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# Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever



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## ABSTRACT

**Objectives:** Twenty-eight states in the U.S have legalized medical marijuana, yet its impacts on severe health consequences such as hospitalizations remain unknown. Meanwhile, the prevalence of opioid pain reliever (OPR) use and outcomes has increased dramatically. Recent studies suggested unintended impacts of legalizing medical marijuana on OPR, but the evidence is still limited. This study examined the associations between state medical marijuana policies and hospitalizations related to marijuana and OPR.

**Methods:** State-level annual administrative records of hospital discharges during 1997–2014 were obtained from the State Inpatient Databases (SID). The outcome variables were rates of hospitalizations involving marijuana dependence or abuse, opioid dependence or abuse, and OPR overdose in 1000 discharges. Linear time-series regressions were used to assess the associations of implementing medical marijuana policies to hospitalizations, controlling for other marijuana- and OPR-related policies, socioeconomic factors, and state and year fixed effects.

**Results:** Hospitalizations related to marijuana and OPR increased sharply by 300% on average in all states. Medical marijuana legalization was associated with 23% ( $p=0.008$ ) and 13% ( $p=0.025$ ) reductions in hospitalizations related to opioid dependence or abuse and OPR overdose, respectively; lagged effects were observed after policy implementation. The operation of medical marijuana dispensaries had no independent impacts on OPR-related hospitalizations. Medical marijuana policies had no associations with marijuana-related hospitalizations.

**Conclusion:** Medical marijuana policies were significantly associated with reduced OPR-related hospitalizations but had no associations with marijuana-related hospitalizations. Given the epidemic of problematic use of OPR, future investigation is needed to explore the causal pathways of these findings.

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## 1. Introduction

As voters in Arkansas, Florida, and North Dakota approved the ballots for medical marijuana legalization in November 2016 (Christensen and Senthilingam, 2016), approximately 60% of the population in the U.S. now lived in states that permitted marijuana use for medical purpose. Despite the increasing support from the public, the scientific research on the public health impacts of medical marijuana legalization has not reached a consensus. Existing evidence primarily concentrated on the changes in the prevalence of marijuana use and provided mixed findings (Sznitman and Zolotov, 2015). The use prevalence, however, is arguably

not the greatest public health concern. While occasional use is not without health risks, marijuana is most harmful to regular users and early initiators and largely harmless to most occasional users (Hall, 2009). Research on stronger indicators of adverse effects of medical marijuana legalization is needed. Given that marijuana is not directly associated with mortality (Sidney et al., 1997), hospitalization probably represents one of the most serious health consequences of marijuana, which imposes substantial economic burdens to the healthcare system and the society (Pacula et al., 2008). No previous studies have investigated how medical marijuana policies were associated with marijuana-related hospitalizations.

In parallel to the heated debate on marijuana legalization, there were overwhelming concerns about the epidemic of opioid pain reliever (OPR) abuse and overdose. In the last two decades, the mortality rate related to OPR overdose and the quantity of prescribed OPR at least quadrupled in the U.S. (CDC, 2011; Warner

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et al., 2014). In 2014, more than 14,000 deaths were related to OPR overdose (CDC, 2016). States have advocated or adopted a series of policies to combat this increasing trend, such as prescription drug monitoring programs and regulations of pain management clinics. The positive effects of these policies on reducing OPR-related outcomes were reported by some studies (Bao et al., 2016; Dowell et al., 2016; Kennedy-Hendricks et al., 2016; Lyapustina et al., 2016; Patrick et al., 2016) but not all (Li et al., 2014; Paulozzi et al., 2011).

Recent studies started to investigate whether medical marijuana legalization would have any influences on the OPR abuse and overdose epidemic. Marijuana has therapeutic effects for chronic pain (Lynch and Ware, 2015) and is being used by patients prescribed with OPR. Around 14–33% patients prescribed with OPR were screened with cannabinoid-positive results (Reisfield et al., 2009). If the patients with legitimate prescriptions for OPR were substituting OPR partially or entirely with marijuana, the increased availability of marijuana as a result of medical marijuana legalizations may reduce the risks of OPR-related health consequences. On the other hand, marijuana use for recreational purpose may serve as a gateway drug to OPR and increase the risk of OPR initiation (Hall and Lynskey, 2005). Should medical marijuana policies have any impacts on marijuana use for medical or recreational purpose, they may unintentionally lead to changes in OPR use and related hospitalizations. Four recent studies reported reduced OPR-related outcomes in association with medical marijuana legalization (Bachhuber et al., 2014; Bradford and Bradford, 2016; Kim et al., 2016; Powell et al., 2015), but the evidence is still limited.

The objective of this study is to examine the associations between medical marijuana legalization and hospitalizations related to marijuana and OPR. Using state-level administrative records of hospital discharges from 1997 to 2014, we focused on the severe health consequences of medical marijuana legalization and exploited the variations of policy implementation in different states at different times. This study is expected to add to the still-limited literature regarding the intended and unintended impacts of medical marijuana legalization and provide implications to OPR policymaking.

## 2. Material and methods

### 2.1. Data

Annual state-level hospitalization data were obtained from the State Inpatient Databases (SID), Developed for Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ), the SID provide administrative records of hospital discharges in community hospitals in participating states. The SID cover the universe of non-federal, short-term, general and other specialty hospitals, regardless of funding sources, as well as the universe of hospitalized patients, regardless of payer (AHRQ, 2016). Containing approximately 97% of all hospital discharges in a state (AHRQ, 2016), the SID offer an almost complete overview of state-level hospitalizations. The advantage of using hospitalization records is to represent objective measures that are free of self-reporting biases commonly seen in survey data.

The annual SID data were obtained between 1997 and 2014. The 14 states that did not participate in the SID as of 2014 were excluded from the study; these states were Alaska, Alabama, Connecticut, District of Columbia, Delaware, Georgia, Idaho, Louisiana, Mississippi, Montana, Ohio, Pennsylvania, South Dakota, and Virginia. We further removed 10 states (California, Illinois, Maine, Maryland, Massachusetts, Minnesota, Nevada, New Hampshire, New Mexico, and New York) from the main analysis, because they do not have full-year observations in the SID before or after implementing medical marijuana policies. The main analysis included 27 states. We

utilized all the years available in the SID for these states with the only exception of Colorado, which implemented recreational marijuana policies at the beginning of 2014. The 2014 Colorado SID data were therefore removed to avoid potential confounding from recreational marijuana legalization. The number of years that a state had the SID data available varied; on average, a state had 14 observations during the study period. There were 382 state-year observations included in the main analysis. Data availability and inclusion and exclusion of states were described in detail in the Supplementary material.

The effective dates of marijuana- and OPR-related policies were obtained from various sources of legal and policy reviews, including RAND Corporation (Pacula et al., 2014a; Powell et al., 2015), the Policy Surveillance Program at Temple University (LawAtlas), National Alliance for Model State Drug Laws (NAMSDL, 2015), and Centers for Disease Control and Prevention (Dowell et al., 2016). The effective dates of these policies for the study sample can be found at the Supplementary material. State socioeconomic data were obtained from Census, Bureau of Labor Statistics, and Tax Foundation.

### 2.2. Variables

The outcome variables were annual rates of hospitalizations related to marijuana and OPR. Specifically, we used International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] to define 3 types of hospitalizations: those involving marijuana dependence or abuse (ICD-9-CM diagnosis codes 304.3 and 305.2), those involving opioid dependence or abuse (ICD-9-CM diagnosis codes 304.0, 305.5, and 304.7), and those involving OPR overdose (ICD-9-CM diagnosis codes 965.00, 965.02, and 965.09). We searched diagnosis codes in all-listed diagnoses including principal diagnosis as well as additional conditions diagnosed at admissions or stays. During 1997–2014, the 27 states had 2.2 million hospitalization records involved with marijuana dependence or abuse, 2.2 million records involved with opioid dependence or abuse, and 0.4 million records involved with OPR overdose. To account for the variations in healthcare utilization across states, we standardized hospitalization rates as the number of discharges for a specific category per 1000 discharges.

We assessed the implementation of medical marijuana policies, the primary policy variable of interest, in three ways. It was first coded as an indicator to represent the presence of medical marijuana policies in the state and year. All the years prior to the implementation year were assigned with value 0, and all the years after the implementation year were assigned with value 1. The value for the implementation year was coded as the number of months adopting the policy divided by 12 months (e.g., 0.25 if the policy was implemented on Oct 1st) to represent partial year of policy implementation (Bachhuber et al., 2014). Among the 27 states included in the main analysis, 9 states implemented medical marijuana policies between 1997 and 2014 (see detailed list in the Supplementary material).

In the second analysis, we allowed for independent effects of permitting medical marijuana dispensaries, the major and most common provision of medical marijuana policies (Pacula et al., 2014b; Powell et al., 2015). The open dates of the first operating medical marijuana dispensary in a state were used to code an indicator for the presence of medical marijuana dispensaries in the state and year. Among the 9 states that implemented medical marijuana policies in our sample, 8 states had operating medical marijuana dispensaries during the study period.

The third model added 1-year, 2-year, and 3-year leads and lags to the contemporary indicator of medical marijuana policy implementation. Adding the series of leads allowed us to test the assumption about identical counterfactual trends in the states adopting and non-adopting medical marijuana policies

(Angrist and Pischke, 2008). The significant associations, if any, will indicate that the implementation of medical marijuana policies endogenously responded to the marijuana or OPR outcomes. If no significant effects are found, any variations in the outcomes can be interpreted as the results of exogenous policy shocks rather than some preexisting differences between states adopting and non-adopting the policies. Whereas adding lagged effects allowed for the detection of heterogeneous policy effects at different time points after policy implementation.

In all the regressions, we included 3 additional time-varying state-level policy variables related to marijuana or OPR: (1) the indicator of marijuana decriminalization, under which marijuana use is illegal but controlled by non-criminal statutes and exempt from criminal processing and consequences (Room, 2010); (2) the indicator for the presence of prescription drug monitoring program; and (3) the indicator for the presence of pain management clinic regulation. Other time-varying state-level factors that may influence marijuana or OPR-related hospitalizations included population size, unemployment rate, median household income in constant 2014 dollars, beer tax rate per gallon in constant 2014 dollars, and uninsured rate. We assessed collinearity of these variables by variance inflation factors and no collinearity was found.

### 2.3. Statistical analysis

We plotted the average hospitalization rates related to marijuana or OPR by year and compared them between the states that did and did not implement medical marijuana policies during the study period.

The unit of analysis was the state-year observation. We assessed the associations between medical marijuana policy implementation and hospitalization rates using linear time-series models with two-way fixed effects. Year indicators were included in all the models to account for unobserved year fixed effects that were common to all the states at the same time, for example, the reformulation of OxyContin. State indicators were also included in all the models to account for unobserved time-invariant factors at state-level, such as social norms. The annual hospitalization rates were log transformed to address right skewness and improve ease of interpretation. The coefficients of policy indicators therefore represented the average percentage difference in hospitalization rates between the periods before and after the policy implementation, controlling for contemporaneous variations in the states that did not adopt the policy. Hospitalizations for marijuana dependence or abuse, opioid dependence or abuse, and OPR overdose were examined in separate regressions.

In addition to the three models that included different forms of medical marijuana policy indicators, we performed a series of robustness checks. First, we replaced the policy implementation date with the policy passage date to identify the presence of medical marijuana policies. Second, we conducted specificity tests by estimating the associations between medical marijuana policies and hospitalization rates of two diseases that are not directly related to marijuana (Bachhuber et al., 2014): heart disease (ICD-9-CM diagnosis codes 390–398, 402, 404, 410–429) and septicemia (ICD-9-CM diagnosis codes 038). Third, we identified hospitalizations using principal diagnosis codes instead of all-listed diagnoses. Because cases with principal diagnoses identified as marijuana dependence or abuse were insufficient to provide statistically meaningful information, we restricted this sensitivity analysis to OPR-related hospitalizations only. Last, the 5 states (Illinois, Maryland, Massachusetts, Minnesota, and New York) that legalized medical marijuana in the last year of the study period and had partial year of post-policy observation were added as states adopting medical marijuana policies in the regressions.

Because the SID provide a census of hospital stays in a state, the data were not weighted. The standard errors in the regressions were clustered at state level to allow for intrastate correlations. All the statistical analyses were conducted with Stata 14 (StataCorp LP, Texas) in 2016. The IRB review was waived by the University of California, San Diego because all the data are secondary, de-identified, and publicly available.

## 3. Results

### 3.1. Descriptive statistics

Fig. 1 demonstrated time trends of hospitalization rates without any adjustment. During 1997–2014, the average hospitalization rates related to marijuana and OPR increased dramatically by approximately 300% in states that did or did not implement medical marijuana policies. In these 18 years, the average hospitalization rates increased from 4.49 to 16.04 per 1000 discharges for marijuana dependence and abuse, from 5.14 to 15.15 per 1000 discharges for opioid dependence and abuse, and from 0.47 to 2.10 per 1000 discharges for OPR overdose. It appears that the gaps in hospitalizations involving marijuana dependence and abuse were continuously widened between the states adopting and non-adopting medical marijuana policies with states adopting medical marijuana policies increased more sharply. Throughout the study period, the states with medical marijuana policies continuously had higher rates of hospitalizations related to opioid dependence or abuse. Hospitalization rates related to OPR overdose were originally higher in the states with medical marijuana policies, but increased less rapidly compared to the states without medical marijuana policies.

### 3.2. Regression analysis

Table 1 reports the associations of hospitalizations to the indicator of medical marijuana policy implementation, controlling for time-varying marijuana-related policies, state-level socioeconomic factors, and state and year fixed effects. The implementation of medical marijuana policies did not have any significant associations with hospitalizations related to marijuana dependence or abuse. However, it was associated with a 23% reduction in hospitalizations related to opioid dependence or abuse ( $p=0.008$ ) and a 13% reduction in hospitalizations related to OPR overdose ( $p=0.025$ ).

In Table 2, the first column for each outcome variable evaluates the indicator of medical marijuana dispensaries. Relative to generic implementation of medical marijuana legalization, the operation of medical marijuana dispensaries had comparable associations with hospitalizations related to opioid dependence or abuse (13% reduction,  $p=0.010$ ) and OPR overdose (11% reduction,  $p=0.006$ ). The second column for each outcome variable reports results including both the indicator of medical marijuana policy and the indicator of medical marijuana dispensaries. Medical marijuana dispensaries alone did not have any independent associations with any hospitalization outcomes after indicators for medical marijuana policy implementation were also included in the regressions.

In Table 3, we explored if any policy effects could be detected in the periods prior to the implementation year of medical marijuana policies. We found no evidence that hospitalization rates of any category differed between states adopting and non-adopting medical marijuana policies in the pre-policy periods. Table 3 also assesses the presence of dynamic policy effects after the implementation year. We found that the reduction in hospitalizations related to opioid dependence or abuse was most salient after 1 year of policy implementation (by 9.4%,  $p=0.031$ ), whereas the reduction in

**Table 1**

Associations between Medical Marijuana Policies and State-Level Hospitalizations Rates Related to Marijuana and Opioid Pain Reliever, State Inpatient Databases 1997–2014.

State-level Explanatory Variable	State-level Outcome Variable: Natural Log of Hospitalization Rates per 1000 Discharges Point Estimate (95% CI)					
	Marijuana Dependence or Abuse		Opioid Dependence or Abuse		Opioid Pain Reliever Overdose	
Medical Marijuana Policy	0.16	(-0.076, 0.41)	<b>-0.23</b>	<b>(-0.41, -0.068)**</b>	<b>-0.13</b>	<b>(-0.25, -0.018)*</b>
Marijuana Decriminalization Policy	0.13	(-0.10, 0.36)	0.094	(-0.15, 0.33)	0.049	(-0.22, 0.32)
Prescription Drug Monitoring Program	-0.088	(-0.21, 0.042)	0.020	(-0.088, 0.12)	0.027	(-0.080, 0.13)
Pain Clinic Regulation	-0.046	(-0.17, 0.078)	0.052	(-0.12, 0.23)	-0.070	(-0.16, 0.025)
Number of State-Year Observations	382		382		382	
Number of Discharges	2,237,916		2,176,326		376,680	
R <sup>2</sup>	0.90		0.96		0.97	

Note: The linear regressions also controlled for state and year fixed effects and state-level time-varying covariates including natural log of population size, unemployment rate, natural log of median household income in constant 2014 dollars, natural log of beer tax per gallon in constant 2014 dollars, and health uninsured rate.

Bold value highlighted statistics with p value smaller than .05.

\* p < 0.05.

\*\* p < 0.01.

**Table 2**

Associations between Operation of Medical Marijuana Dispensaries and State-Level Hospitalization Rates Related to Marijuana and Opioid Pain Reliever, State Inpatient Databases 1997–2014.

State-level Explanatory Variable	State-level Outcome Variable: Natural Log of Hospitalization Rates per 1000 Discharges Point Estimate (95% CI)					
	Marijuana Dependence or Abuse		Opioid Dependence or Abuse		Opioid Pain Reliever Overdose	
Medical Marijuana Policy		0.18 (-0.069, 0.44)		-0.22 (-0.40, -0.044)*		-0.11 (-0.23, 0.013)
Operation of Medical Marijuana Dispensaries	0.011 (-0.11, 0.13)	-0.061 (-0.21, 0.089)	<b>-0.13</b> <b>(-0.23, -0.035)**</b>	-0.048 (-0.15, 0.053)	<b>-0.11</b> <b>(-0.18, -0.034)**</b>	-0.068 (-0.15, 0.020)
Marijuana Decriminalization Policy	0.14 (-0.10, 0.39)	0.17 (-0.096, 0.45)	0.16 (-0.11, 0.45)	0.13 (-0.14, 0.40)	0.12 (-0.17, 0.41)	0.10 (-0.20, 0.40)
Prescription Drug Monitoring Program	-0.086 (-0.21, 0.039)	-0.081 (-0.19, 0.036)	0.032 (-0.084, 0.14)	0.026 (-0.089, 0.14)	0.038 (-0.077, 0.15)	0.035 (-0.075, 0.14)
Pain Clinic Regulation	-0.077 (-0.20, 0.047)	-0.060 (-0.19, 0.071)	0.061 (-0.13, 0.26)	0.041 (-0.14, 0.22)	-0.075 (-0.16, 0.013)	-0.085 (-0.18, 0.0093)
Number of State-Year Observations	382		382		382	
Number of Discharges	2,237,916		2,176,326		376,680	
R <sup>2</sup>	0.90	0.90	0.95	0.96	0.97	0.97

Note: The linear regressions also controlled for state and year fixed effects and state-level time-varying covariates including natural log of population size, unemployment rate, natural log of median household income in constant 2014 dollars, natural log of beer tax per gallon in constant 2014 dollars, and health uninsured rate.

Bold value highlighted statistics with p value smaller than .05.

\* p < 0.05.

\*\* p < 0.01.

**Table 3**

Lead, Contemporary, and Lagged Effects of Medical Marijuana Policies on State-Level Hospitalization Rates Related to Marijuana and Opioid Pain Reliever, State Inpatient Databases 1997–2014.

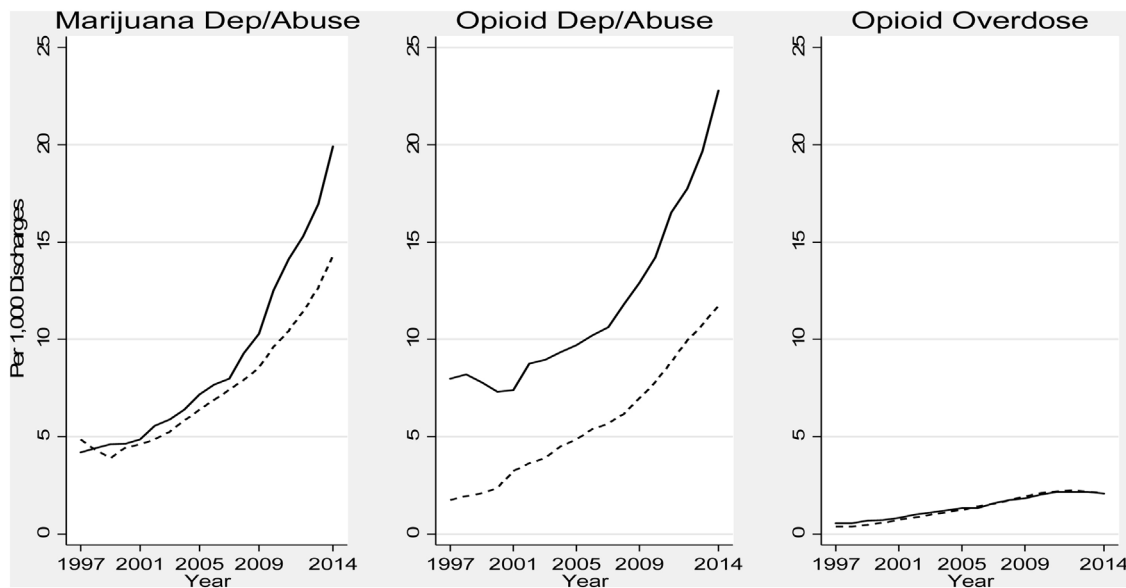
State-level Explanatory Variable	State-level Outcome Variable: Natural Log of Hospitalization Rates per 1000 Discharges Point Estimate (95% CI)					
	Marijuana Dependence or Abuse		Opioid Dependence or Abuse		Opioid Pain Reliever Overdose	
Medical Marijuana Policy, Contemporary	0.10	(-0.020, 0.22)	-0.00	(-0.079, 0.079)	-0.079	(-0.20, 0.042)
Medical Marijuana Policy, Leads:						
1 year lead	0.012	(-0.040, 0.064)	-0.025	(-0.090, 0.039)	0.068	(-0.018, 0.15)
2 year lead	0.089	(-0.064, 0.24)	0.039	(-0.13, 0.21)	-0.11	(-0.22, 0.0039)
3 year lead	0.065	(-0.13, 0.26)	-0.28	(-0.65, 0.080)	0.030	(-0.15, 0.21)
Medical Marijuana Policy, Lags:						
1 year lag	-0.031	(-0.10, 0.044)	<b>-0.094</b>	<b>(-0.18, -0.0095)*</b>	0.0033	(-0.077, 0.084)
2 year lag	-0.0071	(-0.12, 0.11)	-0.036	(-0.15, 0.077)	-0.0049	(-0.067, 0.058)
3 year lag	0.042	(-0.15, 0.24)	-0.084	(-0.23, 0.061)	<b>-0.12</b>	<b>(-0.20, -0.038)**</b>
Marijuana Decriminalization Policy	0.13	(-0.056, 0.33)	0.11	(-0.067, 0.29)	0.096	(-0.15, 0.35)
Prescription Drug Monitoring Program	-0.094	(-0.22, 0.039)	0.029	(-0.083, 0.14)	0.027	(-0.074, 0.12)
Pain Clinic Regulation	-0.036	(-0.17, 10)	0.018	(-0.13, 0.17)	-0.084	(-0.18, 0.013)
Number of State-Year Observations	382		382		382	
Number of Discharges	2,237,916		2,176,326		376,680	
R <sup>2</sup>	0.90		0.96		0.97	

Note: The linear regressions also controlled for state and year fixed effects and state-level time-varying covariates including natural log of population size, unemployment rate, natural log of median household income in constant 2014 dollars, natural log of beer tax per gallon in constant 2014 dollars, and health uninsured rate.

Bold value highlighted statistics with p value smaller than .05.

\* p < 0.05.

\*\* p < 0.01.



**Fig. 1.** Time Trends in Hospitalization Rates in States with and without Medical Marijuana Policies. State Inpatient Databases 1997–2014.

..... Solid lines represent trends in states with medical marijuana policies.

..... Dotted lines represent trends in states without medical marijuana policies.

hospitalizations related to OPR overdose was observed in the third year after policy implementation (by 12%,  $p = 0.006$ ).

With respect to other policy and socioeconomic covariates, uninsured rate was associated with increased OPR overdose hospitalizations. Other covariates including marijuana decriminalization, prescription drug monitoring program, and pain management clinic regulations were generally not associated with any hospitalization outcomes.

### 3.3. Sensitivity analysis

Replacing policy implementation dates with passage dates did not alter the study findings. We found no evidence of the two health conditions (heart disease and septicemia) being associated with medical marijuana policies. The results using principal diagnoses were also similar with the results using all-listed diagnoses for the analyses of OPR-related hospitalizations. We included the 5 states that legalized medical marijuana at the end of the study period in the regressions and obtained similar findings, too.

## 4. Discussion

Using state-level administrative hospitalization data during 1997–2014, we found no convincing evidence that the implementation of medical marijuana policies was associated with a subsequent increase in marijuana-related hospitalizations. This result was robust to the key policy dates defined in different ways. In conjunction with the studies that demonstrated negative or null associations of medical marijuana policies to substance abuse treatment admissions (Pacula et al., 2014b), suicide rates (Anderson et al., 2014), and crime rates (Morris et al., 2014), our study counters the arguments about the severe health consequences that legalizing medical marijuana may bring to the public health. It should be noted that this study does not necessarily contradict some prior research that reported an increase in marijuana use prevalence in association with medical marijuana policies (Chu, 2014; Wen et al., 2015). It just appears that, even if legalization resulted in an increase in the prevalence, it did not contribute to the severe health consequences that concern the public the most. Whether

such findings hold in the long term needs further monitoring and investigations.

This study demonstrated significant reductions in OPR-related hospitalizations associated with the implementation of medical marijuana policies. These findings were supported by the recent studies that reported reduced prescription medications (Bradford and Bradford, 2016), OPR overdose mortality (Bachhuber et al., 2014), opioid positivity among young and middle aged fatally injured drivers (Kim et al., 2016), and substance abuse treatment admissions (Powell et al., 2015) in association with medical marijuana legalization. The mechanisms for the causal connections between marijuana and OPR are not clear. As mentioned earlier, using marijuana can lead to either an increase or a reduction in OPR use depending on the use purposes and the underlying assumptions. This study appears to support the hypothesis that patients prescribed with OPR substitute OPR with marijuana, but it is not directly testable in our data. An alternative explanation for the results reported in this study is that states with medical marijuana legalization may also have tough OPR prescription regulations. However, this hypothesis was not supported by the null associations of OPR prescription regulations estimated in this study. Future empirical evaluations are warranted to explore the use pattern of OPR and marijuana and substantiate the substituting and gateway effects of the two drugs.

Consistent with prior research (Wen et al., 2015), policy effects reported in this study were not static. We found reductions in OPR-related hospitalizations immediately after the year of policy implementation as well as delayed reductions in the third post-policy year. Nonetheless, the availability of medical marijuana dispensaries was not independently associated with hospitalizations as suggested by other studies (Powell et al., 2015). A possible interpretation is that only 1 state in our data legalized medical marijuana but did not have operating medical marijuana dispensaries; a few other states opened medical marijuana dispensaries within only 1–2 years after the legalization of medical marijuana. The lack of variations in policy adoption and timing limited our ability to detect independent effects of detailed policy provisions of medical marijuana legalization.

The 300% increase in hospitalization rates related to marijuana is striking. In contrast, the past-month prevalence of marijuana

use increased at a much slower rate from 6% in 2002–7.5% in 2013 (NIDA, 2015). It is unclear what factors have been driving the huge discrepancies between the trends of use prevalence and the trends of hospitalization rates. Although quite a few states legalized medical marijuana or decriminalized marijuana, this study suggested that they did not contribute to the rise of marijuana-related hospitalizations. One alternative hypothesis is the escalation in marijuana potency (delta-9-tetrahydrocannabinol content), which has tripled from 4% in 1995 to 12% in 2014 in the U.S. (EISOHLY et al., 2016). Nonetheless, empirical evidence again did not find any associations between the potency increase and the legalization of medical marijuana (Sevigny et al., 2014). Studies to understand the growing market share of high-potency marijuana and its associations with marijuana-related hospitalizations are urgently needed.

The unprecedented increase in OPR-related hospitalization rates and other related health outcomes has become a major public health crisis. Compared to the limited research on marijuana, OPR abuse and overdose epidemic has been relatively well studied. It is largely driven by the liberalization of OPR prescription for the treatment of chronic non-cancer pain (Kolodny et al., 2015). Despite lack of evidence in this study, prescription drug monitoring programs and pain management clinic regulations have shown promises to tackle the OPR crisis in some other studies (Bao et al., 2016; Dowell et al., 2016; Kennedy-Hendricks et al., 2016; Lyapustina et al., 2016; Patrick et al., 2016). If the causal relationship indicated in this study can be substantiated in future research, medical marijuana legalization and regulation may be considered as an alternative strategy to reduce OPR-related hospitalizations without aggravating the adverse consequences related to marijuana.

Our study was subject to several limitations, most of which were related to the data used. First, some states included hospitalization records in the SID from non-community hospitals such as psychiatric facilities and Veterans Affairs hospitals, but some states did not (AHRQ, 2016). States may also vary on ICD-9-CM coding practice particularly for drug dependence, abuse, and overdose cases. The coding of opioid dependence or abuse may include heroin cases. The inclusion of state fixed effects should to some extent alleviate these biases in the reporting. Second, the aggregate SID data represented the total number of discharges but not the total number of patients because a patient may be admitted to hospital more than once in a year. The public-use SID were not available before 1997 and not all states participated in the SID during the study period. The findings may not be generalizable to the states that were excluded from this study. Particularly, the results may be inapplicable to California, which has the longest history of medical marijuana legalization as well as the largest population of registered medical marijuana patients and the largest number of medical marijuana dispensaries. Third, although no statistical differences in hospitalization rates between states adopting and non-adopting medical marijuana policies were revealed before policy implementation, we cannot rule out policy endogeneity issues that may be caused by time-varying unobserved factors and were not captured by the two-way fixed effects models. In addition, we were not able to examine detailed policy provisions of medical marijuana legalization such as home cultivation and requirement of patient registry because of small sample size and lack of variations. We were not able to assess OPR-related policies that were adopted by a few states most recently, such as requirements of following OPR prescribing guidelines and mandatory checking prescription drug monitoring program data by providers. This limitation, however, is unlikely to influence the study findings significantly because these policies were not adopted until the very end of the study period or after the study period. Finally, the study findings do not apply to recreational marijuana legalization. In fact, the findings are likely to alter if marijuana for recreational purpose is indeed a gateway drug

to OPR. Examinations on the most recent regulations of recreational marijuana are warranted.

## 5. Conclusions

While the interpretation of the results should remain cautious, this study suggested that medical marijuana policies were not associated with marijuana-related hospitalizations. Instead, the policies were unintendedly associated with substantial reductions in OPR-related hospitalizations. It is still premature to advocate medical marijuana legalization as a strategy to curb the OPR abuse and overdose epidemic, but the policymakers should take into consideration these positive unintended consequences while legalizing medical marijuana. The findings presented in this study merit further investigations especially those to understand the causal pathways.

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## Contributors

Y.S. conceived and designed the study, retrieved data, conducted analysis, interpreted findings, and wrote the manuscript.

## Conflict of interest

No conflict declared.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugalcdep.2017.01.006>.

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