Title

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Authors

Liang, Di
Shi, Yuyan

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The associations of neighborhood availability of marijuana dispensaries and DATA-2000 waivered providers with hospital stays related to opioids

Di Liang[a,*], **Yuyan Shi**[a]

[a]Department of Family Medicine and Public Health,, University of California, San Diego, San Diego, USA

Abstract

Background: Evidence is emerging on how state-wide marijuana legalization and increased supply of DATA-2000 waivered providers may be associated with outcomes related to opioids. It is unknown whether such associations remain at the neighborhood level.

Objectives: This study examined the associations of neighborhood availability of marijuana dispensaries and DATA-2000 waivered providers with opioid-related hospital stays.

Methods: Discharge-level records of inpatient (N=264,013) and observation stays (N=12,621) were obtained from the Washington Comprehensive Hospital Abstract Reporting System from January through June in 2016. Outcomes were indicators for inpatient stays related to opioid use disorder (OUD), inpatient stays related to opioid overdose, and observation stays related to OUD. Primary predictors were the density of marijuana dispensaries and DATA-2000 waivered providers at the zip code level. Multilevel logistic regressions with random intercepts were used to examine the cross-sectional associations, controlling for other patient and neighborhood characteristics.

Results: Patients living in neighborhoods with one more recreational marijuana dispensaries per square mile were more likely (OR=1.54, p=0.017) to be diagnosed with OUD in inpatient stays. Living in neighborhoods with increased density of medical marijuana dispensaries or DATA-2000 waivered providers was not associated with being diagnosed with OUD or opioid overdose in inpatient or observation stays.

Conclusions: Recreational and medical marijuana dispensaries were differentially associated with opioid-related hospital stays. Further investigations are warranted to explore the causal pathways of the findings.

Keywords

marijuana dispensary; buprenorphine; opioids; marijuana; hospitalization

[*]Corresponding Author: Di Liang, PhD, 9500 Gilman Drive, MC0628, San Diego, CA 92093, USA., Telephone: 310-666-5692, dil067@ucsd.edu.

Declaration of interest

The authors have no conflict of interest to declare.

Introduction

The opioid epidemic is a major public health concern in the United States (US) (CDC, 2011; Warner, Hedegaard, & Chen, 2014). The number of opioids prescribed in 2015 was approximately three times as high as in 1999 (Volkow, 2014). At least 11.8 million adolescents and adults misused opioids, and 2.1 million had an opioid use disorder (OUD), in 2016 (SAMHSA, 2017). The opioid-related hospitalizations increased by 64%, and emergency department visits doubled, in 2005-2014 (Weiss et al., 2016). Over the past decade, concerted policy efforts have been made to restrict the prescribing of opioids (Compton & Volkow, 2006; Kolodny et al., 2015).

Expanding access to effective treatments for OUD is essential to reduce its burden (Volkow, Frieden, Hyde, & Cha, 2014). Historically, medications for treating OUD, such as methadone and buprenorphine, were provided only in opioid treatment programs, and, therefore, only a fraction of patients were willing and able to access these medications (Jones, Campopiano, Baldwin, & McCance-Katz, 2015). To expand the clinical ability to treat OUD, the US Drug Addiction Treatment Act (DATA) of 2000 waived the requirement of obtaining a Drug Enforcement Administration (DEA) registration as an opioid treatment program for physicians providing buprenorphine treatment in their offices. Physicians can acquire DATA-2000 waivers if they had a board certification in addiction medicine or psychiatry or completed required training (SAMHSA, 2004). Since 2010, there has been a dramatic increase in the number of DATA-2000 waivered providers (Knudsen, Havens, Lofwall, Studts, & Walsh, 2017). These providers might be more likely to begin prescribing buprenorphine in areas with higher opioid-related mortality rates (Jones et al., 2018; Knudsen et al., 2017). It was hoped that expanding the capacity of buprenorphine treatment could improve access to OUD treatment. The expansion of buprenorphine treatment affected opioid-related outcomes at the population level has remained unexplored.

Parallel with the opioid epidemic, marijuana legalization has expanded throughout the US. As of November 2018, in addition to the District of Columbia, 33 states have legalized marijuana use for medical purposes, 10 of which further legalized marijuana use for recreational purposes. There were two competing hypotheses regarding the relationship between marijuana use and opioid use. First, marijuana use may exacerbate opioid use. Second, marijuana use may substitute for opioid use (Reisfield, Wasan, & Jamison, 2009).

The rationale for the first hypothesis was that marijuana may precede use of opioids, and individuals who used marijuana may share risk factors with individuals who used opioids (Morral, McCaffrey, & Paddock, 2002). As demonstrated by a cohort study, recreational marijuana use was associated with increased likelihoods of opioid misuse and OUD (Olfson, Wall, Liu, & Blanco, 2017). But the data of this study were collected before any states have legalized recreational marijuana use. The evidence on the impact of state recreational marijuana laws on opioid-related outcomes remained scarce, and no positive associations have been documented (Shi et al., 2018; Wen & Hockenberry, 2018).

The rationale for the second hypothesis was the potential therapeutic effects of cannabinoids (e.g., THC, CBD) and smoked marijuana on pain symptoms, which were supported by

systematic reviews of randomized controlled trials (Hill, 2015; Lynch & Campbell, 2011; Lynch & Ware, 2015; Martín-Sánchez, Furukawa, Taylor, & Martin, 2009; Whiting et al., 2015). Chronic or severe pain was, therefore, the most commonly approved condition in the states that legalized medical marijuana. Several ecological studies consistently suggested that state-wide medical marijuana laws were associated with considerable reductions in opioid prescriptions, misuse, overdose deaths, and related hospitalizations at state level (Bachhuber, Saloner, Cunningham, & Barry, 2014; Bradford & Bradford, 2016, 2017; Bradford, Bradford, Abraham, & Adams, 2018; Kim et al., 2016; Liang, Bao, Wallace, Grant, & Shi, 2018; Powell, Pacula, & Jacobson, 2018; Shi, 2017). However, these ecological studies above were not supported by a recent individual-level prospective cohort study in Australia which found no evidence that marijuana use was associated with reduced opioid use among pain patients (Campbell et al., 2018). But in this study, the majority of participants used illicitly obtained marijuana. It is still unknown to what extent the findings can be generalized to the current legal environment in the US.

The availability of marijuana dispensaries and DATA-2000 waivered providers varied substantially across neighborhoods within a state, but its associations with opioid-related outcomes in a neighborhood was unknown (Hansen, Siegel, Wanderling, & DiRocco, 2016; Jones et al., 2018; Mair, Freisthler, Ponicki, & Gaidus, 2015; Morrison, Gruenewald, Freisthler, Ponicki, & Remer, 2014; Rosenblatt, Andrilla, Catlin, & Larson, 2015; Shi, Meseck, & Jankowska, 2016). To fill the knowledge gap, we examined the associations of neighborhood availability of marijuana dispensaries and DATA-2000 waivered providers with hospital stays related to opioids, using hospital records from January through June in 2016 in Washington. We hypothesized that the availability of recreational and medical marijuana dispensaries was associated with a higher and lower risk of hospital stays related to opioids, respectively. According to availability theory, increased access to marijuana may lead to increased marijuana use among the local population (Stockwell & Gruenewald, 2004). Thus, increased availability of recreational marijuana dispensaries may result in increased marijuana use for recreational purposes which may lead to increased opioid or OUD-related health outcomes, while increased availability of medical marijuana dispensaries may results in elevated marijuana use for medical purposes which may lead to alleviated opioid or OUD-related health outcomes. We also hypothesized that the availability of DATA-2000 waivered providers was associated with a lower risk of hospital stays related to opioids. According to the Andersen's behavioral model of health services use, individuals living in areas with more available health care resources were more likely to visit a provider (Babitsch, Gohl, & von Lengerke, 2012). One study reported that living in neighborhoods with more DATA-2000 waivered providers was associated with an increased likelihood of being treated with buprenorphine for OUD (Murphy, Fishman, McPherson, Dyck, & Roll, 2014). Thus, increased availability of DATA-2000 waivered providers may lead to improved opioid- or OUD-related health comes through more accessible OUD treatment.

To analyze the potential differential associations with recreational and medical marijuana dispensaries, we took advantage of the unique policy context in Washington in early 2016, a time when recreational marijuana and medical marijuana dispensaries coexisted. Washington passed the laws to legalize medical marijuana in 1998 and recreational marijuana in 2012. Before recreational marijuana was legalized, medical marijuana dispensaries in Washington

largely operated without regulations. Unlike other states such as Colorado that built its recreational marijuana industry and regulations on top of the existing medical marijuana system, Washington chose to abandon its medical marijuana system and start recreational marijuana regulations from scratch. In 2015, Washington passed the Cannabis Patient Protection Act (SB 5052) requiring that all marijuana dispensaries operate as licensed recreational marijuana dispensaries and obtain a medical marijuana endorsement if they opt to specialize in medical marijuana (WA, 2015). As a result, between July 2014 when the first recreational marijuana dispensary opened and July 2016 when SB 5052 took effect, the old medical marijuana dispensaries that exclusively served medical marijuana patients and the newly licensed recreational marijuana dispensaries that might serve both patients and recreational users operated at the same time in Washington.

Materials and methods

Data Sources and Study Sample

This is a cross-sectional ecological study using secondary de-identified data, and the ethics approval and consent were not needed. We obtained inpatient and observation stay discharge records in all the community hospitals between January 1, 2016 and June 30, 2016 from Washington Comprehensive Hospital Abstract Reporting System (CHARS) administered by the State Department of Health. The records included detailed information on patient demographics, zip code of patient's home address, as well as up to 25 International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis and procedure codes. Patients younger than 12 years of age or living outside of Washington were excluded from the analyses. The final study sample included 264,013 inpatient stay records and 12,621 observation stay records.

Directories and point locations of marijuana dispensaries with physical storefronts in Washington were obtained between March and June in 2016 from a crowdsourced website (weedmaps.com). Weedmaps provides detailed and up-to-date dispensary information contributed by dispensary owners and users. Its data have been validated and used in previous research (Mair et al., 2015; Shi, 2016). Notably, each dispensary on weedmaps self-reports whether it is a medical or recreational marijuana dispensary. This is the only source to differentiate recreational and medical marijuana dispensaries during our study period, as official records for medical marijuana dispensaries were not available until they were regulated in July 2016. Directories and point locations of DATA-2000 waivered providers in Washington were obtained in August 2016 from the Substance Abuse and Mental Health Services Administration. Tobacco and alcohol outlet locations were obtained from business list provider referenceUSA and other contextual factors were obtained from the US Census and the American Community Survey.

Measures

Opioid-related Hospital Stays—The patient-level outcome variables were opioid-related hospital stays, including inpatient stays and observation stays. Inpatient stays were hospital stays after patients were formally admitted to a hospital. Observation stays were short-term hospital stays for patients who were not well enough to go home but not sick

enough to be admitted right away. Observation stays usually lasted for less than 24 hours and rarely exceeded 48 hours. Patients were either discharged or admitted as inpatients after observation stays. In CHARS, if a patient was transferred to inpatient care after an observation stay, this patient would only be recorded as an inpatient. In other words, observation stay discharge records in CHARS captured patients who were discharged after observation stays.

To construct opioid-related hospital stays, we first used ICD-10-CM diagnosis codes to identify OUD (ICD-10-CM diagnosis codes F11.1, F11.2, and F11.9) and opioid overdose (ICD-10-CM diagnosis codes T40.0, T40.1, T40.2, T40.3, and T40.4). A hospital stay with OUD or opioid overdose in all-listed diagnoses, including principal diagnoses as well as secondary diagnoses, was defined as an opioid-related hospital stay. Accordingly, three dichotomized indicators were created to represent inpatient stays involved with OUD, inpatient stays involved with opioid overdose, and observation stays involved with OUD. Observation stays involved with opioid overdose were not analyzed because of insufficient sample size.

The Availability of Marijuana Dispensaries and DATA-2000 waivered providers—The primary explanatory variables of interest were the availability of marijuana dispensaries and DATA-2000 waivered providers in a neighborhood defined by zip code tabulation area (referred to zip code hereafter). Measures for recreational and medical marijuana dispensaries were constructed separately. All the point locations were geocoded using ArcGIS (ArcMap, version 10.4; ESRI Inc., Redlands, CA, USA) and aggregated to zip code level. Availability was measured by the density of marijuana dispensaries or DATA-2000 waivered providers per square mile. In sensitivity analyses, we altered the operationalization of primary explanatory variables to test the robustness of our results. First, we used the total density of recreational and medical marijuana dispensaries. Second, we used three dichotomous variables indicating the presence of any recreational marijuana dispensaries, medical marijuana dispensaries, or DATA-2000 waivered providers because the majority of zip codes did not have any of them. Third, we used three categorical variables to represent 0, 1, and 2+ recreational marijuana dispensaries, medical marijuana dispensaries, or DATA-2000 waivered providers in a zip code, as few zip codes had more than two of them.

Other Patient and Neighborhood Characteristics—Patient-level covariates included age (12-20, 21-34, 35-49, 50-64, or 65+), sex (male or female), primary payer (private insurance, Medicare, Medicaid, or other), and race/ethnicity (non-Hispanic White, Hispanic, non-Hispanic Black, other non-Hispanic minority, or unknown). Zip code level covariates included proportion of population under age 21 (only adults 21 and older can purchase and possess recreational marijuana in Washington), whether the population were predominantly racial and ethnic minority (over 60% of the residents in the zip code were not non-Hispanic White), median household income in thousand dollars of 2016, number of tobacco and alcohol outlets per square mile, and population density (thousand population per square mile).

Statistical Analysis

The descriptive and regression analyses were conducted in STATA 14 (STATA Corp, College Station, TX). We conducted multilevel logistic regressions with random intercepts at the zip code level to examine the associations of the availability of DATA-2000 waivered providers and marijuana dispensaries with opioid-related inpatient or observation stays, controlling for other patient and neighborhood covariates. Multilevel models were used to account for within-neighborhood correlations, as patients nested within zip codes shared the same zip code level explanatory variables of interest and covariates. We examined the variance inflation factors (VIFs) for each model to ensure that the degree of multi-collinearity was low.

We further incorporated spatial dependence in multilevel logistic regressions to account for potential between-neighborhood correlations. We first constructed the rate of inpatient stays involved with OUD per 1000 population, the rate of inpatient stays involved with opioid overdose per 1000 population, and the rate of observation stays involved with OUD per 1000 population, at the zip code level. We then calculated spatially lagged rates of hospital stays related to opioids using GEODA (version 1.12; Center for Spatial Data Science, Chicago, IL, USA). In multilevel logistic regressions, the correspondent spatially lagged variable was added as a zip code level covariate.

Results

Descriptive Statistics

Descriptive results are shown in Table 1. Among 598 zip codes: each zip code on average had 0.29 DATA-2000 waivered providers per square mile, 0.023 recreational marijuana dispensaries per square mile, and 0.037 medical marijuana dispensaries per square mile. Among 264,013 inpatient stay records, 4.5% were related to OUD, and 0.9% were related to opioid overdose. Among 12,621 observation stay records, 2.1% were related to OUD.

Multilevel Logistic Regression Results

Table 2 reports multilevel logistic regression results for inpatient stay records. Patients living in neighborhoods with one more recreational marijuana dispensaries per square mile were more likely (OR=1.54, p=0.017) to be diagnosed with OUD in inpatient stays. Living in neighborhoods with increased density of medical marijuana dispensaries or DATA-2000 waivered providers was not associated with being diagnosed with OUD or opioid overdose in inpatient stays. Regarding patient-level covariates: females (OR=0.82, p<0.001) were less likely to have OUD related inpatient stays than males; individuals aged 21-34 (OR=6.01, p<0.001) had the highest odds of OUD related inpatient stays, while individuals aged 50-64 (OR=1.38, p<0.001) had the highest odds of inpatient stays related to opioid overdose, across age groups; non-Hispanic white had the highest odds of OUD related inpatient stays, while non-Hispanic white and black had the highest odds of inpatient stays related to opioid overdose, across race and ethnic groups; individuals with Medicaid (OR=3.25, p<0.001) had the highest odds of OUD related inpatient stays, while individuals with Medicare (OR=1.45, p<0.001) had the highest odds of inpatient stays related to opioid overdose, among individuals with different health insurance.

Table 3 reports multilevel logistic regression results for observation stay records. The density of medical marijuana dispensaries, recreational marijuana dispensaries, or DATA-2000 waivered providers was not associated with OUD-related observation stays. Regarding patient-level covariates: individuals aged 21-34 (OR=8.55, p<0.001) had the highest odds of OUD related observation stays, across age groups; other non-Hispanic minority had the highest odds of OUD (OR=1.64, p=0.022) related observation stays, across race and ethnic groups; individuals with Medicaid (OR=2.93, p<0.001) had the highest odds of OUD related observation stays, among individuals with different health insurance.

Appendix Tables present sensitivity analysis results. As shown in Appendix Table 1, the density of marijuana dispensaries or DATA-2000 waivered providers was not associated with OUD-related hospital stays. As shown in Appendix Table 2, living in neighborhoods with 1+ recreational dispensary (OR=1.19, p=0.004) was associated with higher odds of being diagnosed with OUD in inpatient stays, while living in neighborhoods with 1+ medical dispensary (OR=0.62, p=0.009) was associated with lower odds of being diagnosed with OUD in observation stays. As shown in Appendix Table 3: compared to patients living in neighborhoods without any recreational marijuana dispensaries, patients living in neighborhoods with one (OR=1.19, p=0.005) recreational marijuana dispensaries were more likely to be diagnosed with OUD in inpatient stays, while patients living in neighborhoods with one medical marijuana dispensary were less likely to be diagnosed with OUD in observation stays (OR=0.49, p=0.005) compared to those living in neighborhoods without any medical marijuana dispensaries.

Discussion

This study is the first attempt to explore the associations of the neighborhood availability of marijuana dispensaries and DATA-2000 waivered providers with opioid-related health outcomes. Utilizing the unique policy environment in Washington, we were able to ascertain the differential associations of recreational marijuana and medical marijuana dispensaries. The findings suggested that the availability of recreational marijuana dispensaries in a neighborhood was associated with a higher likelihood of inpatient stays related to OUD. No associations were detected between the availability of medical marijuana dispensaries or DATA-2000 waivered providers and opioid-related hospital stays.

This study suggested that neighborhood availability of recreational marijuana dispensaries was associated with increased opioid-related hospital stays, yet the availability of medical marijuana dispensaries was not. On the one hand, marijuana use for recreational purpose may lead to increased opioid use (Hall & Lynskey, 2005), which may explain our findings for recreational marijuana dispensaries and previous studies which reported elevated opioid use and misuse among marijuana users (Caputi & Humphreys, 2018; Olfson et al., 2017). On the other hand, because of the therapeutic effects of marijuana on pain (Hill, 2015; Lynch & Campbell, 2011; Lynch & Ware, 2015; Martín-Sánchez et al., 2009; Whiting et al., 2015), patients with pain may use marijuana as a complement or substitute for medical purposes (Reisfield et al., 2009). This may explain why the availability of medical marijuana dispensaries was not associated with increased opioid-related hospital stays. However, our neighborhood-level evidence cannot directly support this assumption at the individual level.

Findings of our main analysis for medical marijuana dispensaries were consistent with a recent individual-level prospective cohort study in Australia (Campbell et al., 2018) but did not support previous state-level investigations (Bachhuber et al., 2014; Bradford & Bradford, 2016, 2017; Bradford et al., 2018; Kim et al., 2016; Liang et al., 2018; Powell et al., 2018; Shi, 2017). Future empirical evaluations are warranted to substantiate the correlations between marijuana and opioid and the individual pattern of drug use.

The null associations between availability of DATA-2000 waivered providers and opioid-related hospital stays do not necessarily indicate a null impact of increased DATA-2000 waivered provider supply on OUD outcomes. DATA-2000 waivered providers may respond to the aggravated opioid epidemic by increasing the supply of OUD treatments. A recent study demonstrated that states with higher opioid overdose had higher rates of growth in the supply of DATA-2000 waivered providers (Knudsen et al., 2017). The observed cross-sectional associations may, therefore, reflect the combined effects of the demand-supply relationship and the true impact of increased treatment capacities on opioid-related outcomes. Also, buprenorphine treatment utilization can also be affected by demand-side factors, such as health insurance coverage and patients' awareness (Babitsch et al., 2012). Future research should utilize longitudinal data to separate the demand-supply factor from the true impact.

The study has limitations. First, the study examined cross-sectional associations instead of causality. Although we controlled for a rich set of patient and neighborhood characteristics, it is likely that some unobserved heterogeneities (e.g., the availability of illicit marijuana and opioids) influenced the estimation of the associations. Second, OUD related to opioids could not be differentiated from that related to illicit opioids (e.g., heroin) in ICD-10-CM diagnosis codes. To ensure consistency of definitions, we, therefore, did not differentiate opioid overdose related to prescription opioids and illicit opioids. Third, the CHARS data had several limitations. Emergency department records were not available in CHARS. Also, no unique identifiers were provided to identify multiple hospital stays of a unique patient, but such cases should be rare in a relatively short time frame (Silva, Schrager, Kecojevic, & Lankenau, 2013; Warner-Smith, Darke, & Day, 2002). Fourth, the directories obtained from SAMHSA may not cover all DATA-2000 waivered providers. Also, we did not control for other resources for treating OUD, such as opioid treatment programs providing methadone, because few neighborhoods had these programs. Fifth, we can only evaluate the impact of the availability of marijuana dispensaries and DATA-2000 waivered providers, rather than the exposure to marijuana and access to OUD treatment. Moreover, the classification of dispensaries (recreational or medical) does not ensure exclusive supply to users using marijuana for recreational or medical purpose, especially during the study period when dispensaries were insufficiently regulated in Washington. Lastly, the first half year of 2016 is a transition period with rapid changes in the policy and neighborhood environments related to marijuana and opioid in Washington. We recognized that the number and classification of marijuana dispensaries and the supply of DATA-2000 waivered providers might not remain constant throughout the entire 6-month study period. The study findings may not be generalizable to Washington after July 2016 when all medical marijuana dispensaries were forced to shut down or transform to recreational marijuana dispensaries or to other states where policy contexts were different.

Conclusion

While the interpretation of the findings should remain cautious, this study suggested that recreational and medical marijuana dispensaries may be differentially associated with opioid-related hospital stays. Policymakers are recommended to consider these potential differences when regulating marijuana dispensaries and products. Future investigations are warranted to explore the causal pathways of the findings.

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Appendix

Appendix Table 1

Sensitivity Analysis Combining Recreational and Medical Marijuana Dispensaries

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	**Inpatient Stays Related to Opioid Overdose (N= 264,013)**	**Observation Stay Related to Opioid Use Disorder (N= 12,621)**
		OR (95% CI)	
Zip-code Characteristics			
Number of marijuana dispensaries per square mile	1.12 (0.95, 1.31)	1.08 (0.93, 1.25)	0.70 (0.41, 1.21)
Number of DATA-2000 waivered providers per square mile	1.05 (1.00, 1.10)	1.03 (0.99, 1.06)	0.99 (0.91, 1.09)
Spatially Lagged Rates of Hospital Stays Related to Opioids	**1.41 *** (1.31, 1.52)**	0.87 (0.60, 1.27)	**3.03 * (1.01, 9.10)**
Proportion of population under age 21	1.19 (0.46, 3.05)	0.71 (0.25, 2.05)	**0.041 * (0.0021, 0.81)**
Racial/ethnic composition			
Predominantly non-Hispanic white	Ref	Ref	Ref
Predominantly racial/ethnic minorities	**0.79 * (0.63, 0.99)**	0.90 (0.71, 1.14)	0.91 (0.45, 1.81)
Median household income †	1.00 (1.00, 1.00)	**1.00 ** (0.99, 1.00)**	**1.01 * (1.00, 1.02)**
Number of tobacco and alcohol outlets per square mile	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.01 (1.00, 1.02)
Population density per square mile ‡	**1.04 ** (1.02, 1.07)**	1.01 (0.98, 1.04)	1.01 (0.93, 1.10)
Individual Characteristics			
Sex			
Male	Ref	Ref	Ref
Female	**0.82 *** (0.79, 0.86)**	1.01 (0.93, 1.10)	0.85 (0.66, 1.10)
Age			
65+	Ref	Ref	Ref
50-64	**3.88 *** (3.64, 4.14)**	**1.38 *** (1.22, 1.57)**	**5.06 *** (3.25, 7.89)**
35-49	**5.05 *** (4.69, 5.43)**	1.11 (0.95, 1.30)	**5.84 *** (3.56, 9.58)**
21-34	**6.01 *** (5.58, 6.48)**	**0.77 ** (0.65, 0.92)**	**8.50 *** (5.08, 14.23)**
12-20	**1.99 *** (1.72, 2.30)**	**0.67 * (0.49, 0.91)**	0.41 (0.055, 3.11)

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	Inpatient Stays Related to Opioid Overdose (N= 264,013)	Observation Stay Related to Opioid Use Disorder (N= 12,621)
		OR (95% CI)	
Race/ethnicity			
Non-Hispanic white	Ref	Ref	
Hispanic	**0.34 *** (0.31, 0.38)**	**0.72 ** (0.59, 0.89)**	**0.39 * (0.19, 0.81)**
Non-Hispanic black	**0.64 *** (0.59, 0.70)**	1.02 (0.85, 1.24)	1.31 (0.68, 2.51)
Other non-Hispanic minority	**0.61 *** (0.56, 0.66)**	**0.64 *** (0.52, 0.79)**	**1.64 * (1.07, 2.51)**
Unknown	**0.67 *** (0.61, 0.74)**	**0.64 *** (0.51, 0.80)**	**0.33 * (0.12, 0.91)**
Primary payer for healthcare			
Private health insurance	Ref	Ref	Ref
Medicare	**3.15 *** (2.96, 3.35)**	**1.45 *** (1.28, 1.65)**	**2.38 *** (1.59, 3.55)**
Medicaid	**3.25 *** (3.08, 3.42)**	**1.42 *** (1.25, 1.61)**	**2.95 *** (2.15, 4.07)**
Other	**1.94 *** (1.76, 2.14)**	**1.27 * (1.03, 1.58)**	0.82 (0.39, 1.73)

* p<.05; ** p<.01; *** p<.001; † Median household income was divided by 1000; ‡ Population density per square mile was divided by 1000. ORs and corresponding 95% CI were in bold if p<0.05. We used multilevel logistic regressions with random intercepts at zip code level.

Appendix Table 2

Sensitivity Analysis Using Dichotomous Indicators for the Availability of Dispensaries and DATA-2000 waivered providers

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	Inpatient Stays Related to Opioid Overdose (N= 264,013)	Observation Stay Related to Opioid Use Disorder (N= 12,621)
		OR (95% CI)	
Zip-code Characteristics			
Number of recreational marijuana dispensaries			
0	Ref	Ref	Ref
1+	**1.19 ** (1.06, 1.34)**	1.03 (0.91, 1.15)	1.17 (0.86, 1.60)
Number of medical marijuana dispensaries			
0	Ref	Ref	Ref
1+	0.98 (0.87, 1.11)	1.04 (0.92, 1.17)	**0.62 ** (0.43, 0.88)**
Number of DATA-2000 waivered providers			
0	Ref	Ref	Ref
1+	1.04 (0.93, 1.16)	0.98 (0.88, 1.09)	1.13 (0.83, 1.53)
Spatially Lagged Rates of Hospital Stays Related to Opioids	**1.41 *** (1.30, 1.53)**	0.81 (0.53, 1.23)	3.03 (0.94, 9.76)
Proportion of population under age 21	1.43 (0.53, 3.87)	0.57 (0.18, 1.79)	0.058 (0.0027, 1.24)
Racial/ethnic composition			
Predominantly non-Hispanic white	Ref	Ref	
Predominantly racial/ethnic minorities	**0.63 ** (0.47, 0.85)**	**0.65 * (0.46, 0.93)**	0.79 (0.34, 1.80)
Median household income †	1.00 (1.00, 1.00)	**1.00 ** (0.99, 1.00)**	**1.01 ** (1.00, 1.02)**
Number of tobacco and alcohol outlets per square mile	1.00 (1.00, 1.00)	1.00 (1.00, 1.01)	**1.01 (1.00, 1.02)**

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	Inpatient Stays Related to Opioid Overdose (N= 264,013)	Observation Stay Related to Opioid Use Disorder (N= 12,621)
		OR (95% CI)	
Population density per square mile‡	**1.05*** (1.02, 1.07)**	1.02 (0.99, 1.04)	1.00 (0.93, 1.07)
Individual Characteristics			
Sex			
Male	Ref	Ref	Ref
Female	**0.82*** (0.78, 0.85)**	**0.99 (0.90, 1.09)**	0.81 (0.62, 1.05)
Age			
65+	Ref	Ref	**Ref**
50-64	**3.88*** (3.62, 4.17)**	**1.43*** (1.25, 1.64)**	**6.04*** (3.77, 9.68)**
35-49	**5.07*** (4.68, 5.49)**	1.08 (0.91, 1.29)	**7.13*** (4.22, 12.03)**
21-34	**6.05*** (5.58, 6.57)**	**0.80* (0.66, 0.96)**	**9.46*** (5.44, 16.45)**
12-20	**2.07*** (1.77, 2.43)**	**0.77 (0.55, 1.07)**	-
Race/ethnicity			
Non-Hispanic white	Ref	Ref	Ref
Hispanic	**0.35*** (0.31, 0.39)**	**0.78* (0.62, 0.97)**	**0.46* (0.22, 0.96)**
Non-Hispanic black	**0.64*** (0.58, 0.70)**	0.94 (0.75, 1.16)	1.46 (0.76, 2.82)
Other non-Hispanic minority	**0.55*** (0.50, 0.61)**	**0.71** (0.57, 0.88)**	1.33 (0.82, 2.17)
Unknown	**0.67*** (0.61, 0.74)**	**0.63*** (0.49, 0.82)**	0.39 (0.14, 1.06)
Primary payer for healthcare			
Private health insurance	Ref	Ref	
Medicare	**3.19*** (2.98, 3.42)**	**1.54*** (1.33, 1.77)**	**2.66*** (1.74, 4.05)**
Medicaid	**3.25*** (3.07, 3.44)**	**1.47*** (1.28, 1.69)**	**2.93*** (2.07, 4.13)**
Other	**1.88*** (1.69, 2.10)**	**1.23 (0.96, 1.57)**	0.81 (0.36, 1.80)

* p<.05; ** p<.01; *** p<.001; † Median household income was divided by 1000; ‡ Population density per square mile was divided by 1000. ORs and corresponding 95% CI were in bold if p<0.05. We used multilevel logistic regressions with random intercepts at zip code level.

Appendix Table 3

Sensitivity Analysis Using Categorical Variables for the Availability of Dispensaries and DATA-2000 waivered providers

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	Inpatient Stays Related to Opioid Overdose (N= 264,013)	Observation Stay Related to Opioid Use Disorder (N= 12,621)
		OR (95% CI)	
Zip-code Characteristics			
Number of recreational marijuana dispensaries			
0	**Ref**	Ref	Ref
1	**1.19** (1.06, 1.35)**	1.04 (0.92, 1.17)	1.07 (0.76, 1.50)
2+	1.14 (0.97, 1.36)	1.05 (0.90, 1.22)	1.21 (0.82, 1.79)
Number of medical marijuana dispensaries			
0	Ref	Ref	Ref

	Inpatient Stays Related to Opioid Use Disorder (N= 264,013)	Inpatient Stays Related to Opioid Overdose (N= 264,013)	Observation Stay Related to Opioid Use Disorder (N= 12,621)
		OR (95% CI)	
1	1.00 (0.87, 1.16)	1.03 (0.89, 1.18)	**0.49 ** (0.29, 0.81)**
2	0.99 (0.85, 1.15)	1.06 (0.92, 1.21)	0.69 (0.46, 1.04)
Number of DATA-2000 waivered providers			
0	Ref	Ref	Ref
1	1.10 (0.96, 1.26)	1.07 (0.93, 1.22)	1.28 (0.86, 1.90)
2+	1.04 (0.93, 1.16)	0.98 (0.87, 1.09)	1.10 (0.81, 1.51)
Spatially Lagged Rates of Hospital Stays Related to Opioids	**1.39 *** (1.30, 1.50)**	0.86 (0.58, 1.26)	**3.71 * (1.27, 10.87)**
Proportion of population under age 21	1.18 (0.45, 3.05)	0.66 (0.23, 1.95)	**0.036 * (0.0019, 0.69)**
Racial/ethnic composition			
Predominantly non-Hispanic white	Ref	Ref	
Predominantly racial/ethnic minorities	**0.79 * (0.63, 0.99)**	0.88 (0.69, 1.12)	0.93 (0.46, 1.88)
Median household income †	1.00 (1.00, 1.00)	**1.00 ** (0.99, 1.00)**	**1.01 ** (1.00, 1.02)**
Number of tobacco and alcohol outlets per square mile	1.00 (1.00, 1.01)	1.00 (1.00, 1.01)	**1.01 * (1.00, 1.02)**
Population density per square mile‡	**1.05 *** (1.03, 1.07)**	1.02 (0.99, 1.04)	0.98 (0.92, 1.05)
Individual Characteristics			
Sex			
Male	Ref	Ref	
Female	**0.82 *** (0.79, 0.86)**	1.01 (0.93, 1.10)	0.85 (0.66, 1.09)
Age			
65+	Ref	Ref	**Ref**
50-64	**3.88 *** (3.64, 4.14)**	**1.39 *** (1.23, 1.57)**	**5.07 *** (3.26, 7.90)**
35-49	**5.05 *** (4.69, 5.43)**	1.11 (0.95, 1.30)	**5.86 *** (3.57, 9.60)**
21-34	**6.01 *** (5.58, 6.48)**	**0.77 ** (0.65, 0.92)**	**8.48 *** (5.06, 14.19)**
12-20	**1.99 *** (1.72, 2.30)**	**0.67 * (0.49, 0.91)**	0.40 (0.053, 3.03)
Race/ethnicity			
Non-Hispanic white	Ref	Ref	Ref
Hispanic	**0.34 *** (0.31, 0.38)**	**0.73 ** (0.59, 0.90)**	**0.38 ** (0.18, 0.79)**
Non-Hispanic black	**0.64 *** (0.59, 0.70)**	1.03 (0.85, 1.24)	1.38 (0.72, 2.64)
Other non-Hispanic minority	**0.61 *** (0.56, 0.66)**	**0.64 *** (0.53, 0.79)**	**1.61 * (1.05, 2.46)**
Unknown	**0.67 *** (0.61, 0.74)**	**0.64 *** (0.51, 0.81)**	**0.34 * (0.12, 0.92)**
Primary payer for healthcare			
Private health insurance	Ref	Ref	
Medicare	**3.15 *** (2.96, 3.35)**	**1.46 *** (1.28, 1.65)**	**2.35 *** (1.57, 3.52)**
Medicaid	**3.25 *** (3.08, 3.42)**	**1.42 *** (1.25, 1.61)**	**2.91 *** (2.12, 4.01)**
Other	**1.94 *** (1.76, 2.14)**	**1.27 * (1.02, 1.58)**	0.81 (0.39, 1.72)

* p<.05; ** p<.01; *** p<.001; † Median household income was divided by 1000; ‡ Population density per square mile was divided by 1000. ORs and corresponding 95% CI were in bold if p<0.05. We used multilevel logistic regressions with random intercepts at zip code level.

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Table 1

Descriptive Statistics of Zip-code and Patient Characteristics

	Mean (95% CI)
Zip-code Characteristics (N=598)	
Number of recreational marijuana dispensaries per square mile	0.023 (0.015, 0.031)
Number of medical marijuana dispensaries per square mile	0.037 (0.019, 0.055)
Number of DATA-2000 waivered providersper square mile	0.29 (−0.13, 0.72)
Proportion of population under age 21, %	26.13 (25.50, 26.77)
Racial/ethnic composition, %	
Predominantly non-Hispanic white	91.64 (89.13, 93.61)
Predominantly racial/ethnic minorities	8.36 (6.39, 10.87)
Median household income in thousand dollars of 2016	57.05 (55.41, 58.69)
Number of tobacco and alcohol outlets per square mile	3.48 (1.63, 5.34)
Population density, thousand population per square mile	1.36 (1.12, 1.60)
Patient Characteristics	
Inpatient Stay Records (N=264,013)	
Related to opioid use disorder, %	4.46 (4.38, 4.54)
Related to opioid overdose, %	0.88 (0.85, 0.92)
Sex, %	
Male	41.19 (41.01, 41.38)
Female	58.81 (58.62, 58.99)
Age, %	
65+	41.19 (41.01, 41.38)
50-64	22.48 (22.32, 22.64)
35-49	13.86 (13.73, 13.99)
21-34	18.79 (18.65, 18.94)
12-20	3.67 (3.60-3.74)
Race/ethnicity, %	
Non-Hispanic white	77.41 (77.25, 77.57)
Hispanic	6.13 (6.04, 6.22)
Non-Hispanic black	4.45 (4.37, 4.53)
Other non-Hispanic minority	6.91 (6.81, 7.01)
Unknown	5.10 (5.01, 5.18)
Primary payer for healthcare, %	
Private health insurance	33.71 (33.53, 33.89)
Medicare	42.93 (42.75, 43.12)
Medicaid	18.93 (18.78, 19.08)
Other	4.43 (4.35, 4.51)
Observation Stay Records (N=12,621)	
Related to opioid use disorder, %	2.12 (1.89, 2.39)
Sex, %	
Male	44.80 (43.93, 45.67)

	Mean (95% CI)
Female	55.20 (54.33, 56.07)
Age, %	
12-20	3.60 (3.29, 3.94)
21-34	11.40 (10.86, 11.97)
35-49	14.72 (14.11, 15.35)
50-64	26.86 (26.09, 27.64)
65+	43.42 (42.56, 44.29)
Race/ethnicity, %	
Non-Hispanic white	82.42 (81.74, 83.07)
Hispanic	7.36 (6.92, 7.83)
Non-Hispanic black	2.07 (1.83, 2.33)
Other non-Hispanic minority	4.56 (4.21, 4.93)
Unknown	3.60 (3.29, 3.94)
Primary payer for healthcare, %	
Private health insurance	31.84 (31.03, 32.65)
Medicare	44.79 (43.92, 45.66)
Medicaid	18.27 (17.61, 18.96)
Other	5.10 (4.73, 5.50)

Table 2

Multilevel Logistic Regressions on Opioid-related Hospital Stays: Inpatient Stay Records (N= 264,013)

	Inpatient Stays Related to Opioid Use Disorder OR (95% CI)	Inpatient Stays Related to Opioid Overdose OR (95% CI)
Zip-code Characteristics		
Number of recreational marijuana dispensaries per square mile	**1.54 * (1.08, 2.21)**	1.04 (0.74, 1.46)
Number of medical marijuana dispensaries per square mile	1.03 (0.86, 1.24)	1.09 (0.92, 1.28)
Number of DATA-2000 waivered providers per square mile	1.04 (0.99, 1.10)	1.03 (0.99, 1.06)
Spatially Lagged Rates of Hospital Stays Related to Opioids	**1.41 *** (1.31, 1.52)**	0.87 (0.60, 1.27)
Proportion of population under age 21	1.26 (0.49, 3.22)	0.71 (0.24, 2.04)
Racial/ethnic composition		
Predominantly non-Hispanic white	Ref	Ref
Predominantly racial/ethnic minorities	**0.78 * (0.63, 0.98)**	0.90 (0.71, 1.14)
Median household income †	1.00 (1.00, 1.00)	**1.00 ** (0.99, 1.00)**
Number of tobacco and alcohol outlets per square mile	1.00 (1.00, 1.00)	1.00 (1.00, 1.01)
Population density per square mile ‡	**1.04 ** (1.02, 1.07)**	1.01 (0.98, 1.04)
Individual Characteristics		
Sex		
Male	Ref	Ref
Female	**0.82 *** (0.79, 0.86)**	1.01 (0.93, 1.10)
Age		
65+	Ref	Ref
50-64	**3.88 *** (3.64, 4.14)**	**1.38 *** (1.22, 1.57)**
35-49	**5.04 *** (4.69, 5.42)**	1.11 (0.95, 1.30)
21-34	**6.01 *** (5.58, 6.48)**	**0.77 ** (0.65, 0.92)**
12-20	**1.99 *** (1.72, 2.30)**	**0.67 * (0.49, 0.91)**
Race/ethnicity		
Non-Hispanic white	Ref	Ref
Hispanic	**0.34 *** (0.31, 0.38)**	**0.72 ** (0.59, 0.89)**
Non-Hispanic black	**0.64 *** (0.59, 0.70)**	1.02 (0.85, 1.24)
Other non-Hispanic minority	**0.61 *** (0.56, 0.66)**	**0.64 *** (0.52, 0.79)**
Unknown	**0.67 *** (0.61, 0.74)**	**0.64 *** (0.51, 0.80)**
Primary payer for healthcare		
Private health insurance	Ref	Ref
Medicare	**3.15 *** (2.96, 3.35)**	**1.45 *** (1.28, 1.65)**
Medicaid	**3.25 *** (3.08, 3.42)**	**1.42 *** (1.25, 1.61)**
Other	**1.94 *** (1.76, 2.14)**	**1.27 * (1.02, 1.58)**

* p<.05; ** p<.01; *** p<.001; † Median household income was divided by 1000; ‡ Population density per square mile was divided by 1000. ORs and corresponding 95% CI were in bold if p<0.05. We used multilevel logistic regressions with random intercepts at zip code level.

Table 3

Multilevel Logistic Regression on Opioid-related Hospital Stays: Observation Stay Records (N=12,621)

	Observation Stay Related to Opioid Use Disorder OR (95% CI)
Zip-code Characteristics	
Number of recreational marijuana dispensaries per square mile	2.50 (0.77, 8.06)
Number of medical marijuana dispensaries per square mile	0.43 (0.16, 1.16)
Number of DATA-2000 waivered providers per square mile	0.99 (0.91, 1.09)
Spatially Lagged Rates of Hospital Stays Related to Opioids	**3.02 * (1.02, 8.96)**
Proportion of population under age 21	**0.038 * (0.0020-0.73)**
Racial/ethnic composition	
Predominantly non-Hispanic white	Ref
Predominantly racial/ethnic minorities	0.92 (0.46, 1.83)
Median household income †	**1.01 * (1.00, 1.02)**
Number of tobacco and alcohol outlets per square mile	**1.01 * (1.00, 1.02)**
Population density per square mile ‡	1.00 (0.92, 1.08)
Individual Characteristics	
Sex	
Male	Ref
Female	0.85 (0.67-1.10)
Age	
65+	Ref
50-64	**5.06 *** (3.25, 7.89)**
35-49	**5.84 *** (3.56, 9.58)**
21-34	**8.55 *** (5.11, 14.31)**
12-20	0.42 (0.055, 3.13)
Race/ethnicity	
Non-Hispanic white	Ref
Hispanic	**0.39 * (0.19, 0.81)**
Non-Hispanic black	1.29 (0.67, 2.47)
Other non-Hispanic minority	**1.64 * (1.08, 2.51)**
Unknown	**0.33 * (0.12, 0.91)**
Primary payer for healthcare	
Private health insurance	Ref
Medicare	**2.37 *** (1.59, 3.55)**
Medicaid	**2.93 *** (2.13, 4.03)**
Other	0.80 (0.38, 1.70)

* p<.05; ** p<.01; *** p<.001; † Median household income was divided by 1000; ‡ Population density per square mile was divided by 1000. ORs and corresponding 95% CI were in bold if p<0.05. We used multilevel logistic regressions with random intercepts at zip code level.