allowance of medical marijuana dispensaries to test for differential changes in outcomes. Given concerns that the adopting states may not be similar to all non-adopting states in terms of pre-policy trends, we also implement a synthetic control approach (Abadie and Gardeazabal (2003); Abadie, Diamond, and Hainmueller (2010); Abadie, Diamond, and Hainmueller (2014)). We find no evidence that medical marijuana laws (broadly specified) are associated with reductions in substance abuse or mortality. However, we find strong evidence that medical marijuana laws legalizing dispensaries reduce substance abuse treatments for opioids. Our estimates imply reductions in treatment admissions of over 15%, with even larger reductions suggested by synthetic control estimation. We also find evidence of reductions in opioid-related mortality. Our difference-in-

differences estimate implies a 16% reduction in opioid-related mortality while synthetic control estimates imply even larger effects of 31% upon the adoption of legal medical marijuana dispensaries. In contrast to prior work (Bachhuber et al. 2014), we find this reduction only in states with dispensaries and not in the broader group of medical marijuana states.

To explore potential mechanisms through which this policy might be working, we examine the influence of the medical marijuana policies on state-level opioid distribution. We find little evidence that states that legally protect medical marijuana dispensaries experience reductions in morphine dose equivalent amounts of opioids distributed to them. This result suggests that legalized medical marijuana distribution replaces illegal opioid acquisition and use, which is not reflected in the legal state supply of opioids.

The rest of this paper is organized as follows. In Section II, we describe the data. Section III provides graphical descriptions of our data, followed by a discussion of our empirical strategy in Section IV. The results are presented in Section V. Section VI includes a discussion and concludes.

II. Data and Measures

Following the literature on opioid-related harm, we use three different measures of opioid use and abuse to study the relationship between medical marijuana laws and potential harm from opioids: opioid-related treatment admissions, opiate-related mortality, and the distribution of opioids to states from the producers of these medications.

First, we use data from the Treatment Episode Data Set (TEDS) to construct the number of treatment episodes related to abuse of pain relievers for the period 1992-2013. States collect data on admissions to treatment facilities receiving public funding (federal block grants, state funds, publicinsurance dollars) even if those facilities also serve privately insured or cash only patients. While not a census of substance abuse treatments in the United States, as facilities serving exclusively privately insured or cash-only patients are not reflected in the sampling frame, examination of national

spending on substance abuse treatment shows that the public sector (via Medicare, Medicaid or other federal, state and local grants or subsidies) have consistently paid over 75% of all substance abuse treatment in the United States since 1998 (Mack et al., 2011). Thus, the TEDS population will capture meaningful shifts in state-level trends in treatment for opioid abuse. The TEDS lists up to three substance of abuse for each admission. We categorize "non-prescription methadone" and "other opiates and synthetics"[2] admissions as related to pain relievers.

A significant fraction of substance abuse treatments are criminal justice referrals (about 21% in our data), and the TEDS data provide information on which treatments are referred by the criminal justice system and which are not. We perform our analysis for all pain reliever substance abuse treatments and also show results for treatments that are not criminal justice referred. We do this because simultaneous changes to state criminal justice systems may alter the interpretation of our results. We find stronger evidence and more precise estimates when we exclude criminal justice referrals, but we find complementary support for reductions in opioid admissions when we include them.

Our second measure of problematic opioid use is opioid-related deaths. This measure is based on mortality data from the National Vital Statistics System (NVSS), a census of deaths in the United States. Opioid related deaths have been the key driver behind prescription drug overdoses for over a decade (Jones et al, 2013). We code deaths as related to prescription opioid pain relievers using the ICD-10 external cause of injury codes (X40-X44, X60-64, X85, or Y10-Y14) and drug identification codes (T40.2-T40.4). We follow the codes used by the CDC to categorize deaths of any intent (unintentional,

[2] These include all non-heroin opiates except non-prescription methadone, such as buprenorphine, codeine, Hydrocodone, hydromorphone, meperidine, morphine, opium, oxycodone, pentazocine, propoxyphene, tramadol, and any other drug with morphine-like effects.

suicide, homicide or undetermined).[3] We limit our analysis to 1999-2013 because prior to 1999, the NVSS used ICD-9 codes for identifying cause of death and opioid-related deaths are difficult to link across ICD coding systems. We used the restricted geocoded data with state identifiers to link medical marijuana laws to opioid-related deaths. We aggregate based on state of occurrence and year.

While the first two data sets measure opioid misuse, we are also interested in opioid use (or general access). Unfortunately, these data are difficult to find at the state-level. However, information on the supply of opioids by drug type through legitimate medicinal channels, one measure of access to opioids, is captured and reflected in the Drug Enforcement Administration's (DEA) Automation of Reports and Consolidated Orders System (ARCOS). The Controlled Substance Act of 1970 requires all manufacturers and distributors to report their transactions and deliveries of all Scheduled II-V substances to the Attorney General. ARCOS is the system that monitors and records the flows of these controlled substances as they move from manufacturers to retail distributors at the local level (down to the street address and zip code). The data include drug purchases across states by a number of specific business activities, including pharmacies, hospitals, practitioners, mid-level practitioners and teaching institutions. However, public data are only available aggregated to the state level.

We received these data by quarter, year, drug type, and state for the years 2000-2011 on all substances. Following prior work, we constructed morphine-equivalent doses of the 8 most commonly abused opioid analgesics (Paulozzi et al., 2011; Paulozzi and Ryan, 2006): fentanyl, hydrocodone (Schedule III), hydromorphone, meperidine, methadone distributed through narcotics treatment programs; methadone distributed through other outlets as an analgesic, morphine, codeine and oxycodone (as OxyContin as well as in other forms). Total grams distributed per capita were converted to morphine equivalent doses drawing on standard multipliers used in this literature (Paulozzi, Kilbourne

[3] See http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6226a3.htm.

and Desai, 2011; Gammaitoni et al., 2003) and aggregated by state and quarter-year. The outcome variable is morphine-equivalent doses of opioid analgesics.

Information on state medical marijuana laws were obtained via original legal research of state statutes and regulations as part of a series of projects funded by the National Institute on Drug Abuse and the Robert Wood Johnston Foundation over the past decade (Chriqui et al., 2002; Pacula, et al., 2002; Pacula et al., 2014). Not all medical marijuana laws are alike and recent evidence suggests that an indicator of "medical marijuana law" adoption does not adequately capture the different features of these laws that can impact behavior (Sevigny et al., 2014; Pacula et al., 2014 and 2015). Thus, our main analysis focuses on the crucial determinant of access to marijuana – whether the law legally protects medical marijuana dispensaries, retail shops that sell marijuana to qualified buyers. We also study effects in states with "active dispensaries," i.e., states with legal or illegal dispensaries but not states that legally protect dispensaries but do not have any in operation. These come from a comprehensive media search of major newspapers in each state for stories mentioning the operation of a cooperative or dispensary. Finally, we estimate effects for states with dispensaries that are both legal *and* active since these are likely to provide greatest access.

III. Descriptive Patterns

To set the stage for our empirical analysis, we begin with a visual display of the trends in our data sources. In Figure 1, we graph the growth in pain reliever substance abuse treatments, opioid-related mortality, and opioid distribution for the respective available years in the data. We normalize all trends to 100 in year 2000. We observe the dramatic increases in opioid use and abuse over this time period in our data. From 2000 to 2012, opioid substance abuse more than quadrupled. Mortality and distribution more than tripled.

We also graph the normalized trends in pain reliever treatments, marijuana treatments, and total treatments for the purposes of comparison in Figure 2. While treatment admissions involving pain

relievers rose tremendously over this period, this rapid growth has not been matched by treatments for any other substance.

Figure 3 graphs trends in opiate treatment admissions by year of adoption of dispensaries, both by the legal date of adoption and the year of the first active dispensary. The listed year of adoption is the first full year of adoption so a partial effect may be observed in the year "prior" to adoption. We do not see any clear consistent patterns in terms of adopting states (or states with active dispensaries) and opioid treatment admissions, although states with active dispensaries have generally lower growth in admissions than the non-adopting states from 2000 forward. Importantly, differential pre-policy trends in treatment admissions across adopting and non-adopting states/states with and without active dispensaries suggest that standard difference in differences methods, which assume parallel trends, may not be appropriate for our analysis. We will address this in our analysis by estimating synthetic control models in addition to more standard difference in differences models.

Figure 4 shows the trend in opioid-related deaths from 1999 to 2013 by medical marijuana dispensary adoption year. Again, we cannot observe any clear differences in trends between non-adopting and adopting (or active) states. Moreover, we see that adopting states appear to be on different trends from the start of the sample period, motivating our use of methods to account for differential trends.

We graph trends in amount of morphine equivalent doses of opioid analgesics distributed to a state by medical marijuana dispensary adoption year in Figure 5. We observe less evidence of dramatic variation across states in this measure than observed for either of our abuse measures, but again we see no strong association of the state dispensary policy on opioids prescribed.

IV. Empirical Strategy

The basis of our empirical strategy is to study changes in our measures of opioid misuse in states adopting medical marijuana laws to those not adopting these laws. We use the timing of adoption of

the marijuana policy for identification. We rely on two complementary methods: (1) a difference-in-differences strategy that uses non-adopting states as controls and differential timing of adoption to estimate the effect and, (2) a synthetic control group strategy that uses a weighted average of all non-adopting states in a "donor pool" of states as controls, with the weights empirically constructed based on the values of covariates and pre-adoption values of the outcome variable (described more below). We adopt the latter approach because of the concern (discussed above) that non-adopting states are not appropriate controls for medical marijuana states. Specifically, they may violate the parallel trends assumption central to a valid difference-in-differences research design, as suggested in Figures 3 and 4.

Our first approach, the traditional difference-in-differences framework, compares changes in outcomes within adopting states to that in non-adopting states. We implement this strategy by including state fixed effects and year fixed effects in the following exponential specification:

$$(1) \qquad y_{st} = exp(\alpha_s + \gamma_t + X'_{st}\beta + MML'_{st}\delta)\eta_{st}$$

where y_{st} represents one of our outcomes for state *s* at time *t*. Although we could estimate a log-linear specification using ordinary least squares, we follow Silva and Tenreyro (2006), which shows that a log-linear specification imposes a multiplicative error term in y while Poisson estimation of an exponential relaxes this assumption, allowing both multiplicative and additive error terms. We also control for time-varying state covariates. We include demographic measures that have been shown to be associated with prescription drug misuse: the percentage of the state population that is male, the percent white, and the age distribution within the state (CDC, 2011b). In addition, we control for the state unemployment rate, which might influence access to insurance/ability to pay for prescription drugs, the state alcohol tax (a potential substitute), and the log of the population. The vector MML represents our two alternative indicators for state medical marijuana laws: any law and a law allowing marijuana dispensaries. Table 1 provides descriptive statistics on our covariates and outcomes.

Nineteen states had operational prescription drug monitoring program (PDMPs) during 1999-2005, but by 2011 nearly all the states had a PDMP. Recent studies find little effect of these laws using similar analytic approaches (Brady et al., 2014; Paulozzi et al., 2011). We instead use in our analyses three specific measures from LawAtlas indicating how aggressive a state's PDMP is in keeping tabs on opioid prescriptions, namely (1) whether a state had a "proactive PDMP", requiring that the state generate and distribute reports to prescribers, dispensers, or law enforcement authorities without being solicited, (2) "mandatory PDMP", which requires all health professionals to report their prescribing in the system, and (3) "real time PDMP," which means that the data in the system is updated at least once a week if not daily, as opposed to being updated quarterly or monthly.[4]

We will also employ a complementary event study approach to estimate lagged effects while also testing for pre-existing trends. For this approach, we estimate equation (1) while allowing for differential effects based on the time relative to adoption. We will include seven indicators per MML dimension, representing 3 years or more before adoption, 2 years prior to adoption, 1 year prior to adoption, year of adoption, 1 year after adoption, 2 years after adoption, and 3 or more years after adoption. As before, we use the first full year of implementation as the year of adoption so it is possible that we should observe a partial effect in the year prior to adoption. We include these seven indicators for each dimension and estimate the event studies for medical marijuana laws and dispensaries jointly.

Our second analytic approach uses the synthetic control group method introduced and developed in Abadie and Gardeazabal (2003); Abadie, Diamond, and Hainmueller (2010); Abadie, Diamond, and Hainmueller (2014). This approach creates weights for each state in the "donor pool" and the weighted average of the outcome variable in the post-period acts as the counterfactual trend that would have been observed for the adopting state. Fixed effect models are equivalent to de-meaning the outcome and explanatory variables in each year, assuming that the average in which each state is

[4] Data available at: http://lawatlas.org/query?dataset=corey-matt-pmp. Last accessed January 30, 2015

given equal weight is an appropriate comparison for the treated states. Synthetic controls models permit different (non-equal) weights to be used to create a "synthetic control" which is more similar to the treated state.

Z_1 is a vector containing all covariates and year-by-year values of the outcome variable for the pre-treated period. Z_0 is a matrix containing the exact same variables for each state in the donor pool. The synthetic control approach creates weights *W* using

$$\widehat{W} = \text{argmin}_W \ \left\| Z_1 - Z_0^{'} \ W \right\|_V$$

$$\text{subject to } w_j \geq 0 \text{ for all } j \text{ and } \sum_j w_j = 1$$

where *W* is a matrix composed of weights represented by w_j. The state-specific weights are constrained to be non-negative. The synthetic control approach is designed to find w_j for all donor states such that $y_{0t} \approx \sum_j w_j y_{jt}$ in the pre-treatment periods. The estimate for each adopting state *i* can be written as the average outcome in the post-adoption period relative to the outcome of the synthetic control:

(3) $$\hat{\beta}_i = \frac{1}{T - T_0} \sum_{t > T_0} \left(y_{it} - \sum_j \hat{w}_j y_{jt} \right)$$

While the synthetic control approach is intended for use when one state adopts a policy, we observe multiple states during our time period adopting medical marijuana laws. To aggregate the estimates, we use

(4) $$\hat{\beta} = \text{argmin}_\beta \sum_{s,t} \left\| y_{st} - \beta(MML_{st}) - \sum_j w_{jt}^s y_{jt} \right\|_V$$

In words, we choose the estimate on the medical marijuana law dummy that minimizes the mean squared error. The synthetic control approach assumes that some weighted average of states in the donor pool can act as an appropriate control for the treated state. This assumption is testable both through visual inspection of the pre-treatment period and through goodness-of-fit measures. *V*

represents a weighting matrix including the inverse of the mean variance in the pre-period such that we downweight states in which the synthetic control is a poor fit and more heavily-weights states in which the synthetic control is a good fit. We also weight by population.

For inference, we adopt and extend the placebo test method suggested in Abadie and Gardeazabal (2003). With one treated state, the idea is to simulate the distribution of estimates under the null hypothesis that there is no effect. This inference approach is implemented by repeating the synthetic control approach for each state in the donor pool, assigning the same year of adoption in each case. The original treated state is assigned to the donor pool. For each state in the donor pool *j,* we obtain a placebo estimate for that state, $\hat{\beta}_i^j$. This approach allows one to simulate the distribution that would be observed randomly and one can compare the true estimate with these placebo estimates. We calculate p-values using

$$\frac{1}{J+1}\sum_{j=1}^{J} 1(|\widehat{\beta}_\iota| > |\hat{\beta}_i^j|) \quad (5)$$

With multiple treated states, we calculate our estimates (equation (4)) as above and simulate the distribution of these estimates. For these simulations, we randomly select a state from the donor pool and assign it the adoption year of California. We then randomly select another state (without replacement) and assign it the adoption year of New Mexico. We do this for all adopting states and obtain a counterfactual estimate of the overall effect. The distribution of these counterfactual estimates provides us with a p-value, comparing the absolute value of our estimated effect to the simulated distribution of the absolute value of the placebo effects. Given the large number of possible combinations, we randomly generate 1000 estimates of the overall effect to simulate the distribution.

In our synthetic control analyses, we first estimate the effect of adoption of any type of medical marijuana law, including all other states in the donor pool. We subsequently estimate the effect of adoption of legal medical marijuana dispensaries using the same donor pool (i.e., we do not include

medical marijuana states without dispensaries in the donor pool[5]). The outcome variables for all synthetic control analyses are expressed per capita.

We will also use the synthetic control approach to study lagged effects in a manner parallel to the event study estimation discussed above. The case study synthetic control method allows for the estimate to vary throughout the post-period. It is straightforward to extend equation (4) to allow for this heterogeneity as well and we will present some results where we estimate effects for first full year of adoption, second full year of adoption, and third (and after) full year of adoption. The synthetic control approach should eliminate any pre-trends so we do not present separate estimates for years prior to adoption. As expected, these pre-adoption year estimates are all statistically insignificant and close to zero.

V. **Results**

V.A. The Availability of Medical Marijuana on Measures of Opioid Harm

We present our main difference-in-differences estimates for pain reliever treatment admissions from the TEDS data in Table 2. We find no statistically significant relationship between medical marijuana laws and pain reliever substance abuse treatments. However, we find statistically significant effects for medical marijuana laws with dispensaries at the 10% significance level. We estimate an effect of -0.170 which implies a reduction in substance abuse of 15.6%.[6] When we exclude criminal justice referrals, we estimate an effect of -0.187 (a 17.1% reduction) and we can reject a null effect at the 5% significance level.

We find little evidence that "active" dispensaries have any effect on opioid abuse. However, we find even larger effects when we study active, legal dispensaries, consistent with our hypothesis that we should expect greater substitution away from opioids towards marijuana in states where access to

[5] Given that we are first testing whether medical marijuana laws without dispensaries have effects, these states are potentially "treated."
[6] The percent reduction is 100*(exp(-.170)-1)%=-15.6%.

marijuana is easiest (both legally and practically). The estimates for these states imply reductions of 28% in opioid substance abuse treatment admissions.[7]

We disaggregate the above results further by studying the effects of medical marijuana laws and legal dispensaries by year relative to adoption. We present our event study estimates with 95% confidence intervals in Figure 6. All of the estimates presented are estimated simultaneously. The estimates for medical marijuana laws are shown in the figure on the left while the dispensary effects are shown in the figure on the right. We observe that the effect of both medical marijuana laws and dispensaries grows over time. By the second year after adoption, dispensaries have a statistically significant effects on opioid substance abuse treatments. We also estimate statistically significant effects for medical marijuana laws more generally for 3+ years after adoption.

Our event study results provide little evidence that pre-trends are driving our results. However, Figure 3 shows that the "parallel trends" assumption may not hold in this context so we implement the synthetic control estimator to further test the robustness of our findings. Each cell in Table 3 represents the estimate from a separate synthetic control regression. We first study the relationship between any MML law and treatment admissions for pain medication using synthetic control methods. Because of the large number of MML adopting states, we present only the overall effects (findings for individual states are provided in the appendix (see the first column of Table A2). We find little evidence of a relationship between MML and treatments. When we focus on legal protection of dispensaries, we find large and statistically significant effects. We estimate an effect of -0.437, corresponding to a 35% decrease in substance abuse treatment admissions. When we exclude criminal justice referrals, we

[7] In states that were the first to adopt laws legally protecting medical dispensaries (CO and CA), dispensaries were already open and active BEFORE the legal protection was provided. In later adopting states, particularly those adopted after the 2009 Ogden Memo, it took 2-3 years for dispensaries to become active post passage of law providing legal protection.

estimate a 53% reduction. Consistent with the Table 2 results, we find especially large estimates for states with legal and active dispensaries.

Next we examine whether medical marijuana laws influenced opioid-related mortality. Given that our panel only begins in 1999, we lose several states as treated states when we examine adoption of any medical marijuana law because these states adopted policies prior to 1999. However, when we look at adoption of an allowance for legal medical dispensaries, we study the same states as before since these policies were adopted much later.

In Table 4, we present the difference-in-differences results. As before, we observe no relationship between general medical marijuana laws and opioid-related deaths, but we do find such a relationship for legal dispensaries. Our estimate of -0.173 in the final column is statistically significant from 0 at the 1% level and implies a reduction in opioid-related deaths of 16 percent. We estimate even larger effects for active dispensaries and active, legal dispensaries. The evidence in Table 4 is relatively consistent that dispensaries reduce opioid-related deaths.

As before, we can estimate lagged effects and test for the importance of confounding trends through an event study. We present the results of our event study analysis in Figure 7. We find little evidence of any effects for medical marijuana laws generally. However, we find further supportive evidence of large mortality effects for dispensaries. By the first year after adoption, we estimate statistically significant effects. We can reject the null hypothesis of no effect for 2 years post-adoption and 3+ years after adoption as well.

The trends in Figure 4 suggest that fixed effect regression techniques may not be appropriate in this context either so we apply the synthetic control approach here as well. Table 5 presents the overall estimates from the synthetic control model examining the relationship between medical marijuana laws and the log of per capita opioid-related deaths. As before, we find estimates larger in magnitude when the synthetic control approach is used to estimate the impact of dispensaries on opioid abuse. For legal

dispensaries, we estimate a significant (at the 10% level) effect of -0.368, which translates to a 31% reduction in opioid overdoses; the precision increases (p-value of 0.069) when we consider legal plus active dispensaries. Overall, we find strong, consistent evidence that medical marijuana dispensaries lead to reductions in opioid-related mortality.

V.B. Medical marijuana laws on measures of opioid distribution

While we have found evidence that medical marijuana dispensaries reduce opioid abuse, as measured by treatment admissions and possibly opioid overdose deaths, we know very little about the mechanism driving this result. To shed some light on mechanisms, we consider the distribution of opioid analgesic medications to legal medical markets using the ARCOS data. Table 6 presents the results for morphine equivalent doses of our 8 primary opioids of abuse pooled together. We estimate that legal dispensaries reduce opioid distribution to the state by over 4%. We also find that medical marijuana laws in general are associated with *increases* in opioid distribution.

Our synthetic control estimates do not confirm either of these relationships, however. Furthermore, our event study analysis does not suggest any significant effects either. In Figure 8, we show the corresponding event study graphs. We find no statistical relationships between our time-relative-to-adoption indicators and legal distribution. In Table 7, we present results from our synthetic control models and find little evidence that medical marijuana laws, even those which legalized dispensaries, have any effect on the distribution of legal opioids to a state. This result suggests that medical marijuana laws do not alter legal opioid access, implying that the opioid abuse increases are resulting from illegal, nonmedical acquisition of opioids.

V.C. Synthetic Control Estimates of Lagged Effects

In Figures 6 and 7, we presented evidence that the impact of legal dispensaries on opioid treatment admissions and mortality grows in magnitude over time. This trend is consistent with medical

marijuana markets growing over time after legalization and the lagged impact of misuse on treatments and deaths. We further study this source of heterogeneity by disaggregating our synthetic control results by time relative to adoption. We present estimates for all of our outcomes in Table 8.

In the first column, we show estimates for substance abuse treatments. The estimate does grow in magnitude over time, though we cannot statistically reject zero when disaggregating the overall effect in this manner. The mortality effects for dispensaries also grow in magnitude over time relative to adoption. The effect is largest and statistically significant from zero for 3+ years after adoption. We also estimates a positive effect for medical marijuana laws more generally, which we did not observe in any prior analysis. We cannot reject the null hypothesis that medical marijuana laws are not associated with any differences in legal distribution of opioids.

Consistent with the results in Section V.B., we find little evidence of effects on legal distribution of opioids (the last column in Table 8). Even 3+ years after adoption, we estimate a small and positive effect of dispensaries on legal opioid distribution.

V.D. Heterogeneous Effects by Demographics

While more men die annually from drug overdoses, women have experienced a larger increase in overdose deaths than men since 1999 (CDC, 2013b). Similarly, people ages 18-25 are most likely to use opioids recreationally, but "middle age is the most vulnerable time for opioid overdoes" (Webster et al., 2011). Consequently, we might expect medical marijuana access to have differential effects on opioid abuse by sex and age.

We replicate our synthetic control results for legal dispensaries, selecting on age and sex. We present results for substance abuse treatment admissions and opioid-related mortality in Table 9. In the case of treatment admissions, we find a robust effect of our legally protected dispensary variable on both men and women as well as young and old. However, we find stronger effects for women than men, which would suggest that woman are even more likely than men to switch to marijuana from

opioids. Similarly, we see much stronger effects on treatment admissions for the older group than the younger group, again suggesting that these policies are having the greatest effect on the groups experiencing the greatest harms from opioid abuse.

However, when we look at the mortality data, we do not see the same patterns. To the contrary, while we find a negative relationship that is marginally significant between the dispensary variable and male mortality, we find no relationship at all between this policy and mortality by women, even though they are the group that has experienced the greatest increase in mortality and our previous result of a large effect on treatment admissions. The effects across age groups (less than 40 and 40+) are relatively uniform too, contrary to our findings on treatment admissions.

VI. Discussion

Considerable attention has been paid in the literature to the potential unintended consequences of medical marijuana laws, with people examining impacts of these policies on youth initiation, recreational marijuana use and abuse as well as drunk driving (Wen et al., 2015; Choi, 2014; Lynne-Landsman et al., 2013; Anderson, Hanson and Rees, 2012 & 2013; Pacula et al., 2013). In this paper we consider a potential unintended benefit of these laws: a reduction in the misuse of prescription opiates.

Our results are intriguing in that we find fairly strong evidence using both difference-in-differences and synthetic control group methods that states providing legal access to marijuana through dispensaries experience lower treatment admissions for addiction to pain medications. We provide complementary evidence that dispensary provisions also reduced deaths due to opioid overdoses. Our estimates are robust to advanced methods that account for differential trends across adopting and non-adopting states. We estimate even larger effects in states that have both legally protected and active dispensaries, further supportive evidence that legal access to medical marijuana substitute for opioid use. The mechanism for this remains a bit unclear, however. We see from the ARCOS data that there is

no effect of these dispensaries on the distribution of opioids through medical channels, suggesting that much of this switch may be driven by the behavior of people using opioids illegally. When we look at treatment admissions data, it appears that women and those over the age of 40 (the two groups for which opioid related deaths have risen the most) are even more affected than men and youth in terms of their responsiveness to this policy. However, we see no similar association between these laws and opioid related mortality by women or differential mortality by age.

These results differ in a few important ways from a prior study showing that medical marijuana laws are negatively associated with opioid-related mortality (Bachhuber et al., 2014). First, we have extra years of data (2011-2013) in which to look for mortality effects, with new states adopting policies during the window of analysis. Second, we account for a unique feature of medical marijuana laws, dispensaries or retail stores, that has been shown to have a direct impact on marijuana use, particularly among adults, and is associated with higher potency (THC/CBD) of marijuana (Sevigny et al., 2014). For many states, policies providing legal protection of dispensaries lagged behind the initial medical marijuana policy, and hence the lagged effects observed in Buchhuber et al (2014) might in fact simply reflect the impact of particular states subsequently providing legal protections to dispensaries (see Table A1 to identify those states). Finally, unlike the prior study, we explicitly test the robustness of our findings in two important ways. We look for consistency in our findings in another measure of opioid abuse (treatment admissions) that is less rare, and hence less sensitive to large outliers. We also consider the influence of pre-policy trend differences in biasing the magnitude of results by using synthetic cohort methods.

The fact that opioid harms decline in response to medical marijuana dispensaries raises some interesting questions as to the extent to which marijuana liberalization policies are potentially beneficial for public health. Marijuana is a far less addictive substance than opiates and the potential for overdosing is nearly zero (Hall and Pacula, 2003). However, it remains unclear from our current analysis

whether the findings we observe are short term or will persist. In addition, we ultimately need to weigh any potential indirect benefits from medical marijuana dispensary provisions in terms of its implied reductions in opiate misuse (or other positive outcomes) against any potential negative impacts of these provisions on other factors, such as drugged driving.

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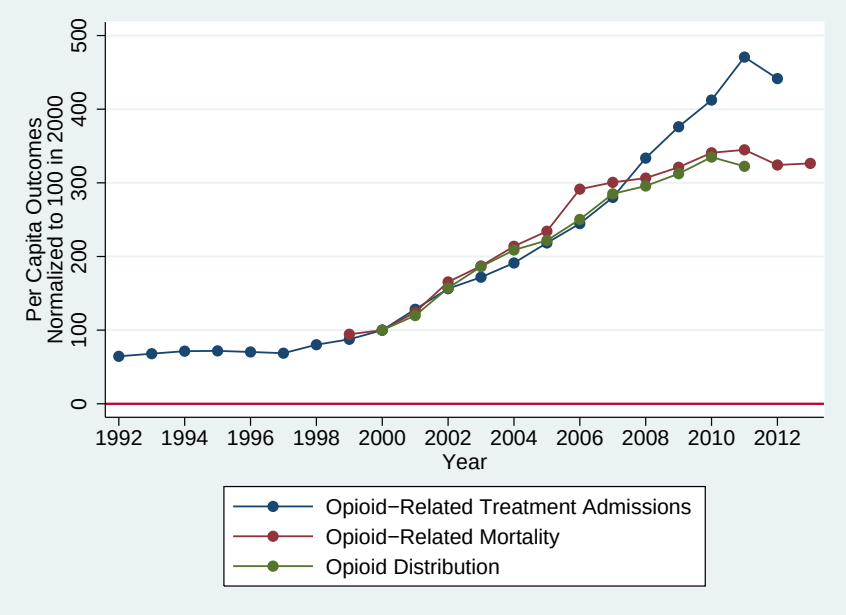
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Figures

Figure 1: Opioid Abuse and Distribution Trends



Notes: Treatment Admissions from TEDS (1992-2012) using only states which report in each year.
Mortality trends from NVSS (1999-2013).
Distribution trends from ARCOS data (2000-2011).

Figure 2: Substance Abuse Treatments Trends by Substance

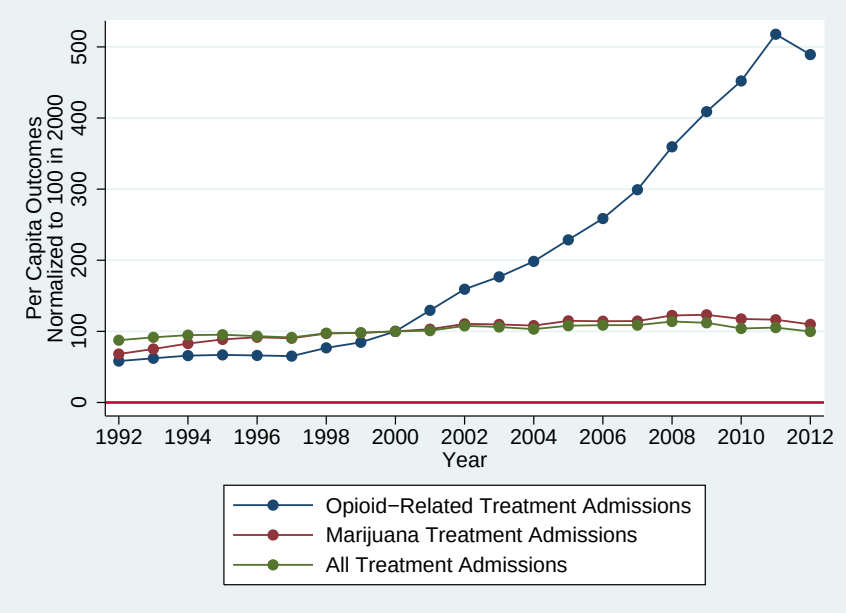
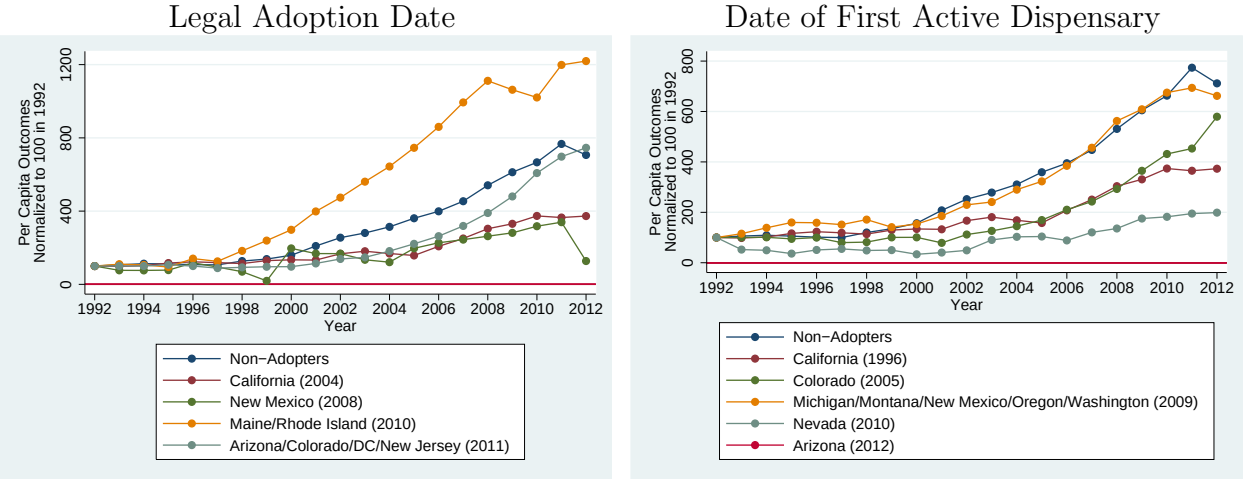
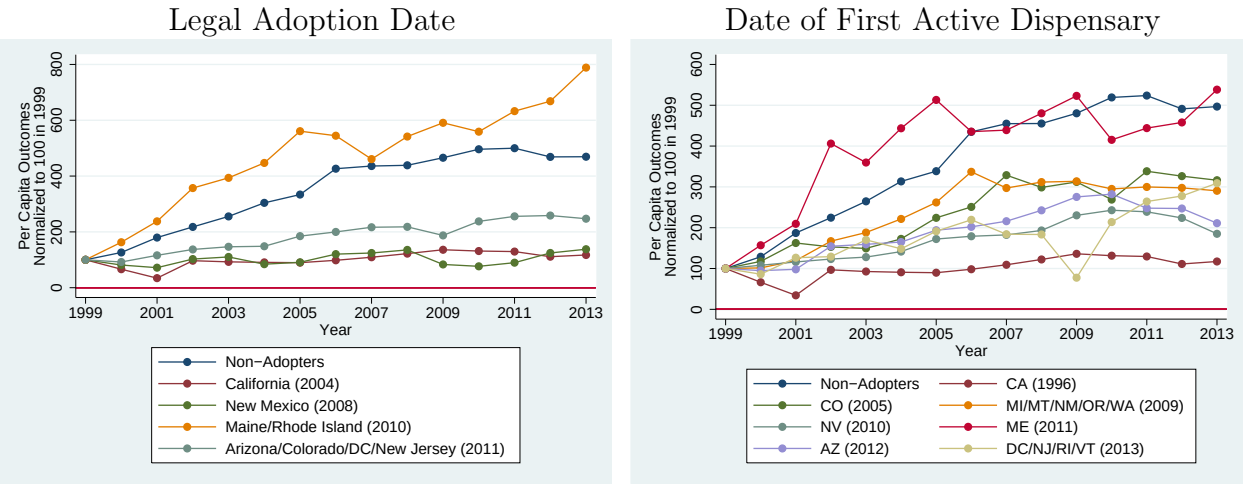


Figure 3: Substance Abuse Treatment Admission Trends by Dispensary Adoption Year



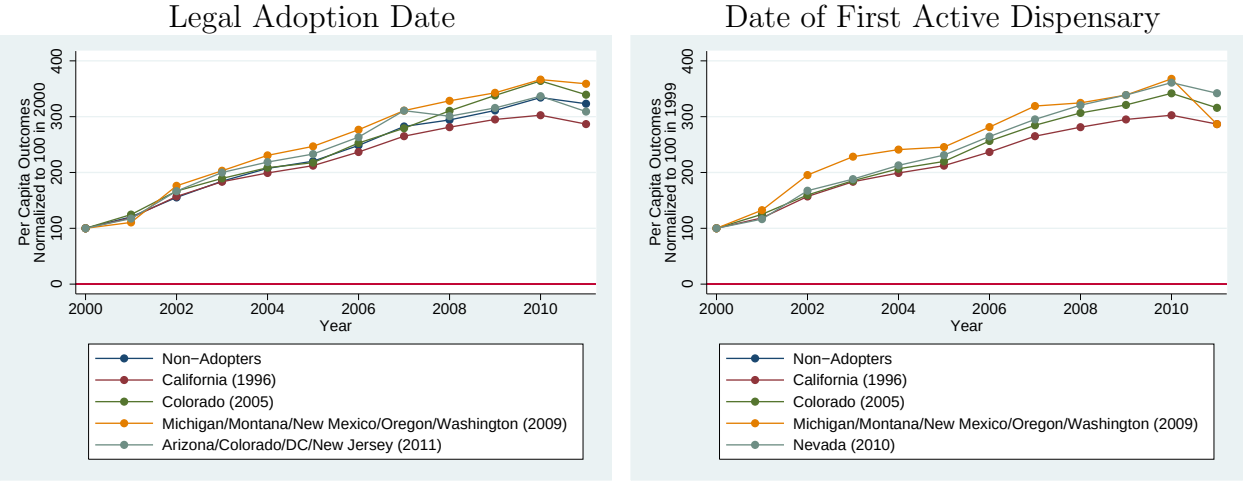
Notes: Dates in parentheses refer to first full year of medical marijuana dispensaries.

Figure 4: Opioid-Related Mortality Trends by Dispensary Adoption Year



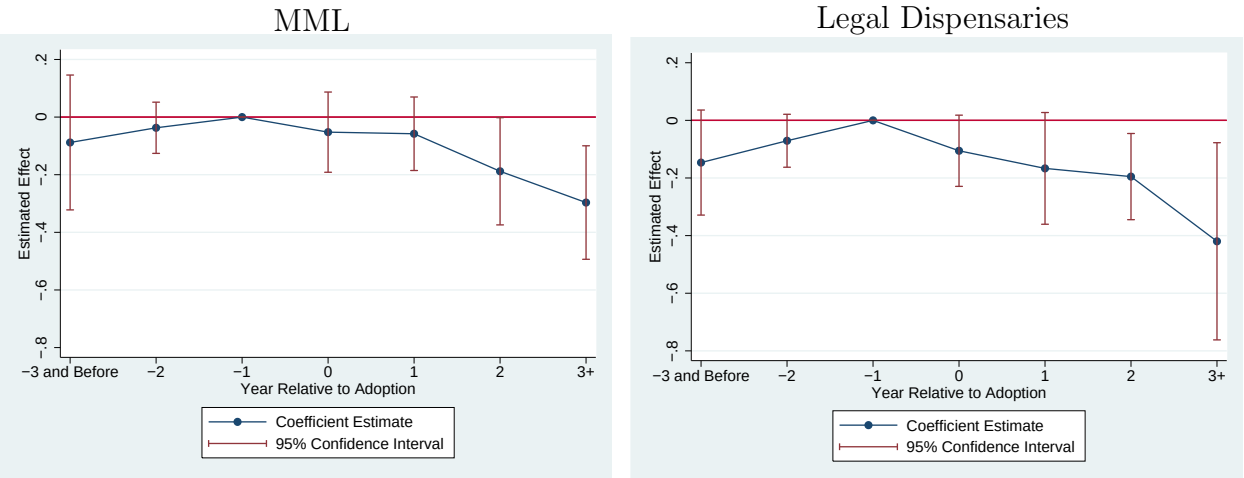
Notes: Dates in parentheses refer to first full year of medical marijuana dispensaries.

Figure 5: Opioid Distribution by Dispensary Adoption Year



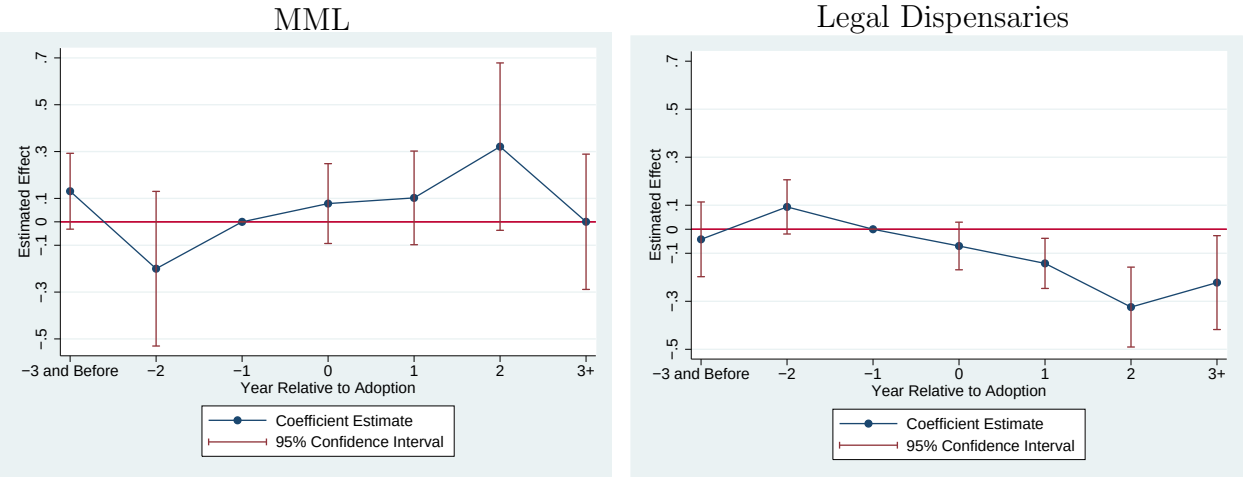
Notes: Dates in parentheses refer to first full year of medical marijuana dispensaries.

Figure 6: TEDS Event Study Results



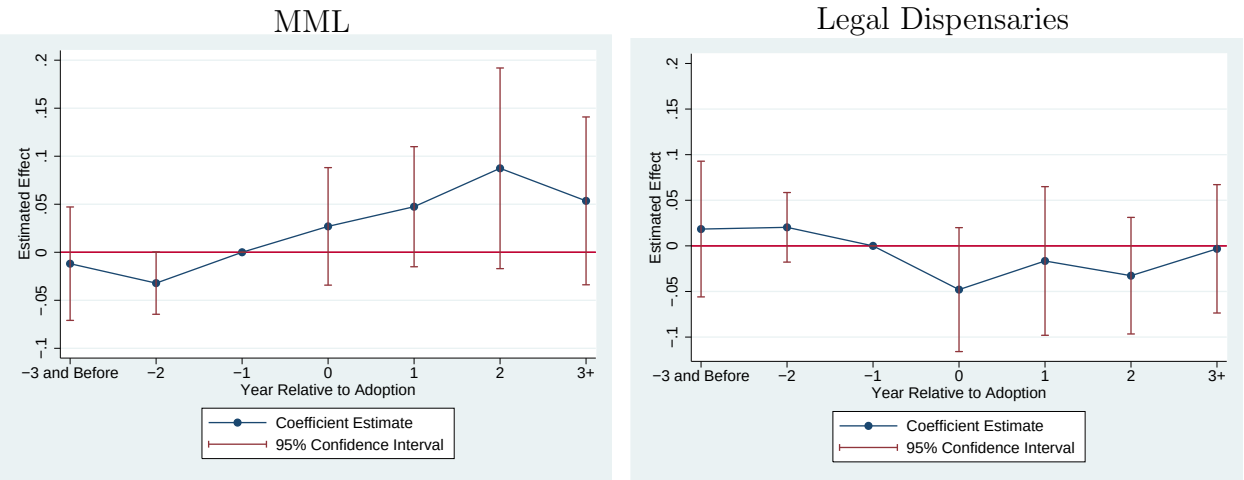
Notes: Estimates in both figures are simultaneously estimated. Year 0 represents first *full* year of adoption so a partial effect for the prior year (-1) may be expected.

Figure 7: Mortality Event Study Results



Notes: Estimates in both figures are simultaneously estimated. Year 0 represents first *full* year of adoption so a partial effect for the prior year (-1) may be expected.

Figure 8: Distribution Event Study Results



Notes: Estimates in both figures are simultaneously estimated. Year 0 represents first *full* year of adoption so a partial effect for the prior year (-1) may be expected.

Tables

Table 1: Summary Statistics

Variable	Mean
Pain Reliever Substance Abuse Treatments (per 10,000)	4.26
Excluding Criminal Justice Referrals	3.35
Opioid-Related Deaths per 100,000	4.11
Morphine-Equivalent Opioid Distribution Per Capita	0.25
Unemployment Rate	6.1
Beer Taxes (cents)	24.7
Any PMP Law	42.7%
Prescriber Responsibility	25.4%
Real Time	12.7%
Proactive Responsibility	4.7%

Notes: All variables refer to state-years in TEDS (1992-2012), except for mortality (1999-2013) and distribution (2000-2011).

Table 2: TEDS Results: Poisson Estimates

Outcome	Opioid Treatment Admissions					
	Full Sample			Excluding Criminal Justice Referrals		
MML	-0.043	-0.045	-0.079	-0.067	-0.063	-0.104
	(0.117)	(0.095)	(0.101)	(0.114)	(0.097)	(0.099)
Legal Dispensaries	-0.170*			-0.187**		
	(0.098)			(0.092)		
Active Dispensaries		-0.071			-0.083	
		(0.108)			(0.104)	
Legal and Active			-0.319***			-0.332***
			(0.090)			(0.098)
PMP Prescriber Data	0.039	0.023	0.056	0.032	0.013	0.049
	(0.066)	(0.060)	(0.069)	(0.071)	(0.063)	(0.074)
PMP Proactive	0.015	-0.012	-0.005	-0.055	-0.087	-0.077
	(0.126)	(0.121)	(0.125)	(0.141)	(0.134)	(0.139)
PMP Real Time	-0.057	-0.059	-0.045	-0.03	-0.033	-0.017
	(0.091)	(0.086)	(0.090)	(0.100)	(0.094)	(0.099)
N	1021	1021	1021	1021	1021	1021

Notes: Significance Levels: *10%, **5%, ***1%. Standard errors in parentheses adjusted for clustering at state-level. Covariates include age distribution, % male, unemployment rate, alcohol taxes, log of the population.

Table 3: Synthetic Control Estimates for Treatment Admissions

log(Per Capita Opioid Treatment Admissions)		
	All	Non-CJ
MML	-0.235	-0.375
	[0.524]	[0.259]
Legal Dispensaries	-0.437	-0.749***
	[0.191]	[0.006]
Active Dispensaries	-0.280	-0.517
	[0.486]	[0.255]
Legal and Active	-0.500	-0.805***
	[0.115]	[0.006]

Notes: Significance Levels: *10%, **5%, ***1%. P-values in brackets calculated using placebo tests. Synthetic controls calculated using pre-treatment outcomes for each pre-treatment year and mean of covariates (age distribution, % male, unemployment rate, alcohol taxes, log of the population). "Donor pool" includes states which never adopt any medical marijuana law. Only states which report in each year of TEDS (1992-2012) included. Each estimate in the table is derived from a separate synthetic control regression.

Table 4: Mortality Results: Poisson Estimates

Outcome	Opioid-Related Mortality		
MML	0.087	0.163	0.053
	(0.116)	(0.102)	(0.106)
Legal Dispensaries	-0.173***		
	(0.063)		
Active Dispensaries		-0.236***	
		(0.090)	
Legal and Active			-0.178***
			(0.064)
PMP Prescriber Data	-0.057	-0.090**	-0.054
	(0.039)	(0.041)	(0.040)
PMP Proactive	-0.01	-0.032	-0.029
	(0.090)	(0.107)	(0.098)
PMP Real Time	0.003	0.012	0.006
	(0.039)	(0.042)	(0.039)
N	765	765	765

Notes: Significance Levels: *10%, **5%, ***1%. Standard errors in parentheses adjusted for clustering at state-level. Covariates include age distribution, % male, unemployment rate, alcohol taxes, log of the population.

Table 5: Synthetic Control Estimates for Mortality

log(Per Capita Opioid-Related Deaths)	
MML	0.274*
	[0.054]
Legal Dispensaries	-0.368*
	[0.083]
Active Dispensaries	-0.012
	[0.927]
Legal and Active	-0.396*
	[0.069]

Notes: Significance Levels: *10%, **5%, ***1%. P-values in brackets calculated using placebo tests. Synthetic controls calculated using pre-treatment outcomes for each pre-treatment year and mean of covariates (age distribution, % male, unemployment rate, alcohol taxes, log of the population). "Donor pool" includes states which never adopt any medical marijuana law. Each estimate in the table is derived from a separate synthetic control regression.

Table 6: ARCOS Results: Poisson Estimates

Outcome	Total Opioid Distribution		
MML	0.053**	0.040	0.039
	(0.027)	(0.034)	(0.030)
Legal Dispensaries	-0.047*		
	(0.027)		
Active Dispensaries		-0.002	
		(0.036)	
Legal and Active			-0.028
			(0.030)
PMP Prescriber Data	0.092***	0.085***	0.089***
	(0.024)	(0.024)	(0.024)
PMP Proactive	0.025	0.025	0.023
	(0.020)	(0.020)	(0.021)
PMP Real Time	-0.072**	-0.071**	-0.071**
	(0.030)	(0.030)	(0.030)
N	612	612	612

Notes: Significance Levels: *10%, **5%, ***1%. Standard errors in parentheses adjusted for clustering at state-level. Covariates include age distribution, % male, unemployment rate, alcohol taxes, log of the population. Outcome variable is translated into morphine equivalent units.

Table 7: Synthetic Control Estimates for Distribution

log(Per Capita Opioid Distribution)	
MML	-0.027
	[0.712]
MML, Dispensaries	0.034
	[0.747]
Active Dispensaries	0.06
	[0.335]
Legal Plus Active	0.043
	[0.700]

Notes: Significance Levels: *10%, **5%, ***1%. P-values in brackets calculated using placebo tests. Synthetic controls calculated using pre-treatment outcomes for each pre-treatment year and mean of covariates (age distribution, % male, unemployment rate, alcohol taxes, log of the population). "Donor pool" includes states which never adopt any medical marijuana law. Each estimate in the table is derived from a separate synthetic control regression.

Table 8: Synthetic Control Event Study Estimates

	Treatments		Deaths		Distribution	
	MML	Dispensaries	MML	Dispensaries	MML	Dispensaries
1st Full Year	-0.157	-0.356	0.15	-0.057	0.011	0.066
	[0.611]	[0.164]	[0.607]	[0.900]	[0.853]	[0.442]
2nd Full Year	-0.229	-0.511	0.179	-0.256	-0.015	0.078
	[0.552]	[0.101]	[0.608]	[0.406]	[0.839]	[0.511]
3+ Years	-0.262	-0.502	0.443***	-0.641***	-0.050	0.037
	[0.531]	[0.155]	[0.001]	[0.001]	[0.669]	[0.875]

Notes: Significance Levels: *10%, **5%, ***1%. P-values in parentheses generated through placebo tests.

Table 9: Heterogeneity in Dispensary Effect: Synthetic Control Estimates

Sub-Group	Men	Women	Under 40	40+
Treatment Admissions	-0.281***	-0.794***	-0.378*	-0.506***
	[0.002]	[0.001]	[0.070]	[0.004]
Mortality	-0.345*	-0.086	-0.379*	-0.365*
	[0.065]	[0.675]	[0.072]	[0.084]

Notes: Significance Levels: *10%, **5%, ***1%. P-values in brackets calculated using placebo tests. Synthetic controls calculated using pre-treatment outcomes for each pre-treatment year and mean of covariates (age distribution, % male, unemployment rate, alcohol taxes, log of the population). "Donor pool" includes states which never adopt any medical marijuana law. Each estimate in the table is derived from a separate synthetic control regression.

A Appendix Tables

Table A1: Summary of Assumptions Regarding Effective Dates for State Medical Marijuana Laws and Legally Protected Dispensaries During our Study Period 1992-2013~~1~~

State	Medical MJ Enactment Date	Medical MJ Effective Date	MJ Dispensary Legally Protected? (Year Dispensaries Became Legally Protected and Were Open)
Alaska	11/3/1998	3/4/1999	No
Arizona	11/2/2010	12/14/2010	Yes (2011)
California	11/8/1996	2/3/1997	Yes (2004)
Colorado	11/7/2000	12/31/2000	Yes (2001)
Delaware	5/13/2011	5/13/2011	Yes (NA)
Washington DC	5/21/2010	7/27/2010	Yes (NA)
Hawaii	6/14/2000	6/14/2000	No
Maine	11/22/1999	12/23/1999	Yes(2010)
Maryland	5/22/2003	10/1/2003	No
Michigan	11/4/2008	12/4/2008	No
Montana	11/2/2004	11/2/2004	No
Nevada	6/14/2001	10/1/2001	No
New Jersey	1/18/2010	7/1/2010	Yes(2011)
New Mexico	4/3/2007	7/1/2007	Yes(2008)
Oregon	12/3/1998	12/3/1998	Yes(NA)
Rhode Island	1/3/2006	1/3/2006	Yes(2010)
Vermont	5/26/2004	7/1/2004	Yes (NA)
Washington	11/3/1998	12/3/1998	No

Note: States that adopted medical MJ policies outside of our time period are treated as "control states", including MA (2012), IL (2013), New York (2014) and Maryland (2014). In some instances, dispensaries were legally allowed in subsequent state policies that fell outside of our evaluation window (e.g. Vermont and Oregon). In other cases, the state policy that passed medical marijuana did not provide immediate legal protection for dispensaries (as they had to go through a particular process (e.g. DC), or they emerged in subsequent law (e.g. CA). Thus, and "NA" in the third column indicates that the dispensaries that were permitted by the policy were provided legal protection outside of our study period.

Table A2: State-by-State Dispensary Estimates

	TEDS	Mortality	Distribution
Arizona	n/a	-0.198	-0.113
p-value		[0.500]	[0.229]
pre-treated squared error		0.198	0.005
California	-0.505	-0.514	-0.240
p-value	[0.208]	[0.125]	[0.143]
pre-treated squared error	0.172	1.466	0.576
Colorado	-0.123	-0.076	0.060
p-value	[0.667]	[0.750]	[0.514]
pre-treated squared error	0.388	0.040	0.001
DC	n/a	0.585	-0.109
p-value		[0.125]	[0.200]
pre-treated squared error		3.730	0.153
Maine	0.981**	-0.147	-0.022
p-value	[0.042]	[0.563]	[0.857]
pre-treated squared error	8.9	0.314	0.006
New Jersey	0.235	0.382	0.035
p-value	[0.500]	[0.250]	[0.743]
pre-treated squared error	0.096	8.895	0.004
New Mexico	-0.788**	-0.215	0.098
p-value	[0.042]	[0.406]	[0.486]
pre-treated squared error	2.989	0.521	0.002
Rhode Island	0.207	0.188	-0.086
p-value	[0.500]	[0.500]	[0.457]
pre-treated squared error	2.36	0.385	0.047

Notes: Significance Levels: *10%, **5%, ***1%. P-values in brackets calculated using placebo tests. Synthetic controls calculated using pre-treatment outcomes for each pre-treatment year and mean of covariates (age distribution, % male, unemployment rate, alcohol taxes, log of the population). "Donor pool" includes states which never adopt any medical marijuana law. Each estimate in the table is derived from a separate synthetic control regression.